Tumors of the Skull Base

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17.1 Introduction

The skull base is affected by a wide range of tumor pathologies. They are often slow-growing, benign, extra-axial tumors that cause symptoms by involvement of the cranial nerves or a mass effect on the brain stem and cerebellum. They are often located in critical areas within the cranium that are especially hard to reach with routine surgical techniques. Involvement of cranial nerves and vessels makes these lesions particularly challenging to treat surgically. Due to the benign nature of most of these lesions, complete surgical removal often affords a cure, although some skull-base tumors require a combination of surgical and radiation therapies.

According to the Central Brain Tumor Registry of the United States (CBTRUS), the incidence of all primary benign and malignant brain tumors is 14.0 cases per 100,000 persons per year [1]. If we exclude metastatic lesions to the skull base and include pituitary tumors, neoplasms involving the base of the skull would constitute 25% of all primary intracranial tumors.

This chapter will focus on three specific pathologies within the skull base: chordomas, meningiomas, and paragangliomas. Other tumors that involve the skull base, including schwannomas and other nerve sheath tumors, pituitary tumors, metastases, and carcinomas, are covered in other chapters of the text.

17.2 Chordoma and Chondrosarcoma

Chordomas and chondrosarcomas are often considered together because of their similarities in presentation, location, radiographic appearance, and surgical treatment. Despite this fact, these tumors are distinct

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pathological entities and display different biological behavior and prognosis.

Chordomas and chondrosarcomas are rare, slow-growing tumors within the skull base. Chordomas are thought to originate from remnants of the primitive notochord, while chondrosarcomas are thought to originate from mesenchymal cells or embryonic rests of the cartilaginous matrix of the cranium [2]. Virchow originally described chordomas in 1846 as small, soft, jelly-like tissues arising from the synchondrosis spheno-occipitalis, which he thought were associated with cartilaginous tumors. The tumors were named *eccondrosis physaliphora* due to the large vesicular, plant-like cells called *physaliferous cells* that are within chordomas [3]. Muller called these tumors *chordomas* or *ecchordosis* in 1925, after identifying their origin as remnants of the notochord.

17.2.1 Epidemiology

Chordomas are rare tumors that are thought to originate from the remnants of the primitive notochord. The annual incidence is 0.2–0.5 per 100,000 persons per year and account for 0.1–0.7% of intracranial tumors and 6% of all primary skull-base tumors. Chordomas arise in patients of all ages, but typically become symptomatic in the third to fifth decades of life. The average age at diagnosis is 43 years. Fewer than 5% of chordomas occur in children [4]. There appears to be a male preponderance with a ratio of ~2:1 reported in some series, while others report no sex preponderance. It has been described that chordomas do not occur in people of African-American decent, but that does not seem to be true for chondrosarcomas. These are often slow-growing tumors, and the time from first symptom to diagnosis often exceeds 12 months. Recent increases in the use of CT and MRI have allowed earlier diagnosis. Chordomas are found to be metastatic in 10% of cases.

Chondrosarcomas are thought to originate from mesenchymal cells or from embryonic rests of the cartilaginous matrix of the cranium. They are also extremely rare tumors with a similar presentation to chordoma. Chondrosarcomas have a male preponderance and present at younger ages (within the second and third decades of life).

Due to the fact that chordomas originate from remnants of the notochord, they can occur anywhere along the spinal axis. They most frequently arise in the sacrococcygeal area (~50% of the time), followed by the skull base (~25–35%), and finally in the remainder of the spine (~15%). Within the skull base, chordomas usually arise from the midline clivus and are thought to originate specifically from the spheno-occipital synchondrosis, and may be entrapped by bone. They often have extensions to the sella, parasellar region, sphenoid sinus, cavernous sinus, foramen magnum, prepontine cistern, posterior fossa, occipital condyle, infratemporal fossa, first cervical vertebra, and retropharyngeal spaces. The cavernous sinus is found to be involved in up to 50% of cases. Chondrosarcomas often originate laterally along the petrous apex or sphenoid ridge as opposed to the midline origin of chordomas.

17.2.2 Symptoms and Clinical Signs

As with other skull-base tumors, chordomas cause symptoms and signs depending on their location and direction of extension. The most common complaints reported are headaches, diplopia, visual changes, and lower cranial nerve pareses. Tumors that are located more cephalad in the basisphenoid tend to cause dysfunction of the extraocular muscles, usually through dysfunction of the sixth cranial nerve. Permanent or intermittent diplopia is the first symptom reported in most patients. Tumors in this location also present with endocrine dysfunction and other upper cranial nerve symptoms, such as decreased visual acuity, and facial numbness. More caudally located tumors in the basiocciput cause dysfunction of the lower cranial nerves, resulting in facial weakness, hearing loss, dysphagia, hoarseness, and swallowing difficulties. Patients with tumors in this location often have compression of the brain stem and cerebellum, resulting in the presence of long-tract signs, motor and sensory deficits, as well as cerebellar dysfunction with ataxia and dysmetria. Tumors extending further into the occipital condyles may cause occipital headaches that are worsened by movement of the neck. Involvement of the anterior portion of the occipital condyles causes hypoglossal nerve dysfunction seen with unilateral tongue weakness. Retropharyngeal and nasal extension can cause symptoms including Eustachian tube blockage, nasal obstruction, epistaxis, dysphagia, dysarthria, and throat fullness. When the tumor extends laterally, unilateral symptoms are found.

Cranial neuropathies are detected on neurological examination and are found in 40–90% of patients at presentation. The most frequently noted symptom on physical examination is extraocular muscle weakness secondary to sixth nerve involvement. Often a retropharyngeal mass can be seen on examination of the nasopharynx with an office endoscope.

17.2.3 Diagnostics

Synopsis. The diagnosis of chordoma requires pathological evaluation of tumor tissue. The suspicion of chordoma can be raised using brain MRI and CT in combination for a radiographic diagnosis. Chordoma is suspected in a patient with a clival mass demonstrating destruction of the bony clivus without hyperostosis, along with nasopharyngeal extension. A tumor mass within the nasopharynx can be biopsied for diagnosis.

The radiographic diagnosis of chordoma requires the use of both MRI and CT in combination. CT scanning typically demonstrates a well-defined, midline, soft-tissue, expansile mass arising from the clivus, often with lytic destruction of adjacent bony structures and minimal sclerosis (Fig. 17.1). High-resolution, thin-cut CT scans through the skull base allow for close evaluation of the extent of bony destruction. Three-dimensional reconstructions of volumetric data can be beneficial in assessing the extent of bony destruction. Tumors are usually isodense or hypointense to brain tissue and display varying degrees of contrast enhancement. Slight to moderate contrast enhancement is seen in all cases. Calcification is seen in 47–71% of chordomas and is thought to be due to sequestered bony fragments within the tumor instead of dystrophic calcification by the tumor. Solitary or multiple zones of low attenuation are often seen within the soft-tissue mass. These zones are thought to represent myxoid and gelatinous material seen on pathology. CT is also optimal for the evaluation of tumor extension into the retropharyngeal space and sphenoid and paranasal sinuses. Assessing soft-tissue extension within the posterior fossa is limited with CT scanning due to significant levels of bony artifact.

MRI is the technology of choice in chordoma for examining the extent of soft-tissue involvement, compression of vascular structures, and intradural extension of tumor. Chordomas appear iso- to hypointense to brain on T1-weighted images and hyperintense on T2-weighted images due to the high fluid content of the vacuolated cells (Figs. 17.1 and 17.2). Some tumors demonstrate multiple, scattered, small foci of very high signal on T1-weighted sequences. These areas are thought to correspond to small sites of hemorrhage and mucinous collections seen on pathologic examination. Most chordomas have heterogeneous signal intensity with lobulated regions of high signal intensity, separated by areas of low signal intensity. Gadolinium injection usually produces moderate to extensive heterogeneous contrast enhancement, although some tumors enhance homogeneously, and some tumors show no contrast enhancement. Postcontrast fat suppression sequences highlight the tumor inside the usually fatty clivus.

MR angiography and conventional catheter angiography may be used in combination with CT and MRI in cases with significant involvement of the vasculature. The vertebrobasilar and petrous internal carotid vascular systems are often displaced or encased by chordomas and are involved in up to 79% of cases. Knowledge of the vascular anatomy is often critical in treatment planning.

