Meningiomas and Meningeal Tumors

4

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4.1 Definition

Meningiomas are tumors arising from the arachnoidal coverings of the brain [45]. They are responsible for the vast majority of meningeal tumors and occur anywhere on the brain surface, including the skull base, and rarely also in the ventricular system.

Other than meningiomas, hemangiopericytomas and meningeal sarcomas belong to the group of intrinsic meningeal tumors [45]. As with every other tissue, both metastases and lymphoma can also be found in the meninges.

4.2 Epidemiology

Epidemiological data for most tumors of the central nervous system are difficult to obtain as cancer registries tend to be regional or at best national as in the Scandinavian countries [12]. A very comprehensive source is the statistical report published by CBTRUS (Central Brain Tumor Registry of the United States); the latest 2007/2008 edition covers the data collection period 2000–2004.

Meningiomas show a rising incidence with age. In unselected autopsy series, 2.7% of the male and 6.2% of the female population over the age of 80 had meningiomas that up to that point had been undiscovered. The reported incidence is variable between different investigations, but disregarding the changing proportions from the growing incidence of cerebral metastases with better oncological therapies, one can assume that meningiomas are responsible for about 15% of all intracranial tumors in males and 30% in females. Not considering the autopsy cases, the reported numbers on a population base vary between 1.6 and 5.5 per

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100,000. CBTRUS reports an incidence of 5.51 per 100,000 person years, resulting in 33.3% of all tumors of the central nervous system. As a rule the tumors are reported to be 1.5–3 times more frequent in females. In the 2000–2004 period the rate given by CBTRUS was 3.29 for males and 7.19 for females, showing a slight increase over the years that, however, may still be a reflection of the broader availability of and access to diagnostic procedures. Peak incidence is the sixth decade of life (median age at diagnosis for CBTRUS is 65 years). Pediatric meningiomas are very rare, with 2% of all tumors being in that population [44].

There does not seem to be any association with race or any geographical preference that cannot be explained by the access to medical care or pattern of reporting.

An unselected 10-year series from the University of Hamburg Department of Neurosurgery reflects these demographics with a female to male ratio of 507:172 (2.9:1) (Table 4.1).

4.3 Molecular Genetics

The majority of patients who suffer from neurofibromatosis type 2 (NF2) develop meningiomas [34, 36, 50]. In sporadic meningiomas *NF2* gene mutations are detectable in up to 60% and thus represent the most frequent gene alteration. The *NF2* tumor suppressor gene is located on chromosome arm 22q, and mutations in one allele are typically associated with either monosomy 22 or large deletions involving the other allele. Absent or strongly reduced immunoreactivity of the NF2 gene product merlin (schwannomin) has also been demonstrated in meningiomas. Merlin belongs to the 4.1 family of structural proteins that link the cytoskeleton to proteins of the cytoplasmic membrane. Recently, another member of this family, the 4.1B/DAL-1 protein has been implicated in meningioma pathogenesis. 4.1B/DAL-1 expression is lost in 70–80% of meningiomas. No mutations were detected in the *4.1B/DAL-1* gene, which is located on chromosome arm 18p. However, loss of heterozygosity (LOH) involving the *4.1B/DAL-1* region on 18p was identified in 70% of meningiomas [33].

Inactivation of the *NF2* and *4.1B/DAL-1* genes occurs with approximately equal frequency in benign (WHO grade I), atypical (WHO grade II) and anaplastic (WHO grade III) meningiomas, suggesting that both represent relatively early events in tumorigenesis. In contrast, several other genetic alterations have been identified more frequently in the more malignant tumor forms and are therefore believed to be associated with meningioma progression [63]. In the approximate order of their frequency, these alterations are allelic losses on chromosome arms 1p, 14q, 10q, 9p and 17q. However, with the exception of the *CDKN2A*, $p14^{ARF}$ and *CDKN2B* genes on 9p, which display alterations in the majority of malignant meningiomas, no other tumor suppressor genes could consistently be identified as altered in meningiomas.

Gene expression analyses by array-based techniques have been used also in meningioma research, and in a series where spinal and cranial meningiomas were compared that way, a distinct set of 35 genes distinguishing between these entities was identified [52], but as such there are no surprising new insights from micro-array techniques in the analysis of meningioma.

Table 4.1 Meningiomas in an unselected departmental series ($N = 679$ cases, 1992–2001) (Emami et al., unpublished results)

Location	*n*	Histology[a]	*n*	Age (years)	*n*
Convexity	291				
Skullbase	153				
Posterior fossa/tentorium	93				
Orbit	28				
Ventricular	5				
		Meningiothe liomatous	250		
		Fibrillary	142		
		Transitional	163		
				0–30	35
				31–50	190
				51–70	361
				71–90	93

[a]The three most frequent histological subtypes
Source: Emami et al. (unpublished results)

4.4 Etiology and Prevention

Meningiomas should be considered spontaneous tumors. Very early on, they were found to be associated with a complete or partial loss of chromosome 22 [65], but that has so far not provided any clues for the origin of these tumors. The only established association is

with ionizing radiation; this was obtained from the large series of immigrants into Palestine in the early 1950s who were regularly irradiated for tenia capitis and then had a much higher than normal incidence of meningiomas with a delay of about 35 years [51]. Likewise, the follow-up of citizens from Hiroshima and Nagasaki who were exposed to the atomic blasts has shown that in this population there was a higher incidence of meningiomas with a very similar delay [46]. The doses producing meningioma with this long delay should be considered rather low as high doses of therapeutic radiation for neoplasm lead to meningiomas with a shorter delay (around 5 years [57]) or rather induce anaplastic gliomas. The literature about the role of diagnostic exposure to radiation is most likely limited to specific dental procedures [37].

As meningiomas occur most frequently in postmenopausal women [58] and meningiomas are known to have high levels of steroid hormone receptors, establishing a relationship between steroid hormones and the growth of meningiomas has long been attempted [23, 25]. The only vague association comes from the observation that in some cases, meningiomas that had gone undetected became symptomatic during pregnancy [62] (Fig. 4.1) and even grew so rapidly that they spontaneously hemorrhaged. In that context there is a constantly ongoing debate whether women who are known to have a meningioma or have had a meningioma removed should be on hormonal replacement therapy. Currently there does not appear to be a risk in respect to contraceptives, but there is a hint of an indication that hormonal replacement therapy may increase the risk for meningioma [13]. As, however, no study has been done up to now in which the use of steroid replacement has been evaluated in a randomized, controlled, prospective fashion in these patients and likely never will be, their management remains in the hands of physicians who have to observe the patient closely and make individual decisions about what is best.

4.5 Signs and Symptoms

There are no typical signs or symptoms that are unequivocally specific for meningiomas. The clinical symptomatology is basically determined by the location of the lesion, the size and the impact on its immediate surroundings. For clinical purposes, meningiomas are subspecified according to their site of origin, and this classification allows the description of the most frequent signs associated with the typical locations (Table 4.2).

The direct symptoms also depend very much on the size of the tumor and the growth rate. Large tumors that have grown over many years may have produced only very few symptoms because the surrounding brain had a chance to adapt while slowly becoming displaced (Fig. 4.2). In cases of caudal skull base meningiomas, this may lead to extreme brain stem compression almost without any symptoms (Fig. 4.3). As meningiomas also differ in their respect for the arachnoidal boundary–independent of size–the less the brain shows any reaction to the tumor, the bigger the tumor

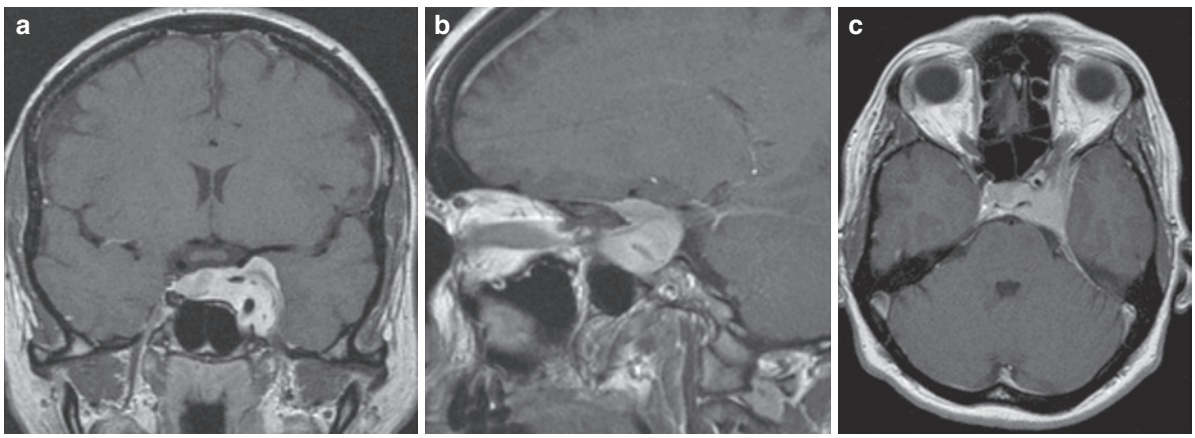

Fig. 4.1 Cavernous sinus meningioma of a 30-year-old woman that during two pregnancies caused transient visual problems in the left eye. Despite extension into the sellar lumen, there is no endocrine dysfunction. The tumor has been biopsied and is under observation with the option of radiotherapy in case of progressive symptoms. (Three planes review Gd enhanced MRI)

Table 4.2 Symptoms of meningiomas according to location

Location	Typical symptoms
Convexity	
Frontal	Affective disorders
Parietal	Seizures
	Motor or sensory disorder, hemiparesis
Temporal	Speech disorders, memory impairment
Parasagittal	Seizures
	Motor or sensory disturbance
Olfactory meningioma	Loss of olfaction
	Affective disorders
	Loss of activity
Tuberculum sellae meningioma	Visual field or visual acuity loss
Clinoid process meningioma	Visual field or visual acuity loss
Cavernous sinus meningioma	Diplopia, facial pain, or numbness ocular venous congestion
Optic sheath meningioma	Loss of vision
Orbital meningioma	Exophthalmos
Sphenoid wing meningioma	
Medial	Loss of vision, diplopia
	Psychmotor seizures
	Schizoaffective disorders
Lateral	Seizures
	Speech problems
Tentorial meningioma	Hydrocephalus, seizures, visual field loss
	Ataxia
Cerebellar meningioma	Ataxia, vertigo, hydrocephalus
Foramen magnum meningioma	Hydrocephalus, symptoms of dorsal, lateral, or ventral brain stem compression
Cerebellopontine angle meningioma	Unilateral cranial nerve dysfunction
petroclival or clivus meningioma	Unilateral or bilateral cranial nerve dysfunction and symptoms of ventral brain stem compression
Ventricular meningioma	Partial hydrocephalus

usually is. Seizures are more frequent in the typical ictogenic regions, particularly when lesions extend exophytically into the temporomesial region or the perirolandic area.

There are also many ways for meningiomas to affect the brain indirectly and produce symptoms. Meningiomas at the tentorial edge, whether supra- or infratentorial, can lead to compression of the CSF pathways and thus result in occlusive hydrocephalus, as do large meningiomas in the posterior fossa (Fig. 4.4). Meningiomas that produce an extraordinary amount of edema (frequently of the secretory type [7]) cause an indirect mass effect exceeding their own mass several fold and can cause drowsiness and even loss of consciousness up to the extreme of herniation (Fig. 4.5). Meningiomas occluding a major sinus such as the falcine meningiomas or parasagittal meningiomas or those of the torcular or transverse sinus can cause venous congestion and generalized edema to the extreme of chronic intracranial hypertension with papilloedema and impairment of visual acuity (Fig. 4.6). It is frequently seen that even after complete resection of a meningioma, an edema-like change in signal intensity in the magnetic resonance imaging (MRI) can remain for many years (Fig. 4.6).

It is a general rule that the risk of surgical treatment of a meningioma can be very well assessed when edema and neurological symptoms are present. When these symptoms disappear with appropriate steroid treatment (see below), surgery will be much less risky than when the symptoms persist despite edema resolution.

4.6 Staging and Classification

As described in the chapter on histopathology of CNS tumors, meningiomas are graded according to the WHO grading system into well-differentiated meningiomas of the WHO grade I, atypical meningiomas WHO grade II and anaplastic meningiomas WHO grade III [14]. In addition, there are several subtypes, of which two in themselves are equivalent to a higher grade [45]. Due to serially acquired genetic aberrations, progression from a lower grade to the next higher grade is possible [34] (Fig. 4.7), and this is also accompanied by increasing production of angiogenic factors [35] and the late incidence of metastasis in the situation of anaplastic meningioma [27].

