THE MANAGEMENT OF MENINGIOMAS OF THE SPHENOIDAL WING

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ABSTRACT

This is a retrospective study of the clinical characteristics, neuroradiologic features, histology, and outcome of treatment among 95 patients with meningiomas of the sphenoidal ridge. The patients were treated in the Departments of Neurosurgery, Ludwig-Maximillians University Munich (56 patients), and the University of Bern in Switzerland (39 patients). The Munich series consisted of admissions between 1988 and 1994. Some of these were readmissions for recurrent disease therefore longer follow up data from as far back as 1978 were available for them. All the Munich patients were followed up for at least 5 years. The average follow up for the Bern patients was 28.1 months. Recurrence-free survivals, overall recurrence rates and the benefits of radiation for subtotally excised tumours are evaluated.

The ages of the patients ranged from 30 to 81 years with a mean of 59 years. The peak tumour frequency was in the age range 46.4 years to 68.6 years. The male:female ratio was 1:2.4. There was a preponderance of medial over lateral tumours (63% medial, 34% lateral) and 3% were *en plaque* lesions extending from the pterion for varying extents toward the midline. Two patients had multiple meningiomas. The symptoms could be clearly separated into those due to medial tumours and those due to lateral tumours with visual complaints occurring in medial tumours and one sided symptoms in lateral tumours.

The neuroimaging modality was CT scan and selective angiography in all cases and in addition MRI in 50 (53%) patients. CT imaging gave a diagnostic yield of 96% but the MRI had a superior resolution and was able to demonstrate vascular involvement. The blood supply was from branches of the ethmoidal artery in 41%, from branches of the middle meningeal artery in 26% and from intracavernous branches of the internal carotid artery in 25% of cases.

Surgery was performed in 91 patients. In 42 (46%) patients the excision was complete (Simpson grade 1). When Simpson grades 1 and 2 were considered together (68 cases) they constituted 75% of all excisions. Macroscopic residual tumour (Simpson 3 and 4) was present in 25% of cases. In the Munich series failure of complete removal was due to cavernous sinus invasion in 7 (12.5%) cases and extensive bone involvement in 4 (7.7%). The overall surgical mortality was 3.4%. Tumour recurrence/progression was 5.5% for totally excised tumours and 23% for subtotally excised tumours at 5 years. Radiotherapy was offered in 11 patients in the Munich series but not in the Bern series. There was a trend towards a beneficial outcome after radiation in the control of subtotally excised tumours where the progression-free survival of 75% at 5 years in this group was better than the expected survival of 45% to 59%. Owing to the small number of irradiated patients the outcome of radiation treatment could not be subjected to a statistical evaluation. It is concluded that from the trend observed radiation therapy has a place in the treatment of subtotally removed meningiomas. Prospective studies are recommended.

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DECLARATION

I declare that this dissertation is my own work and that it has not been submitted to any other University or academic institution for a similar or any other academic award

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2 INTRODUCTION

The sphenoidal wing is the third commonest location for intracranial meningiomas which themselves constitute 13-18 per cent of all intracranial tumours. In this location meningiomas present certain well-known, sometimes very difficult practical management problems. The problems are largely related to the anatomical proximity of the tumour to neurovascular structures. These are the optic, the oculomotor, the trochlear, trigeminal, and the abducent nerves, the cavernous sinus and the carotid artery with its branches. The involvement of these structures is often responsible for the difficulties encountered during the surgery of tumours in this area.

As it enters the intracranial cavity the carotid artery is not uncommonly displaced and/or encased to varying extents by a medially situated tumour. This encasement may lead to narrowing of the vessel. When the vessel wall is itself invaded by tumour complete surgical excision is made difficult or impossible without injuring the artery. The compression of the optic nerve may lead to visual field defects, to unilateral blindness or even to total blindness. Paralysis of ocular movements in the affected eye may result from direct compression of the oculomotor nerve or from invasion of the carotid sinus. Furthermore the not uncommon presenting clinical picture of progressive exophthalmos is a result of the retrobulbar mass lesion of the medially situated meningioma or of hyperostotic changes.

Meningiomas of the sphenoidal wing tend to infiltrate bone more commonly than its counterparts elsewhere. This tendency adds to the causes of incomplete surgical

removal with the resulting higher recurrence rates even in the face of improved microsurgical techniques. In case of bone involvement the surgeon does not have the advantage of a rapid section histology during the surgery itself because of the time required for bone to be decalcified before it can be stained and examined histologically. As the margin between affected bone and healthy bone cannot be visually determined with accuracy it is common for tumour to be left behind. Furthermore, adequate bone removal could be limited by the risk of increased morbidity.

As meningiomas are mostly benign tumours lending themselves to total surgical excision they are considered to be curable neoplasms. Since, however, as will be evident later, medial sphenoidal meningiomas are not invariably amenable to complete excision this tumour may offer an opportunity to evaluate modalities of treatment other than surgery alone. At the time of preparation of this manuscript there was already a proliferation of reports in the world literature with varying views regarding the benefits of radiation. While many gave evidence of improvement in tumour-free survival rates among patients with incomplete tumour removals some showed no conclusive evidence of beneficial effects. A few authors have reported significant complications such as cranial nerve damage and cerebral infarction following conventional radiotherapy for meningiomas in certain locations. On the other hand, progress in conventional radiotherapy and new radiosurgical technique such as the gamma-knife and modified LINAC do offer hope for optimal tumour control in the future.

Meningiomas have been extensively studied and many of their characteristics established. There are, however, still many areas of the subject that require further studies. Series on sphenoidal wing meningiomas have been generally small series of retrospective studies covering one or another aspect of the disease. Notable among these aspects are the problems of recurrence and high morbidity after surgery in meningiomas located along the sphenoid wing. These problems have been largely reduced by improved neuroimaging techniques and by a better understanding of the microneuroanatomy at the skull base. Improved microsurgical techniques especially in those tumours which invade the cavernous sinus have improved the rates of completeness of excision. Tumour recurrence, however, remains high following surgery of medial sphenoid wing meningiomas.

The present study was prompted by the management challenge presented by this tumour. It takes advantage of the large amount of data on meningiomas available at the Großhadern University Hospital in Munich to revisit the clinical characteristics, the outcome of management, recurrences and effects of modalities of treatment in addition to conventional surgery. This work was inspired by the personal experience of the author's teacher and mentor Professor H.-J. Reulen and by the stimulating if controversial literature on the sphenoidal wing meningiomas. The dissertation is presented in two parts:

- **The Background:** This outlines a brief history of meningiomas, its aetiology, pathology, neuroimaging and clinical presentation and management. In this part

the current world literature on the management and the outcome of treatment of meningiomas of the sphenoidal wing will also be reviewed.

- **The present study:** which constitutes the main part of the dissertation presents the objectives, patients and methods, results and a critical discussion of the results

2 THE BACKGROUND

2.1 THE HISTORY OF MENINGIOMA

By the time the term „meningioma“ was coined by Harvey Cushing in 1922[1] to describe a generally benign tumour of the meninges this tumour had been known for well over two centuries. In the early 1600's a Swiss physician Felix Plater[2] described autopsy findings of his patient Caspar Bonecurtis as follows, „...a round fleshy tumour like a corn. It was hard and full of holes and was as large as a medium sized apple. It was covered in its own membrane and was entwined with veins. However, it was free of all connections with the mater of the brain so much so that when it was removed by hand it left behind a remarkable cavity.“

In 1774 Antonie Louis described a group of 20 patients with *tumeurs fongueuses de la dure-mere*. His detailed description of each of these patients indicates that most of them had meningiomas.[3] Many other authors reported on tumours under various names whose descriptions were similar to what we know today to be meningioma.[4,5,6,7,8]

The terminology used in describing meningioma was complicated in the early days by conflicting views regarding their cell of origin. The Paccionian granulations first described by Paccioni in 1705[9] were later suggested to be of meningeal origin by Rainey in 1846[10] and further acknowledged as such by Luschka in 1852,[11] Meyer in 1859[12] and Key and Retzius in 1876.[13] However, the connection between these granulations and meningeal tumours remained unknown. Although John Cleland[14]

and Robin[15] did attribute the origin of these tumours to the arachnoid in 1864 and 1869 respectively it was Martin Schmidt[16] who in 1902 after careful microscopic examinations showed that their structure resembled the endothelial cell clusters capping the arachnoid villi. Cushing and Weed were to confirm in 1915 what had first been proposed by Cleland 50 years earlier.[17] The surgery of meningioma long predated the understanding of its pathogenesis. Lawrence Heister of Helmsted in Germany attempted in 1743 to treat a meningioma by applying a caustic of lime to the tumor.[18] The patient developed an infection and died. This therapeutic attempt probably marked the first recorded „surgical" treatment for meningioma. More conventional early attempts at surgical removal were by Olaf Acrel in Sweden in 1768, also with a fatal outcome,[19] and by Berlighieri and Zanobi Pecchioli.[5] William Macewen performed a successful excision of a left olfactory groove meningioma in Glasgow in 1879.[20] The first successful meningioma excision in the U.S.A. was performed by William Keen in 1887, whose patient survived for 30 years and 44 days.[21] Historically the most important meningioma operation was probably Cushing's operation on Major General Wood, Chief of Staff of the US Army in 1905.[22] Cushing was to state that the success of Wood's operation led to a positive attitude to the possibilities of brain surgery.[23] His unequalled overall contribution to the surgery of meningiomas marked a significant turning point in the development of neurosurgery as a whole. This achievement was undoubtedly made possible by the parallel development of aseptic technique, anaesthesia and electrosurgery.[15]

In his famous Cavendish Lecture in 1922[1] Cushing said, „There is today nothing in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery, especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable and though disappointments are still many, another generation of neurological surgeons will unquestionably see them largely overcome."

2.2 THE AETIOLOGY OF MENINGIOMA

There is no single known cause of meningioma but there have been significant observations over the years regarding the roles of trauma, ionising radiation, viruses and genetic factors. Furthermore, developments in cytogenetics and molecular biology have not only helped identify the possible common pathway in meningioma pathogenesis but they also hold a promise for possible genetic control of this tumor in the future.[24]

2.2.1 Molecular Biology and Cytogenetics

A number of chromosomal abnormalities associated with meningioma have been determined, the most common and most consistent abnormality being the deletion of part or even the whole of the long arm of chromosome 22.[25] It is probable that most meningiomas will have some gene loss on chromosome 22.[26] Some of them may, however, manifest chromosomal changes too subtle to be determined by traditional karyotyping.[24] A technique that can identify smaller changes than traditional karyotyping techniques utilises the restriction fragment length polymorphisms

(RFLPs). These are pieces of DNA localised to a chromosome or portions thereof on which they serve as markers. They are stably inherited variations in the chromosome structure.[24] Their identification allows the distinction between chromosomes from different tissues. This provides an opportunity to compare the structure of chromosome 22 in normal tissue to that in neoplastic tissue such as meningioma material. Utilising RFLPs probes mapping of chromosome 22 Seizinger *et al.*[27] studied chromosome 22 in 40 meningioma patients who were heterozygous in their normal cells. They found loss of heterozygosity in 43% of tumour cells in comparison to normal cells in at least one chromosome 22 marker. This indicated loss of at least part of one copy of a pair of chromosome 22 in 43% of tumours. Seizinger[28] and Rouleau[29] showed similar proportions of chromosome 22 loss in meningioma associated with bilateral acoustic neurofibromatosis (BANF), speculating that the association between meningiomas and acoustic neuromas in BANF was an indication of a common mechanism of development of the two tumours. Zankl and Zang[30] have shown that monosomy of chromosome 22 occurs in up to 72% of cases but most other workers have demonstrated an occurrence of about 40%.[24,28] Of the remainder 60% without apparent abnormality, Rachlin and Rosenblum[24] suggest that the changes on chromosome 22 are too small (i.e. point mutations) to be demonstrated by routine RLFP analysis.

The *modus operandi* of chromosome 22 monosomy in meningioma growth has been proposed.[24,31] One of the pair of genes on the chromosome could be a recessive oncogene whose phenotype will be expressed if its opposite dominant normal allele

is deleted in a mutation. An alternative explanation is that chromosomes may contain tumor suppressor genes which when lost in a chromosome deletion allow tumor to form unchecked. The sporadic form of meningioma would require the simultaneous occurrence of two events: (i) Mutation to form a recessive oncogene on chromosome 22 and (ii) The loss of the dominant normal allele from the second copy of chromosome 22.

2.2.2 Radiation

In order to implicate radiation as the cause of a specific tumour (i) the tumour must appear in the field of radiation, (ii) a long latent period should exist between the time of radiation and the appearance of tumour, and (iii) the radiation-induced tumor must be histologically distinct from any previously existing tumour.[24]

Numerous case reports and short series have implicated radiation as a cause of meningioma.[32,33,34,35,36,37] In one report[33] Iacano *et al.* reported on a patient who developed both supratentorial and infratentorial meningiomas 19 years after irradiation for a medulloblastoma. They also reviewed 35 documented cases of post-irradiation meningioma. Modan *et al.*[38] studied 10,912 Israeli children who had received low dose irradiation to the scalp for Taenia Capitis by the Keinboeck-Adamson method.[39] They found a 4 fold increase in the occurrence of meningioma in this group as compared to a control group. The Keinboeck-Adamson method delivered 450-850 rad to the scalp and about 70-175 rad to the brain.[40] Since the arachnoid is so closely applied to the brain it receives a radiation dose close to that

received by the brain. This group of children constitutes a group whose tumour is a result of low dose irradiation.

A higher irradiation dose offered for head and neck tumours (2300-7200 rad) although more commonly causing sarcoma has also been associated with meningioma induction.[24] Iacano *et al.*[33] found a 31.3 year meningioma induction interval for the low dose group and 20.8 years for the high dose group-a significant difference at the 95% confidence level. Citing the statistically increased incidence of meningioma in irradiated patients, the proximity of these tumours to other radiation changes in the surrounding brain and overlying scalp, and the dose related induction interval Iacano *et al.*[33] suggest that irradiation is indeed a stimulus for the induction of meningioma. Since ionising irradiation is known to cause chromosomal deletion or translocations [24] such a deletion may be the mechanism for tumour induction by causing loss of tumor suppressor sequence on chromosome 22. The deletion of chromosome 22 has not, however, been demonstrated following radiation.

2.2.3 Viruses

The role of viruses in meningioma causation is not at present conclusive. However, the methods currently available for identifying small pieces of DNA and viral proteins in human tumours may provide a better understanding in the future.

Papovaviruses occur commonly in human beings. Most adults have circulating antibodies against them probably acquired during asymptomatic infections in childhood.[24] Serum antibodies against BK virus for example have been found in 83%

of adults[41] while antibodies against JC viruses have been demonstrated in 65% of adults.[42] Among a total of 336 human intracranial tumours examined for human papovavirus tumour antigen (TAg) 36 were found positive. Of these 32 were meningiomas.[43,44,45,46] Rachlin and Rosenblum[24] suggest that the protein identified in meningiomas as viral protein may in fact be a cellular protein of meningioma cells with significant homology with the papovavirus TAg. Using the Southern blot which is currently the most sensitive and specific method for identifying specific genes and cellular DNA[47] Rachlin *et al.*[48] found two of nine meningiomas (22%) to have DNA sequences homologous to SV40 DNA.