The differential diagnosis of tumors with this appearance includes other skull-base tumors that occur in this location. Meningiomas can often be differentiated from chordoma because they often have sclerotic bony changes and hyperostosis. Chondrosarcomas can mimic chordoma in both clinical and radiographic appearance. Chondrosarcomas are thought to be centered off-midline along the petrous apex, while chordomas are more often centered in the midline clivus. Despite this difference, pathological evaluation of tumor tissue is required to distinguish the two entities. Other tumors in the differential diagnosis are nasopharyngeal carcinomas, pituitary tumors, and metastatic tumors.

17.2.4 Staging and Classification

Synopsis. Chordomas and chondrosarcomas are classified pathologically. Three pathological subtypes have been identified: chordoma, chondroid chordoma, and chondrosarcoma. The difference between classic chordoma and chondrosarcoma is evident with pathology and immunohistochemical staining, but chondroid chordomas lie in a continuum between chordoma and chondrosarcoma and may be difficult to differentiate. The overall pathological appearance is taken into

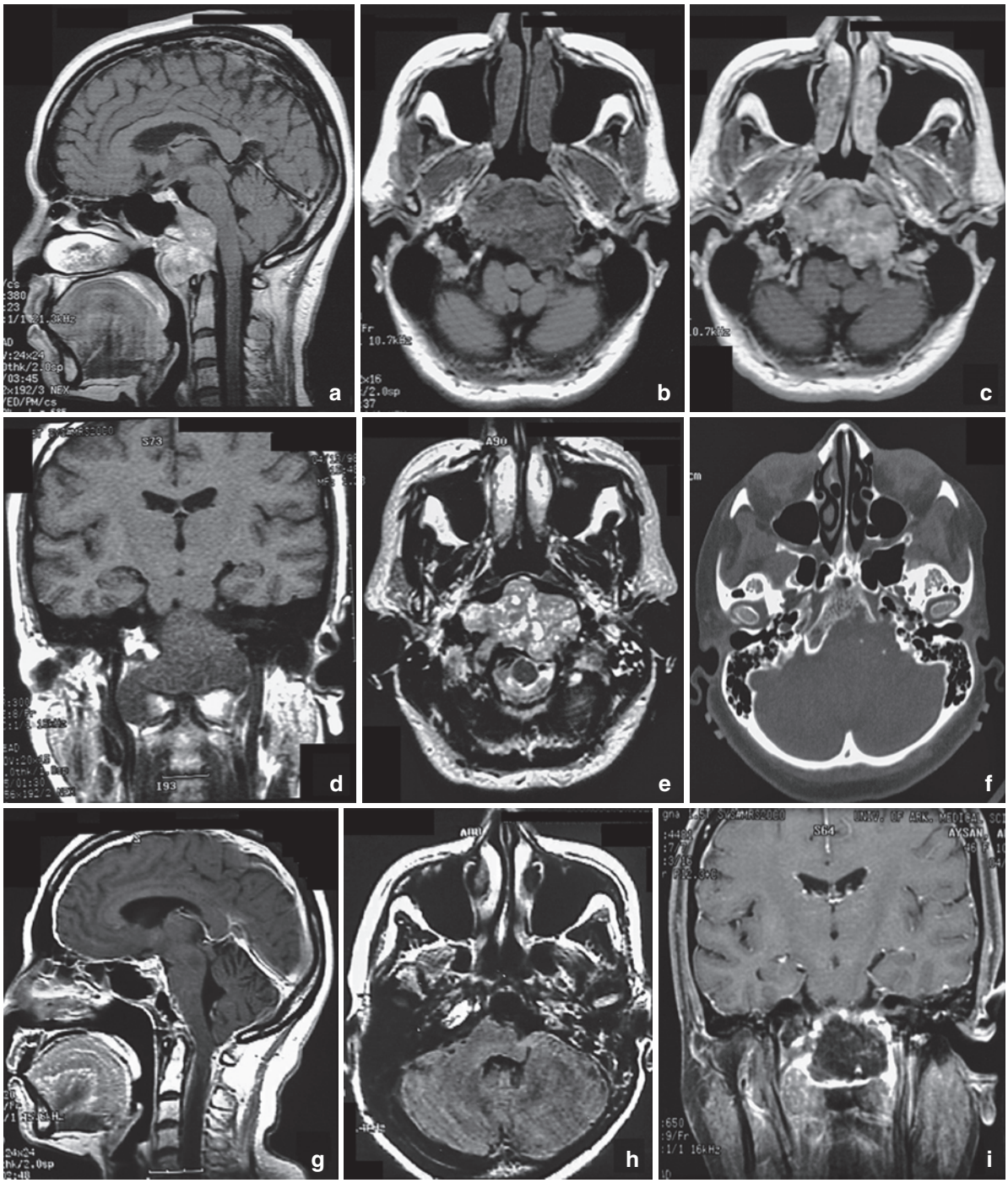

Fig. 17.1 (**a**–**i**) Imaging of chordoma. (**a**) Preoperative contrast-enhanced T1 sagittal image demonstrating tumor arising from the clivus with brain stem compression. Preoperative T1 axial image without (**b**) and with (**c**) contrast. (**e**) High T2 signal intrinsic within chordoma. (**f**) Preoperative CT demonstrating erosion of the bony skull base and calcium inclusions within the tumor. (**g**–**i**) Postoperative imaging in sagittal, coronal, and axial planes demonstrating resection of tumor

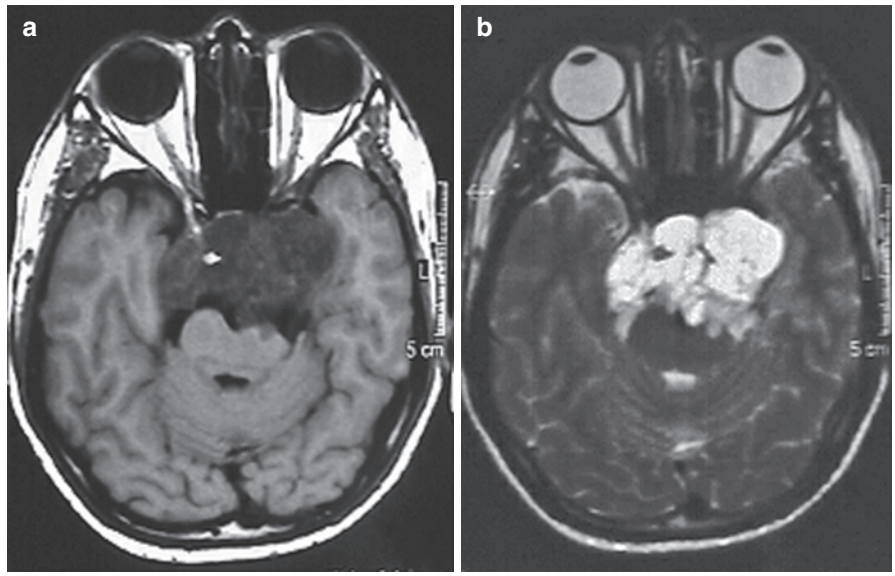

Fig. 17.2 (**a**, **b**) Imaging of chordoma. (**a**) Large midline chordoma with brain stem compression. (**b**) Typical bright T2 signal characteristic of chordoma