There is no clinical staging for the extent of the disease or the aggressiveness of the tumor, but there is for the resection (see below). The significance of the histological grading is related to the decision making for adjuvant therapies (see below) and the follow-up regimen. In general, there is a correlation of the grades with survival, but only when the tumors are in comparable locations and similar extents of resection can be achieved. On the other hand, there is a much better prognosis for a completely resected atypical meningioma (WHO grade II) of the convexities compared to

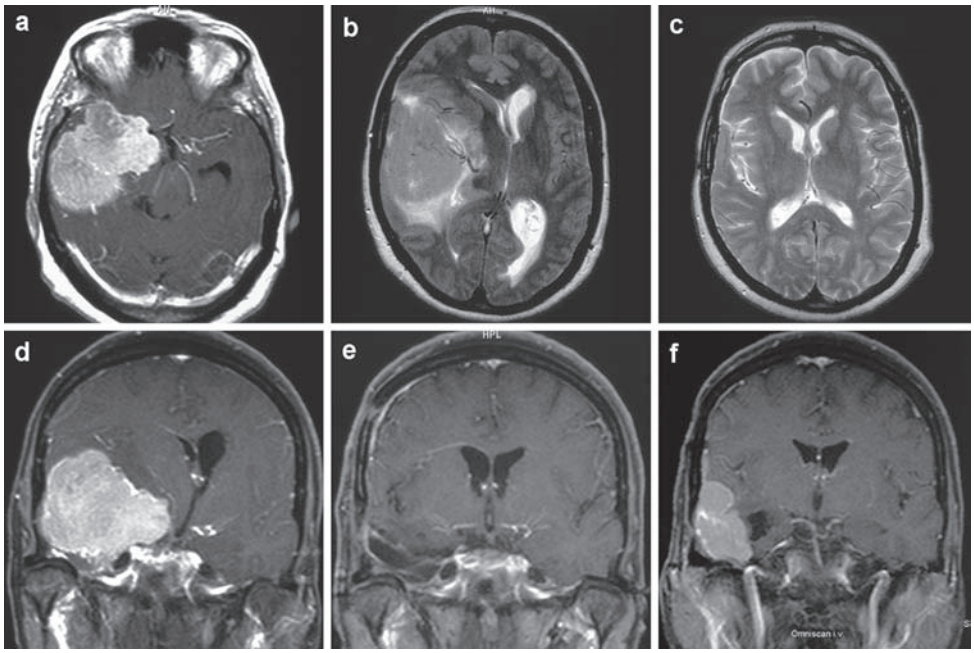

Fig. 4.2 Large temporal meningioma with impressive midline shift, but no specific symptoms (**a, b, d**). The diagnosis was made after lack of concentration and inability to complete simple tasks in daily life led to cranial imaging. Despite the appearance of encased large vessels, the tumor was completely removed without any deficits (**c, e**). The minimal perilesional edema was reflected by a good dissection plane over most of the tumors surface. The definitive diagnosis being an atypical meningioma, the tumor recurred 4 years later (**f**)

a non-resectable meningioma WHO grade I of the skull base (Fig. 4.8).

4.7 Diagnostic Procedures

Many meningiomas are found incidentally because of unrelated complaints such as a dizzy spell, a transient ischemic attack or uncharacteristic headache, or because after a minor trauma an MRI has been performed (Fig. 4.9). Otherwise, any of the symptoms summarized in Table 4.2 above may specifically lead to some kind of neuroimaging.

Computed Tomography (CT): CT shows meningiomas usually as well-described mass lesions with uniform contrast enhancement located at the surface of the brain, either at the convexity or the base of the skull. A non-enhanced scan must be obtained in the first place because it may show extensive calcification, which is mostly associated with very slow growth and thus only a relative indication for therapy. Especially in fronto-orbital tumors it is important to have thin sections and a series of bone windows because they define the borders of infiltration and resection if there is not even resectability. CT is the optimal modality to assess intraosseous components of frontobasal skull base meningiomas (Fig. 4.10) or to detect primary intraosseous meningiomas (Fig. 4.11).

Magnetic Resonance Imaging (MRI): MRI is now the major modality for the diagnosis of meningiomas, especially as many lesions have some skull base component or extensions into compartments that are not as well visualized or differentiated in the CT. Again, the mass of the tumor will show not only homogeneous contrast enhancement, but also tail-like extensions in the meninges will be seen [the so-called *meningeal tail sign* [Fig. 4.12]] and infiltration of neighboring structures. Petroclival meningiomas, for example, can be assessed anatomically for their complex extension towards the optic canal and into the cerebellopontine angle (Fig. 4.13). The carotid artery, which is regularly encased by petroclival meningiomas, can be judged for its width, shape and patency. When considerable narrowing is present, a "time-to-peak" analysis after gadolineum application comparing the timing of gadolineum arrival in the two hemispheres already allows some estimate of hemodynamic relevance of the stenosis and

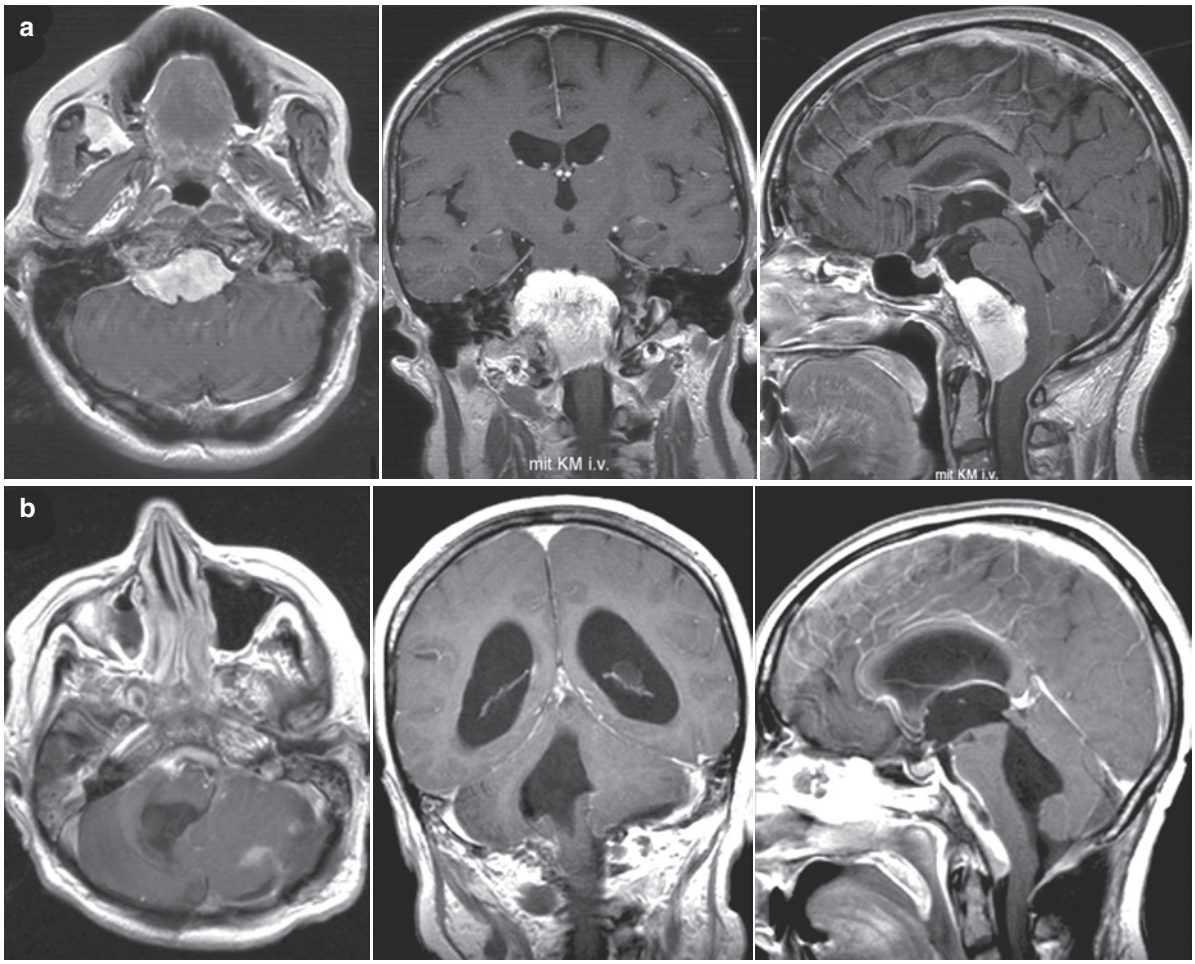

Fig. 4.3 (**a**) Large meningioma of the clivus extending mostly into the right CP angle. The removal required approaches from both sides because of encasement of the caudal cranial nerves on both sides. The dura of the clivus was completely invaded and was left in place after extensive coagulation. (**b**) The course has been stable with no indication of growth of the possible extradural tumor layer seen at the level of the foramen magnum (*bottom right*). Postoperatively, the patient developed a malresorptive hydrocephalus that required shunting

indication for bypass surgery (Fig. 4.14). Frontobasal meningiomas are occasionally not much more than a thin layer of contrast enhancement, and this is especially true for optic sheath meningiomas, which will be missed except on thin-sliced MRI with special attention to all three planes (Fig. 4.15). When close to a sinus or originating from a sinus wall, extension of the tumor into the sinus or patency of the sinus can be seen on T2-weighted images and MR angiography (Fig. 4.16).

The extent of edema is shown equally well in CT and MRI. The major differential diagnosis is a solid metastatic lesion because the age groups with the peak incidence overlap. Clues to decide for meningioma would be the extent of dural involvement and especially a reaction of the bone-like hyperostosis (Fig. 4.17). Meningiomas may also occur in multiple locations in the same patient (Fig. 4.18), but multiplicity is much more common in metastasis, and for three metastatic lesions it would be very unusual to have all of them on the surface of the brain. In tumors over 1 cm, MR spectroscopy is an additional tool showing a characteristic spectrum of metabolites that can provide an increasingly reliable estimate of the nature of the lesion [18]. Diagnostic pitfalls are the rare cystic meningiomas with an appearance similar to a pilocytic astrocytoma or a cystic metastasis (Fig. 4.19).

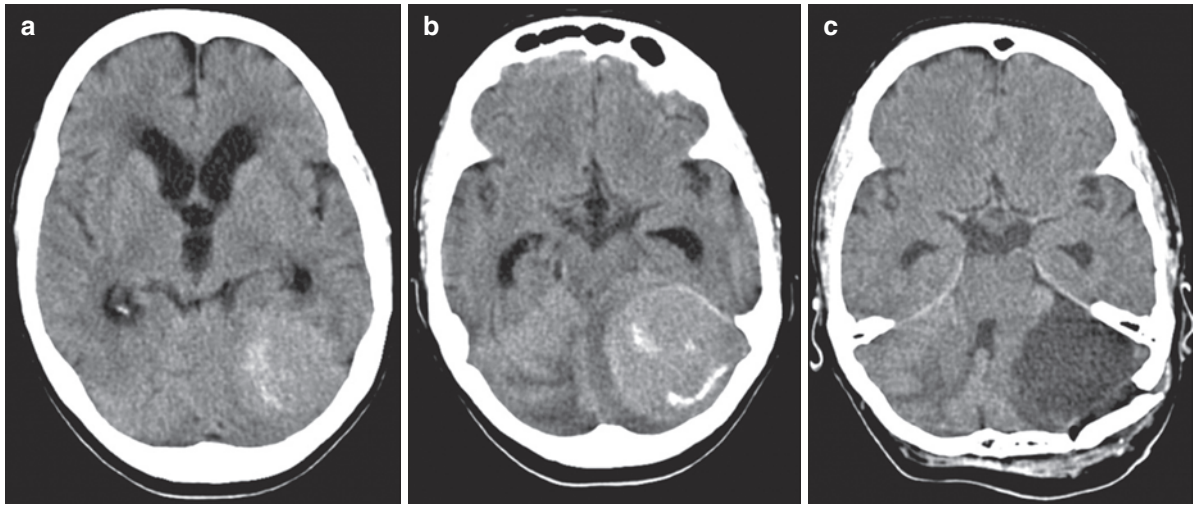

Fig. 4.4 Computed tomography (CT) of a large meningioma in the posterior fossa that over months led to occlusive hydrocephalus, which is seen to result in distended temporal horns and periventricular capping over the frontal part of the lateral ventricles (**a, b**). A few days after removal, the fourth ventricle is again visible, and the temporal distension is slowly regressing (**c**)

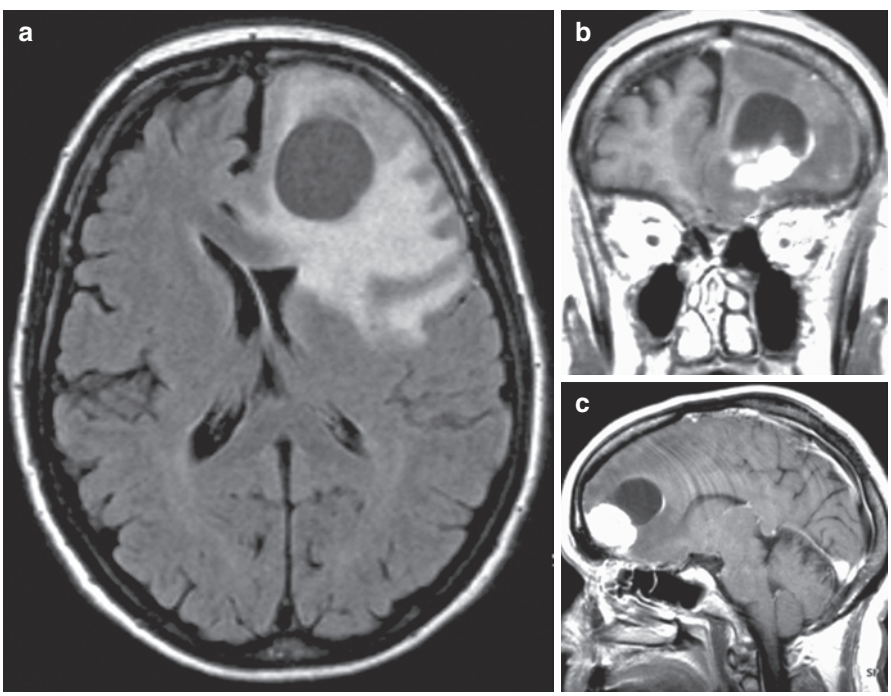

Fig. 4.5 Magnetic resonance imaging (MRI) of a patient with a massive edema resulting from a meningioma of the secretory type. As seen in the T2 images (**a–c**), the amount of space occupation is mostly due to the edema and not so much due to the mass effect of the tumor

Angiography: This diagnostic tool is only used to answer specific questions related to the surgical strategy and has no use for diagnosis itself. It is indicated to determine the patency of sinuses, collateralizations and the hemodynamic relevance of a stenosis within a sinus. Angiography provides a good overview of the vascularization (Fig. 4.19) and in some cases provides an opportunity for preoperative embolization, especially when there is a major blood supply from the tentorial or mastoidal meningeal arteries that would be caught only later in the surgical procedure.