In summary the presence of viral particles in human meningiomas is an attractive but insufficient premise to prove its causative role in meningioma induction. Indeed the virus may have infected the cell after the neoplastic transformation has occurred. Theoretically, nevertheless, the virus could transform the cell by acting as a mutagen or by acting in concert with a cofactor for another mutagen. In this role the virus could act as a mutagen or maintain the transformed state. At the present time despite biochemical evidence associating DNA virus with meningioma, the role of virus in the development of human meningioma remains unclear.[24]

2.2.4 Neurofibromatosis

At least two forms of this genetic disorder, namely von Recklingshausen's Neurofibromatosis (VRNF) and Bilateral Acoustic Neurofibromatosis (BANF) are

known to be associated with meningioma. Neurofibromatosis is an autosomal dominant genetic disorder occurring in 1 of 3000 births.[49] Both BANF and VRNF patients may develop intracranial or spinal meningioma[24] but BANF patients have in addition always bilateral acoustic neurofibromata[50] that occur at a relatively younger age than do the sporadic acoustic neuromata. BANF is also more commonly associated with meningioma than is VRNF.[24] In both BANF and meningiomas there is a similar loss of genes on chromosome 22.[28]

2.2.5 Trauma

Cushing and Eisenhardt reviewed 295 cases of intracranial meningiomas and found 93 cases in which a history of head injury was given or evident as for example in case of tumour underlying an old fracture.[51] This led Cushing to believe strongly that trauma was a significant factor in the development of meningiomas. Although many small series and case reports have supported the head injury factor [52,53,54] case control studies have failed to identify a correlation between trauma and the development of meningioma.[55,56,57]

2.2.6 Role of Sex Hormones

Several clinical features suggest that meningiomas may be related to sex hormones. Cushing and Eisenhardt first noted that meningiomas could increase in size during pregnancy.[58] Similar observations have been made by others.[59,60] It is further known that meningiomas occur more commonly in women than in men and are positively

correlated with breast, ovarian and endometrial carcinomas.[61] Bellur *et al.*[62] have reported on a frequent association between obesity and meningioma.

Many authors have investigated meningiomas for the presence of oestrogen and progesterone receptors. Table 1 shows a summary of findings by various workers. Unlike in breast tissue, progesterone activity in meningioma tissue is not dependent upon the activation of oestrogen receptors but rather it can occur independently.[25] Early reports indicated the presence of both oestrogen and progesterone receptor activity.[63,64] More recent studies, using more specific binding criteria provide evidence for the presence of progesterone receptor binding but not oestrogen receptor (ER) binding in most meningiomas.[65] Markwalder *et al.*[146] have found a positive correlation between progesterone receptor status and tumour histology. In their study of 44 patients they detected progesterone receptor activity in 77%. A negligible number of tumours were ER positive. They also found that 96% of progesterone receptor positive tumours were meningothelial, 71% were transitional and 48% were fibrous. Rubinstein *et al.*[149] have demonstrated a statistically higher incidence of ER and progesterone receptor concentration in recurrent as compared to initially excised tumours and conclude that these higher hormone levels may indicate a higher degree of aggressiveness.

Table 1. Sex Hormone receptor detection by competitive binding in meningiomas

Series (ref.)	Number of patients	Oestrogen	Progesterone
Brentani [137]	6	2 (33%)	6 (100%)
Markwalder [146]	44	Negligible	34 (77%)
Poisson [138]	25	None	24 (96%)
Whittle [150]	29	None	16 (55%)
Blankenstein [151]	45	7 (15.6%)	40 (88.9%)
Kornblum [152]	29	None	8 (3.4%)

Other receptors have also been identified in meningioma material. Brentani *et al.*[137] found androgen receptors in all of six meningiomas they examined while another group[138] found androgen receptor activity in 23 of 25 meningiomas. Furthermore, Lesch *et al.*[139] found a positive correlation between androgen and ER activity. They suggested that oestrogens might regulate androgen receptors through the ER system. Receptor binding sites for insulin growth factor 1 and epidermal growth factor receptor have been detected in meningioma material.[140,141] Somatostatin[142] and dopamine D1[143] receptor activity have also been demonstrated.

Employing stimulation and inhibition studies, investigators have evaluated the effects of oestrogens and progesterone on meningiomas. Progesterone was shown by Maiuri et al.[144,145] to diminish growth in six tumours which had progesterone receptors. They found that in these six tumours oestrogen had no effect on tumour growth. It has been reported by Waelti and Markwalder[147] that medroxyprogesterone

acetate diminished growth in 35% of tumours. RU486, a progesterone antagonist, has been shown by Olson[148] to inhibit three of three meningiomas.

In summary, there is mounting evidence that sex hormone activity is present in meningiomas and that these hormones may play a role in the pathogenesis and in the behaviour of this tumour. Their precise pathogenetic role requires further studies to elucidate.

2.3 THE PATHOLOGY OF MENINGIOMA

Meningiomas arise from arachnoid cap cells of the arachnoid granulations. A positive correlation exists between the density of arachnoid granulation cells and the distribution of meningiomas. However, this tumour also occurs in locations where no arachnoid cap cells are expected, as in the extreme cases of ectopic meningiomas.[66]

Tumour location along the sphenoid wing has been classically described as medial, middle and lateral.[67] This description was first proposed by Cushing[51] and was intended to group the tumours according to their clinical characteristics. Bonnal *et al.*[68] have modified this classification somewhat, breaking it up into groups A-E namely:

Group A: Deep or clinoidal or sphenocavernous
Group B: Invading en plaque of the sphenoid wings
Group C: Invading en masse of the sphenoid wing which combines the features of A and B
Group D: Middle ridge tumour
Group E: Pterional global tumour or Sylvian point tumour

On the other hand the concept of an anatomical continuum of all meningiomas involving the cranio-orbital junction has been proposed by Stern.[69] Other authors recognise a distinction between only two groups namely, the medial clinoidal group and the lateral group for which distinctive clinical, radiological and surgical features exist.[70] This classification will be used in this dissertation.

Two morphological varieties of meningioma are described, namely the globular and the *en plaque* forms. The latter is more commonly found along the sphenoidal wing than at any other intracranial location.[71] This morphologic variety of meningioma grows as a carpet of neoplastic tissue along the dura producing hyperostosis of the sphenoid wing.

Although histologically benign, meningiomas frequently infiltrate bone as well as the dura and dural venous sinuses. Recently, Kotapka *et al.*[72] have shown that the carotid artery is also not uncommonly infiltrated. Bone infiltration is recognisable as erosion and/or hyperostosis. The latter which is the commoner lesion is frequently found in sphenoidal wing meningiomas.[73] In both forms of bone involvement tumour may be found to a variable extent in the bone. Bone erosion has been shown to be a feature commoner among meningiomas that tend to recur.[74]

Medial tumours arise from the clinoid process and may displace, encase or less commonly invade the internal carotid artery and its branches.[76] The optic nerve can similarly be compressed by tumour invading the dura of the optic foramen and canal leading to reduced vision or blindness in the ipsilateral eye.[77,78,79] A larger tumour

might lead to the well-described Foster-Kennedy syndrome characterised by optic atrophy on the side of the tumour and papilloedema on the contralateral side.[80,126] The oculomotor, trochlear, trigeminal and abducens nerves can also be involved by the meningioma. Their preservation presents one of the main technical difficulties for the surgeon attempting excision of the tumour.[82] Hyperostotic bone in case of *en plaque* tumour may compress the optic nerve in the optic canal as well as cause exophthalmos.

2.3.1 Macroscopic Features

Meningiomas are characteristically well circumscribed tumours with a focal attachment to the dura. Typically the tumour is globular, can attain varying sizes and grows centrifugally towards the brain which it compresses but does not invade except when the tumour is malignant.[83] There is usually an arachnoid interface between the tumour and the pia mater. The tumour itself is well encapsulated and may present a cobblestone or bosselated appearance. The colour varies from tan to red depending on the extent of vascularisation. A yellow tinge may be found indicating xanthomatous changes. The cut surface of the fresh specimen is pale and presents a semitransparent appearance or a reddish brown colour. A gritty consistency is often found indicating the presence of psammoma bodies which are described below. Haemorrhage into meningiomas is uncommon but when it occurs it tends to be associated with angiomatous meningiomas.[84] In very large tumours and in those which have undergone malignant degeneration necrosis may be present.[85]

2.3.2 Histologic Features of Meningiomas

2.3.2.1 Meningotheliomatous meningioma

As mentioned above, meningiomas are tumours of neuroectodermal origin arising from arachnoid cap cells. Other cells such as fibroblasts and endothelial cells of the pia, the arachnoid or dura mater may also give rise to meningiomas.[86] The usual histological appearance is one of high cellularity consisting of epithelial-like cells arranged in lobules or islands with a syncytial appearance. The cells have ill-defined borders, and show a discretely eosinophilic cytoplasm, sometimes homogeneous and sometimes finely granular. Nuclear characteristics are variable but one most often finds a nucleus of average size which may be rounded or elongated, containing uniformly stippled chromatin with 1-2 nucleoli.[87] The nucleus may show vacuolation, the vacuoles either appearing optically empty or containing eosinophilic inclusions.[87] The cell appearances described above are further characterised by the subdivision of the neoplastic mass they form into neoplastic territories by an interstitial collagenous stroma. Meningothelial cells, like their counterpart the non-neoplastic arachnoid cells, can arrange themselves in spiral clumps forming the typical whorls among which collagenous fibres may be deposited and which may then undergo hyalinization and calcification to become psammoma bodies. This description of tumour has been called endotheliomatous, meningotheliomatous or syncytial. Meningotheliomatous and transitional meningiomas together constitute about 75% of all histological types.[88]

2.3.2.2 Fibroblastic Meningioma

The second main histological grouping of meningioma forming 10% to 20% of all histologic tumour types is the fibroblastic type. It is characterised by multilaminated sheets of interlacing elongated spindle cells with intervening reticulin fibres and collagen. The nuclear properties are rather similar to those of syncytial meningioma but lacking are the typical whorls and syncytial nature characteristic of a meningotheliomatous meningioma.[90] Isolated palisading of nuclei may be observed introducing a confusion with a schwannoma.[91]

2.3.2.3 Transitional meningioma

This is a histological pattern which contains features of both the syncytial and fibroblastic meningioma typically consisting of cellular whorls separated by elongated cells with focal deposition of collagen. Frequently whorls are to be found around a central blood vessel but can also form around hyalinized collagen, a single meningothelial cell or even muscle fibres.[92]

Other numerous histological appearances of meningioma are described but the pattern does not seem to offer a reliable prognostic indicator of the overall behaviour of the tumour. On the other hand various constellations of histological features do seem to have a prognostic significance. A widely accepted histopathologic classification that does have a limited prognostic value is the WHO classification (Table 2). This classification gives an indication of the degree of aggressiveness

which in the case of meningiomas cannot be determined from a single histologic appearance taken in isolation.[93]

2.3.2.4 Malignant meningioma

As stated above the definition of precise histologic criteria of malignancy in meningiomas is difficult. In a series of 657 primary tumours,[154] using the WHO criteria 1.0% were considered malignant, 4.7% atypical and 94.3% benign. Many of the features usually denoting increased aggressiveness such as invasion of the brain, papillary and haemangioperycytic morphology, focal necrosis, increased mitotic figures, prominent nucleoli and nuclear pleomorphism have been observed in tumours that follow a benign clinical course.[108] Furthermore, metastatic spread although generally uncommon in meningiomas is not an invariable indicator of histologic malignancy.[109] Some histologic varieties such as the papillary meningiomas have a propensity for metastatic spread.[110] Metastatic spread has been linked to invasion of vascular structures and dissemination through the circulation.[109] The most common sites for metastatic deposits are the lungs (60%), abdominal organs (34%), vertebral bodies (11%), long bones, pelvis and skull (11%).[111]

Table 2. Histopathologic classification (WHO) of meningioma

CLASS	SUBTYPE	PREDOMINANT FEATURE
A. Classic	1. Meningotheliomatous	Syncytial cells with lobules
	2. Fibroblastic	Spindle cells with collagen
	3. Transitional	Mixture of above types
	4. Psammomatous	Exuberant psammoma bodies
	5. Angiomatous	Abundant sclerosing blood vessels
B. Angioblastic	6. Hemangioblastoma	Capillary endothelial cells with lipid stromal cells
	7. Hemangiopericytoma	Poorly differentiated pericytic cells with reticulin
C. Aggressive	8. Papillary	Papillary pattern with few anaplastic features
D. Malignant	9. Anaplastic	Invasion of brain parenchyma Metastases

The WHO has further developed a scoring system for meningiomas. Histologic signs of anaplasia are scored on a three step scale of loss of architecture, increased cellularity, nuclear polymorphism, mitotic figures, focal necrosis, and the presence or absence of brain infiltration.[94] For each of the first five parameters a score is assigned as follows: Absent=0, uncommon=1, common=2, and plentiful=3. In case of brain invasion, 0=no invasion, 1=brain invasion. A grade is then assigned based on the total score: grade I, benign, 0-2 points; grade II, atypical, 3-6 points; grade III, anaplastic, 7-11 points; and grade IV, sarcomatous, 12-18 points.

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2.4 LITERATURE REVIEW ON THE MANAGEMENT AND OUTCOME

Complete surgical removal of tumour remains the hallmark of meningioma therapy. Advances in neuroimaging, a better understanding of microneuroanatomy, brain protection and intraoperative neuromonitoring have substantially reduced the surgical mortality and morbidity of sphenoidal wing meningiomas.[153] Tumour recurrence, however, which depends in most cases on the completeness of surgery [99] remains a challenge in operations on medial tumours. Older series have given complete excision rates as low as 47% for medial as compared to rates of 91% for lateral sphenoidal tumours.[96] Improved microsurgical techniques have made more radical excision possible.[95] In a series of clinoidal meningiomas Al-Mefty[153] showed that of 19 Al-Mefty type II tumours complete excision (Simpson 1) was achieved in 18. He found on the other hand that complete excision of Al-Mefty type I tumours was almost impossible and was associated with a definite morbidity. Even when apparently total removal has been achieved the risk of recurrence remains substantial.[95,79,98,99] There is further evidence that 100% cures for meningioma in whatever location are probably not attainable.[100] Much work in the last few decades has therefore also been directed at evaluating adjunctive therapy for meningiomas that cannot be completely excised or whose risk of recurrence despite complete removal is high.

Many workers have reported beneficial effects of fractionated radiotherapy in the control of meningiomas.[101,102,103] Most recently Goldsmith *et al.*[104] have reported on a retrospective analysis of 140 patients treated with post operative irradiation at the

University of California San Francisco from 1967-1990. They found an overall 5-year survival rate of 85% and a progression-free survival rate of 89% for patients irradiated following incomplete excision of benign meningiomas. They found this to be a better outcome in comparison to rates of 43% and 59% respectively that are obtained with subtotal resection followed by observation only.[102] Moreover, the outcome compares favourably with that obtained in series of complete excision which remains the benchmark of meningioma therapy. Mirimanoff, *et al.*[100] reported a 5-year progression free survival rate of 93% and Taylor, *et al.*[102] reported an 82% 5-year actuarial local control whereby in both series the tumour was completely excised. Mirimanoff, *et al.*[100] as well as Barbaro *et al.*[105] have noted in regard to cases of subtotal resection, that patients undergoing radiation have more favourable outcomes than those not receiving irradiation.

Al-Mefty *et al.*[106] have found significant long-term complications in a series of patients treated with irradiation for benign CNS tumours, including meningioma. Sandler [107] has suggested that the liberal use by the Al-Mefty group of the term „complication“ in their series was probably unjustified. Goldsmith, *et al.*[104] in a careful long-term follow-up review of their series found no significant complications. They did cite a case of post-irradiation blindness in a patient treated before 1980. Another of their patients developed fatal cerebral necrosis after treatment with radiation. Following this patient's death their institution no longer uses high-dose opposed lateral fields technique for irradiation of the central nervous system.

2.5 THE ANATOMY OF THE SPHENOIDAL WING

The sphenoid ridge forms an arcuate posteriorly concave ridge of bone that separates the middle from the anterior cranial fossa. It consists of the body of the sphenoid, the greater wing, the lesser wing and the pterygoid plates. Medially the body of the sphenoid is saddle-shaped to form the sella turcica that accommodates the hypophysis. The lesser wing, the *Ala parva,* whose posteromedial extremity is the anterior clinoid process lies anteromedially. The lesser wing articulates anteriorly with the frontal bone and in the midline with the cribriform plate of the ethmoidal bone. In the midline anteriorly lies the crista galli.