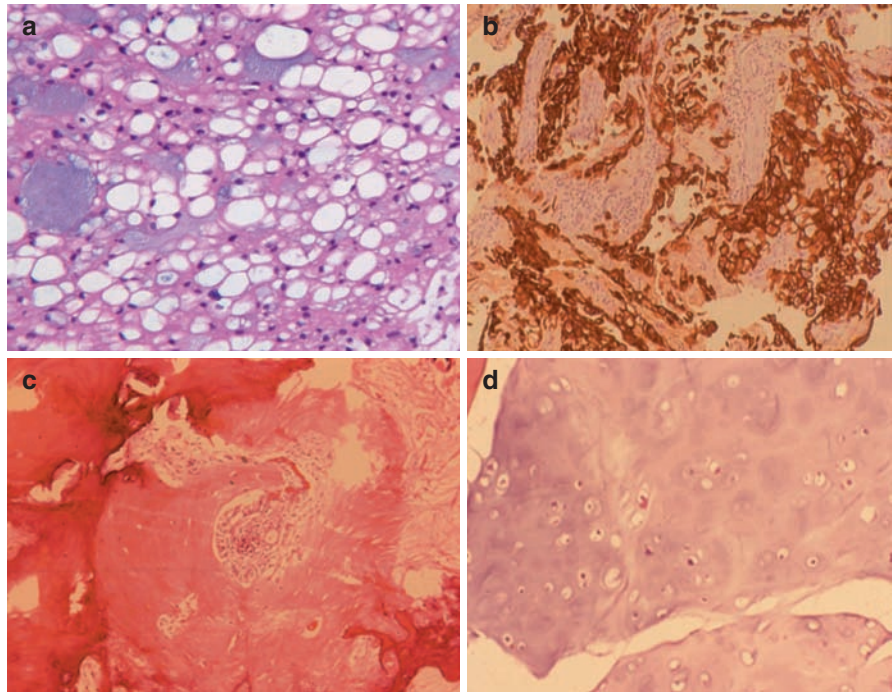

Fig. 17.3 (**a**–**d**) Pathology of chordoma and chondrosarcoma. (**a**) Pathology of classic chordoma with large physaliferous cells. (**b**) Cytokeratin immunohistochemistry demonstrating strong positive staining of chordoma specimen. (**c**) Pathology slide of chordoma demonstrating bony invasion by tumor. Note the rests of tumor cells deep within the bone. (**d**) Histology of classic chondrosarcoma

account in combination with immunohistochemistry to make this distinction. Chondrosarcomas are further subdivided into three groups based on pathological characteristics.

The pathological characteristics of chordoma (Fig. 17.3a) include containing fibrous strands that create lobulations and pseudoencapsulation. These lobules are found to contain either sheets of physaliferous cells or pools of mucin. Physaliferous cells contain varying amounts of cytoplasmic mucin, giving these cells their characteristic vacuolated appearance. The pools of mucin contain cords of eosinophilic syncytial cells.

Chondroid chordoma is a subtype of chordoma that contains foci of cartilaginous hyaline stroma within a chordoma background in varying proportions. This subtype may have similar pathological findings to chondrosarcoma and often requires immunohistochemistry for differentiation.

Classification of chondrosarcomas takes into account the predominant cellular type on pathology to differentiate between classic, mesenchymal, and dedifferentiated chondrosarcomas. Classic chondrosarcoma (Fig. 17.3d) is the most common type and is identified by the large, atypical chondrocytes within a hyaline cartilaginous matrix background. Classic chondrosarcomas have further been divided into grades I–III, with higher grades displaying increased mitotic rates, cellularity, and decreased chondroid matrix. The mesenchymal class of chondrosarcomas displays regions of undifferentiated mesenchymal cells and cartilage. Dedifferentiated sarcomas are more aggressive, with characteristics similar to anaplastic sarcomas.

Immunohistochemistry has been important to differentiate the three pathological subtypes. Due to their origin from notochordal remnants, most chordomas and chondroid chordomas stain positively for the epithelial markers cytokeratin (CK) (Fig. 17.3b) and epithelial membrane antigen (EMA). Chondrosarcomas lack these epithelial markers and will not stain positively, thus positive staining for CK and EMA confirms the diagnosis of chordoma or chondroid chordoma. However, lack of CK and EMA staining does not exclude a diagnosis of chordoma. Many chordomas will also stain positively with carcinoembryonic antigen (CEA), whereas chondrosarcomas will not. Within the continuum of chordoid and chondroid tumors containing aspects of both types of tumors, it has been suggested that all tumors positive for CK and EMA as well as those tumors with CK and EMA negative staining that display predominantly chordoid patterns should be classified as chondroid chordomas. Tumors with predominantly chondroid patterns without CK and EMA staining should be classified as chondrosarcomas.

17.2.5 Treatment

Synopsis. Two treatments have proven beneficial for chordomas, maximal surgical resection and high-dose radiation. The main challenge in the treatment of chordomas is local recurrence, thus a combination of radical resection and high-dose radiation therapy is required. Local recurrence is thought to be due to local bony invasion by tumor cells, with nests of tumor deeper within the skull-base bone than is seen at surgery (Fig. 17.3c). Due to their midline location in the bone of the skull base, surgical resection proves challenging. Even with radical surgical resection, chordomas tend to recur. The current treatment practices combine aggressive surgical resection and proton beam radiation.

17.2.5.1 Surgery

The advent of skull-base surgical techniques has allowed for the surgical exposure and radical resection of chordomas. These tumors are located in the midline skull base within the bone of the clivus, often with extensions into multiple different compartments of the cranium. Specifically, chordomas can extend into the sellar and parasellar spaces, sphenoid sinus, cavernous sinus, foramen magnum, prepontine cistern, posterior fossa, occipital condyle, infratemporal fossa, and retropharyngeal spaces. Due to this localization and extension, multiple different surgical approaches are required for the treatment of these tumors, and often multiple approaches are utilized within the same patient. Surgical treatment must be tailored for each case, specifically taking into account the areas of the skull base involved, overall health of the patient, and previous surgical resection.

Attempts at radical resection are crucial to the effective treatment of chordomas. Average survival with untreated chordoma is estimated at 28 months after onset of symptoms. After total or near total surgical resection, the overall survival rate at 5 years has been reported to be between 13% and 51%, and between 18% and 35% at 10 years. Recurrence rates range from 12% to 60% with a mean follow-up of 1.9–30 years [5]. Patients who have not had previous surgery have a higher chance with radical resection and better recurrence-free survival rates than patients who have undergone prior surgery [6].

Surgical approaches require the ability to access the skull base from multiple different strategies. The midline anterior skull-base approaches (transsphenoidal, extended transsphenoidal, and transmaxillary) are used for tumors in the clivus and for extensions into the nasopharynx, sella, parasellar regions, and sphenoid sinus. Lateral extension of the tumor along the petrous pyramid and cavernous sinus requires the

addition of lateral approaches (middle fossa, cranio-orbito-zygomatic). Tumor extension into the posterior fossa and occipital condyles requires transpetrosal and transcondylar approaches. Patients requiring multiple different approaches often benefit from staged resection.

These multiple surgical approaches are accompanied by potential complications. Due to the location of these tumors in the midline skull base, access is limited, and thus obtaining a watertight closure of the dura is a difficult task. Cerebrospinal fluid (CSF) leakage is the main complication associated with surgical treatment of chordomas, occurring in 8–30% of patients. Since access to these regions is often through the nose and mouth, meningitis is a potential problem in patients with CSF leak, occurring in 0–10% of these patients. Surgical complications also include transient and permanent cranial neuropathies, which occur in 0% to 80% of patients. Surgical mortality is reported between 0% and 8%. Patients who underwent previous surgical therapy are at higher risk of both surgical morbidity and mortality.

Care must be taken during surgical resection of chordomas due to the possibility of chordoma cells seeding and growing in distant sites [7]. Specifically, chordoma cells can seed the operative route in the nasal mucosa, bone, dura, and muscle distant from the primary tumor site, along the surgical access route. Also, tumor seeding has been reported in the abdominal fat harvest sites. Postoperative and follow-up imaging should examine the surgical route to assess for tumor seeding. The operative technique should be altered in patients with suspected chordoma. Specifically, the surgical route is coated with fibrin glue and large patties. The fat graft is harvested after changing gowns and gloves with a separate set of instruments, within a separate surgical field. The fat graft is placed into the resection bed after surgical patties have been removed from the surgical route. Closure takes place after changing surgical drapes and towels, and gowns and gloves.

17.2.5.2 Radiotherapy

Adjuvant radiotherapy has become a mainstay in the treatment of chordomas, although chordomas were once considered radioresistant tumors. The dose required to treat mesenchymal tissue tumors is in the range of 70–80 Gy, while the radiation tolerance of surrounding neural structures, including the brain stem, is 60 Gy. However, improving technology has allowed more conformal dosing of photon and proton radiation to the tumor beds. Intensity-modulated radiotherapy and three-dimensional conformal radiotherapy technologies have allowed the treatment of these tumors with fractionated photon beam therapy with higher accuracy and conformal dosing.

Radiosurgery with gamma-knife and LINAC-based systems is being used for patients with chordoma. Currently, there are insufficient published results using this technology, particularly in the long term.