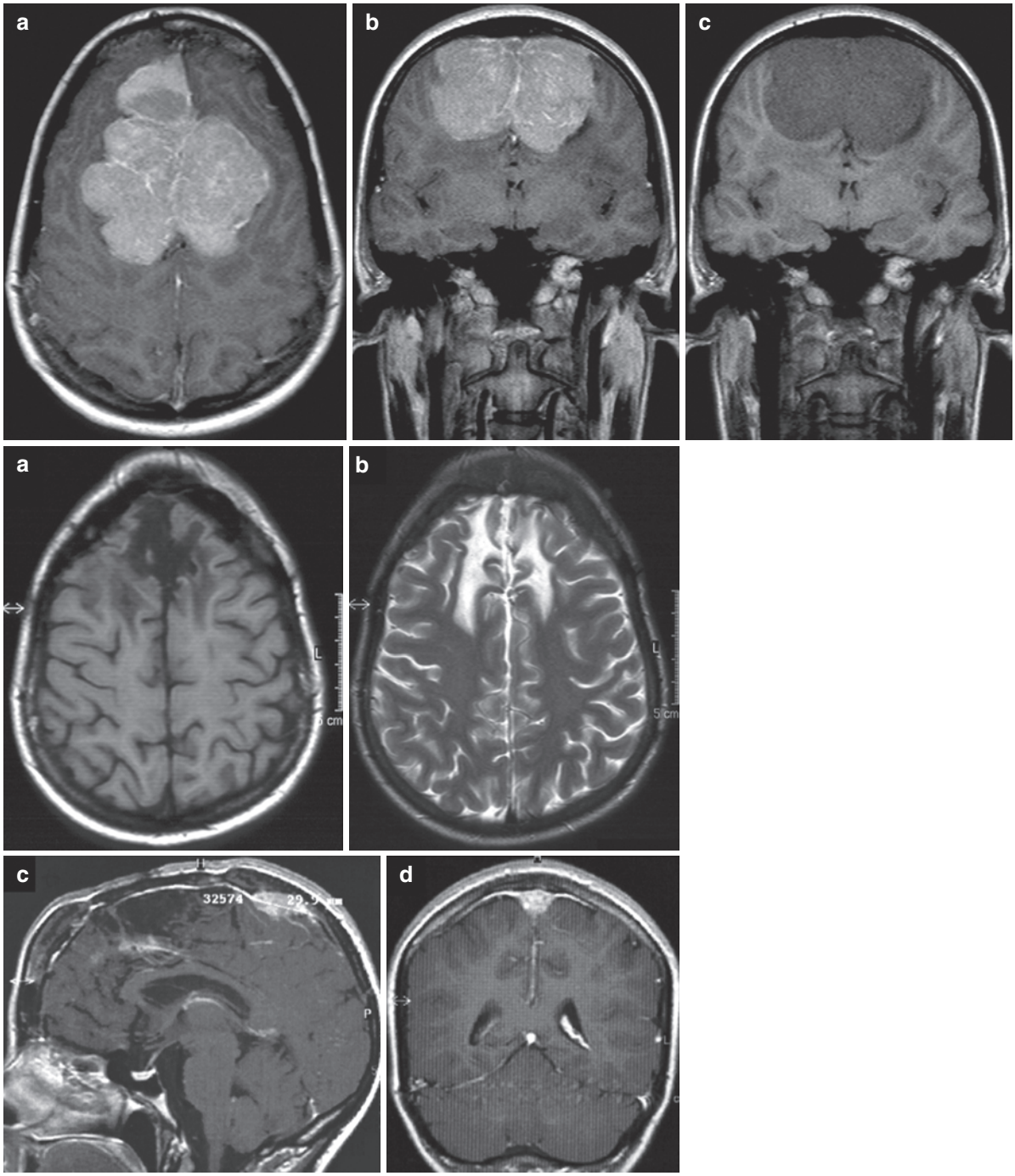

Fig. 4.6 Very sharply demarcated bilateral falx meningioma of a 28-year-old woman who had papiledema and developed optic nerve atrophy from constant pressure. The sinus was removed in its occluded parts (*Top row*, **a–c**). The edema that was present only in the most central aspects around the tumor was still present 5 years after follow-up (*middle panel* **a, b**) at which time also a recurrence was seen in the distal part of the sagittal sinus (*bottom panel* **c, d**). This is asymptomatic and will be observed until a sufficiently large tumor has developed to warrant another operation and sufficient collaterals have formed so that that segment can be removed without congestive sequelae

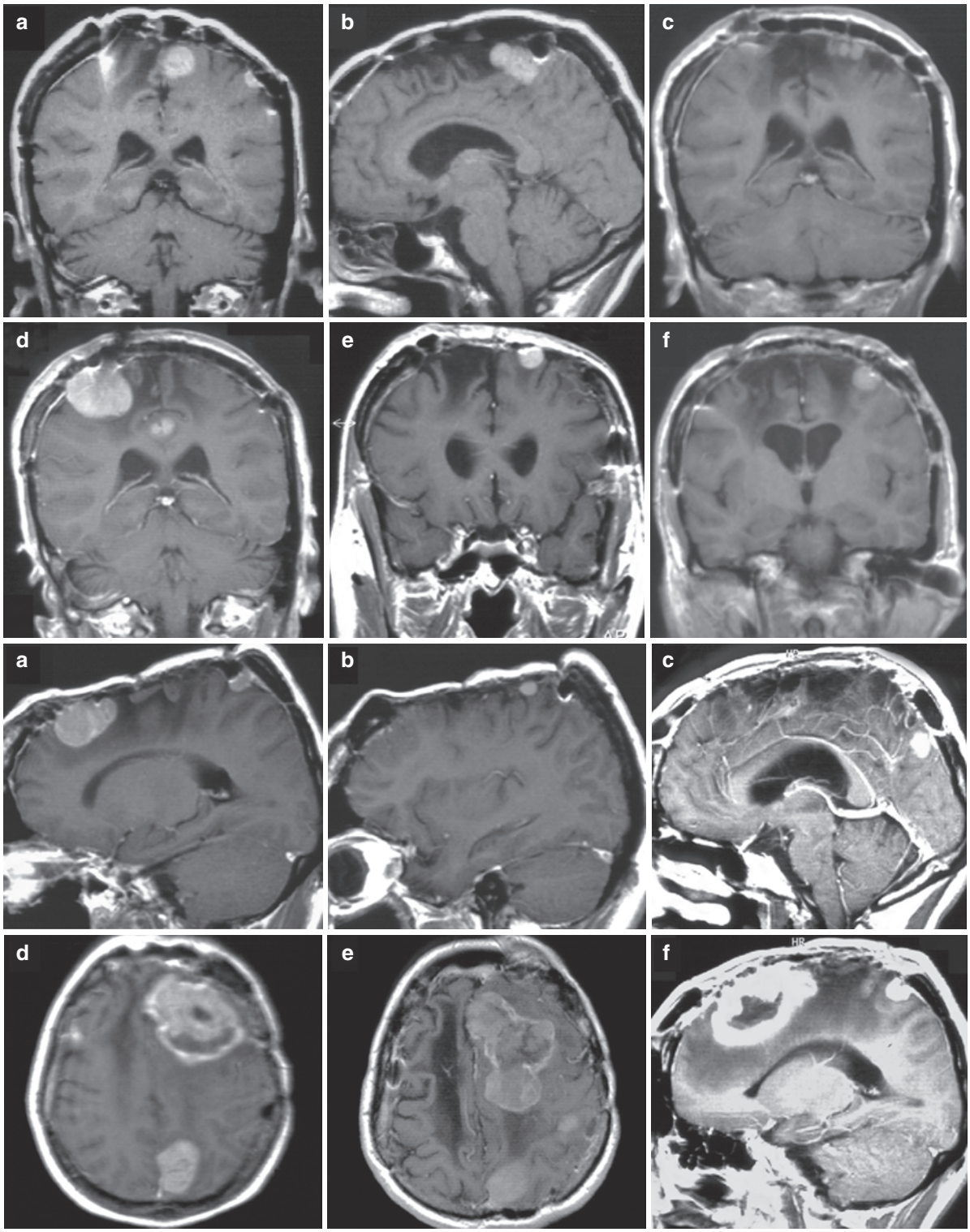

Fig. 4.7 Progressive dedifferentiation of a meningioma that was originally operated on in 1978. Altogether six operations for multifocal recurrences with accumulation of more genetic alterations (34) were performed (**a–c**, top panel and **d–f** top panel are from two recurrences in the late 90ies). Increasingly difficult wound conditions followed (bottem panel after removal of bone flap and more recurrences then scheduled for radiosurgery, **a–c** bottom panel). Shortly after radiosurgery very rapid growth and neurological deterioration was seen (bottom panel **d–f**) so that no further therapy except high dose steroids was available

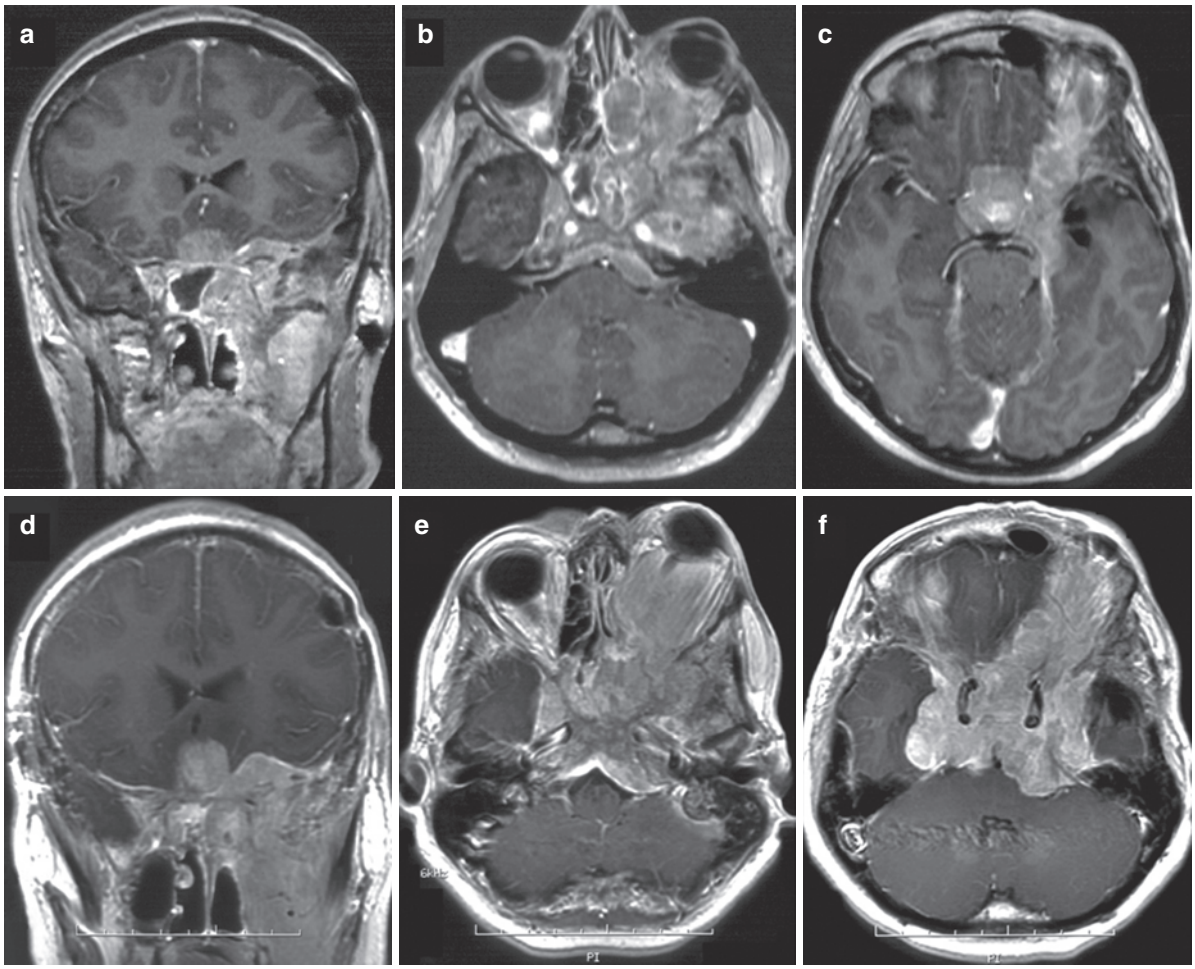

Fig. 4.8 Surgically not manageable, extensive fibrillary meningioma WHO I of the skull base that was partially decompressed twice to save vision on the right eye. The tumor is rapidly progressive and radiosurgery, bromocryptine, anti-progesterone and hydroxyurea treatments failed. Time between the two series (**a–c** and **d–f**) is one year

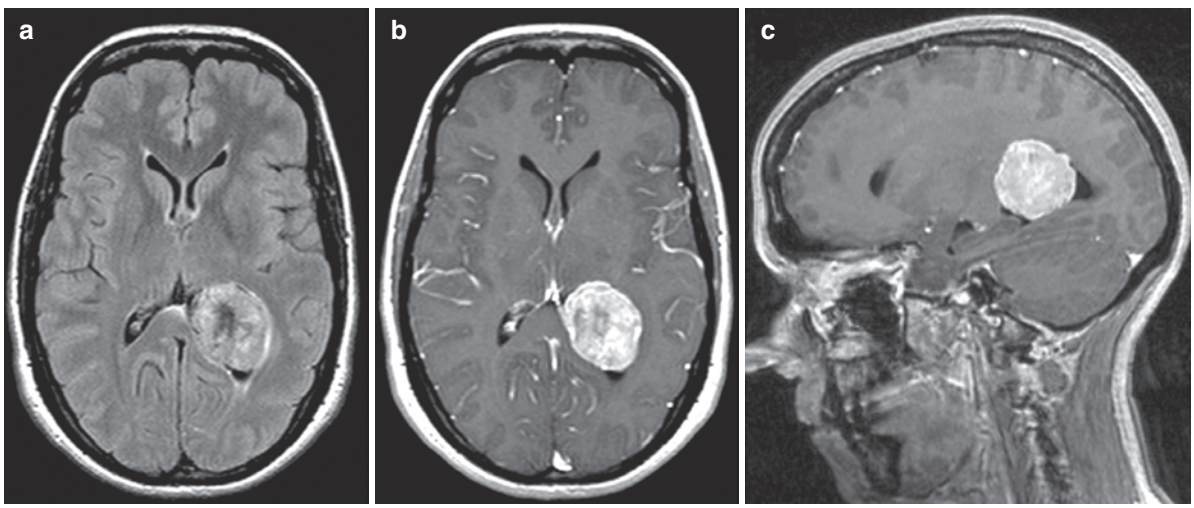

Fig. 4.9 A ventricular meningioma that was diagnosed because of intermittent headache, which is completely non-reactive in the brain. The intact, non-invaded ependymal surface allowed for unrestricted CSF passage so that not even a partial hydrocephalus developed