The body of the sphenoid articulates with the clivus posteriorly. On either side of the body of the sphenoid is a groove-the carotid sulcus in which the internal carotid artery runs first anteroinferior and later inferolateral to the optic nerve. The latter runs from the orbit posteromedially in the optic canal to reach the optic chiasma in the midline. The cavernous sinus lies on the slanting walls of the sphenoid body enclosed by double dural folds with attachments to the anterior clinoid process anteriorly and the posterior clinoid posteriorly here continuing into the free margin of the tentorium cerebelli. Together with the intracavernous carotid the oculomotor, the trochlear and the abducent nerves run in the sinus and reach the orbit through the superior orbital fissure whose medial end lies covered by the anterior clinoid process.

The greater wing, the *Ala magna*, lying posterior to the lesser wing articulates with the parietal, and the squamous and petrous temporal bones. In the medial side of the

greater wing in a roughly anteroposterior distribution are the foramina rotundum, ovale and spinosum. They are traversed by the maxillary branch of the trigeminal nerve, the mandibular branch of the same nerve and the middle meningeal artery respectively. The carotid artery gains the middle cranial fossa through the foramen lacerum. The pterygoid plates protrude inferiorly from the body of the sphenoid almost vertically about 1.5 cm on either side of the vomer which articulates with the body of the sphenoid in the midline inferiorly.

The relation of the meninges to the carotid artery is of surgical significance. The carotid artery emerges from the cavernous sinus inferomedial to the anterior clinoid process entering the subdural space to be vested in the carotid cistern. The carotid cistern is bordered superiorly by the dura over the anterior clinoid process and the gyrus rectus of the frontal lobe. Inferiorly it is bordered by the dura covering the superior aspect of the cavernous sinus. The arachnoid does not follow the carotid artery into the cavernous sinus. It is also not attached to the anterior clinoid process. Therefore between the dura of the cavernous sinus and the investment of the carotid cistern are 1-2 mm of carotid artery without arachnoid investment. Medially the carotid cistern shares a wall with the chiasmatic cistern and is bounded laterally by the medial temporal lobe and the free margin of the tentorium. The inferior part of the carotid cistern and the superior part of the interpeduncular cistern are in apposition and thus create a single Liliequist membrane.

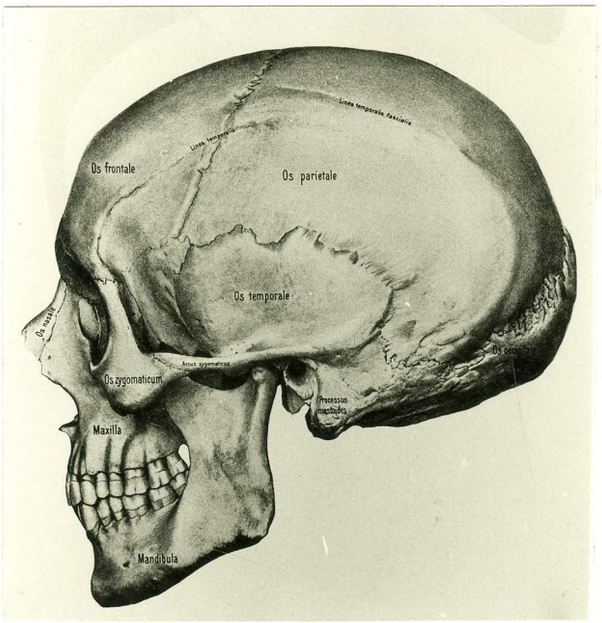
Thus in case of meningiomas arising proximal to the end of the carotid cistern such as at the inferior aspect of the anterior clinoid process the segment of the carotid

artery not invested with arachnoid becomes enwrapped in tumour which may actually invade the adventitia because an arachnoid membrane is lacking. The growing tumour advances the arachnoid ahead of it allowing further adventitia invasion which may extend into the middle cerebral artery. Such tumours are difficult to dissect free from the vessels without injury to the latter.

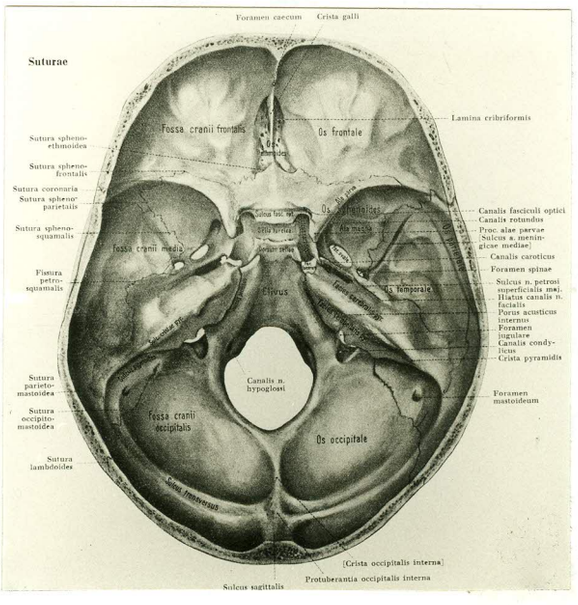
Tumours arising from the lateral or the superior aspect of the clinoid process are related to the segment of the carotid artery invested in the carotid cistern. In this case therefore an arachnoid interface exists between the tumour and the vessel. Dissection of tumour from the encased vessel is therefore possible without an added morbidity.

From the anatomy of the sphenoidal wing area it is possible to appreciate the nature of clinical presentation of tumours in this location. Medial tumours are in close relation to the optic nerve and may lead to visual disturbances. They may also invade the neighbouring cavernous sinus leading to compression of the third fourth, and sixth cranial nerves. Lateral tumours on the other hand first compress the brain and have room to grow large before symptoms are experienced. The understanding of the anatomy also brings the expected surgical difficulties into perspective.

Plate 1. a). A lateral view of the skull showing the pterion which is formed by the greater wing of the sphenoid, the frontal the parietal and the temporal bones
b). A photograph of the skull base showing the arcuate shaped shenoid wing which forms a separation between the anterior and the middle cranial fossae.



a)



b)

3 THE PRESENT STUDY

3.1 METHODOLOGY

3.1.1 Objectives

1. To study the clinical and neuroradiologic features of sphenoidal wing meningiomas and determine their value in management decisions and in the prediction of outcome.

2. To study the anatomy of the blood supply of the tumours at the various locations on the sphenoidal wing.

3. To study the histological patterns of sphenoidal wing meningiomas and their influence on the clinical behaviour of tumour.

4. To study the complications and outcome of management in particular the influence of radiotherapy on the recurrence rate and survival.

3.1.2 Patients and Methods

The Central Medical Archives at the Klinikum Großhadern maintains an up-to-date inventory of all case notes of patients discharged from the wards on a computer data bank. Since 1990 the department of Neurosurgey itself also keeps a computer record of all discharges containing details of name and date of birth, diagnosis, operations if any, complications and outcome at discharge. Further, histology reports on all tumours operated upon or biopsied are kept by year in alphabetical order within the

department. The names of all patients with a histologically confirmed diagnosis of meningioma were obtained and their case notes retrieved from the Central Medical Archives. Case notes of patients with sphenoidal wing meningioma were selected and studied. In nearly every instance the case notes contained a discharge medical report. This was a detailed record of the clinical history, physical findings, and outcome of surgery. A record of the operative procedure was similarly available in the case notes. Neuroimaging records were in most cases separately available from the Central Archives. In cases where radiation therapy had been offered the pertinent information regarding such treatment was included in the discharge medical report. For each new admission of the same patient a new case note was issued and details pertaining to the current admission entered. All patients seen between 1988 and 1994 were included in the study. Some of them were readmissions whose tumours had initially been diagnosed and treated well before this period. The effective follow up therefore extended to periods before 1988. The longest follow up was from 1978 to 1994. A total of 71 case notes were retrievable. Of these all the required information pertaining to clinical data, neuroimaging, operative procedure and further therapy as well as follow up was available for 56 patients.

Similar raw data was obtained for patients treated at the neurosurgical department of the University of Bern, Switzerland and those variables which were available in both series were analysed together.

3.1.3 Questionnaire

A questionnaire was developed partly based on one previously used in the study of a related subject at the Neurosurgical Department of the University of Bern, Switzerland by Reulen and associates. The present questionnaire (appendix 1) was structured to take into account standardised descriptions such as completion of surgery according to Simpson,[112] and type of vascular encasement by tumour as described by Al-Mefty[75] in order to find a basis for comparing outcome in patients treated by different surgeons. Apart from the computer data base that was developed to record and streamline the data, this questionnaire was also completed for each case by the author himself.

3.1.4 Neuroimaging

Patients' initial and follow-up CT scans, pre-operative angiograms and MRIs when available were studied in detail for each patient to determine the following:

- Exact anatomic location of tumour
- The approximate size of the tumour
- The presence or absence of peritumoral oedema. The oedema was approximately quantified by measuring the extent of the peritumoral hypodensity on the CT scans. Values of up to 2.5cm were considered to correspond to moderate oedema and those larger than 2.5cm to severe oedema.
- The feeding vessels
- The presence of vascular displacement and/or encasement

3.1.5 Operative Technique

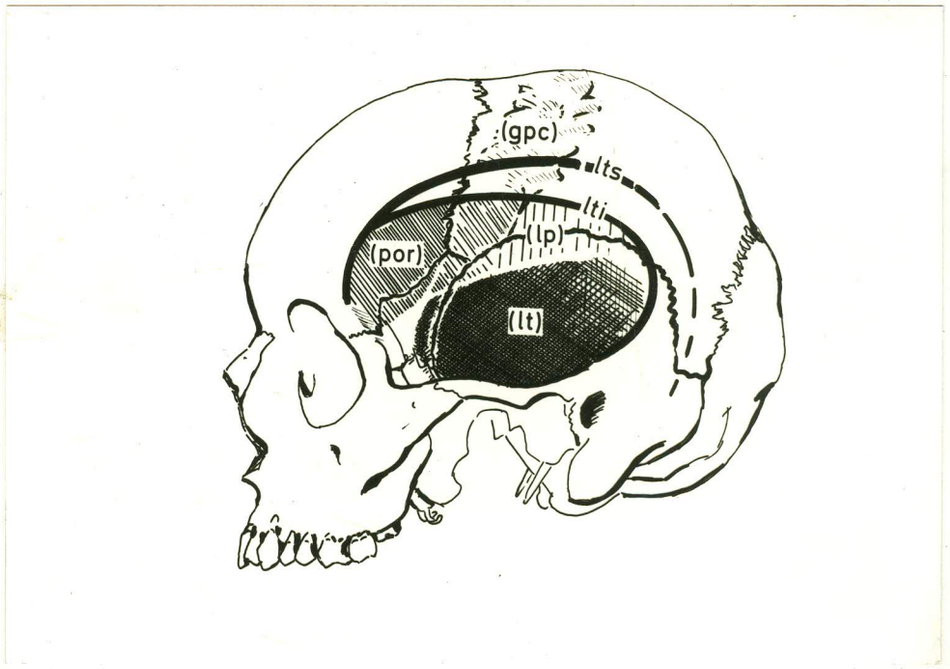
Surgery was carried out under general anaesthesia with the patient in the decubitus position. The shoulder on the side to be operated on was slightly raised with the help of a small pillow and the head rotated 30-45 degrees to the opposite side with the vertex 15-30 degrees to the horizontal and secured in a Mayfield head clamp. The surface markings of the scalp incision were outlined. Mannitol was infused at the commencement of the scalp incision. The approach most commonly used was the fronto-pterional craniotomy (plate 2). The lateral end of the sphenoid wing was drilled off using the high-speed drill. For those tumours which were mainly osteoclastic, the operation now proceeded extradurally, the tumour-containing sphenoid ridge was drilled away with a high speed drill, and bone excision carried through the foramen ovale and superior orbital fissure to decompress the optic nerve when this was found to be compromised by a hyperostotic tumour. For tumours which were globular early dural opening was carried out using a curvilinear incision across the plane of the Sylvian fissure, which latter was then partly laid open to allow the retraction of the frontal and temporal lobes. In case of large tumours one of the operators (H.-J. Reulen) preferred at this step to resect the anterior pole of the temporal lobe and decompress the tumour in the middle fossa before opening the Sylvian fissure.

The tumour was now removed piecemeal using the cutting diathermy loop or the ultrasonic aspirator, care being taken not to damage encased nerves or vessels.

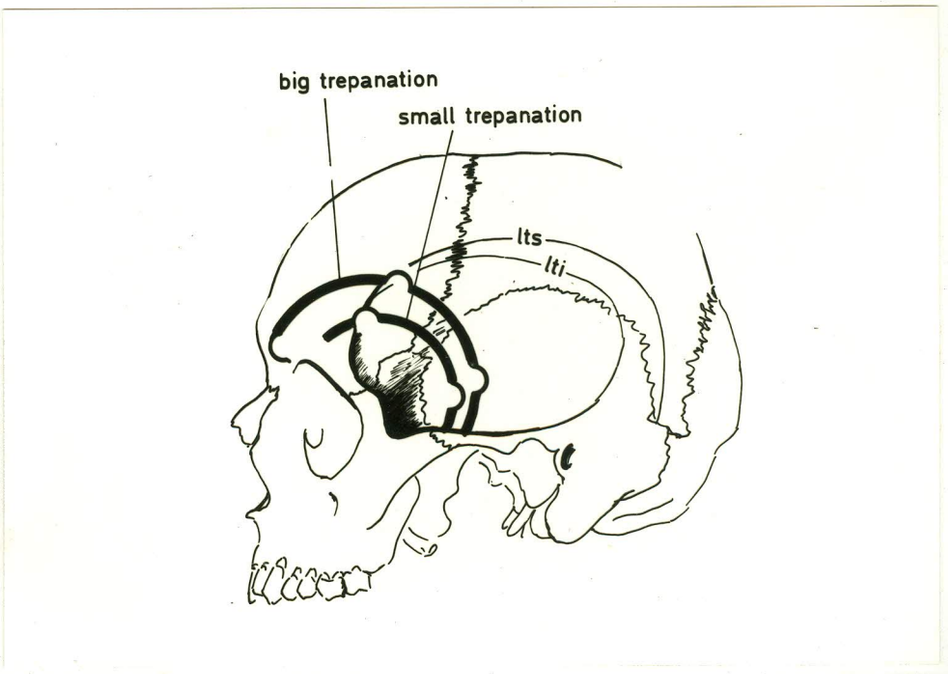
Finally dura and bone macroscopically involved was removed as far as possible. The

dead space created by extensive bone resection is obliterated with bone cement and the cranial floor repaired so as to remain water tight. The extent of tumour, dura and bone removal was almost always carefully described in the operative notes.

Plate 2. Schematic diagram of the skull to show (a) surface markings and projected locations of underlying brain. Diagram (b) shows two craniotomy approaches: the big trepanation is used for sphenoidal meningioma. **Abbreviations:** *gpc*=pre-central gyrus projection, *lts*=superior temporal line, *lti*=inferior temporal line *lp*=Projection of the parietal lobe, *por*=orbital gyrus of the frontal gyrus III, *lt*=temporal lobe.