Proton beam therapy has become the radiation treatment of choice for chordomas. Protons allow radiation delivery in highly conformal dose distributions without an exit dose. This also allows proton therapy to be used for irregular tumor boundaries.

Currently, there are two proton beam facilities in the USA, in Massachusetts and in California, and one in Orsay, France. With the use of proton beam therapy at doses of 65–83 cobalt gray equivalents (CGE), the 3- and 5-year local recurrence-free survival rates were between 94% and 95% for chondrosarcoma and 67% to 73% for chordoma. Five-year survival rates were 91–100% for chondrosarcoma and ~80% for chordoma [8, 9].

17.2.5.3 Chemotherapy

There are currently no reports of chemotherapy treatments that have proven effective in treating chordoma or chondrosarcoma. There have been a few reports with limited numbers of patients using experimental treatments for chordoma [10]. Use of chemotherapy may be considered in infants with chordoma who are too young for radiation therapy. This strategy is employed potentially to halt tumor growth until the child is old enough to tolerate radiation therapy.

17.2.6 Prognosis/Quality of Life

Untreated chordoma is associated with an average survival of 28 months after diagnosis. A combined surgical and radiation treatment regimen affords the patient the best chance at progression-free survival. Chondrosarcoma is associated with a significantly better prognosis than chordoma when treated with both modalities. Chondroid chordomas behave similarly to chordoma.

The extent of tumor resection and adjuvant radiation therapy are related to the prognosis. Extent of resection has been shown to affect outcome. Patients who have had a gross total resection of tumor have higher 5-year survival rates and recurrence-free rates than patients who underwent only partial resection. Chordoma patients can be divided into good-prognosis and poor-prognosis groups. The former includes patients who after surgical resection have either gross total resection or small residual tumor size and absence of tumor along critical dose-limiting neural structures, such as the brain stem and optic apparatus. Patients in the latter groups achieve only temporary slowing of tumor growth, even at higher radiation doses. These patients should be considered for aggressive surgical resection to improve the ability to deliver high-dose radiation.

Adjuvant radiation therapy, especially proton beam treatments, prolongs the survival and recurrence-free survival of patients.

Age is a controversial prognostic factor for adult patients, with studies showing conflicting results. Age less than 5 years is associated with a worse prognosis and with a more malignant pathology.

Cytogenetic studies on tumor tissues may show prognostic differences. There was no significant difference in karyotype between patients with chordoma and chondroid chordoma. Abnormal karyotype was seen more frequently in chordoma than chondrosarcoma. An abnormal karyotype was also associated with higher recurrence rates. Tumors with loss of the tumor suppression loci at 1q and 13q demonstrated more aggressive behavior.

17.2.7 Future Perspectives

Since chordoma is a rare disease, there has been limited treatment information in the form of large studies. With the emergence of proton beam therapy as the adjuvant treatment of choice, most of the patients are being concentrated at two centers allowing for such large trials. The surgical management of these tumors also requires improvement to increase the number of patients with gross total resection while limiting complications. Recent advances in surgery, including intraoperative monitoring of cranial nerves, and frameless stereotactic guidance have improved the surgical results. Further understanding and study of the biology of these tumors will also be required to improve future therapies.

17.3 Skull-Base Meningiomas

17.3.1 Epidemiology

Meningiomas occur frequently, constituting 20% or more of all intracranial tumors. Their incidence between community-based series and clinical series varies from 1 to 6 cases per 100,000 persons per year and on average is estimated to be around 2.6 cases per 100,000 persons per year [1]. Meningiomas are frequently located at the skull base, with 40% of meningiomas being in this location. The sphenoid ridge is the most commonly involved location at the skull base (Table 17.1). Other locations include the olfactory groove, planum sphenoidale, tuberculum sella, anterior clinoid, cavernous sinus, cerebellopontine angle, clivus and petroclival area, and foramen magnum.

Meningiomas occur more commonly in African-Americans than in white people. Several African studies show a significantly higher incidence of meningiomas among that population. This finding may be of importance from a genetic and molecular biologic perspective. The results of three large studies of intracranial neoplasms indicate a higher incidence of meningiomas in women. The ratio of male to female incidence ranges from 1:1.4 to 1:2.8. The incidence of intracranial meningiomas increases with age, with a peak incidence of 6/100,000 population in men between 60 and 69 years of age and 9.5/100,000 population in women in the 70–79 years age group. Meningiomas are rare in the pediatric population and account for 1–2% of brain tumors in this age group. When occurring in children, the majority of these tumors affect boys.

Several analytic epidemiologic studies have been performed to identify etiologic risk factors for intracranial meningiomas. They apply to meningiomas at the skull base and meningiomas in other locations. The studies with the strongest designs and most patients are those linking ionizing radiation to the development of

Table 17.1 Intracranial location of meningiomas

Falx/parasagittal	25%
Sphenoid wing	20%
Convexity	20%
Olfactory groove	10%
Posterior fossa/petrosal	10%
Suprasellar	10%
Others[a]	5%

[a] Optic sheath, clivus, foramen magnum, intraventricular, tentorial, cerebellopontine angle

meningiomas. Among the first were the studies of children treated for tinea capitis using low-dose radiation. In a cohort of 10,834 children treated with a dose of radiation estimated at 1.5 Gy, 19 patients developed meningiomas, for a relative risk of 9.5. The mean interval from radiation exposure to diagnosis was 20.7 years. Most of the tumors in this study were at the convexity where the dose of radiation was 60% greater than at the skull base [11]. Several other studies demonstrated a dose-response relationship between ionizing radiation to the head and the occurrence of meningiomas. The latency of meningioma occurrence following low-dose radiation appears to be considerably longer than that for meningiomas following higher doses of radiation.

Another source of low-dose radiation that has been linked to the development of meningiomas is exposure to dental radiographic examination. The full mouth series has been performed since the introduction of dental radiography and involves taking 10–20 individual radiographs. The skin exposure with various machines varies from 1 to 3 Gy. Several studies have examined the risk of meningioma with dental radiographs. Two studies did not find an association between meningioma and dental amalgam fillings. Two other studies found that the likelihood that the meningioma was at the skull base increased with increasing numbers of full mouth radiographs. This was the region of the cranium that was presumed to have received the greatest radiation exposure. From the previous studies and discussion, it is clear that ionizing radiation may be a cause of intracranial meningioma. Less clear are the most important sources of radiation and how many meningiomas can be attributed to ionizing radiation. Three criteria have to be fulfilled to be considered a radiation-induced tumor: (1) it has to occur in the irradiated field; (2) it has to appear following an appropriate, usually long, period of latency following irradiation; (3) it has to differ from any preexisting neoplasm.

Radiation-induced meningiomas have been shown to behave differently than non-radiation-induced meningiomas [12]. The age at presentation with radiation-induced meningiomas appears to be related to the dose of radiation received, and on average is at a younger age. The latency period from exposure to the diagnosis of meningioma also appears to be dose related. These tumors behave more aggressively and have a 100% recurrence rate (Fig. 17.4). On pathological examination, these tumors are higher grade, stain for a higher proliferative index, and have multiple, complex, cytogenetic alterations, including chromosomes 1p and 6q.

Other factors that have been clearly linked to the occurrence of intracranial meningiomas are genetic. It has been recognized for many years that meningiomas occur with a higher frequency in patients with neurofibromatosis type 2 as well as in certain familial aggregates. It is now accepted that meningiomas arise when there is loss of NF-2 or other tumor suppressor genes in combination with the activation of proto-oncogenes. Most meningiomas with deletions on chromosome 22 map to 22q12, which is the same locus responsible for producing the NF-2 tumor suppressor gene. The NF-2 gene locus is not involved in familial meningiomas; however; rather a different tumor suppressor gene is speculated to be responsible.

Sex hormones and their receptors seem to play an important role in the development of meningiomas as suggested by epidemiologic features of this tumor: It is two to four times more common in women; it grows more rapidly during pregnancy and during the luteal phase of the menstrual cycle, and it has been linked with breast carcinoma. It is also well established that estrogen and progesterone receptors are present in meningiomas. Most estrogen receptors identified in meningiomas are type II receptors, which have a lower affinity and specificity for estrogen than the type I receptor classically found in breast cancers. It is currently believed that estrogen binds in less than 20% of meningiomas. Progesterone receptors are much more common, occurring in 50–100% of tumors tested. The biologic significance of these receptors remains uncertain, with their presence correlating with less aggressive tumors.