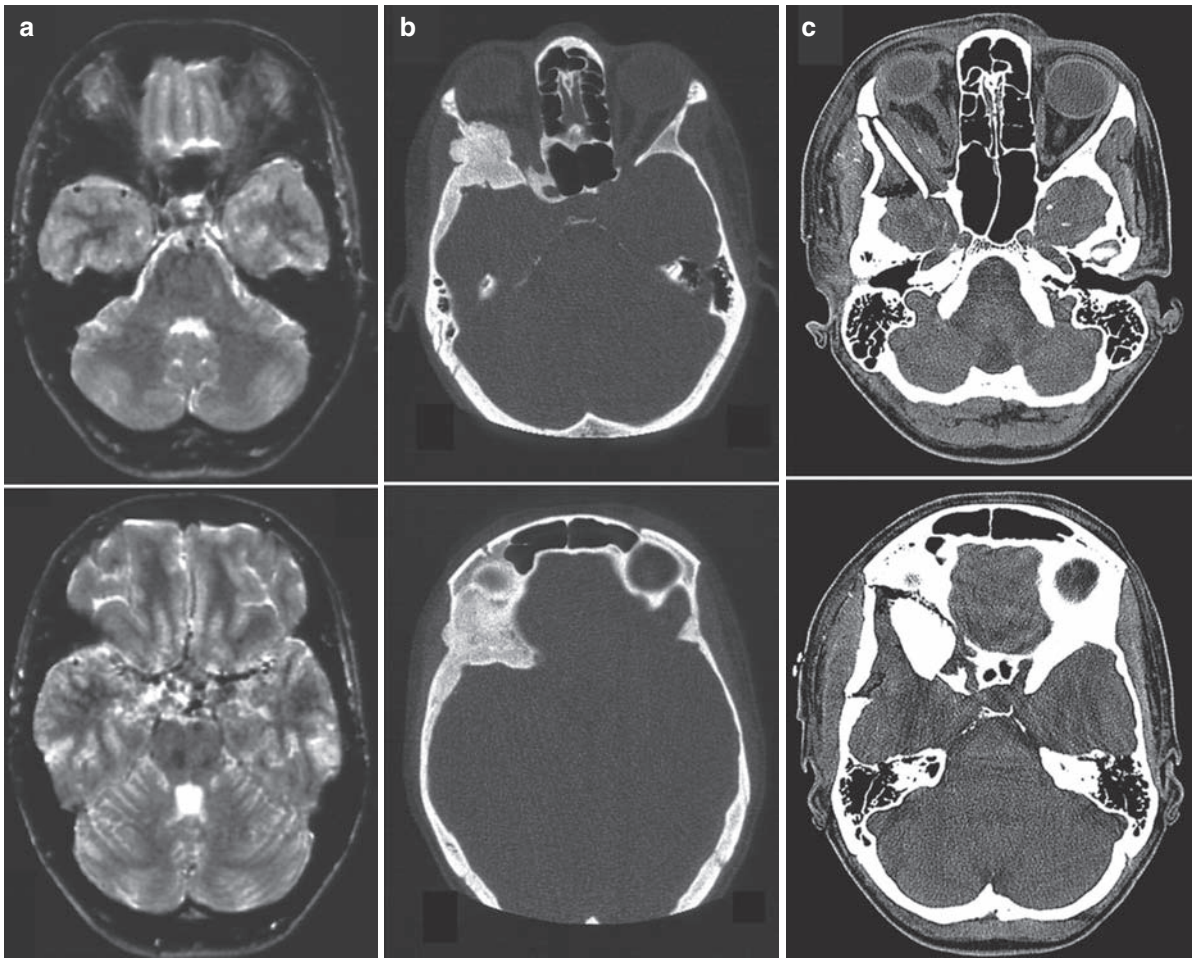

Fig. 4.10 Osseous meningioma of the lateral sphenoid wing, completely taking up the lateral wall of the orbit. No soft tissue components are present. Removal requires extensive drilling of the bone and decompression of the optic canal. The bone is reconstructed with methyl-methylacrylate providing an orbital roof (*right top*) and a lateral wall (*right bottom*)

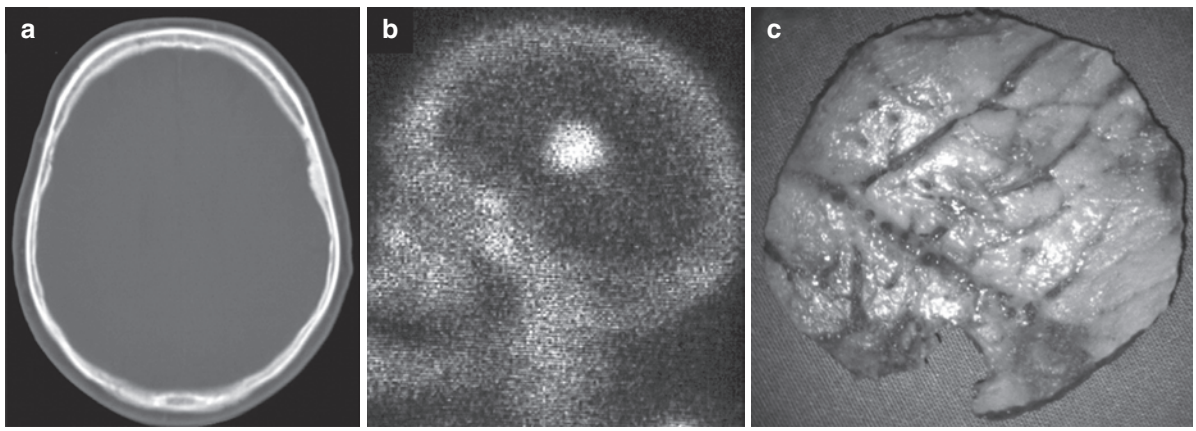

Fig. 4.11 Primary intraosseous meningioma (**a**) that was found because of staging for prostate carcinoma involving a whole skeletal scintigraphy (**b**). The only sign of the tumor was a slight thickening of the bone and a changed bone structure. The tumor itself could be seen as pale sclerotic bone (**c**). The dura underneath the tumor was completely free of tumor and unreactive. There was no indication for any metastatic involvement

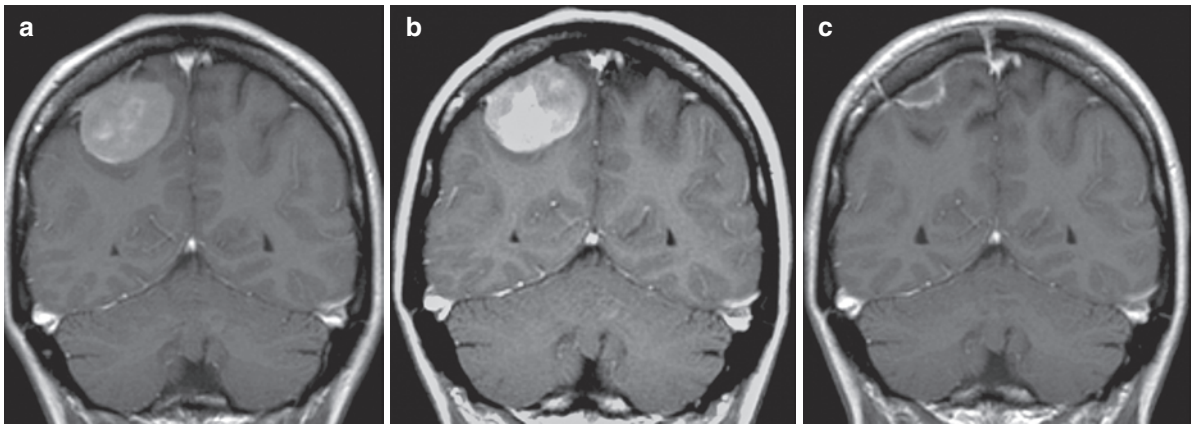

Fig. 4.12 Typical convexity meningioma with a broad dural attachment that extends further than the tumor (meningeal tail sign). Removal of the tumor (*right*) should include all the infiltrated zone that is to be replaced with periosteum

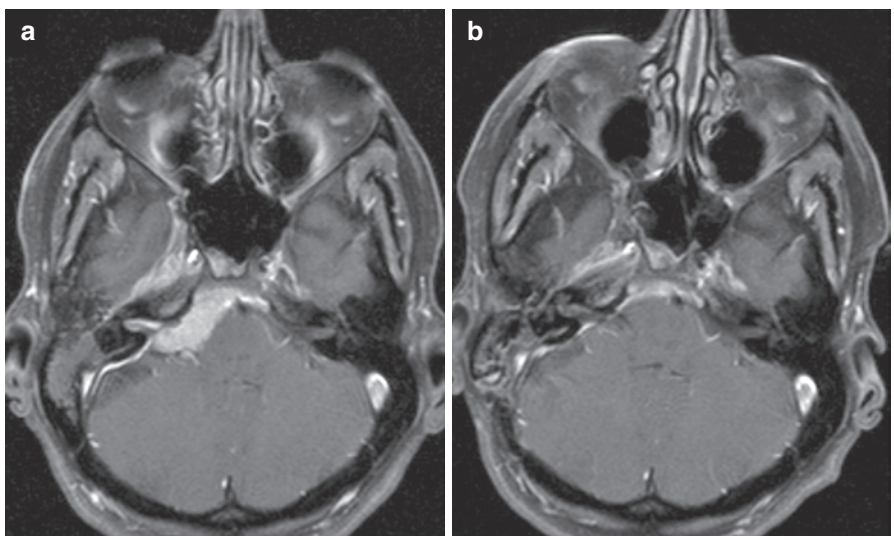

Fig. 4.13 Extensive, non-resectable meningioma of the clivus, CP angle, cavernous sinus, sellar lumen and jugular foramen with extracranial extension (partially not shown). Removal of the intracranial parts to decompress the brain stem and free the cranial nerves together with coagulation of the clival and posterior petrosal dura was performed right and the whole residual was irradiated by fractionated stereotactic radiation

4.8 Therapy

4.8.1 Surgery

Therapy of meningiomas is generally surgical [2, 3]. Especially for the skull base locations, over last the decade it has become more interdisciplinary [22], with additional treatment opportunities also for radiotherapists and radiosurgeons with their improving tools [29]. The refinement of microsurgical approaches offers a resective option, or at least a partial one, for almost all meningioma locations [2, 3]. Again, as for the symptoms, surgical management differs according to location.

The most important question is whether a meningioma needs to be treated at all or can be left to observation, keeping in mind that many lesions are found accidentally. Especially with incidental, calcified meningiomas in the elderly, repeated imaging within 6 months or even a year is justified; when no increase in size is seen, the lesion is left to observation. Calcification in CT as such does not indicate a presumably slow growth as the tumor upon resection may still be well vascularized and vital, and all the hyperdensity might have been due to microcalcification (Fig. 4.20). Tumors may even change their growth characteristics over time. A tumor may recur, or a residual may slowly grow with advancing age, and then slow down and remain constant for many years (Fig. 4.21).

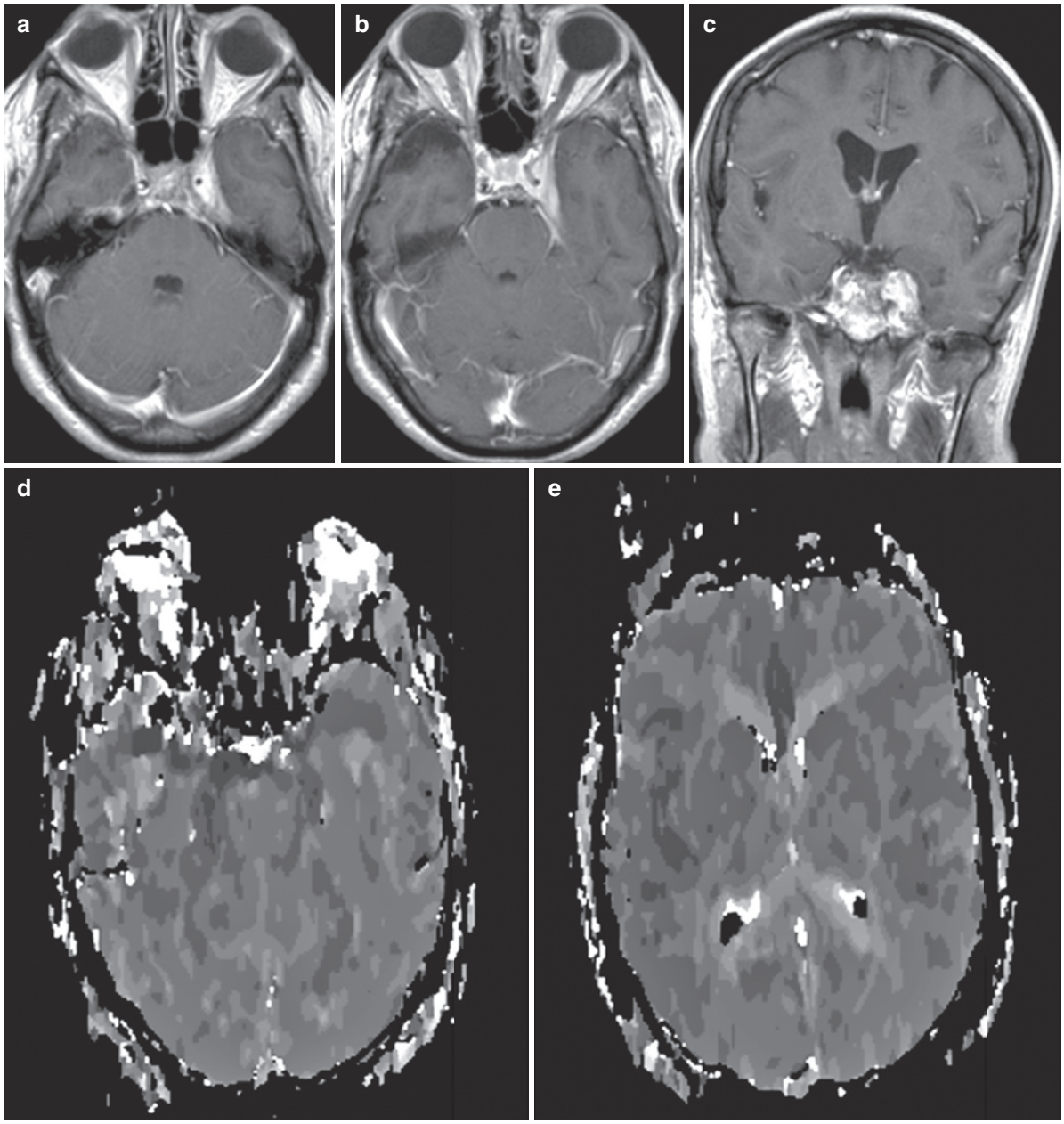

Fig. 4.14 Very compact meningioma of the anterior part of the cavernous sinus with significant narrowing of the left carotid, but no symptoms of ischemia (*top panel*). In these situations further progression of the tumor or the sequelae of radiosurgery may lead to "silent" occlusion of the carotid in case of sufficient collateralization. To assess the risk, a very easy screening method is the so-called time-to-peak measurement of the gadolineum distribution in both hemispheres in perfusion weighted MRI (*bottom panel*). In case the peaks are reached simultaneously, there is no hemodynamic relevance of the stenosis, and bypass surgery is not indicated