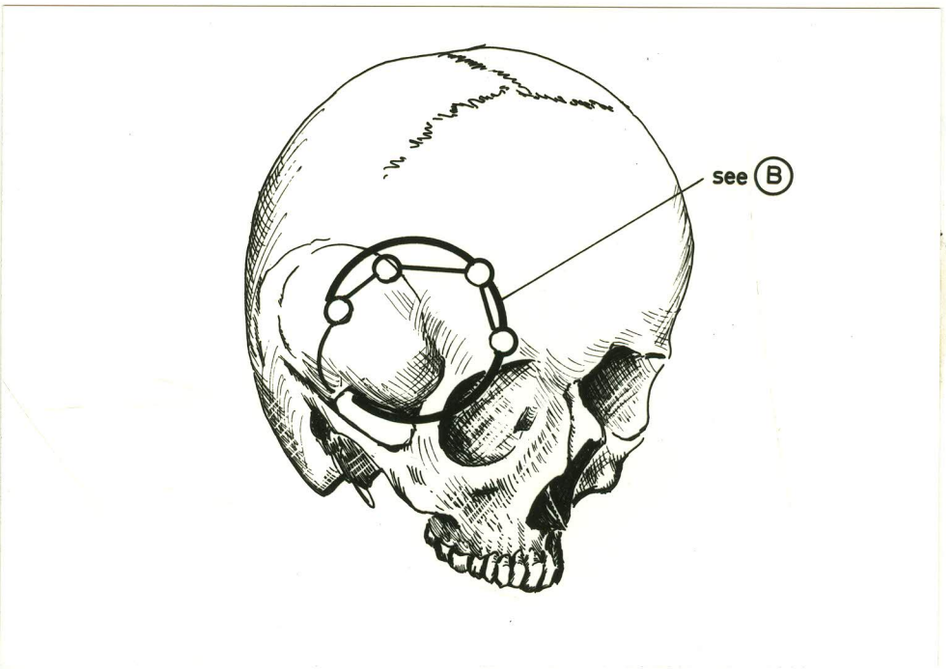
a)



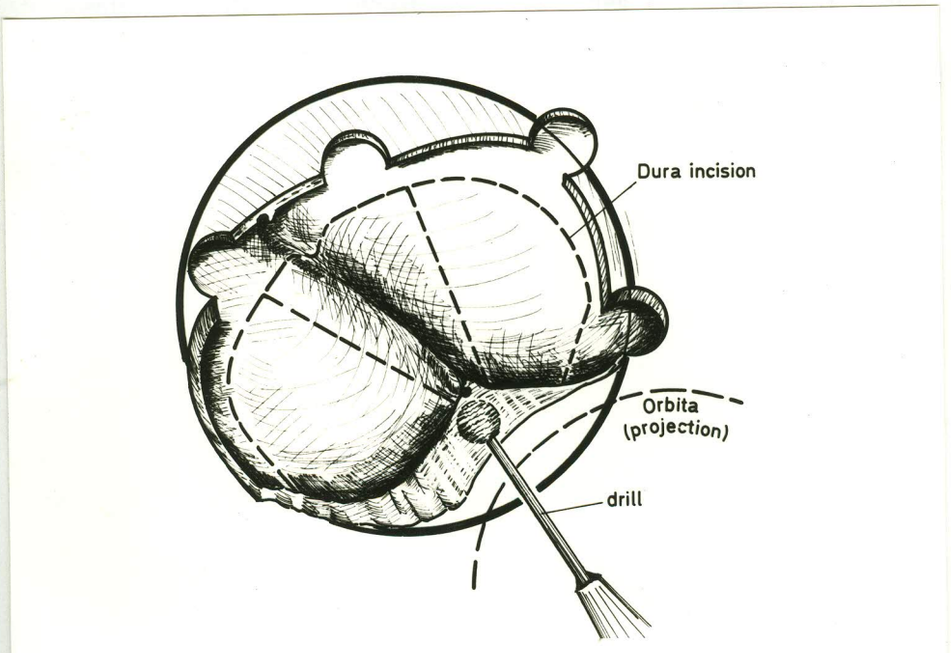
b)

Plate 3. a)An anatomical sketch of a pterional craniotomy
b)an enlarged craniotomy view after removal of the bone.

a)



b)



Incomplete removal was usually due to neurovascular encasement, invasion of the cavernous sinus or diffuse bone involvement. In such cases some operators used laser to necrotise irremovable visible tumour. The use of laser was, however, not based on a unified indication and as such could not be standardised. In this study, the surgeon's description of the operation was used to determine the degree of the completeness of surgery as proposed by Simpson [112] and shown below:

Grade 1: Complete tumour resection with resection of dura and abnormal bone.

Grade 2: Complete removal with coagulation of dural attachment.

Grade 3: Complete removal without resection of dura or coagulation as in the case of. sinus or bone involvement

Grade 4: Subtotal removal.

Grade 5: Decompression or simple biopsy

In unpublished data Kobayashi and associates have proposed a new scheme of classification of completeness of surgery with the plausible argument that Simpson's classification which was formulated before the operating microscope came into use is no longer entirely satisfactory.[114]

3.1.6 Classification of Tumour

The tumours of the sphenoid wing were classified for the purpose of this work into medial and lateral. Truly cavernous sinus tumours were excluded from this series since they constitute a different clinical and surgical entity.[115] The medial group was

further reclassified according to Al-Mefty into groups I, II and III on the basis of cerebral arterial involvement by tumour as found at surgery.[75]

Al-Mefty I

The tumour origin is infraclinoid. There is no arachnoid mater interface between tumour and the vessel encased by it.

Al-Mefty II

The tumour origin is supraclinoidal or lateral clinoidal. There is an arachnoid interface between tumour and the encased vessel.

Al-Mefty III

The tumour arises from the optic foramen or canal with an arachnoid interface being present or absent between tumour and nerve.

Although MRI and angiography are very helpful in the determination of the presence or absence of vascular involvement by the tumour, Al-Mefty's classification was worked out from the description of the operation. Finally tumours were also classified according to the predominant histological picture.

3.1.7 Complications of Surgery

Complications following surgery were grouped into two categories:

1. Early complications occurring within six months of surgery and
2. Late complications which occurred more than six months post-operative

3.1.8 Follow up

An outpatient record is maintained on a separate case note which during the first three years of follow up is kept at the outpatient clinic and can easily be retrieved. Case notes of patients followed up for longer than three years are submitted to the Central Medical Archives. Patient's initial follow up data was therefore usually readily available. The routine follow up schedule was at one, three and five years post-operative. Long term data and follow up information in the periods between these regular follow up intervals was, however, more difficult to obtain. Enquiries sent to family physicians were generally not promptly replied to. A follow up letter was therefore designed and mailed to the patients themselves in order to obtain the most pertinent information desired (appendix 2).

The case notes studied were those of patients admitted between the years 1988 and 1994. Twelve of these patients had been first seen and treated from as far back as 1978. The follow up period therefore extended to periods before 1988.

3.1.9 Data Analysis

Rates of actuarial overall survival and tumour-free or progression-free survival were calculated from the date of surgery or radiation in the case of primary radiotherapy to the time of death or first determination of recurrence.

Recurrence was defined as evidence of tumour on Follow-up CT or MRI or as neurological deterioration attributable to the tumour. Progression in the case of subtotally excised tumours was similarly defined. Selected clinical variables were

subjected to univariate analysis as a continuous and/or as a dichotomous variable. A Wald chi-square test was used for both the continuous and the dichotomous variables to test the association between these variables and the outcome.

3.2 RESULTS

3.2.1 Clinical features

3.2.1.1 Age and Sex distribution

A total of 95 cases were available for the study. Figure 1 shows the age and sex distribution among the patients. The Male:Female ratio was 1:2.4. The age at diagnosis ranged between 30 and 81 years with a mean of 59 years. The standard deviation was 11.4, and the standard error of the mean 1.5 at the 95% confidence level. The peak tumour frequency was between the ages 46.4 and 68.6 years overall. There was no apparent age-dependent incidence in males when this group was evaluated separately. The age range of highest tumour incidence was therefore a feature peculiar to female patients.

Fifty nine (62%) of the tumours were medial, 28 lateral (29%) and 8 (9%) *en plaque* lesions involving varying extents of the sphenoid wing. The medial tumour was significantly commoner than the lateral (p=.05). Two patients had multiple meningiomas. One had a cerebello-pontine angle meningioma and another 46 year old patient two other CNS tumours: a suprasellar meningioma and a parasagittal meningioma. The second patient had cutaneous stigmata of von Recklinghausen neurofibromatosis.

Figure 1. Ages and Sex of Patients with Sphenoidal wing Meningiomas n=56

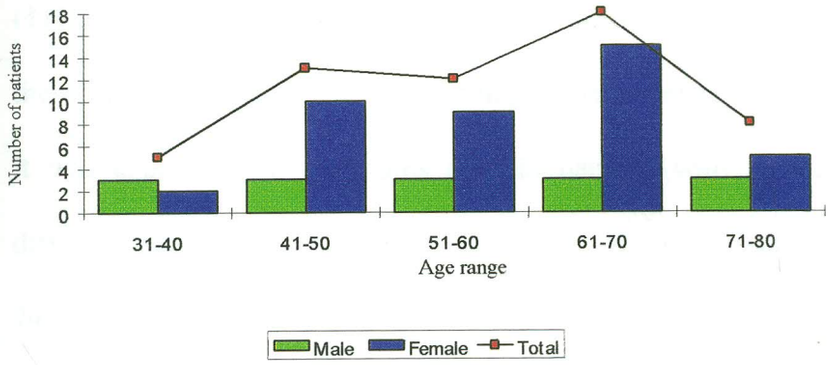


Table 3. Tumour location on the sphenoid wing. n=78*

	Right	Left	Total
Medial	22	33	55
Lateral	19	13	32
Total	41	46	87

3.2.1.2 Symptoms and signs

The commonest presenting symptoms in this series were visual complaints (54%) ranging from reduced visual acuity to overt blindness; headaches (44%),

* Eight of the tumours were en plaque lesions

exophthalmos (20%) and gait disturbances (17%). Apart from headaches other symptoms and signs indicating cerebral compression were not infrequent. They included speech difficulties (15%), memory lapses (12%), nausea and vomiting (11%), personality changes (15%) and one-sided extremity signs (15%). Table 4 lists these findings. When the clinical findings were correlated with the location of tumour it was apparent that symptoms seen in patients with medially situated tumours differed from those in patients with lateral tumours. Visual deterioration (medial 74%; lateral 14%), and exophthalmos (medial 19%; lateral 14%) were commoner in patients with medial tumours. One sided symptoms and signs such as hemiparesis (medial 10%; lateral 29%), speech abnormalities (medial 10%; lateral 29%), memory disturbances (medial 10%; lateral 18%) were more frequent in laterally located tumours. Oculomotor involvement occurred only in medial tumours. Four patients with *en plaque* tumours presented with exophthalmos. From this data it seems evident that symptoms and signs of sphenoidal wing meningiomas located medially on the wing tend to be a result of local pressure on contiguous structures such as the optic nerve and the eye ball while lateral tumours present with features of cerebral compression.

3.2.2 Radiological Findings

3.2.2.1 Computer tomography

Details of computer tomographic features were available only for the Munich series. Forty seven of 56 patients in this series (84%) presented with CT findings of iso- to

slightly hypodense lesions with intense uniform enhancement while 8 (14%) demonstrated non-homogenous enhancement. Of the 8 patients showing

Table 4. Symptoms and signs by tumour location

Symptoms and signs	Medial n=59	Lateral n=28	*En plaque* n=8	**Total n=95**
Headaches	26	15	1	42
Reduced vision				
Ipsilateral	24	2	1	27
Bilateral	6	1	1	8
Homonym.	7	1	1	9
Blindness				
Ipsilateral	6	0	0	6
Bilateral	1	0	4	5
Exophthalmos	11	4	0	15
Gait disturbances	6	10	0	16
One-sided symptoms	6	8	0	14
Speech abnormalities	6	8	0	14
Personality changes	7	7	0	14
Trigeminal involvement	5	1	0	6
Oculomotor involvement	6	1	0	7
Memory disturbances	6	5	0	11
Dizziness	5	4	0	9
Nausea and vomiting	6	4	0	10
Facial paralysis	3	1	0	4
Seizures				
Generalised	10	3	0	13
Focal	6	1	0	7
Complex partial	1	3	0	4
Disorientation	0	1	0	1

inhomogenous enhancement 3 had tumours with extensive calcification, 4 were *en plaque* lesions and 1 showed cystic degeneration. Only one patient had a tumour without significant enhancement. Slight to extensive peritumoral oedema was observed in 24 patients (43%) (Table 5). When tumor enhancement was related to the

presence or extent of peritumoral oedema no positive correlation was found (p=.05). Oedema was present in 21 (45%) and absent in 26 (55%) of 47 intensely enhancing tumours. Similarly no correlation could be found between enhancement or oedema and the clinical behaviour or histological pattern. Reduced inhomogenous enhancement was found in 8 patients 3 of who showed oedema and 5 no oedema. The number of scans showing poor enhancement were, however, too small for statistical evaluation. The small numbers were consequent upon the low rate overall of occurrence of reduced contrast enhancement (14%) seen in the study cases.

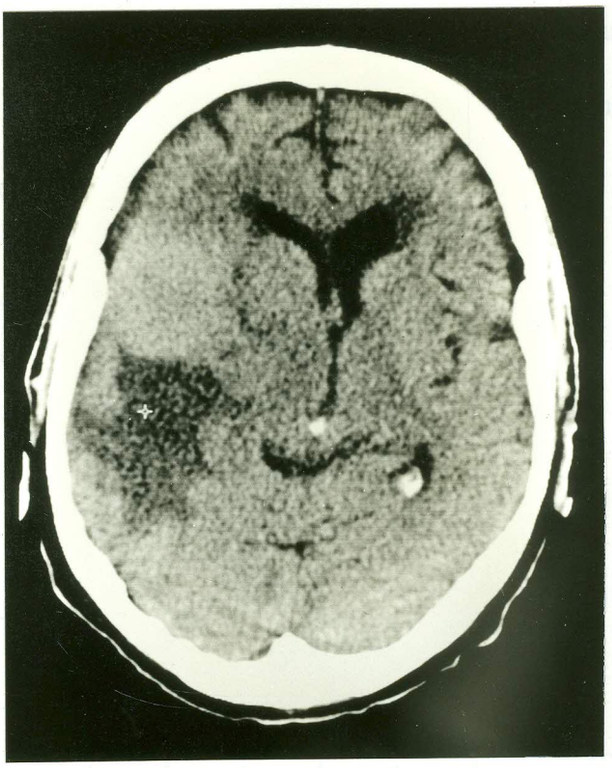
Table 5. Peritumoral Oedema in relation to contrast enhancement

Enhancement	Oedema present	No oedema	Total
Intense homogeneous	21	26	47
Inhomogeneous	3	5	8
None	0	1	1

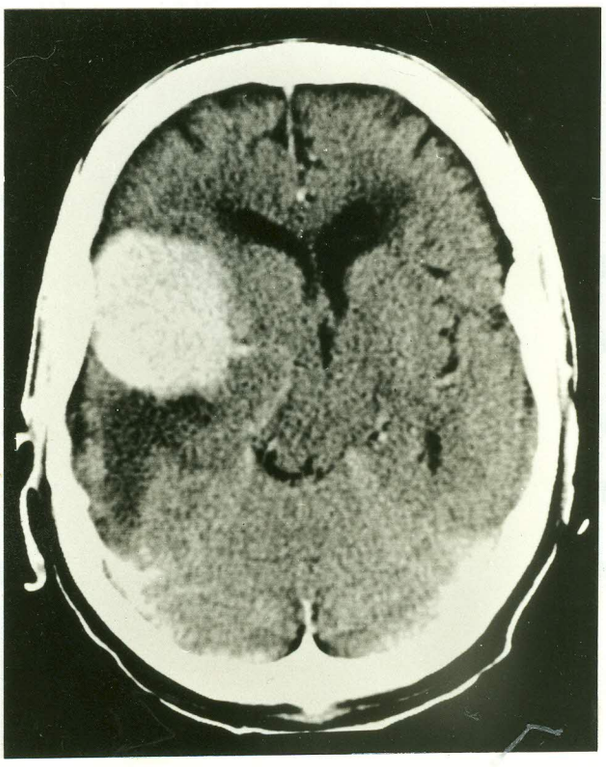
The diagnosis of meningioma could be made with confidence on the basis of CT films alone in 54 of 56 cases (96%). The two doubtful cases were an *en plaque* lesion and one with cystic changes. The typical diagnostic characteristics were the tumour's relationship to the dura, the intense homogenous contrast enhancement, location of the tumour and its circumscribed nature. Further, all of the *en plaque* tumours were associated with typical hyperostosis of the underlying sphenoidal wing and in all instances involved the pterional end of the shenoidal ridge. They then extended for varying distances towards the medial end of this bone.