Although it is known that certain viruses will produce central nervous system tumors when inoculated in laboratory animals, their actual role if any in the development of meningiomas is still undefined.

Head trauma has initially been suggested by Cushing to play a role in the development of meningiomas. Several recent studies have failed to show an increase in the incidence of meningiomas in cohorts of patients with head injuries.

17.3.2 Symptoms and Clinical Signs

There is no single symptom or sign that can identify which patients harbor an intracranial meningioma. Indeed, some tumors are identified fortuitously in patients who have no symptoms or signs of intracranial

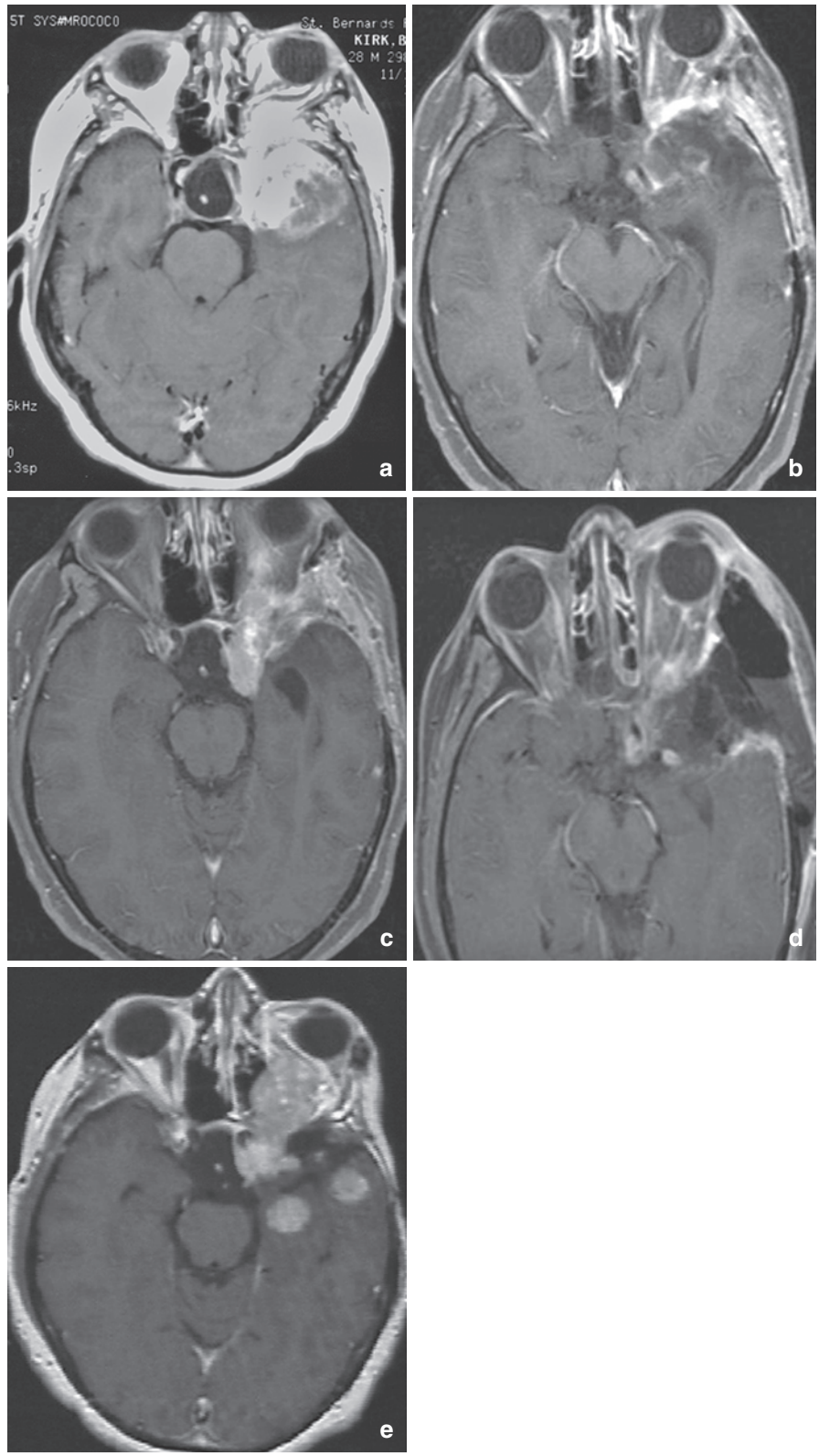

Fig. 17.4 (**a**–**e**) Radiation-induced meningioma demonstrating multiple recurrences. (**a**) Meningioma imaging at diagnosis. (**b**) MRI demonstrating gross total resection (**c**) Tumor recurrence 1 year later. (**d**) MRI after repeat resection. (**e**) Repeat recurrence after another year

disease. Other patients have a variety of presenting features, including headaches, paresis, seizures, personality changes, confusion, and visual impairment. In population-based studies, headaches and paresis were found to be the most common symptom and sign. An increased incidence of abnormal physical findings was found in patients with malignant meningiomas. Patients with skull-based meningiomas may have additional signs and symptoms depending on where the lesion is located. Olfactory groove meningiomas present most commonly with slow onset of changes in mental status, particularly in mood, insight, judgment, and motivation. Late in their course, the patients may have headache, reduced vision, and seizures. Rarely do patients complain of loss of sense of smell, and only 3 of 29 cases reported by Cushing and Eisenhardt had this as their primary symptom. The Foster Kennedy syndrome of anosmia, unilateral optic atrophy, and contralateral papilledema is, in fact, uncommon. Most patients with tuberculum sellae meningiomas present with an insidious onset of progressive visual loss, usually a chiasma syndrome with ipsilateral optic atrophy and incongruous bitemporal hemianopsia. Panhypopituitarism can happen, but is rare.

Clinoidal meningiomas most often present with monocular visual loss. Cavernous sinus meningiomas may result in proptosis, diplopia, facial hypoesthesias, or aberrant oculomotor regeneration. Meckel's cave meningiomas may present with a petrous apex syndrome consisting of facial numbness or pain and diplopia secondary to a sixth nerve palsy. Petroclival meningiomas usually present with signs and symptoms of brain stem compression as well as facial numbness, diplopia, hearing loss, and facial weakness. Foramen magnum tumors are usually associated with nuchal and suboccipital pain as well as a stepwise, appendicular sensory and motor deficit.

17.3.3 Diagnostics

CT scanning can detect the majority of meningiomas and can in most instances determine their extent. CT at wide window and level settings optimally identifies bone involvement, either hyperostosis or bone lysis. This capability is especially used for skull-base tumors because it aids in the specificity of diagnosis and in planning the extent of surgical resection required to rid the patient of the meningioma. On nonenhanced CT scans, the typical meningioma is isodense to slightly hyperdense to brain and of homogenous density, although calcification may be present and may range from tiny punctate areas to dense calcification of the entire lesion. Edema, which appears as low density on CT, is often evident to various degrees, the extent of which has few predictable correlates. Bone changes, which are best imaged with CT, occur in approximately 25% of meningiomas and vary from hyperostotic to destructive lesions (Fig. 17.5). Intravenous contrast usually shows intense, homogeneous enhancement, and morphologic features, such as sharp demarcation and a broad base against the bone or free dural margins, are easily seen. On CT, approximately 15% of benign meningiomas have an unusual appearance. Areas of hyperdensity, hypodensity, and nonuniform enhancement may be seen and may represent hemorrhage, cystic degeneration, or necrosis, respectively. Aggressive meningiomas may at times be distinguished by preoperative imaging, findings of indistinct or irregular margins, or mushroom-like projections from the main tumor mass.

High-resolution CT, MRI, and MR angiography have to a large extent supplanted angiography, which once played a preeminent role in the diagnosis of intracranial meningiomas. Indeed, the determination of venous sinus patency, historically the purview of the angiogram, can be well visualized on MRA, thus eliminating this indication for angiography. Some suggest that angiography can still be performed routinely for old meningiomas to help identify any pial vascular supply to the tumor. However, from a practical point of view, this information is unlikely to alter the management of these patients significantly. Angiography remains a vital means by which the feasibility and safety of preoperative embolization can be determined. Furthermore, pertinent collateral circulation can be identified. To date, only selected angiography can resolve the generally small communicating branches present between the internal carotid arteries and vertebral arteries and the external carotid arteries, the presence of which to a large extent determines the safety of embolization of intracranial meningiomas. Angiography helps also in the preoperative evaluation of the venous complex of the vein of Labbe, especially when the petrosal approach is indicated or when the tentorium needs to be cut. This venous anatomy can sometimes be evaluated with an MRV, but angiography remains the best study to do so.