The classical, typical meningioma of the convexity or lateral sphenoid wing should be resected, including its origin, likewise meningiomas of the falx or the frontal skull base. Excision of the dura should be performed as far as the preoperative imaging showed any enhancement (meningeal tail sign). In most cases there will be sufficient periosteum to substitute the resected dura. If not, artificial materials exist that can be used instead. When the bone appears to be affected, it can be drilled out at the suspicious site, and if it is completely

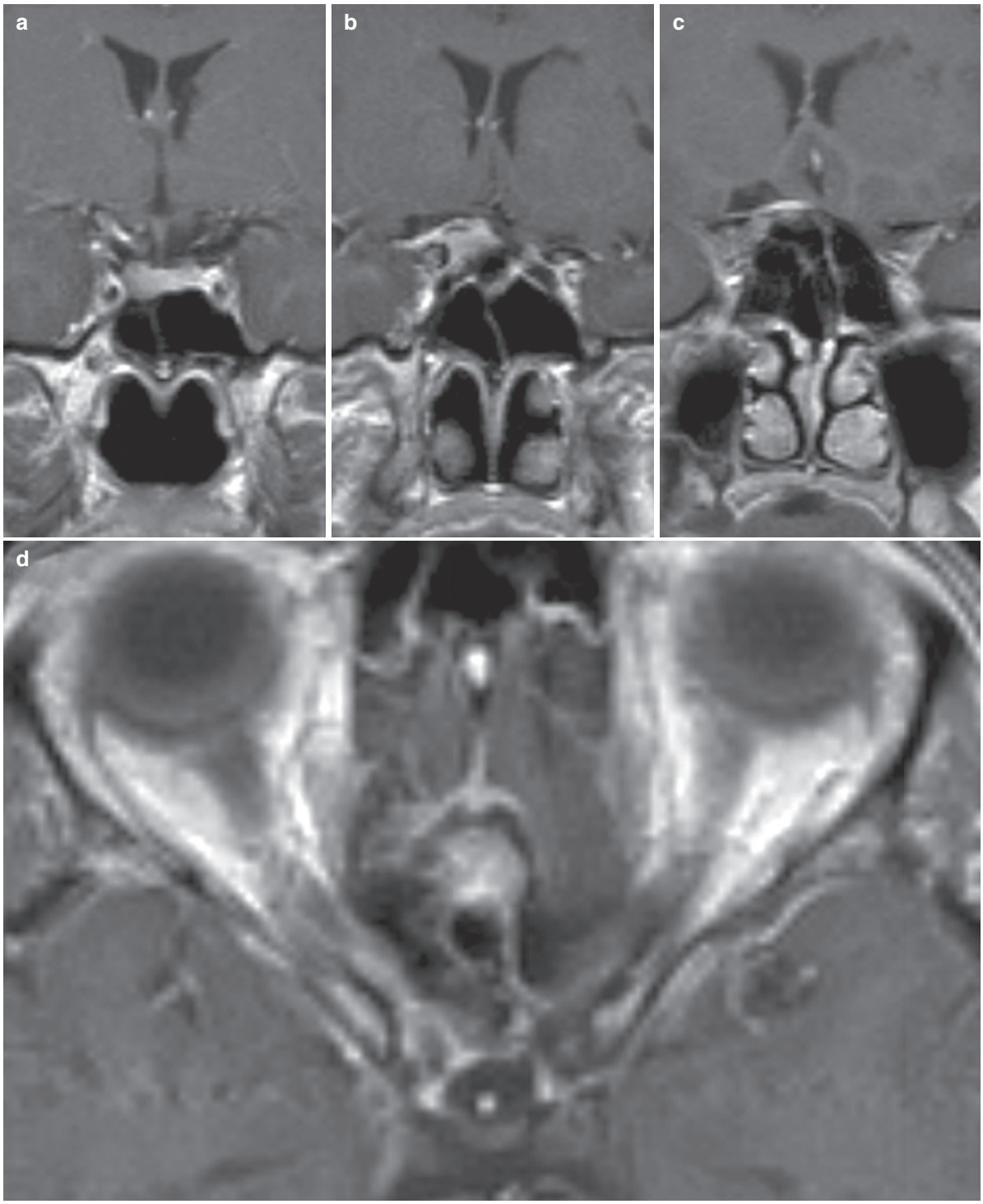

Fig. 4.15 Very small meningioma of the optic nerve that led to visual impairment. Only in the coronal view (*top panel* **a–c**) can one see the enhancement, which is minimal in the other planes. The only option is decompression of the optic canal

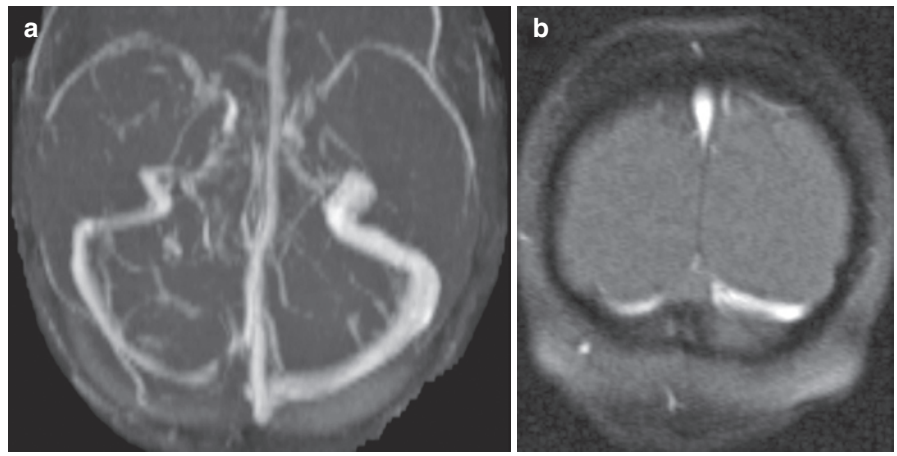

Fig. 4.16 Intrasinusoidal residual of an infratentorial meningioma involving the torcular area. This tumor is seen best as a "negative" impression in the MRI and was not removed because the sinus still carried significant amounts of blood. This tumor is under observation following a single-dose radiosurgical procedure

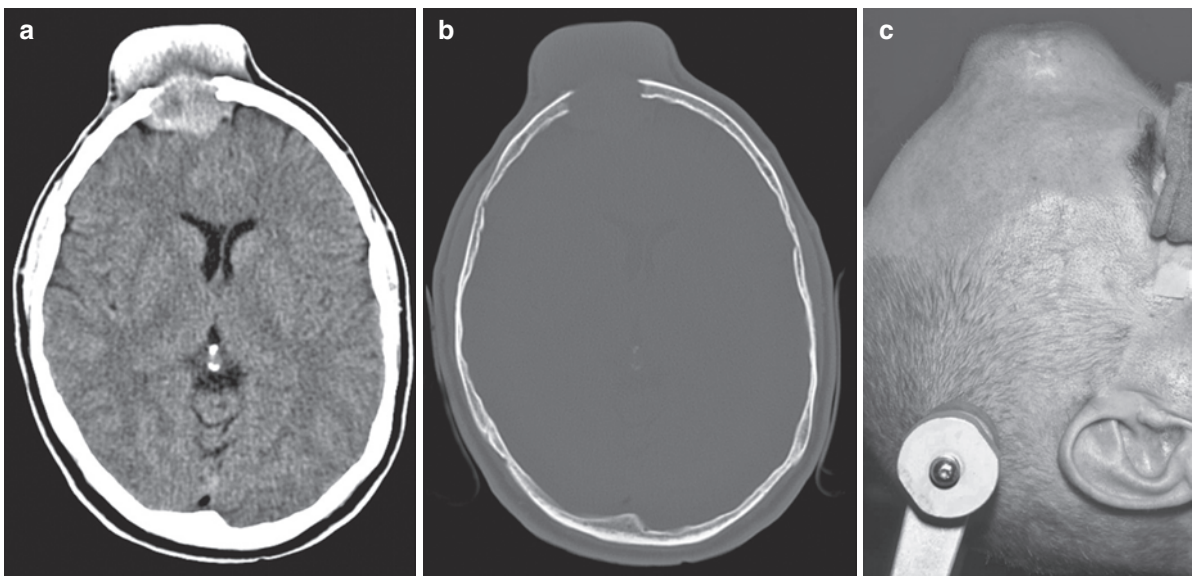

Fig. 4.17 Meningioma that has grown through the bone and can be seen extracranially as a deformity of the skull

infiltrated, it has to be replaced as well. Thus, in some cases the reconstruction is more laborious than the resection itself, especially in cases of fronto-orbital meningiomas or olfactory groove meningiomas where it may be necessary to close a bony destruction of the frontal skull base with split bone and periosteum [8].

Involvement of the sinuses poses a specific problem. When the sagittal sinus in its frontal part is involved or a transverse sinus that has become hemodynamically irrelevant and is compensated by the other side, it can be sacrificed for the sake of a radical resection as there are good collaterals. If the sagittal sinus in its parietal aspect or the confluents or a dominant transverse sinus is involved and still patent and infiltrated to an extent that is beyond what can be easily patched during surgery, the wall and any intrasinusoidal part should be left. It can be irradiated or left to grow on and occlude the sinus slowly while forming collaterals, which usually happens over years and as a rule goes unnoticed. Then the whole residual can be removed in one block. There are papers about sinus repair, but the rates of complication exceed that of this "wait-and-see" and "second look" approach [54]. Only in selected individual cases is it advocated to attempt venous repair after radical resection [55]. Reports about focal irradiation have not yet been published, but it is to be expected that this will lead to some

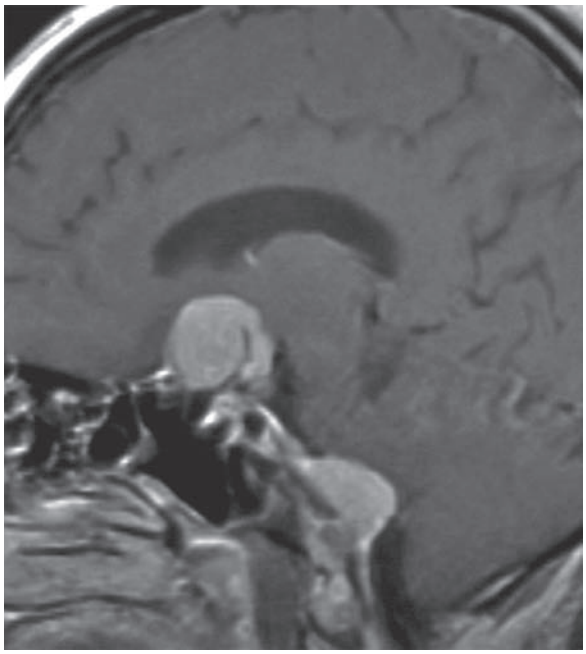

Fig. 4.18 Multiple meningiomas of a patient who was seen because of visual problems on the right eye as a result of a suprasellar meningioma. The MRI revealed a second, non-connected lesion in the right CP angle, which was removed in a separate session

better local control either arresting the tumor or leading to a longer delay until the sinus is closed.

The use of preoperative embolization has not become standard [5, 47]. Although many meningiomas would lend themselves to this approach, it is an unnecessary risk for the patient because with most tumors, the surgical approach to the lesion already involves extensive devascularization and achieves the same result as embolization. Fibrin glue and particles have been used mostly as embolic materials, and this leads to necrosis in the tumor, which can make histopathological classification more difficult. Also there may be swelling with ensuing neurological deficits necessitating more urgent surgical intervention than anticipated. The indication for preoperative embolization should be very strict and limited to cases where there is a clear surgical advantage or a situation in which blood transfusions are anticipated but cannot be recommended in general [48].