Plate 4. Axial CT scans of a lateral sphenoidal wing meningioma
a) Plain scans and b) After contrast enhancement. To note are the intense contrast enhancement, the peritumoral oedema in the white matter and distortion of the ventricles with a midline shift.

a)

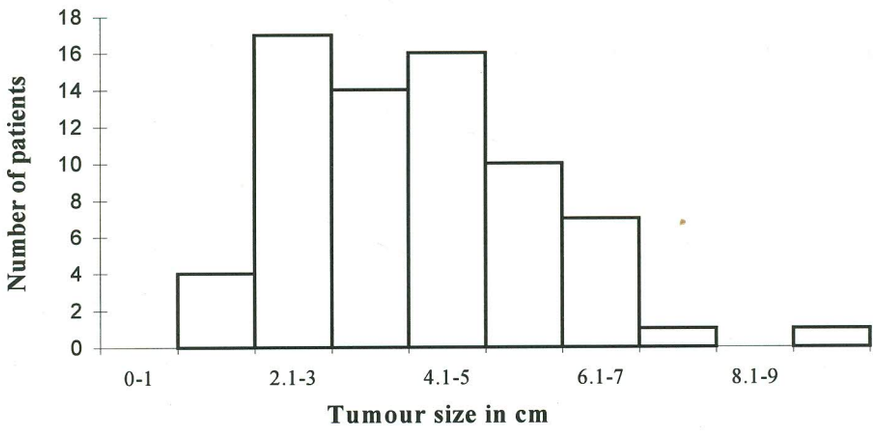


b)



In both the Munich and the Bern cases the size of the tumour was estimated as the largest diameter of the lesion as seen on the CT scans. Such an estimate of tumour size was also possible from the angiograms and from the MRI films and yielded similar results . The average tumour diameter ranged from 1.5 centimetres (cm) to 10 cm with a mean of 4.4 cm, and a median of 4 cm. Figure 2 shows a graphic representation of tumour size.

Figure 2. The distribution of tumour size estimated as the average diameter of the tumour in cm



3.2.2.2 Magnetic Resonance Imaging

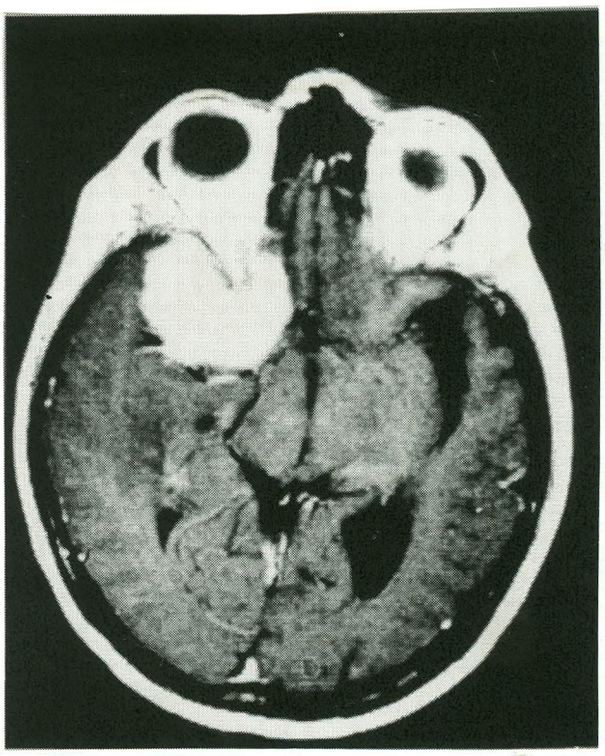
Since this neuroimaging technique has become routinely available relatively recently not all cases in this series were subjected to magnetic resonance imaging (MRI). Fifty patients had been evaluated with MRI. The principal imaging features were comparable to those of CT scans but at the skull base there were MRI findings which proved superior to those of CT scans. The gadolinium enhanced scans delineated

tumour in the bone distinctly and were superior in this regard to the CTs which simply showed hyperostotic changes. Twenty five tumours showed varying extents of oedema formation. Notable was the MRI evidence of oedema in 5 cases where no clear evidence of oedema was apparent on CTs. Furthermore MRI gave findings of vascular encasement and/or displacement which were comparable to angiographic findings. The quality of the imaging features was such that the nature of vascular involvement by tumour as seen in MRI scans could be very accurately determined. Optic nerve displacement or encasement seen on MRI scans correlated positively with operative findings. The MRI was therefore superior to the CT in the imaging of tumours in this area. Furthermore angiograms offered no information not available from the MRI studies

Plate 5. Left clinoidal meningioma. MRI in T1 sequence, (a) before and (b) after gadolinium injection. In the unenhanced scans the tumour is isointense with brain. Contrast uptake is intense and homogeneous.

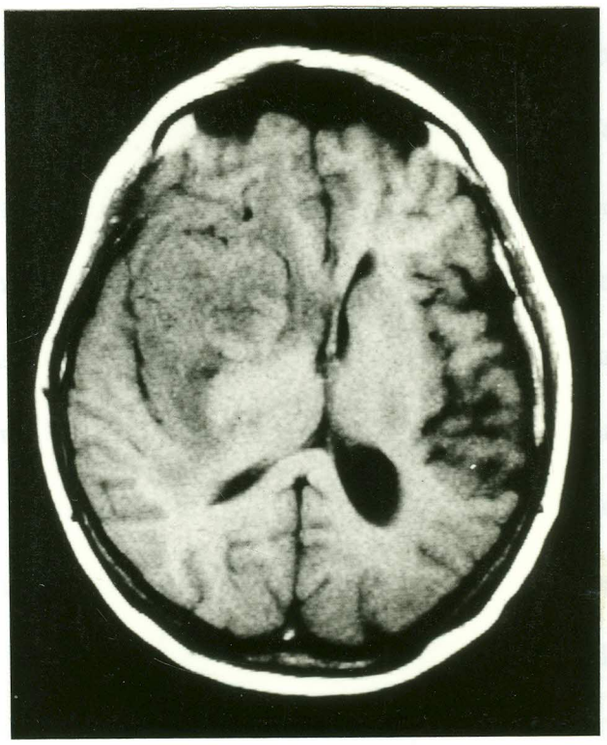


a)

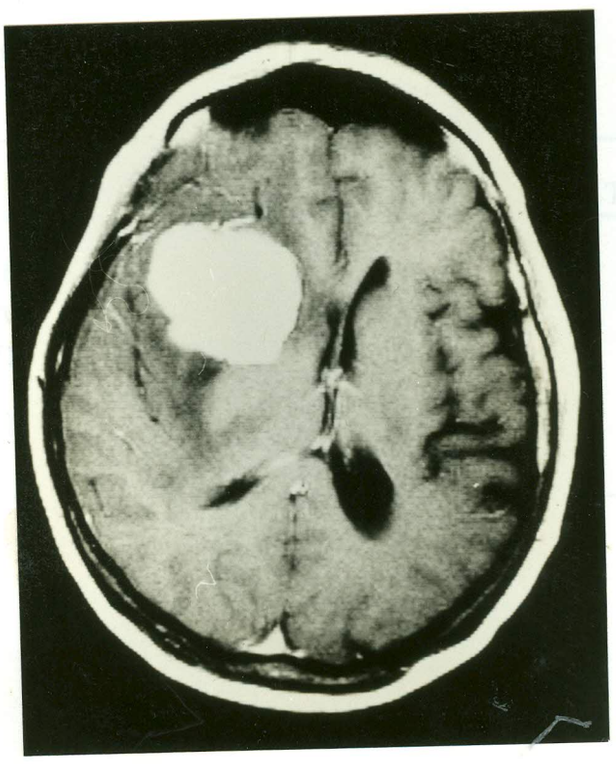


b)

Plate 6. Intense homogeneous enhancement seen in T1 MRI sequences: (a) before and (b) after gadolinium injection. The images are of high resolution. Notice the ventricular distortion and the midline shift.



a)



b)

3.2.2.3 Angiographic findings

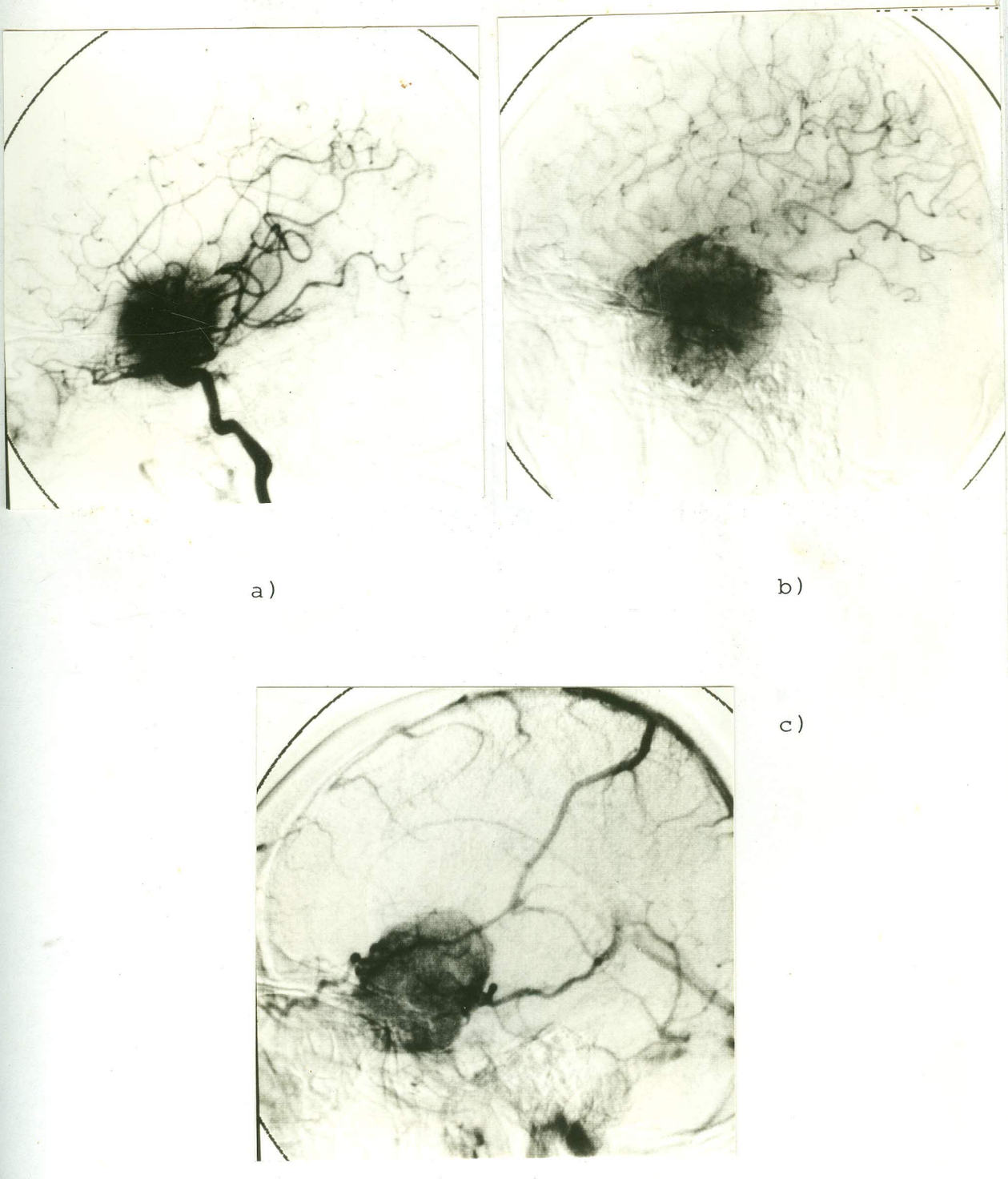
All patients underwent angiography in addition to CT. The studies were performed to complement the CT findings and with the view to performing embolisation when this was indicated and feasible in order to reduce intraoperative haemorrhage. In every case the method of examination was by the Digital Subtraction Technique (DSA). The typical features of a tumour blush of varying intensity appearing early and persisting through the capillary and venous phases (plate 7) characterised 84 studies. The main arterial feeders were the ethmoidal artery (41%), the middle meningeal artery (26%), and intracavernous branches of the internal carotid artery (25%). The middle cerebral, the ethmoidal, and the maxillary arteries constituted the remaining blood supply. One tumour was supplied by the Arteria Tentorii (Table 6). From the data available it did not appear that pre-operative embolization had been performed for any of the tumours.

Table 6. Arterial supply to sphenoidal meningiomas:

Feeding artery	Frequency		
	Medial	Lateral	Total
Ethmoidal artery	31	8	39
Middle meningeal artery	12	13	25
Caroticocavernous trunk	22	2	24
Middle cerebral artery	2	5	7
Maxillary artery	2	1	3
Meningohypophyseal trunk	1	0	1
Arteria tentorii	1	0	1

The middle cerebral artery was displaced by tumour in 35 cases (36%), the internal carotid artery in 24 cases (25%), and the anterior cerebral artery in 6 instances (6%). Encasement of the internal carotid artery was evident in 12 cases (13%). The middle cerebral artery was encased by tumour in only one instance. There was no case of encasement of the anterior cerebral artery.

Plate 7. Digital subtraction angiogram to show a typical meningioma blush occurring early in the arterial phase (a) and persisting through the capillary (b) and venous phases (c).

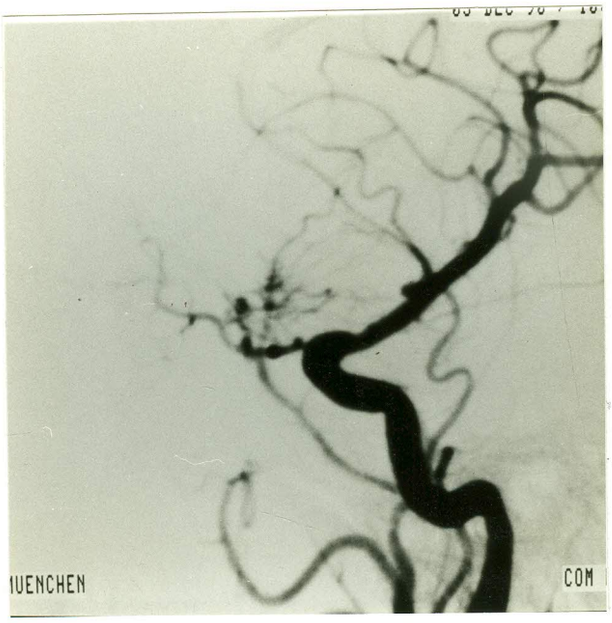


a)

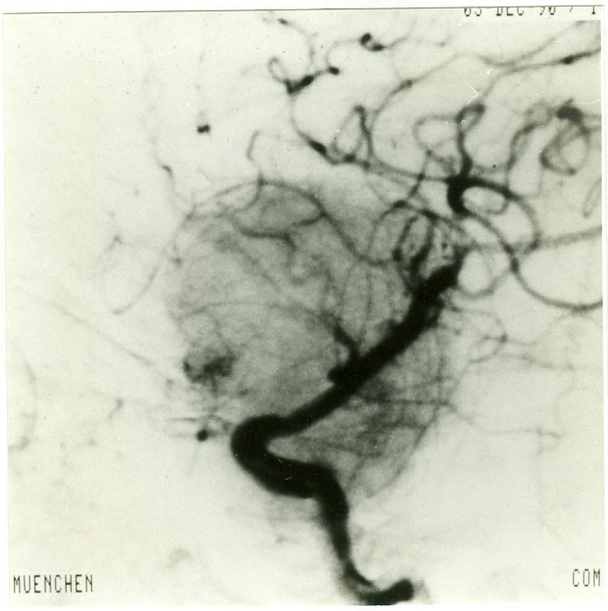
b)

c)

Plate 8. Digital subtraction angiogram of the left common carotid artery; lateral view showing (a) Narrowing and irregularity of the supraclinoid ICA and the MCA (indicating arterial encasement) and enlargement of the ophthalmic artery supplying the tumour. (b) Tumour outlined by blush.