The high-field MRI characteristics of meningiomas are relatively consistent. On T1-weighted images,

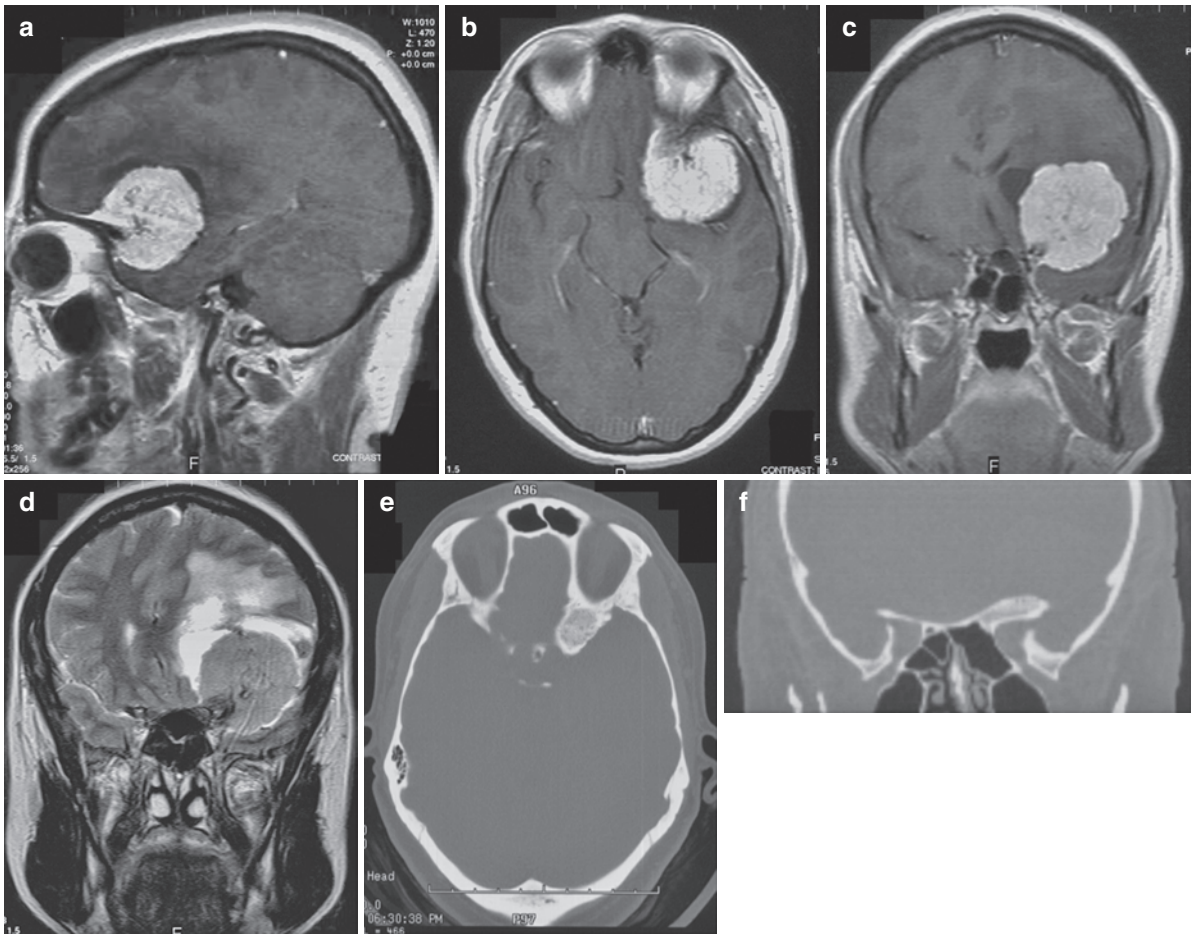

Fig. 17.5 (**a**–**f**) Imaging of meningioma. (**a**–**c**) Sagittal T1 imaging of basal clinoidal meningioma demonstrating bright, homogeneous contrast enhancement and the dural tail. (**d**) T2 imaging of meningioma demonstrating significant vasogenic edema with surrounding brain. (**e**, **f**) Preoperative axial and coronal CT scans demonstrating hyperostosis of the underlying skull base at the sphenoid wing and clinoid

60–90% of meningiomas are isointense, whereas 10–30% are mildly hypointense compared with gray matter. T2-weighted imaging reveals that 30–45% of meningiomas are of increased signal intensity, whereas approximately 50% are isointense to gray matter. MRI better assesses vascular distortion or encasement and tumor vascularity than CT scanning. Flow voids produced by flowing blood identify the vasculature local to the tumor. The ability to decide on an extra-axial localization of a neoplasm is also heightened on MRI. Typical marginating characteristics include displacement of blood vessels, the presence of CSF clefts between the tumor and the brain, and inward displacement of the gray/white junction. The ability of T2-weighted images to subtype meningiomas is controversial, with some studies showing 75–90% accuracy and others finding no correlation. The amount of cerebral edema present in association with meningioma may also help to subtype some of these tumors. However, making such distinctions is of little clinical value in the treatment of meningiomas. High signal intensity on T2-weighted images has also been correlated with microscopic hypervascularity and soft tumor consistency. It may also help to predict the ease with which the tumor can be resected from the surrounding brain. Contrast-enhanced MRI provides the highest level of detection of meningiomas. Most meningiomas enhance intensely and homogeneously with intravenous paramagnetic contrast material (Fig. 17.6), and in approximately 10% of cases, small additional meningiomas are encountered that are