The most consequential new therapeutic development over the last decades has been the inclusion of radiosurgery. For several tumor locations, the treatment paradigms over the last years have shifted, and the extensive skull base approaches with bypass surgery and cranial nerve interpositions have been left in favor of a radiosurgical treatment component (Fig. 4.22). It is now common to approach large skull base meningiomas that involve the cavernous sinus as a whole or in parts opportunistically. This applies to petroclival meningiomas and some lesions of the clivus and cerebellopontine angle. Any exophytic parts will be aggressively removed and the tumor reduced to the part containing encased cranial nerves and blood vessels that will be left. This part can then be treated with conformal fractionated radiation or radiosurgery with any of the radiosurgical tools (Fig. 4.22) [22]. With growing experience the possible risks of radiosurgery become apparent [15, 41] and lead to the conclusion that radical surgery should really be attempted wherever possible so that radiation treatment is only applied when surgical risks are too high. In particular, the possibility of an accelerated aggressive growth after radiotherapy might be considered [15].

Another specific situation occurs in optic sheath meningiomas (Fig. 4.23) [42]. These meningiomas are usually very difficult to treat and pose a major dilemma. In an attempt to temporarily stabilize the disease, surgery is limited to decompression of the optic nerve canal and splitting of the sheath as much as the tumor infiltration allows. Attempts at resection almost always result in severe immediate deterioration of vision. With decompression only, visual loss will come gradually and may be postponed for a long time. There are reports about radiotherapy that show that in the majority of cases stable disease can be secured, although long-term results over several decades are not available yet [4]. Whatever therapy is selected, care should be taken that it is administered only to patients with progressive disease because the course can be stable without treatment for many years [17].

Radiosurgery as a *primary* modality is reserved for cases in which surgical manipulation is associated with presently unacceptable morbidity and the likelihood of only subradical resection. As with meningiomas that have a radiosurgical component in the interdisciplinary strategy, the locations are mostly at the skull base, with true intracavernous meningiomas being the largest group, but also locations in the cerebellopontine angle and the perisellar region. In addition to location, age, comorbidities and general status of health have to be included into the decision making (Fig. 4.24). The results of larger series show that disease control can be achieved in the majority of cases

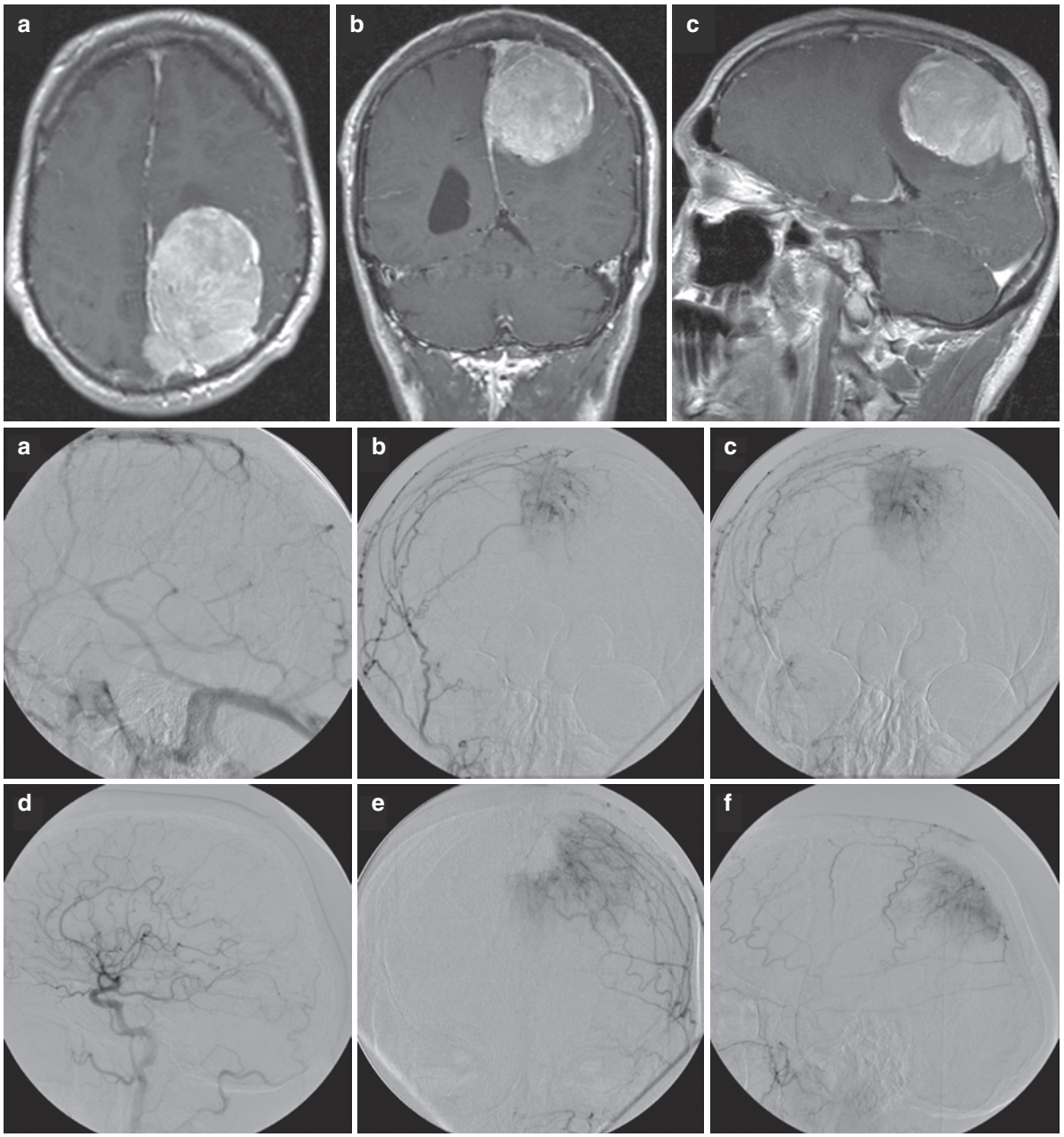

Fig. 4.19 Large bilateral meningioma of the falx that has occluded the sinus and results in pronounced edema, which was the cause of the neurological deficit and which completely resolved within a week of surgery (*top panel* **a–c**). The vascularization is exclusively via the external carotid artery (*bottom panel* **a–f**) and is completely eliminated when performing the dural circumcision as the first part of the surgery. Consequently, this tumor was an avascular mass during the removal without preoperative embolization

with acceptable morbidity, which, however, is not negligible [21]. Total remissions, however, are rare, which is expected when the induction of fibrous changes and stable disease is the major goal in these rather slowly proliferating lesions [29].

Chemotherapy has almost no role in the treatment of meningiomas. Even in anaplastic meningiomas, there is only limited experience and limited efficacy for the classical chemotherapeutic agents [10, 11, 31]. Hope has long rested with the discoveries about the

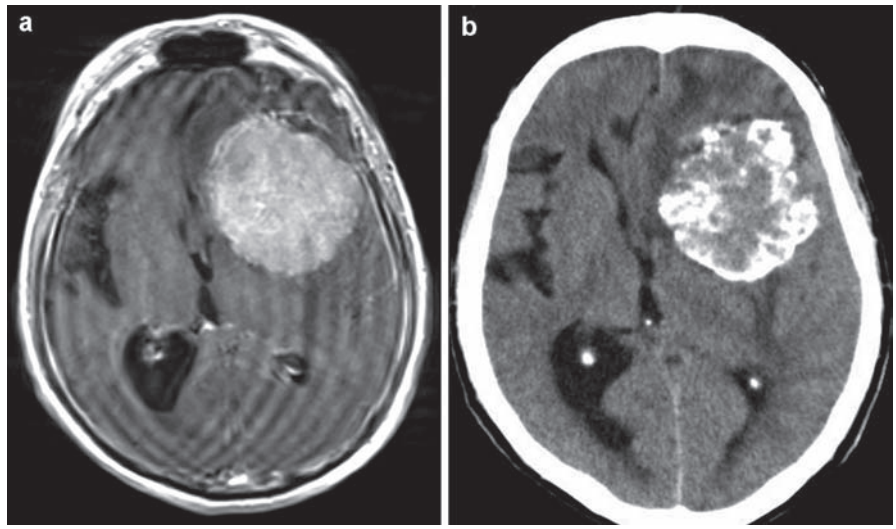

Fig. 4.20 Large sphenoid wing meningioma hyperdense on CT suggesting extensive calcification (**a**). The enhancement on MRI (**b**) already indicates that the tumor may consist mostly of vital tissue, and indeed this was a soft meningioma in which the calcification apparently was microscopic

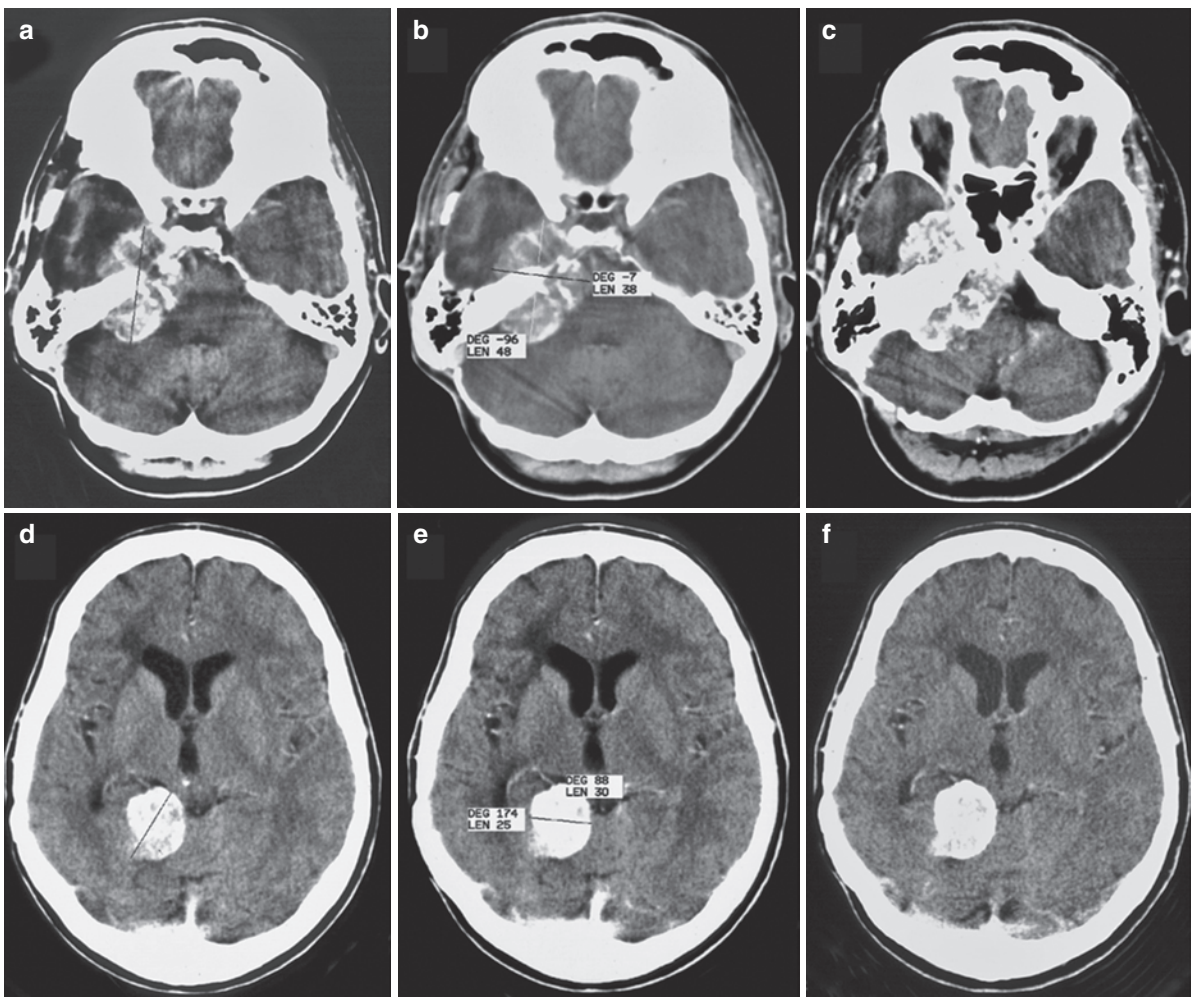

Fig. 4.21 Residuals of a meningioma that was operated on 10 years before the first CT scan seen in this follow-up (**a, d**). The patient felt no symptoms at the time and had other health problems that resulted in the decision to remain in follow-up without any surgical therapy. Further follow-up (**b, e**) 2 years; (**c, f**) 5 years showed that there was almost no further growth, and the patient is in stable condition without neurological deficits

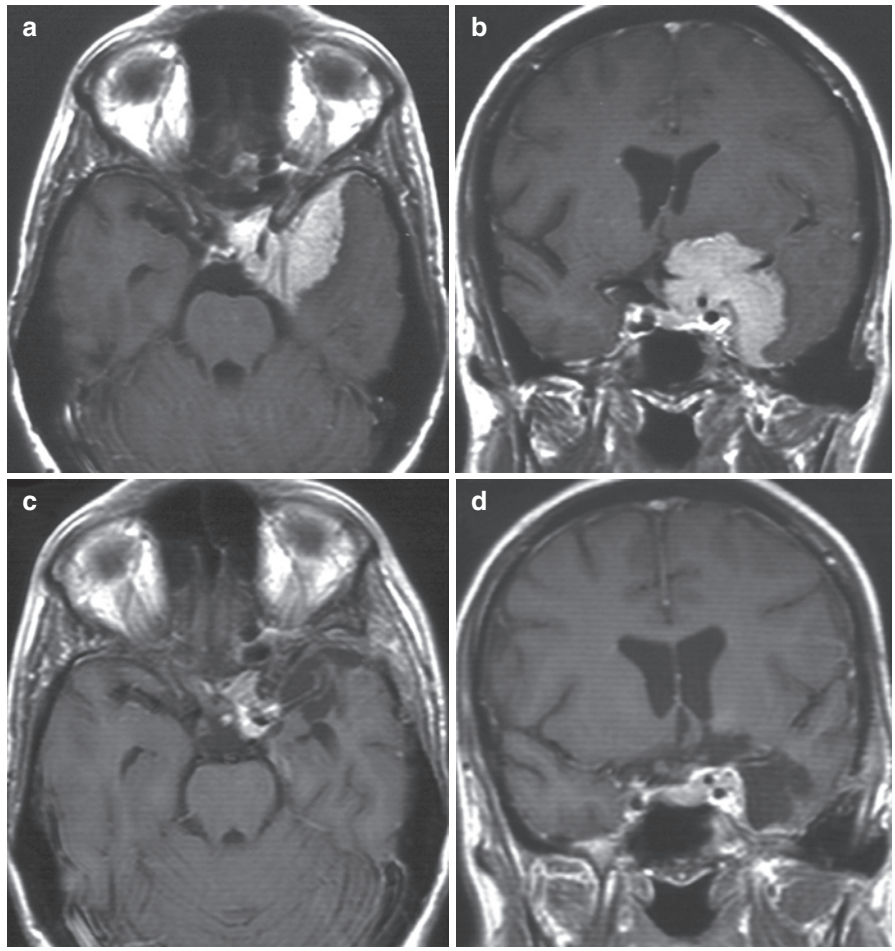

Fig. 4.22 Exophytic meningioma of the anterior clinoid process extending into the cavernous sinus and around the optic canal (*top panel*). Small residuals of the tumor were left, and at the first sign of progressive growth (*bottom right*) fractionated stereotactic surgery was indicated