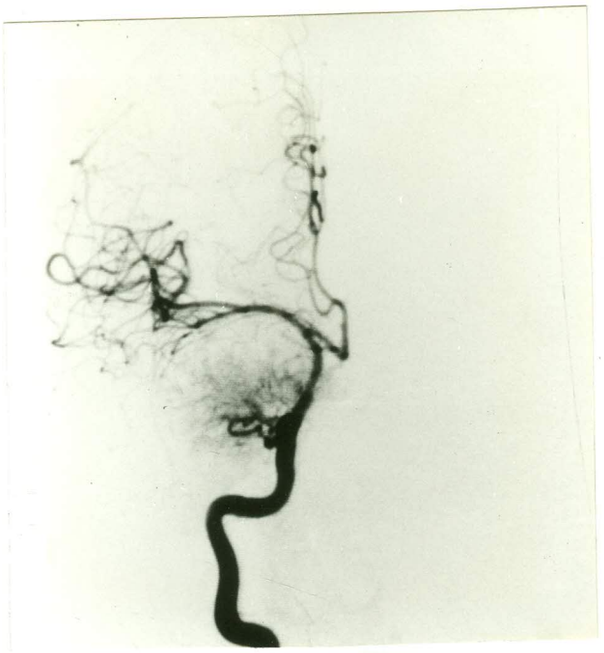


a)

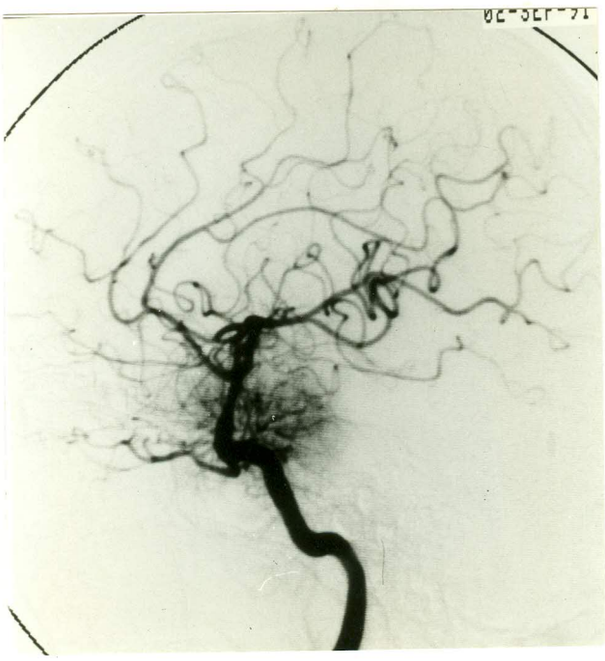


b)

Plate 9. Digital subtraction angiogram showing in AP views (a) displacement and narrowing of the carotid and middle cerebral arteries and in lateral view (b) tumour blush, narrowing and irregularity of the ICA and MCA.

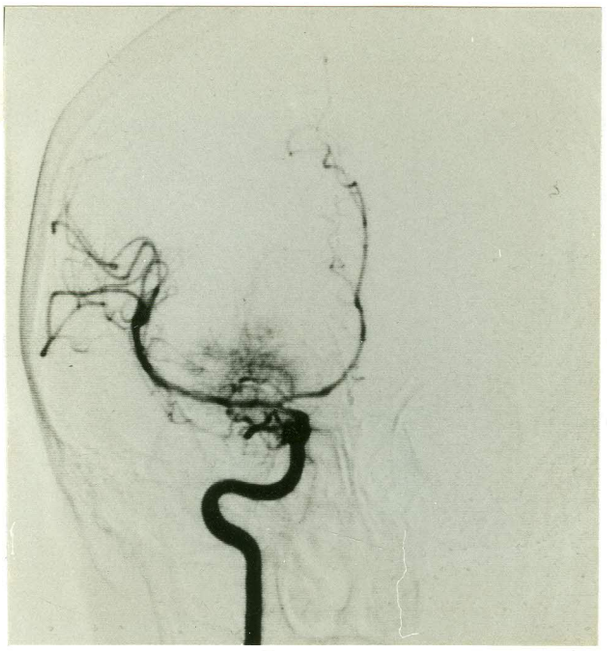


a)



b)

Plate 10. AP views of a medial tumour showing stretching and displacement of the MCA and ICA laterally and medially respectively. Note the intense tumour blush in (b).



a)



b)

3.2.3 Treatment and Outcome of Treatment

3.2.3.1 Surgical treatment

Surgery was the mainstay of treatment. Of the 95 patients 91 (96%) were offered surgery. The completeness of surgery according to Simpson was: Grade 1 43 cases (47%), grade 2 29 cases (32%), grade 3 10 cases (11%), and grade 4 9 cases (10%). The reasons for subtotal (Grade 4) tumour removals were invasion of the cavernous sinus in 2 cases and extensive bone involvement in 4 cases. In this series no tumour was simply biopsied. Al-Mefty type I encasement was seen in 7 patients, type II in 24 and type III in 3 patients (Table7). Table 8 shows the arterial involvement

Table 7. Al-Mefty Classification of tumours n=34

Al-Mefty I	7 (8%)
Al-Mefty II	24 (26%)
Al-Mefty III	3(3%)

by tumour according to Al-Mefty [75] as seen at operation and its relationship to the completeness of tumour removal for 17 Munich cases for which this information was available. Of the Al-Mefty type I tumours 2 could be completely excised, one was completely excised but the dura only coagulated, and 2 could only be subtotally removed. It must be mentioned, however, that the two subtotally removed Al-Mefty I tumours also invaded the cavernous sinus and this, rather than the Al-Mefty status was the reason for failure of complete removal Simpson 1 and Simpson 2 removal in 4

4 cases each of Al-Mefty type II tumours were achieved. In Al-Mefty type III lesions two tumours could be totally excised and one tumour only subtotally excised. Again in this group the failure of complete excision was not a result of the Al-Mefty status but rather it was due to extensive infiltration of bone.

Table 8. Extent of Tumour Removal by Al-Mefty Classification n=16

Al-Mefty class	Completeness of surgery (Simpson)			
	Grade 1	Grade 2	Grade 3	Grade 4
I n=5	2	1	0	2
II n=8	4	4	0	0
III n=3	2	0	0	1

The Holmium laser was used in 7 instances as an adjunct to microsurgical extirpation of tumour. In these instances the completeness of surgery was Simpson 1 in 2 cases Simpson 2 in 4 cases and Simpson 4 in 1 case. The indication for the use of laser was not clear. This form of treatment was applied in 6 of the 7 cases by one of the operators who had a special interest in laser surgery. As these cases were too few, however, no conclusions could be drawn regarding the influence of laser surgery on the surgical outcome.

3.2.3.2 Immediate Postoperative outcome

The immediate post operative clinical state was gauged by the level of consciousness before and after the operation. Table 9 shows that preoperatively 88 patients were alert and 3 were drowsy. Postoperatively 84 patients (95%) were alert, 5 were drowsy and 2 were unarousable. The two unarousable patients constituted the subsequent mortality in this series.

Table 9. Perioperative Level of consciousness n=92

Level of consciousness	Before surgery	After surgery
Awake	88	84
Drowsy	4	6
Stuporous	0	2
Coma	0	0

3.2.3.3 Histologic findings

Table 10 shows the histologic findings for 92 meningiomas in the study. Meningothelial meningiomas constituted 69 cases (75%), transitional 10 cases (11%), and fibroblastic meningiomas 4 (4%) cases. Atypical features were seen in 5 tumours while 2 were angiomatous meningiomas. Two tumours had features of hypercellularity, increased mitoses, loss of architecture, focal necroses and brain invasion. These appearances indicated histological malignancy. There was no positive correlation between histologic features and clinical findings.

Table 10. Histologic findings

Meningothelial meningioma	69(75%)
Transitional meningioma	10(10.9%)
Fibroblastic meningioma	4(5.3%)
Atypical meningioma	5(5.4%)
Angiomatous meningioma	2(2.2%)
Malignant meningioma	2(2.2%)

3.2.3.4 Complications of Surgery

The complications observed in this series are shown in table 12. Noteworthy complication occurred in 18 patients (19.5%). Early complications were brain swelling 4 cases, CSF cysts 10 cases, wound infection 3 cases, cerebral infarction with hemiparesis 4 cases, aphasia 6 cases and unilateral blindness 2 cases. Third nerve paresis occurred in 8 cases 3 of which recovered completely. Trochlear nerve paralysis was observed in 2 cases. Long term complications included third nerve paralysis 5 cases, pituitary insufficiency 1 case, hemiparesis 3 cases, seizures one case and unilateral blindness 2 cases. Table 11 shows the neurological deficits before and soon after surgery. Whereas 38 patients were free from any deficits preoperative, 45 were without neurological symptoms postoperatively.

Table 11. Neurological Deficits Before and After Surgery n=92

Type of lesion	Preoperative	postoperative
None	38	45
Visual deterioration	12	9
Ipsilateral blindness	4	6
C. N. III lesion	6	13
C. N. IV lesion	1	4
C. N. V lesion	1	1
C. N. VI lesion	0	2
Hemiparesis	8	12
Aphasia/dysphasia	11	11

Table 12. Complications of surgery

Type of complication	Medial tumours	Lateral tumours	Total
Severe brain swelling	3	1	4
Cerebral infarction	3	1	4
Hemiparesis	3	1	4
Aphasia	2	4	6
Blindness	2	0	2
Third nerve paralysis	8	0	8
Trochlear nerve paralysis	2	0	2
Organic brain syndrome	1	0	1
Seizures	3	0	3
Pituitary insufficiency	1	0	1
Wound infection	3	0	3
Meningitis	1	0	1
Cerebrospinal cyst	5	5	10
Pneumonia	3	0	3
Brachial artery embolism	1	0	1
Femoral artery embolism	1	0	1
Pulmonary embolism	4	1	5
Deep venous thrombosis	2	1	3
Renal insufficiency	1	0	1
Postoperative haematoma	1	1	2
Hydrocephalus	1	0	1

Vascular complications leading to cerebral infarction mentioned above were observed in 3 patients with Al-Mefty type I carotid artery encasement. In 2 of them there was no intraoperative evidence of arterial injury but in both cases cerebral infarction involving the anterior choroidal artery territory with permanent hemiparesis followed. Treatment with the elevation of blood pressure and calcium channel blockers did not reverse the vasospasm. In the third case the carotid artery was injured during dissection and had to be temporarily clipped and repaired. This patient suffered permanent hemiparesis. In one other patient hemiparesis occurred

soon after surgery with a massive cerebral hemispheric swelling with infarction thought to be of venous aetiology. Operative vascular injury did not occur among the patients with Al-Mefty type II lesions. There were two deaths that occurred within ten days of the operation giving a primary operative mortality of 3%. Both deaths occurred with persistent neurologic deficits consequent upon cerebral infarction.

3.2.3.5 Intercurrent Medical Conditions

Twenty two patients had intercurrent medical conditions which could have affected their general response to therapy (Table 13). Cardiac disease was found in 9 patients, arterial hypertension in 13 and renal insufficiency in 1 patient. None of the two operative deaths occurred in patients with heart disease or any of the other medical conditions. One of the patients with a previous history of coronary bypass had a protracted post operative recovery with permanent hemiparesis. Duodenal ulcer, asthma, cholelithiasis, hypothyroidism and hyperthyroidism were the other medical conditions among the remaining patients. One patient had been previously operated upon for a uterine carcinoma and for a hypernephroma making the present meningioma her third tumour.

3.2.3.6 Radiotherapy

Conventional external beam irradiation was used in 9 cases and gamma knife therapy in 2 cases (Table 14). In 4 of these cases conventional radiotherapy was used as salvage therapy to reduce the rate of tumour progression in patients offered the

Simpson grade 4 operation. Radiotherapy was also offered to one patient following initial Simpson 1 surgery and after two cases each of Simpson grade 2 and 3.

Table 13. Intercurrent medical conditions

Cardiac	9
Arterial hypertension	13
Lung disease	3
Obesity	5
Cholelithiasis	1
Duodenal ulcer	1
Asthma	1
Hydrocephalus	1
Hypothyroidism	1
Hyperthyroidism	1
Obstructive uropathy with renal insufficiency	2
Previous history of hypernephroma and uterine carcinoma	1

Table 14. Outcome of radiation treatment

Type of therapy	Number of cases	Remarks	Outcome
Gamma Knife after conventional therapy	1	Transitory deafness after initial radiotherapy	Tumour regression after Gamma knife treatment.
Gamma Knife	1	Primary radiation	No progression at 4 years
Conventional radiotherapy	3	Radiation after Simpson 4 surgery	1 tumour progressed No tumour regressed No progression at 5 years in 2 cases
	2	Radiation after Simpson grade 3 surgery	No progression at 5 years
	1	Radiation after Simpson grade 1 surgery (malignant meningioma)	No recurrence at 5 years
	2	Radiation after Simpson grade 2 surgery (atypical meningiomas)	1 recurrence at five years
	1	Primary radiation	Tumour progression

operations. The indication for additional treatment with radiotherapy in the completely excised tumours was histological malignancy in one case and atypical tumours with an increased proliferative tendency in 2 cases. Two patients were offered radiation as a primary modality of treatment because due to tumour location the operative risk was considered too high.

3.2.3.7 Outcome of Treatment

The Glasgow Outcome Score (GOS) was used to evaluate the outcome of treatment. The overall outcome of surgery was very good. Table 15 shows the Glasgow Outcome Score for the 92 operated patients at about six months following surgery. The primary surgical mortality was 3%. Full recovery (GOS I) was observed in 58 patients (63%). Eighty four patients (91%) had a GOS of I to II. Severe disability (GOS IV) was observed in 1 and death occurred in 2 patients. Of the 29 Munich patients showing full recovery, 18 (62%) had lateral sphenoidal wing tumours and 2 (6.9%) purely *en plaque* lesions. All the lateral wing tumours scored I. The 2 deaths, 1 severe disability and 3 moderate disabilities occurred among medial tumours. The outcome was therefore significantly superior for the lateral sphenoidal wing tumours ($p<.05$). For the Bern series the GOS was not available as a function of tumour location.

Table 15. Glasgow Outcome Score at 6 months

GOS		Medial n=34	Lateral n=18	*en plaque* n=4	Bern cases all groups n=36	Total n=92
I	*Full recovery* Patient can lead a normal and independent life no neurological deficit	9(26.4%)	18(100%)	2(50%)	29(80.5%)	58(63%)
II	*Minimally disabled* patient can lead a full independent life with minimal neurological deficit	19(55.8%)	0	2(50%)	4(11.1%)	25(27.2%)
III	*Moderately disabled* Patient has neurol-ogical or intellectual impairment but is independent	3(8.8%)	0	0	2(5.6%)	5(5.4%)
IV	*severely disabled* patient is conscious but totally depend-ent on others to manage the activities of the day	1(2.9%)	0	0	0	1(1.1%)
V	*Dead*	2(5.8%)	0	0	1(2.8%)	3(3.3%)

Long term outcome was evaluated by establishing the ability of the patients to return to gainful employment after surgery. Table 16 shows that such information was available for 72 patients. Fifty two of these (72.2%) were able to return to their previous employment, 11 (15.3%) had to change to lighter work and 9 (12.5%) were unable to be gainfully employed.