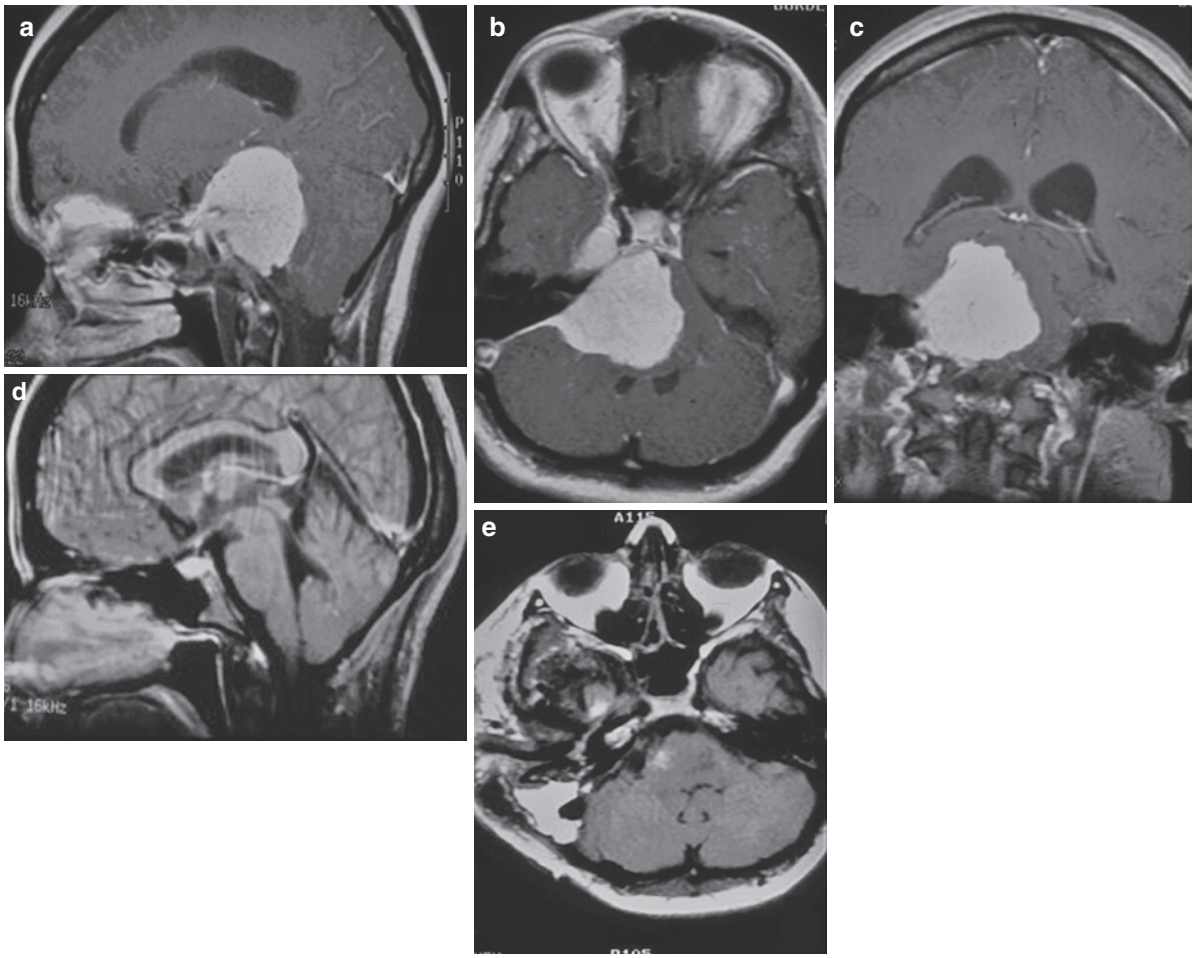

Fig. 17.6 (**a**–**e**) Imaging of meningioma. (**a**–**c**) Preoperative T1, postcontrast images of large petroclival meningioma demonstrating bright homogeneous contrast enhancement and dural tail. (**d**, **e**) Postoperative images in the same patient after surgical resection using petrosal skull-base approach demonstrating complete resection. Note fat within area of mastoid resection used in the surgical approach

missed on unenhanced MR images. Likewise, contrast enhancement of the dura extending away from the margins of the mass is typical of meningioma, although it can be seen with other dural-based lesions (Figs. 17.5 and 17.6). This dural tail can represent tumor extension, and its resection is important to lessen the risk of recurrence. Postoperative enhanced MRI has also been found to be more sensitive and specific in the detection of residual or recurrent meningioma (Fig. 17.6). Thick and nodular enhancement has a high correlation with recurrent or residual neoplasm.

Meningiomas express somatostatin receptors, allowing the use of octreotide scintigraphy in their imaging (Fig. 17.7). All meningiomas show an intensely positive scan, while other skull-base tumors are negative. This technology may be used to differentiate between meningiomas and other skull-base tumors, or may be used in the follow-up of patients to assess for recurrence [13].

17.3.4 Staging and Classification

Most meningiomas are benign and can be graded as WHO grade I. However, certain histological subtypes are associated with a less favorable clinical outcome and correspond to WHO grades II and III [14] (Table 17.2). Grade II meningiomas include chordoid meningiomas, clear-cell meningiomas, and atypical meningiomas. Chordoid meningiomas contain regions that

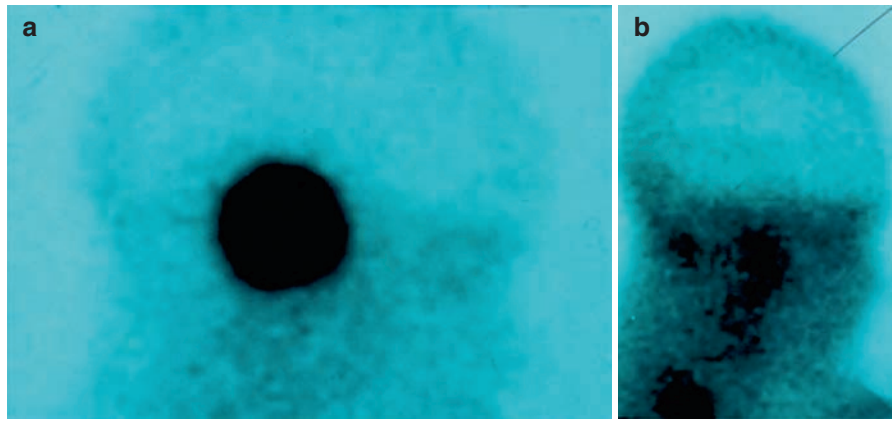

Fig. 17.7 (**a**, **b**) Octreotide scintigraphy of meningioma. (**a**) Preoperative octreotide scan of a patient with a skull-base meningioma. The tumor demonstrates bright octreotide uptake. (**b**) Postoperative scan in the same patient demonstrating lack of octreotide uptake

Table 17.2 Revised World Heath Organization grading of meningiomas [14]

Meningiomas with low risk of recurrence and aggressive growth:
Grade I
Meningothelial
Fibrous/fibroblastic
Transitional (mixed)
Psammomatous
Angiomatous
Microcystic
Secretory
Lymphoplasmocyte rich
Metaplastic
Meningiomas with greater likelihood of recurrence and/or aggressive behavior:
Grade II
Atypical
Clear cell
Chordoid
Grade III
Rhabdoid
Papillary
Anaplastic
Meningioma of any subtype with high proliferation index and/or brain
Invasion

Table 17.3 Mayo Clinic criteria for atypical and anaplastic meningiomas [15, 16]

Criteria for atypical meningiomas:
High mitotic index: ≥4 mitoses/10 HPF (≥2.5/mm^2)
or presence of three of the following four features:
Sheeting
Prominent nucleoli
Small-cell formation
Hypercellularity (≥53 nuclei/HPF; ≥118/mm^2)
Or
Brain invasion
Criteria for anaplastic meningiomas:
Excessive mitotic activity: ≥20 mitotic figures/10 HPF (≥12.5/mm^2)
Or
Focal or diffuse loss of meningothelial differentiation resulting in carcinoma-, sarcoma-, or melanoma-like appearance

are histologically similar to chordoma with trabeculae of eosinophilic vacuolated cells in a myxoid background. They are interspersed with typical regions of meningioma. Clear-cell meningiomas are often patternless meningiomas composed of polyclonal cells with a clear glycogen-rich cytoplasm. A meningioma with increased mitotic activity or three or more of the following features (increased cellularity, small cells with high nuclear-cytoplasm ratio, prominent nucleoli, uninterrupted patternless or sheet-like growth, and focus of spontaneous necrosis) is considered atypical [15, 16] (Table 17.3). Papillary meningiomas as well as rhabdoid and anaplastic meningiomas are considered WHO grade III. A papillary meningioma is a rare meningioma, a variant defined by the presence of a very vascular pseudo-papillary pattern in at least part of the tumor. They tend to occur in children. A rhabdoid meningioma is also an uncommon tumor containing patches or extensive sheets of rhabdoid cells, which are rounded tumor cells with eccentric nucleoli. Finally, a meningioma is considered anaplastic if it has histologic features of frank malignancy far in excess of the abnormalities present in atypical meningiomas [16].

Malignant progression of benign meningiomas has also been described [17]. There has been documented progression from benign to atypical and anaplastic

histologic grades based on pathological evaluation of tumors at original presentation and at recurrence. Along with progression of histological grading, there has also been an increase in the proliferative indices as the tumor becomes more malignant. These tumors are associated with complex cytogenetic abnormalities, with deletions at chromosomes 22, 1p, and 14q. Interestingly, these complex chromosomal changes are present at the time the tumors are benign. This indicates that tumors with complex genetic alterations are at risk of recurrence and malignant progression [17].

17.3.5 Treatment

17.3.5.1 Meningioma Surgery

Harvey Cushing described surgery for meningiomas in 1938: "Few procedures in surgery may be more immediately formidable than an attack upon a large tumor [meningioma] and that the ultimate prognosis hinges more on the surgeon's wide experience with the problem in all its many aspects than is true of almost any other operation that can be named" [18]. This description still holds true over 60 years later.