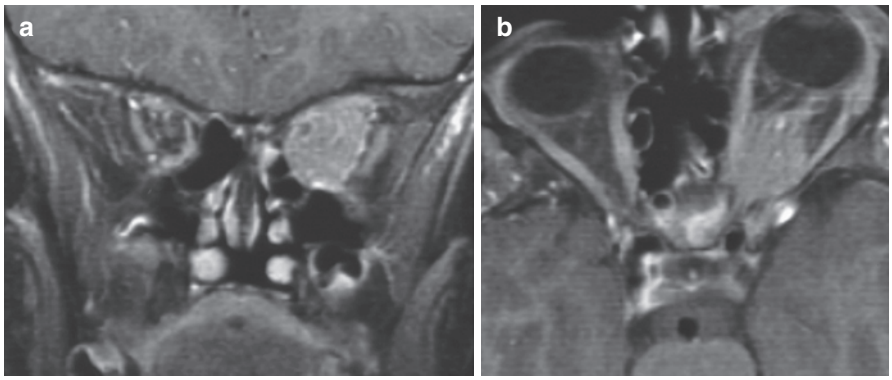

Fig. 4.23 Biopsy-proven meningioma of the optic nerve in a young boy, which upon inspection proved to be unseparable from the nerve and thus could not be removed without risking blindness, which in this case was not yet present. Should the eye lose sight at some point, a complete resection might be attempted with the risk that the eyeball completely degenerates when disconnected from the nerve

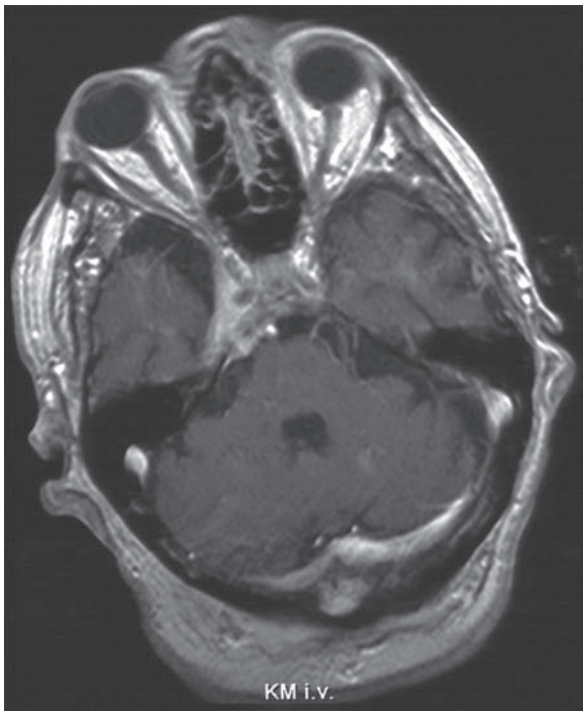

Fig. 4.24 Primarily radiated meningioma of the cavernous sinus in an otherwise severely disabled patient. Such cases are the domain of primary radiotherapeutic interventions

cell biology of meningiomas and the possibility to develop targeted approaches, which in the context of meningioma hold only limited promise [43]. But neither the presence of progesterone receptors nor the presence of dopamine receptors [9] has lead to therapeutic opportunities despite phase II clinical trials [20] since those cells expressing the progesterone receptor do not divide [60]. The only option with some limited efficacy comes from drawing an analogy to chronic lymphatic leukemia, which also is a slowly proliferating disorder. Hydroxyurea, which is effective in that disorder, has shown a therapeutic effect also in some patients [38, 40], but a large randomized prospective phase III trial is still unavailable.

4.9 Prognosis

The prognosis of meningiomas depends on their grade and their location. It can only be determined in the individual patient from regular follow-up. It has been difficult to find prognostic parameters based on histological markers except for grade and subtype. All other markers do not seem to have prognostic relevance. Based on the resection, the completeness of removal has been classified and basically distinguishes between a radical resection including the origin (Simpson grade 1), resection with coagulation of the origin (Simpson grade 2), partial resection (Simpson grade 3) and a mere biopsy (Simpson grade 4) [53].

Evidently there is better prognosis with more radical resection, but this may need to be revisited with the now widespread use of radiotherapeutic techniques for residual tumors. As a rule of thumb, one can expect permanent cure of a convexity meningioma of WHO grade I or II, which is fully resected in over 90% of the cases. Skull base meningiomas even when completely reduced to their site of origin will recur in 50% of the cases.

Anaplastic meningiomas have a poor prognosis and will eventually even metastasize.

4.10 Follow-Up

Patients with resected meningiomas need to be followed regularly after treatment, and thisat may require interdisciplinary cooperation. At first there should be follow-up intervals with imaging of 6 months or 1 year and later every 2 years. MRI is generally the best modality, but in cases of bone involvement at the skull base, CT may need to be done as well. Because imaging changes may be subtle in some patients, other monitoring modalities may need to be included, such as regular ophthalmological assessment or audiograms, when the tumor is in the area of the respective compromised cranial nerves and recurrence/progression impairing their function is feared. As it has been reported that patients with radiosurgical treatment for residual tumor may experience sudden aggressive growth with years of delay, special attention must be given to patients with such combined treatments.

Only when after 10 years there is no evidence of any disease activity can patients be dismissed from regular follow-up. Bearing in mind that tumors may alter their growth characteristics over years, patients can be advised that not each indication of new tumor activity needs to be treated right away because it may not cause any symptoms and can be safely watched for some time. However, it must be pointed out that exactly because of the usually slow-growing nature, regular follow-up is important

because symptoms from a recurrent or progressing lesion may arise only late, and then optimal therapeutic opportunities may have been missed. There are no blood tests that allow monitoring of tumor activity.

4.11 Future Perspectives

Optimal definition of the treatment modalities in an interdisciplinary setting and evaluation of that concept in larger series with meticulous follow-up will make treatment of meningiomas safer and more efficacious on a much more individualized basis. Given the absence of any pharmacological treatment option and lack of perspective of such in the near future, therapy will be resting on surgery and radiation for a long time. It is to be hoped that refined and meticulously clinically correlated gene expression analyses will lead to the definition of candidate genes for truly targeted therapies.

4.12 Other Meningeal Tumors

Hemangiopericytoma comprises about 2% of meningeal tumors [24]. They tend to occur at a younger age than the meningiomas, with a peak incidence in the fourth and fifth decades. Also, there appears to be a slight prevalence in the male sex. By WHO grading they are allocated to the grades II and III, but the parameters distinguishing the two still need to be fully validated. The genetic alterations are different from meningioma, with alterations of the chromosome 22 absent. Most alterations are found on chromosomes 12q13 and 6p21.

As for clinical signs and symptoms, there is no difference between meningiomas and hemangiopericytomas. The neuroradiological features are slightly different from meningiomas. The tumors tend to cause lytic lesions in bone and do not grow through the bone like the meningiomas, which with rare exceptions either cause hyperostosis or just distend the bone without completely destroying it. The tumors are highly vascularized and upon angiography show a wealth of pathological vessels [39]. In contrast to meningiomas, calcifications are rare.

Treatment of hemangiopericytoma is more complex than that of the average meningioma. The tumors should be removed as completely as possible, and then there is a consensus that the region needs to be irradiated [1], because otherwise the rate of recurrence is 91% [60]. Also, these tumors have a tendency to metastasize, primarily into bone [56]. No chemotherapeutic regimen has emerged as an effective standard [16]. Corresponding to the aggressiveness of the disease, patients need to be followed closely, especially to detect metastases. The high rate of recurrence and metastases are the cause for mortality, and despite aggressive treatment, up to 60% of the patients may have succumbed to the disease within 15 years [61].

4.12.1 Dural Lymphoma

Dural lymphomas present as contrast-enhancing lesions with an extension like a subdural hematoma, like a nodular meningioma with a dural tail, like an en-plaque meningioma or just like dural hypertrophy. Particularly suspicious is an extension deep into the arachnoid spaces and sulci (Fig. 4.25). Primary dural lymphomas are rare and not to be mistaken for primary CNS lymphoma (see Chap. 19). They are mostly of the MALT type [19, 49], although other kinds and regular Hodgkin's disease have been reported [26]. They seem to have a better prognosis than PCNSL and respond well to cranial radiation [6]. Many of the reported dural lymphomas were unexpected, and therefore, some were resected like en-plaque meningiomas. Cranial radiation is to be recommended even after resection, but certainly after biopsy.

4.12.2 Dural Metastases

Metastatic disease to the brain is seen with increasing frequency, but in comparison to the parenchymal or leptomeningeal variants, purely dural involvement is rare and is detected most frequently in the context of suspected meningioma [32, 59]. Whereas in intracerebral disease where a metastasis is more readily suspected because of imaging characteristics and has a known primary in about 80% [64], the diagnosis of a dural metastasis is made much more frequently when the primary tumor is still unknown [59]. This can be

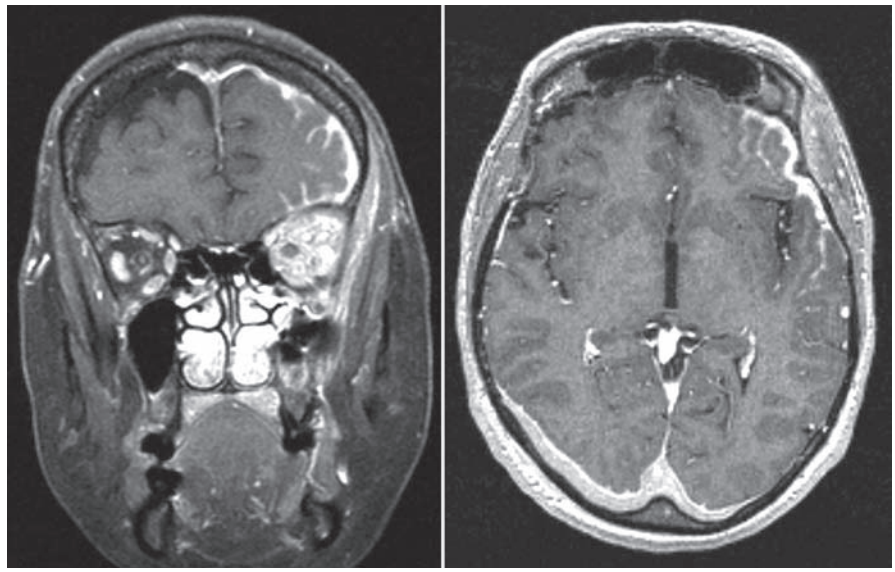

Fig. 4.25 Gd-enhanced MRI of a left frontal lesion, which was observed for 5 years in a patient with deteriorating vision who decidedly declined all offers for a biopsy. When the lesion was biopsied because of an increasing exophthalmos, it turned out to be the metastasis of a slowly growing lymphoma, a cervical manifestation of which had been treated 7 years ago

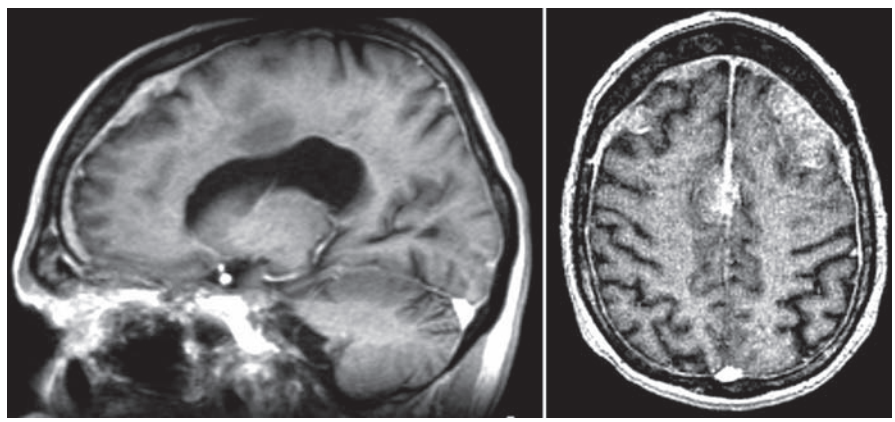

Fig. 4.26 Bihemispheric, mostly frontal en plaque and nodular manifestation of a prostate carcinoma known for 6 years treated only with endocrine therapy. The patient presented with beginning signs of disorientation. No treatment was given because of rapid deterioration

partially explained by the fact that dural metastases may occur in any type of cancer, but show a different spectrum from intracranial disease. A large combined surgical and autoptic series showed a surprisingly broad spectrum, including the expected high numbers of breast cancer as primary, but an even higher number of underlying prostate cancer, which can have extensive manifestation (Fig. 4.26), and also such primaries as the larynx, gall bladder and stomach, which otherwise rarely metastasize to the brain [28].