Table 16. Long term outcome of surgery n=72

Patients able to return to previous employment	52
Patients able to do lighter work	11
Patients unable to take up employment	9

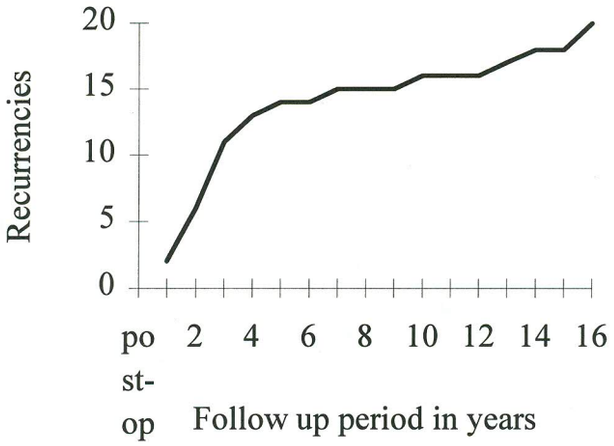
3.2.4 Tumor Recurrence and Progression

Figure 3 shows the observed cumulative recurrence of the study cases. The overall recurrence including tumour progression in case of incomplete excisions at 5 years was 23%. When the extent of tumour removal was taken into consideration the recurrence rates were for Simpson grade 1, 2.6%, and grade 2, 21% at 5 years. In the case of subtotal excision tumour progression was 39% at 5 years. There was a statistically significant favourable difference in the recurrence/progression rates for completely excised tumours as compared to that for subtotally excised ones (p=.05). Table 17 shows overall tumour recurrence by tumour location and completeness of surgery.

Table 17. Overall tumour recurrence by tumour location and completeness of surgery

Simpson classification	Operated cases	Recurrence		Total Recurrence
		Medial	Lateral	
1	42	1	0	1
2	26	3	2	5
3	11	3	0	3
4	12	8	4	12
5	0	0	0	0
Total	91	15	6	21

Figure 3 Cumulative recurrence of surgical cases

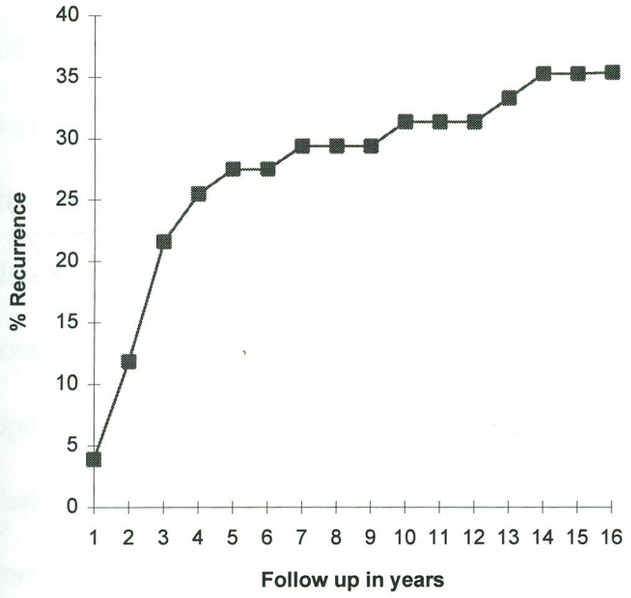


As only 11 cases were treated with radiation this modality of treatment could not be statistically evaluated. Furthermore the follow up for irradiated patients was not more than 5 years. There was, nevertheless a trend towards a favourable outcome at five years in the cases treated. Table 14 shows that radiotherapy was offered for incomplete tumour removals or as a primary form of therapy in 8 of 11 patients. Among these 8 patients tumour progression occurred in 2 despite radiation. That is 6 of 8 tumours (75%) showed no progression at 5 years. One of the 6 tumours showing a positive response had been previously subtotally excised but failed to respond to conventional irradiation. This tumour showed definite regression after a subsequent therapeutic attempt with stereotactic radiosurgery.

The one malignant meningioma in this series irradiated after Simpson grade 1 surgery was free of recurrence at 5 years. Radiation did not influence the course of the disease in 3 patients 1 of whom had a recurrence at 5 years after Simpson grade 2

surgery followed by irradiation. Two tumours progressed:-1 grade 4 tumour and 1 medially located tumour treated by radiation alone. In this series therefore, 8 of 11 patients treated with radiation benefited from it.

Figure 4. Cumulative percent recurrence of all tumours



No neurologic complications were recorded after radiotherapy except in one patient who developed transitory reduced hearing following external beam irradiation to a medially located tumour. She had undergone a Simpson grade 3 operation prior to the radiation. She went on to recover fully from this complication but the tumour progressed despite the radiation. In 1993 she was offered treatment with the gamma knife and is the patient who at follow up in September 1994 showed significant tumour regression.

3.3 DISCUSSION

3.3.1 Clinical features

3.3.1.1 Age and Sex Incidence

The age incidence range, the peak age incidence and the male:female incidence ratio in this series are similar to those reported by other workers.[112] Female preponderance begins in the fourth decade and seems to decrease after the age of 70 years. At the extremes of age the incidence of meningioma seems to be the same for both sexes. Although the majority of studies demonstrate a predominance of meningioma in women this predominance occurs in the USA only among White and Asiatic populations. In a US study no sex difference was seen in African Americans in Washington DC, and in the Los Angeles County female predominance was less prominent in African Americans.[113] Odeku and Adeloye[114] found intracranial meningioma to be commoner among males in a study of this disease in Nigerian Africans. In their study 20% of the meningiomas occurred during the second decade of life, an age for which most studies show an equal distribution of meningioma between women and men.[115,116]

Autopsy series have given contradicting results of equal distribution of meningiomas between men and women[117] and female preponderance.[118] These findings also show an increase with age in the occurrence of multiple meningiomas (8.2%)[118] as compared to that in clinical data (1% to 2%).[119] In the present study multiple meningiomas occurred in 2 (2%) of 95 cases. It has been suggested that the increase

in incidence of multiple meningiomas with age may mean that loss of the suppressor gene may be age-dependent.[118]

Age-dependent variations in meningioma incidence in women are related to hormonal activity in pregnancy and during the reproductive age in general.[59,60] Meningiomas have been reported to coexist with other hormone-dependent tumours such as breast, ovarian and endometrial carcinoma.[61] The finding in the current series of meningioma in a patient previously treated for endometrial carcinoma adds to these recorded instances.

3.3.1.2 Symptoms and Signs

The clinical symptoms and signs of sphenoidal wing meningiomas were already known to Cushing to be determined by the location of the tumour along the sphenoidal wing.[51] Indeed the description of tumour according to its location partly indicates the recognition of the nature of clinical presentations at each site and partly the surgical technique required and difficulties to be anticipated. It has already been pointed out that, although the classical description has tended to divide sphenoidal wing meningiomas into three groups: the medial, middle and lateral,[51] the findings in the present study have shown a distinct difference between completely medial and completely lateral tumours.

Sixty four percent of medial as compared to 5% of lateral tumours manifested visual deterioration and visual field defects. Similarly exophthalmos occurred in 29% of medial tumours and in 4% of lateral tumours. Oculomotor and optic nerve

involvement occurred only in medial tumours. Hemisymptomatic findings of hemiparesis and speech abnormalities were commoner among the lateral tumours. Notable were also a higher occurrence of memory and gait disturbances among the patients with lateral tumours. There was no difference in the frequency of headaches and seizure disorders in the two tumour groups.

The difference in symptomatology can be explained on the basis of the anatomic relationships at the two main locations. Medial tumours arise in the region of the anterior clinoidal processes and are in close proximity to the optic nerve which they may compress, displace and/or encase. Furthermore tumours can grow anteriorly into the optic canal, further compressing the ipsilateral optic nerve.[77,78,79] In this way visual symptoms are likely to present earlier than the other *mass lesion* features. Bilateral optic nerve compromise by tumours involving this area and localised to one side of the midline has been well described.[80,81]

On the other hand laterally located tumours originating at the lateral end of the sphenoid wing may remain relatively silent until they are large enough to manifest with symptoms of local compression. As they then grow larger they compress the cortex and this way lead to contralateral signs such as hemiparesis or hemisensory deficits. The symptoms may be aggravated by peritumoral oedema. Depending on the size of tumour the middle part of the sphenoid wing was encroached upon to varying extents. The findings were, however, of either typically medial or typically lateral symptoms. It would seem from the foregoing that tumours of the sphenoid wing can well be classified into medial and lateral groups.

Among 4 patients with *en plaque* tumour exophthalmos was the only presenting symptom in 3. In one headache was an additional complaint. This type of tumour is known to grow insidiously and to cause displacement of the eyeball forward by practically crowding it out of the orbit whose wall is involved in hyperostotic changes. The exophthalmos may go unnoticed for many years. In some cases, even after it has been discovered, patients have been treated for other causes of exophthalmos such as Grave's disease before the correct diagnosis has been made by neuroimaging.

3.3.2 Neuroimaging

3.3.2.1 Computer tomography

The imaging of meningiomas of the sphenoidal wing requires that the typical features of this tumour be brought out in order to characterise the meningioma and exclude lesions that constitute the differential diagnosis in this area. It must therefore successfully show the extra-axial nature of the tumour, its bony relationships and/or invasion, its involvement of the vessels which it may encase or displace, and possibly its histologic nature. The CT scan has largely satisfied these requirements and has increased the diagnostic yield of neuroimaging substantially.[133]

Computer tomographic features of meningiomas have been well described.[25] The typical appearances are of a well circumscribed, dura-based, intensely enhancing lesion with or without hyperostosis of the adjacent bone. Not only is the aetiologic diagnosis possible on the CT scans but the histologic nature of the meningioma can

sometimes also be inferred from the imaging appearances.[112] Calcification for example, especially when homogeneous, occurs in transitional and fibroblastic tumours. Low attenuation areas or irregular margins are suggestive of angioblastic or syncytial forms.

Malignant tumours do not usually display calcification and rarely manifest less than moderate peritumoral oedema on CT scans.[120] Other radiological features thought to be typical of malignant meningioma include indistinct tumour margins, fringes of tumour extending deeply into brain substance, marked bone destruction, prominent low density necrosis and „mushrooming."[121] Mushrooming refers to an extension of tumour pannus along the surface of the brain at a distance from the main globular mass of the lesion.[121] It must be, however, stated that malignant meningiomas cannot be distinguished with certainty on computer tomography.[25] The difficulty in precisely categorising meningiomas as malignant even on histological criteria has been discussed above. One of the reasons is that tumours that may appear histologically malignant can follow a clinically benign course. On the other hand, apparently benign meningiomas can also metastasise to distant sites while many apparently malignant ones do not necessarily do so. Metastasis is generally rare even in aggressive meningiomas.

Plain and contrast-enhanced axial CT scans were an effective method of diagnosis for meningiomas of the sphenoid wing in the present series. In 98% of cases meningioma could be diagnosed with certainty from the CT scan images alone. The only instances in which doubt existed about the diagnosis were in one *en plaque*

lesion and in a small tumour with a large cyst around it. In the *en plaque* lesion there were bone changes of hyperostosis extending from the pterion to involve the lateral orbital wall. The lack of CT evidence of soft tissue tumour whatsoever even on contrast enhancement introduced a doubt about the bony changes not being those of a meningioma. The tumour was suspected to be primarily a bone tumour, possibly an osteoma. The suspicion that this was a meningioma came only during surgery because the consistency of the tumour was not like that of an osteoma. Subsequent histological examination confirmed that it was a meningioma of the meningothelial type.

Using bone windows and direct coronal scanning the CT scan displays bone involvement at the skull base very well.[133] Along the sphenoid wing this point is important since bone involvement by tumour is particularly frequent and often a determining factor for the completeness of surgery.[134] Hyperostosing *en plaque* meningiomas are almost exclusively pterional in location (plate 10) constituting 90% of all hyperostosing *en plaque* meningiomas.[71] Although CT appearances of hyperostosing *en plaque* meningiomas are characteristic elsewhere, the differential diagnosis of ossifying fibroma, osteoma or cavernous haemangioma in skull base lesions may have to be considered.[71] In this series one truly pterional *en plaque* hyperostosing meningioma was found in a 46 year old female patient. The CT findings were of a thickened pterional area with hyperostosis extending to the orbital wall. No *en masse* or distinctly *en plaque* tumour was to be seen in relation to this thickening giving the impression that this was probably a primary bone lesion.

Hyperostosing *en plaque* meningiomas are interesting tumours.[68] Since their original description by Cushing,[51] very few papers have been published on this subject.[71] Except for isolated cases, only a few series are found in the literature.[68,96,122]

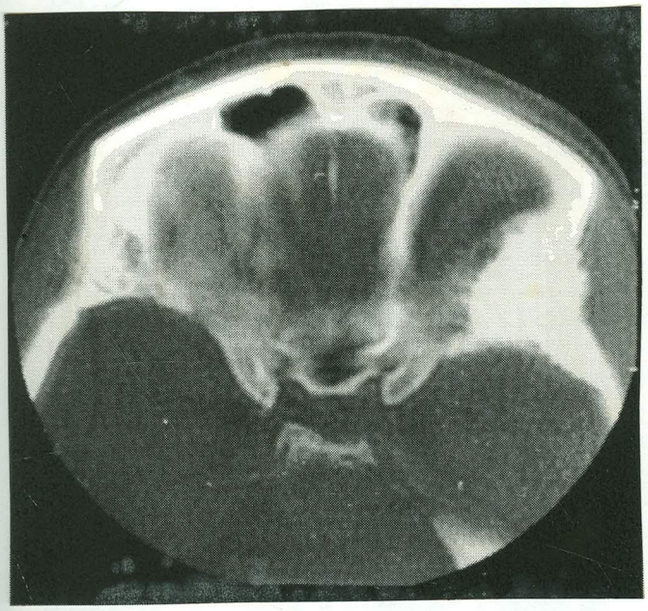
3.3.2.2 Magnetic Resonance Imaging

Magnetic resonance imaging was the other neuroimaging technique used in the diagnosis of meningiomas in this series. The imaging properties of the MRI are basically similar to those of the CT scan although the basic imaging principles are entirely different. MRI offers the advantage of multiplanar imaging (plate 11), the absence of beam hardening artefact of bone, and a higher tissue contrast which improves tumour resolution. These features make the MRI particularly advantageous in the imaging of tumours at the skull base. The tumour on unenhanced MRI is isointense (60%) or mildly hypointense (30%) to grey matter on T1-weighted images. On T2-weighted and proton density (PD) images the tumour is isointense (50%) or moderately hyperintense to cortex (40%). The gadolinium-enhanced MRI image shows an intense and uniform enhancement except in the case of dense calcification or a cystic lesion. In so doing it provides the highest level of both detection and characterisation of meningiomas possible.[123] Furthermore, considering the extra-axial situation of the lesion which is the hallmark of meningioma diagnosis, the inversion recovery (IR) sequence of the MRI dramatically improves the grey/white contrast.[123] This allows for a high diagnostic yield of meningiomas by this technique because the relation of the cortex to the tumour can be more clearly

appreciated. Another feature that is of value in establishing the extra-axial location of the tumour and which can be seen in 95%[135] of cases is the presence of an interface between the tumour and the adjacent brain (plate 12). This interface is produced by venous or arterial structures at the margins of the lesion, or by a CSF film in a preserved subarachnoid space. When, occasionally as in one of the cases in this series the subarachnoid space becomes encysted, a large secondary arachnoid cyst could be formed obscuring a small meningioma.[123]

The MRI and CT are best considered complimentary in meningioma imaging. However, MRI is superior in evaluating the effects of meningiomas on adjacent vascular structures.[135] In CT images the brain and vessels are isodense before and after contrast enhancement while in MRI a signal void is produced by flowing blood providing a high contrast to the adjacent tumour intensity. Therefore using MRI it is possible to determine displacement, encasement, and narrowing or occlusion of vessels by meningiomas of the sphenoid wing. Furthermore the developments in the technique of MR angiography will improve this role of the MRI in the determination of vascular relationships to the tumour.

Plate 11 (a) Axial CT scans showing a right pterional hyperostotic meningioma extending into the orbital wall. (b) shows a higher magnification
(c) Plain skull x-ray showing thickening of the right pterional area extending medially along the sphenoidal ridge



a)



b)

c)

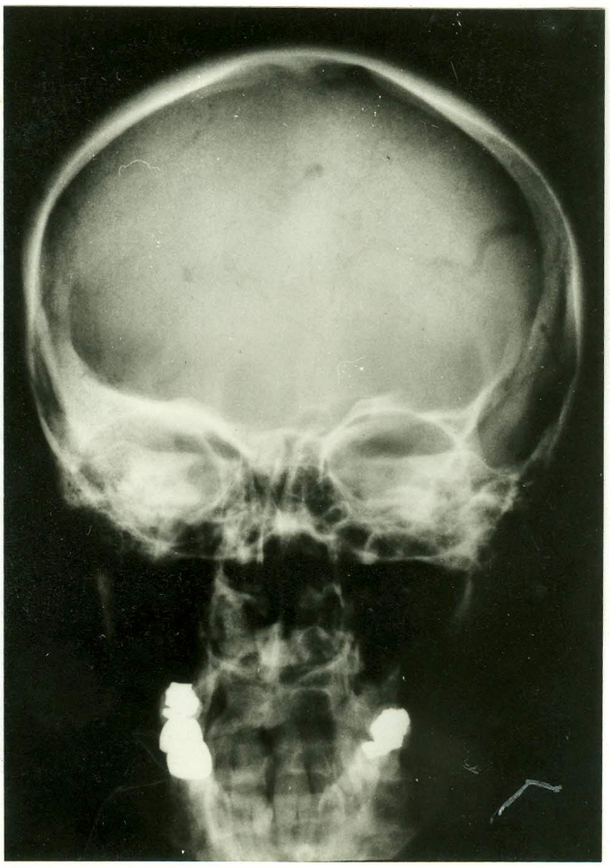
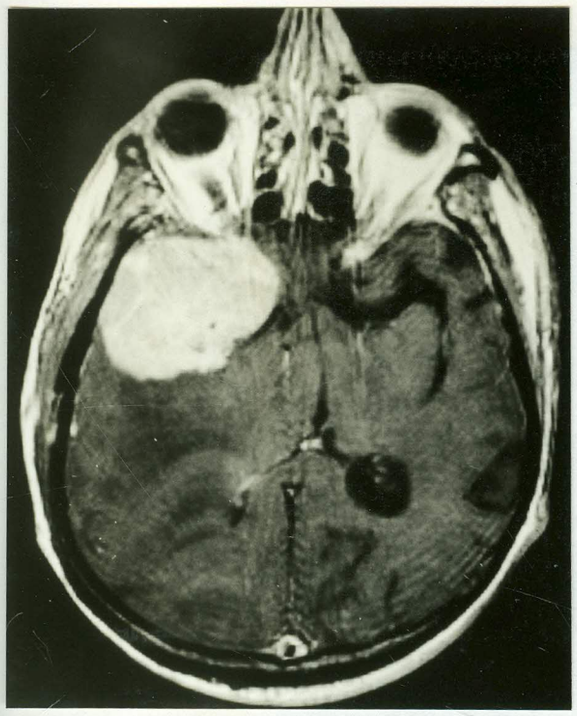


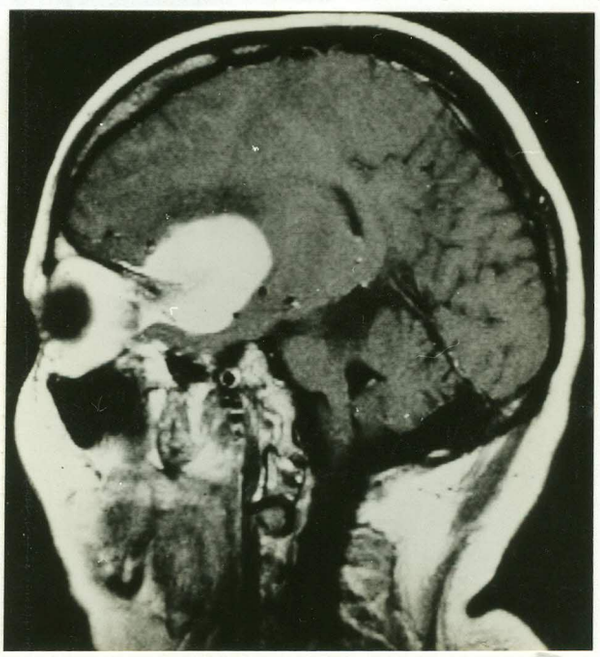
Plate 12 MRI images of a clinoidal meningioma in T1-weighted sequences showing the tumour in axial (a), coronal (b) and sagittal views (c).



a)



b)



c)

Plate 13. Direct coronal CT scans after contrast enhancement showing a medial clinoidal tumour with peritumoral oedema. The quality of resolution is clearly inferior to that of the MRI scans on plate 12

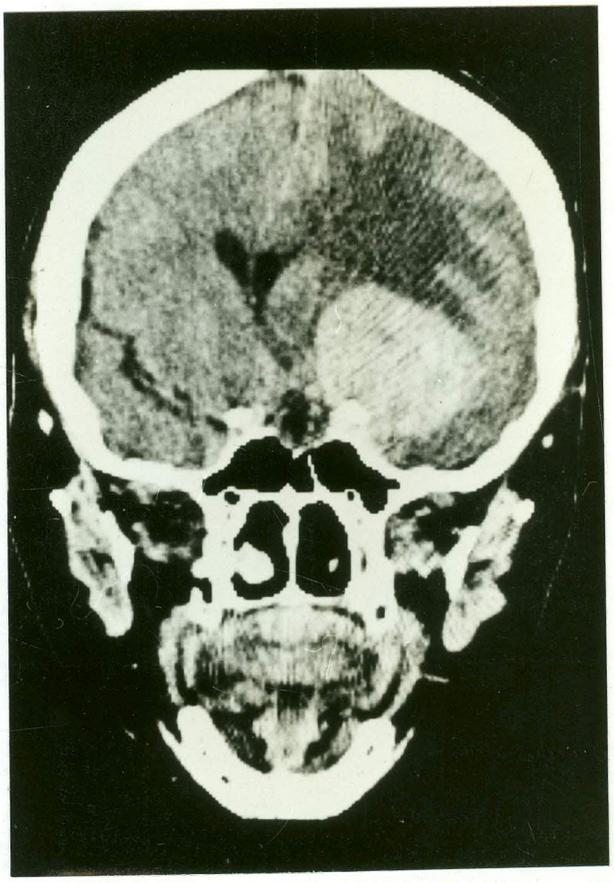


Plate 14. Unenhanced T1-weighted MRI scans showing a signal void around the tumour due to an arachnoid interface delineating the tumour clearly.



3.3.2.3 Angiography

In this study all patients were subjected to a selective angiographic study of the internal and external carotid arteries. Since most of the information required regarding tumour diagnosis, location and characteristics was available from the CT and MRI scans, the role of angiography was to determine the arterial supply, the extent of vascularity and confirm the nature of arterial and venous involvement by tumour. It would have also been useful for assessing the need and the possibility for preoperative embolization which reduces intraoperative haemorrhage and which can soften the tumour by causing tumour necrosis thus making the surgery lighter.[124] Embolization is not usually possible for medial tumours. However, it is not clear why in this series no lateral tumour was embolised preoperatively. One argument could well be that, when tumours were supplied by branches of the ethmoidal artery or anastomotic networks involving it, embolization could have risked occlusion of the retinal artery leading to blindness. Lasjaunias and Berenstein[124] have indicated that the limitation of devascularization by particles is related to the internal carotid artery branches arising from the C4 and C5 segments as well as to the ophthalmic and cerebral arterial supply to the tumour. They state that these vessels are not usually embolized except in special situations where the need for more aggressive tumour removal outweighs the risk of sacrificing an important functional artery.

The arterial supply to tumours of the sphenoidal area originates from three main sources:- The middle meningeal artery, branches of the intracavernous carotid artery and branches of the ophthalmic system. The vascular dural pedicle of lateral

sphenoidal meningiomas are branches of the middle meningeal artery (MMA), which latter may take its origin from the external carotid artery (ECA), from the internal carotid artery (ICA), or from the vertebral system.[125] From the ECA the MMA may arise from either maxillary artery, or from the ascending pharyngeal artery. From the ICA its source may be the ophthalmic artery, the inferolateral trunk (ILT), or the intrapetrous internal carotid artery.[125]

3.3.3 Long Term Outcome of Management

The outcome of meningioma treatment can be evaluated by examining the standard parameters of operative morbidity and mortality, the recurrence rates and the recurrence-free survivals. The recurrence of sphenoidal wing meningiomas of 23% at 5 years overall in this series is favourably comparable to that of other series which show a recurrence of 40% to 50% overall for tumours in this area.[136] The overall outcome was influenced by the location of tumour (medial or lateral), which correlated positively with the completeness of surgical removal. Other authors have also remarked on the striking difference in mortality, morbidity, failure of total removal and recurrence when medial sphenoidal meningiomas are compared with lateral shenoid lesions.[67,68,125]

3.3.4 The Role of the Completeness of Surgery

Complete surgical removal remains the benchmark for meningioma surgery.[100] In the present series Simpson grade I excision was associated with a 5 year recurrence of 2.6%, grade II with 21% recurrence and grade IV excision with a 39% tumour

progression at 5 years. The differences between the recurrence rates were statistically significant. Simpson found recurrence rates of 9% following grade I surgery and 19% recurrence following grade II surgery.[99] Other authors have quoted for the two grades 11%; 22%[124] and 8%; 16%.[125] These finding are in keeping with the established concept that in meningioma surgery completeness of surgery is the single most important factor influencing the outcome of treatment. The completeness of removal of tumour is in turn influenced by anatomic considerations which depend on tumour location and its relationship to surrounding vital structures such as blood vessels and cranial nerves. Recurrence in medial tumours constituted 70% of the overall recurrence in the current series.

The nature of vascular involvement as descried by Al-Mefty has been implicated as a possible cause of removal failure.[75] When the tumour is adherent to the carotid artery because of the lack of an arachnoid interface between it and the tumour,(Al-Mefty I tumours) it is likely that tumour will be left on the artery whose adventitia it has probably invaded. Attempts at radical excision of these tumours may lead to major morbidity due to vascular injury.[75] In this study two of the Al-Mefty type I tumours could not be completely excised. The failure of complete excision in these cases was, however, apparently a result of cavernous sinus invasion rather than the vascular involvement *per se.* It is, nevertheless significant that in the three Al-Mefty type I tumours 2 of which were completely excised and one totally excised but the dura only coagulated and left in place, major vascular complications followed. It could be construed that had less than complete excision been attempted the complications

could have been averted albeit at the risk of an increased recurrence.[104] Since meningiomas are slow-growing tumours it could be argued that severe morbidity does not justify aggressive tumour removal in order to minimise recurrence. Fortunately, however, improved surgical techniques are making it possible to remove difficult medial tumours with an acceptable morbidty.[75] All Al-Mefty type II tumours were totally excised without vascular complications. These tumours, with an arachnoid interface between them and the carotid artery they enclose lend themselves well to complete microsurgical excision without added risks of morbidity.[75]

3.3.5 Complications of Surgery

3.3.5.1 Morbidity and Mortality

Significant complications were recorded in 18 patients (19.5%). Mild cranial nerve compromise generally improved during post-operative follow up so that of the 8 cases in which oculomotor paresis occurred 3 went on to recover completely and the remaining 5 showed varying degrees of recovery. Unilateral blindness followed surgery in 2 cases. Unlike in other meningiomas in the suprasellar area visual recovery in clinoidal meningiomas is poor.[127,128] Cranial nerve injury has been ascribed to actual contact injury during surgical manoeuvres. Surgical manoeuvres could cause injury of the optic nerve in case of Al-Mefty type III tumours. In this type of lesion the tumour arises from the optic foramen and extends into the optic canal and the tip of the anterior clinoid process. Arachnoid may not be present between these tumours and the optic nerve although it may intervene between the tumour and the carotid artery.[75]

In this series a mortality of 3% overall was observed. This was primarily an operative mortality occurring within ten days of surgery and following persistent neurological deficits. The deaths occurred in patients with medially located tumours giving a mortality of 5.5% for this group and were associated with massive cerebral ischaemia leading to fatal infarction. Considering clinoidal tumours alone the mortality rates of 32% and 42% have been reported by Uihlein and Weyland [126] and by Bonnal *et al.*[68] respectively. In many series the cause of surgical mortality was injury to major cerebral vessels.[67,68,126] These findings are similar to those of the present series where no surgical mortality was recorded in tumours of the lateral sphenoidal wing and where all deaths were a result of vascular compromise. It is notable that in two of the deaths no arterial damage was apparent although the dissection of the tumour from the carotid artery was described as difficult. The patients went on to develop severe ischaemia with Doppler sonographic and angiographic evidence of vasospasm. Only in one Al-Mefty I case was there an intraoperative injury to the carotid artery requiring repair to control the ensuing haemorrhage. This patient survived her complication.

As might be expected from the age structure of this series intercurrent medical conditions were found in a number of patients. Significant cardiac conditions constituted 23% of all the intercurrent diseases. Systemic hypertension was the other medical condition which occurred in 33% of all those with intercurrent medical conditions. There was no evidence that these patients faired worse than those without medical problems. This could be attributed to the high quality multidisciplinary care

available at the university hospital. Only one patient with a previous coronary bypass followed a protracted post operative course, developing hemiparesis which could not be explained by the surgical procedure. Furthermore the early mortality did not seem to have been influenced directly by the intercurrent medical conditions.

3.3.6 Radiotherapy

A favourable response of meningiomas to a non-surgical treatment can be recognised not only as tumour regression but also as the absence of progression [129] Tumour progression can be determined by deterioration of clinical symptoms as well as by neuroimaging. The corollary is that the lack of anticipated neurological deterioration in patients whose tumours have been only subtotally or not at all excised implies a response to the treatment modality

It has been mentioned above that the number of patients in this series treated with radiation was small and the follow up not longer than 5 years. For this reason it was difficult to apply statistical tests of significance to the apparent impact of this treatment. A definitely favourable trend was, nevertheless discernible from the findings among the 11 patients treated with radiation. Seven of the 11 patients showed no tumour progression at 5 years and one showed no progression at 4 years. It should be noted that 8 of these patients had either subtotal tumour removal prior to radiation (6 patients) or had been offered radiation as a primary form of therapy (2 patients). In 1 of the 8 patients showing a favourable response to radiation there was evidence of tumour regression on control MRI. In this irradiated group of patients

with incomplete tumour removal the progression free survival was 75% at 5 years and there was no mortality. The outcome of radiation therapy in this study for incompletely excised tumours is good when compared with the relapse/progression free survivals for patients offered incomplete excision followed by observation only of 43% to 59% at 5 years.[101,102,103,105]

Early reports on radiation treatment following incomplete surgical removal of meningiomas indicated that radiation had little or no beneficial effect in the control of residual meningiomas.[99,130 131,132] In these reports the doses of radiation used were lower than those used currently. In more recent reports of patients treated with doses of 5,000 to 6,000 cGy beneficial effects of radiation on subtotally excised meningiomas have been obtained.[102,105] In an analysis of 140 patients treated with radiation after incomplete surgical excision Goldsmith *et al.*[104] found an overall 5 year survival rate of 85% for benign tumours and 58% for malignant tumours. Their 5 year progression-free survival rates were 89% and 48% for benign and for malignant tumours respectively. This study with a follow up for up to 23 years showed that irradiation benefited patients who had undergone incomplete excision of their meningiomas.

The present series also shows a definite tendency that irradiation for subtotally excised meningiomas improves the progression-free survival from an expected 43% to 59% up to 75%. Radiotherapy was not associated with significant complications. In the future, prospective studies are likely to be able to establish with certainty the place of radiation therapy on subtotally excised meningiomas.

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