When purely dural and having an appearance like meningioma, the differential diagnosis is close to impossible without a tissue diagnosis because the neuroradiological techniques may not provide sufficient parameters for differentiation [30]. The tumors may be dural with a flat spread, nodular or show a combination of subdural–dural–skull extension. Depending on the context of the overall status of the patient, there may be an indication for resection, especially when the differential diagnosis toward meningioma cannot be made without histology and there is no known primary. As the spectrum of histological origins is very heterogeneous, there are no published series about the role of radiotherapy or chemotherapy as there are for leptomeningeal metastatic disease. How to proceed after histological verification of a dural metastasis will depend on the established treatment paradigms for the primary tumor and has to be determined in an interdisciplinary tumor board.

References

1. Alen JF, Lobato RD, Gomez PA, Boto GR, Lagares A, Ramos A, Ricoy JR. (2001) Intracranial hemangiopericytoma: study of 12 cases. Acta Neurochir (Wien) 143:575–586
2. Al-Mefti O. (1991) Meningiomas. Raven, New York
3. Al-Mefti O. (1998) Operative atlas of meningioma. Lippincott-Raven, Philadelphia, PA
4. Becker G, Jeremic B, Pitz S, Buchgeister M, Wilhelm H, Schiefer U, Paulsen F, Zrenner E, Bamberg M. (2002) Stereotactic fractionated radiotherapy in patients with optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys 54:1422–1429
5. Bendszus M, Rao G, Burger R, Schaller C, Scheinemann K, Warmuth-Metz M, Hofmann E, Schramm J, Roosen K, Solymosi L. (2000) Is there a benefit of preoperative meningioma embolization? Neurosurgery 47:1306–1311; discussion 1311–1302
6. Beriwal S, Hou JS, Miyamoto C, Garcia-Young JA. (2003) Primary dural low grade BCL-2 negative follicular lymphoma: a case report. J Neurooncol 61:23–25
7. Buhl R, Hugo HH, Mehdorn HM. (2001) Brain oedema in secretory meningiomas. J Clin Neurosci 8(Suppl 1):19–21
8. Bull WJ, Vandevender D, Cimino VG. (2003) Reconstruction of defects of the cranial base. Tech Neurosurg 9:106–112
9. Carroll RS, Schrell UM, Zhang J, Dashner K, Nomikos P, Fahlbusch R, Black PM. (1996) Dopamine D1, dopamine D2, and prolactin receptor messenger ribonucleic acid expression by the polymerase chain reaction in human meningiomas. Neurosurgery 38:367–375
10. Chamberlain MC. (2004) Meningiomas. Curr Treat Options Neurol 3:67–76
11. Chamberlain MC, Tsao-Wei DD, Groshen S. Temozolomide for treatment-resistant recurrent meningioma. Neurology 62:1210–1212
12. Christensen HC, Kosteljanetz M, Johansen C. (2003) Incidences of gliomas and meningiomas in Denmark, 1943 to 1997. Neurosurgery 52:1327–1333; discussion 1333–1324
13. Claus EB, Black PM, Bondy ML, Calvocoressi L, Schildkraut JM, Wiemels JL, Wrensch M. (2007) Exogenous hormone use and meningioma risk: what do we tell our patients? Cancer 110:471–476
14. Collins VP. (2004) Brain tumours: classification and genes. J Neurol Neurosurg Psychiatry 75(Suppl 2):ii2–11
15. Couldwell WT, Cole CD, Al-Mefty O. (2007) Patterns of skull base meningioma progression after failed radiosurgery. J Neurosurg 106:30–35
16. Ecker RD, Marsh WR, Pollock BE, Kurtkaya-Yapicier O, McClelland R, Scheithauer BW, Buckner JC. (2003) Hemangiopericytoma in the central nervous system: treatment, pathological features, and long-term follow-up in 38 patients. J Neurosurg 98:1182–1187
17. Egan RA, Lessell S. (2002) A contribution to the natural history of optic nerve sheath meningiomas. Arch Ophthalmol 120:1505–1508
18. Fountas KN, Kapsalaki EZ, Gotsis SD, Kapsalakis JZ, Smisson HF, 3rd, Johnston KW, Robinson JS, Jr., Papadakis N. (2000) In vivo proton magnetic resonance spectroscopy of brain tumors. Stereotact Funct Neurosurg 74:83–94
19. Goetz P, Lafuente J, Revesz T, Galloway M, Dogan A, Kitchen N. (2002) Primary low-grade B-cell lymphoma of mucosa-associated lymphoid tissue of the dura mimicking the presentation of an acute subdural hematoma. Case report and review of the literature. J Neurosurg 96:611–614
20. Grunberg SM. (1994) Role of antiprogestational therapy for meningiomas. Hum Reprod 9(Suppl 1):202–207
21. Han JH, Kim DG, Chung HT, Park CK, Paek SH, Kim CY, Jung HW. (2008) Gamma knife radiosurgery for skull base meningiomas: long-term radiologic and clinical outcome. Int J Radiat Oncol Biol Phys 72(5):1324–1332
22. Hart DJ, Gianotta SL. (2003) Complex cranial base meningioma: combined management. Tech Neurosurg 9:86–92
23. Hsu DW, Efird JT, Hedley-Whyte ET. (1997) Progesterone and estrogen receptors in meningiomas: prognostic considerations. J Neurosurg 86:113–120
24. Jääskeläinen J, Louis DN, Paulus W, Haltia M. (2000) Haemangiopericytoma. In: Kleihues P, Cavanee WK (eds) Tumors of the central nervous system: pathology and genetics. IARC Press, Lyon
25. Jhawar BS, Fuchs CS, Colditz GA, Stampfer MJ. (2003) Sex steroid hormone exposures and risk for meningioma. J Neurosurg 99:848–853
26. Johnson MD, Kinney MC, Scheithauer BW, Briley RJ, Hamilton K, McPherson WF, Barton JH, Jr. (2000) Primary intracerebral Hodgkin's disease mimicking meningioma: case report. Neurosurgery 47:454–456; discussion 456–457
27. Kaminski JM, Movsas B, King E, Yang C, Kronz JD, Alli PM, Williams J, Brem H. (2001) Metastatic meningioma to the lung with multiple pleural metastases. Am J Clin Oncol 24:579–582
28. Kleinschmidt-DeMasters BK. (2001) Dural metastases. A retrospective surgical and autopsy series. Arch Pathol Lab Med 125:880–887
29. Kondziolka D, Nathoo N, Flickinger JC, Niranjan A, Maitz AH, Lunsford LD. (2003) Long-term results after radiosurgery for benign intracranial tumors. Neurosurgery 53:815–821; discussion 821–812
30. Kremer S, Grand S, Remy C, Pasquier B, Benabid AL, Bracard S, Le Bas JF. (2004) Contribution of dynamic contrast MR imaging to the differentiation between dural metastasis and meningioma. Neuroradiology 46:642–648
31. Kyritsis AP. (1996) Chemotherapy for meningiomas. J Neurooncol 29:269–272
32. Laidlaw JD, Kumar A, Chan A. (2004) Dural metastases mimicking meningioma. Case report and review of the literature. J Clin Neurosci 11:780–783
33. Lamszus K. (2004) Meningioma pathology, genetics, and biology. J Neuropathol Exp Neurol 63:275–286
34. Lamszus K, Kluwe L, Matschke J, Meissner H, Laas R, Westphal M. (1999) Allelic losses at 1p, 9q, 10q, 14q, and 22q in the progression of aggressive meningiomas and undifferentiated meningeal sarcomas. Cancer Genet Cytogenet 110:103–110
35. Lamszus K, Lengler U, Schmidt NO, Stavrou D, Ergun S, Westphal M. (2000) Vascular endothelial growth factor, hepatocyte growth factor/scatter factor, basic fibroblast

growth factor, and placenta growth factor in human meningiomas and their relation to angiogenesis and malignancy. Neurosurgery 46:938–947; discussion 947–938
36. Lamszus K, Vahldiek F, Mautner VF, Schichor C, Tonn J, Stavrou D, Fillbrandt R, Westphal M, Kluwe L. (2000) Allelic losses in neurofibromatosis 2-associated meningiomas. J Neuropathol Exp Neurol 59:504–512
37. Longstreth WT, Jr., Phillips LE, Drangsholt M, Koepsell TD, Custer BS, Gehrels JA, van Belle G. (2004) Dental X-rays and the risk of intracranial meningioma: a population-based case-control study. Cancer 100:1026–1034
38. Loven D, Hardoff R, Sever ZB, Steinmetz AP, Gornish M, Rappaport ZH, Fenig E, Ram Z, Sulkes A. (2004) Non-resectable slow-growing meningiomas treated by hydroxyurea. J Neurooncol 67:221–226
39. Marc JA, Takei Y, Schechter MM, Hoffman JC. (1975) Intracranial hemangiopericytomas. Angiography, pathology and differential diagnosis. Am J Roentgenol Radium Ther Nucl Med 125:823–832
40. Mason WP, Gentili F, Macdonald DR, Hariharan S, Cruz CR, Abrey LE. (2002) Stabilization of disease progression by hydroxyurea in patients with recurrent or unresectable meningioma. J Neurosurg 97:341–346
41. Muracciole X, Regis J. (2008) Radiosurgery and carcinogenesis risk. Prog Neurol Surg 21:207–213
42. Newman SA. (2003) Optic nerve sheath meningiomas. Tech Neurosurg 9:64–77
43. Norden AD, Drappatz J, Wen PY. (2007) Targeted drug therapy for meningiomas. Neurosurg Focus 23:E12
44. Perry A, Dehner LP. (2003) Meningeal tumors of childhood and infancy. An update and literature review. Brain Pathol 13:386–408
45. Perry A, Louis DN, Scheithauer BW, Budka H, von Deimling A. (2007) Meningiomas. In: Louis DN, Ohgaki H, Wiestler OD, Cavanee WK (eds) WHO classification of tumors of the central nervous system. IARC Press, Lyon, pp. 164–172
46. Preston DL, Ron E, Yonehara S, Kobuke T, Fujii H, Kishikawa M, Tokunaga M, Tokuoka S, Mabuchi K. (2002) Tumors of the nervous system and pituitary gland associated with atomic bomb radiation exposure. J Natl Cancer Inst 94:1555–1563
47. Probst EN, Grzyska U, Westphal M, Zeumer H. (1999) Preoperative embolization of intracranial meningiomas with a fibrin glue preparation. AJNR Am J Neuroradiol 20:1695–1702
48. Rosen CL, Ammerman JM, Sekhar LN, Bank WO. (2002) Outcome analysis of preoperative embolization in cranial base surgery. Acta Neurochir (Wien) 144:1157–1164
49. Rottnek M, Strauchen J, Moore F, Morgello S. (2004) Primary dural mucosa-associated lymphoid tissue-type lymphoma: case report and review of the literature. J Neurooncol 68:19–23
50. Ruttledge MH, Sarrazin J, Rangaratnam S, Phelan CM, Twist E, Merel P, Delattre O, Thomas G, Nordenskjold M, Collins VP, et al (1994) Evidence for the complete inactivation of the NF2 gene in the majority of sporadic meningiomas. Nat Genet 6:180–184
51. Sadetzki S, Modan B, Chetrit A, Freedman L. (2000) An iatrogenic epidemic of benign meningioma. Am J Epidemiol 151:266–272
52. Sayagues JM, Tabernero MD, Maillo A, Trelles O, Espinosa AB, Sarasquete ME, Merino M, Rasillo A, Vera JF, Santos-Briz A, de Alava E, Garcia-Macias MC, Orfao A. (2006) Microarray-based analysis of spinal versus intracranial meningiomas: different clinical, biological, and genetic characteristics associated with distinct patterns of gene expression. J Neuropathol Exp Neurol 65:445–454
53. Simpson D. (1957) The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 20:22–29
54. Sindou M. (2001) Meningiomas invading the sagittal or transverse sinuses, resection with venous reconstruction. J Clin Neurosci 8(Suppl 1):8–11
55. Sindou MP, Alvernia JE. (2006) Results of attempted radical tumor removal and venous repair in 100 consecutive meningiomas involving the major dural sinuses. J Neurosurg 105: 514–525
56. Soyuer S, Chang EL, Selek U, McCutcheon IE, Maor MH. (2004) Intracranial meningeal hemangiopericytoma: the role of radiotherapy: report of 29 cases and review of the literature. Cancer 100:1491–1497
57. Strojan P, Popovic M, Jereb B. (2000) Secondary intracranial meningiomas after high-dose cranial irradiation: report of five cases and review of the literature. Int J Radiat Oncol Biol Phys 48:65–73
58. Swensen R, Kirsch W. (2002) Brain neoplasms in women: a review. Clin Obstet Gynecol 45:904–927
59. Tagle P, Villanueva P, Torrealba G, Huete I. (2002) Intracranial metastasis or meningioma? An uncommon clinical diagnostic dilemma. Surg Neurol 58:241–245
60. Tonn JC, Ott MM, Bouterfa Hikerkans S, Kapp M. (1997) Inverse correlation of cell proliferation and expression of progesterone receptors. Neuosurgery 41:1152–1159
61. Vuorinen V, Sallinen P, Haapasalo H, Visakorpi T, Kallio M, Jaaskelainen J. (1996) Outcome of 31 intracranial haemangiopericytomas: poor predictive value of cell proliferation indices. Acta Neurochir (Wien) 138:1399–1408
62. Wan WL, Geller JL, Feldon SE, Sadun AA. (1990) Visual loss caused by rapidly progressive intracranial meningiomas during pregnancy. Ophthalmology 97:18–21
63. Weber RG, Bostrom J, Wolter M, Baudis M, Collins VP, Reifenberger G, Lichter P. (1997) Analysis of genomic alterations in benign, atypical, and anaplastic meningiomas: toward a genetic model of meningioma progression. Proc Natl Acad Sci USA 94:14719–14724
64. Westphal M, Heese O, de Wit M. (2003) Intracranial metastases: therapeutic options. Ann Oncol 14(Suppl 3): iii4–10
65. Zang KD. (2001) Meningioma, a cytogenetic model of a complex benign human tumor. Cytogenet Cell Genet 93: 207–220