Positioning of the patient should be done in a fashion that maximizes the patient's safety, the accessibility of the tumor, the allowance for unimpeded venous drainage, the beneficial effects of gravity, and the surgeon's comfort. Most patients with either supra- or infratentorial meningiomas may be placed in the supine position. Monitoring for air embolism, which should be used with any position that involves placing the head above the heart level, is particularly important during meningioma surgery since many tumors are closely related to the venous sinuses and their large tributaries. As well as taking advantage of the effects of gravity, several methods are employed to minimize brain retraction, among which is spinal drainage. However, contraindications, such as large tumors or obstructive hydrocephalus, should be considered. Hyperventilation to a PCO2 of 25–30 contributes to the degree of brain relaxation. The best means of reducing brain retraction, however, is to eliminate the need to do so by using one of the basal approaches. Since these approaches utilize orbital and zygomatic osteotomies and increase removal of the bony skull base, they allow a low, flat route to basally located tumors. Scalp flaps, which should be wide based to allow for a rich blood supply and designed to facilitate any subsequent reoperation, should be linear, gently curvilinear, or bicoronal incisions rather than horseshoe flaps. In the vast majority of first operations for meningiomas, a layer of arachnoid separates the tumor from the brain parenchyma, cranial nerves, and blood vessels. When it does, the chances of neural and/or vascular injury can be greatly reduced by defining and staying within the surgical plane. One maneuver that facilitates the definition of this arachnoid border is extensive debulking of the tumor, thus allowing the tumor capsule to collapse inward. The method used to debulk the tumor, which may be suction, coagulation, sharp excision, or use of the ultrasonic aspirator or the surgical laser, depends on the tumor consistency, vascularity, and location. Once the mass of the meningioma is resected, careful attention must be given to removing the involved dura and bone. The extent of bone that must be removed can be determined by inspection of the preoperative CT scan's bone windows. All of the hyperostotic bone should be considered contaminated by neoplastic cells. In fact, areas of hyperostosis resected at the time of surgery show tumor invasion histologically in most patients [19]. The fear of entering the mastoid air cells or paranasal sinuses is not cause for failing to remove this diseased bone. A wide margin of dura should be resected, and the defect should be repaired with pericranium, temporalis fascia, or fascia lata.

Cushing and Eisenhardt established a landmark particularization of meningiomas, and since that time, the common practice has been to classify meningiomas by their site of origin [18]. This has been helpful not only in planning the surgical approach, but also in understanding the relationship of the tumor to the surrounding brain parenchyma, neurovascular structures, and arachnoid cisterns. When the site of origin of the meningioma is determined, its pattern of growth in relation to the surrounding critical structures and the number of arachnoid layers separating it from them is better understood. Using those layers of arachnoid separating the tumor from the adjacent elements is the essence of safe surgical resection of meningiomas.

Meningiomas of the Anterior Cranial Base: Tuberculum Sellae Meningiomas. Small tuberculum sellae meningiomas are usually resected through the unilateral supraorbital approach. Bigger lesions in this location, as well as olfactory groove meningiomas, are resected through the bilateral supraorbital approach. For both approaches, the patient is placed supine and

the trunk elevated 20°, the head moderately hyperextended and fixed in a Mayfield headrest to allow the frontal lobes to fall backward. The head is kept straight to facilitate orientation. The scalp incision is started 1 cm anterior to the tragus and continued behind the hairline to the level of the superior temporal line on the opposite side. In this manner, the superficial temporal artery course is posterior to the incision, while the branches of the facial nerve are anterior. The scalp behind the incision is elevated and freed from the pericranium, leaving the thick areolar tissue with the pericranium. A large pericranial flap base on the supraorbital and frontal vessels is then incised as far posteriorly as possible, dissected forward, and reflected over the scalp flap. Both layers of the temporalis fascia are incised posterior to and along the course of the upper branches of the facial nerve until muscle fibers are seen. The deep fascia, the fat pad, and the superficial fascia are then retracted anteriorly. The upper portion of the temporal muscle is detached from its insertion anteriorly and is retracted posteriorly, exposing the junction of the zygomatic, sphenoidal, and frontal bones. The bone flap used depends on the size and location of the tumor. The flap can be either unilateral supraorbital for small tuberculum sellae meningiomas or bifrontal supraorbital for bigger tuberculum sellae meningiomas and olfactory groove meningiomas. In adults, the midline hole will invariably pass through the anterior and posterior walls of the frontal sinus. The mucosa is exenterated after the bone flap is removed. The posterior wall of the sinus is removed, and the sinus is packed with a small piece of temporal muscle. After the bone flap is removed, the dura is tacked up and opened under the microscope. Once the bifrontal approach is used, the sagittal sinus is divided between two silk sutures, and the falx is cut at its lowest limit. Elevation of the frontal lobe should be minimal. The olfactory nerve is located and preserved by dissecting it for some distance from the base of the frontal lobe. Tumor feeders are intercepted early; they are coagulated and severed on the basal aspect of the tumor. Devascularization is restricted to midline to avoid injury to the optic nerve on either side. Midline orientation is maintained by observing the falx position. The tumor is debulked with suction, ultrasonic aspirator, or a bipolar coagulator and microscissors. Once the dissection approaches the neurovascular structures, only bipolar cautery and microdissection should be used. After the tumor is debulked, the optic nerves, which are displaced laterally, are identified. The tumor is slowly stripped from the flattened or engulfed nerve. Despite apparent encasement of or severe adherence to the nerve, a plane of dissection can be obtained under high magnification. To preserve any remaining vision, dissection of the optic nerve and its blood supply must be meticulous. Dissection may need to begin at the chiasm so that the surgeon can locate and dissect an obscured optic nerve on the opposite side. Arterial structures should be preserved through the same method of sharp microdissection into an arachnoidal plane. The carotid artery is dissected free from the tumor with an array of microinstruments, including bipolar forceps, microdissectors, and scissors. Carotid dissection continues to free the ophthalmic artery, the posterior communicating artery, the anterior thalamic perforators, and the choroidal artery. Further dissection of the tumor progresses to the bifurcation of the internal carotid artery and into the Sylvian fissure. Dissection is then continued to free the middle and anterior cerebral arteries. In most cases, the tumor has simply displaced each vessel and their perforators, and rarely actually engulfs them. The A1 segments in particular are usually severely stretched or adherent and tend to tear. Should this occur, temporary clips should be applied distal and proximal to the bleeding point and the arterial wall sutured with fine 8.0 Prolene sutures. Although arterial twigs of the anterior cerebral arteries may supply the tumor, the surgeon must first be certain that these vessels are, indeed, tumor feeders and not hypothalamic perforators or the optic tract blood supply. Thus, each arterial branch should be dissected and followed to ascertain its eventual course. Particular precision is needed to spare the artery of Heubner and the vital branches to the striatum. As dissection continues, both A1 arteries and the anterior communicating artery are freed from the tumor. The membrane of Liliequist is intact, making tumor removal from the posteriorly displaced basilar artery easy. The pituitary stalk can be recognized by its distinctive color and vascular network. A tumor extending backward under the hypothalamus usually displaces the pituitary stalk backward and to one side. Some tumors actually engulf the pituitary stalk and require meticulous and tedious dissection. The blood supply to the pituitary gland should be preserved. The tumor impinging on the hypothalamus can be removed gently if the surgeon maintains a plane of cleavage. Excessive downward retraction of the tumor, however, should be avoided. The arachnoid membrane of Liliequist provides an excellent plane of dissection for tumor removal. Often this membrane comes away with the tumor, leaving the rostral pons, midbrain, oculomotor nerves, and

basilar artery and its branches in full view. When the tumor extends into the cavernous sinus or optic canal, the anterior clinoid process, the roof of the optic canal, and the roof of the superior orbital fissure are drilled away with the diamond bit of the high-speed air drill. The dura is then opened along the optic nerve. Tumor tissue around the optic nerve is removed with bipolar and microdissectors, and the surgeon must pay particular attention to preserving the hypothalamic and central retinal arteries. This bony drilling exposes the superior aspect of the cavernous sinus, and the internal carotid artery emerges through the superior wall and is surrounded and firmly anchored to the dura by a ring. Beginning at this emergence, an incision is made in the exposed dura and extended posteriorly toward the posterior clinoid process. The internal carotid artery is then followed in retrograde fashion into the cavernous sinus where it is dissected. In the cavernous sinus space, the tumor is dissected with bipolar coagulation and microdissectors. Venous hemorrhage is controlled with surgical paddies. After the tumor has been removed, its dural attachment should be resected or coagulated. Involved bone should be removed with a diamond bit of a high-speed air drill. Any opening into a paranasal sinus requires thorough repair of the dural defect. If the sphenoid sinus was entered, its mucosa is exenterated, and the sinus is packed with fat taken from the patient's thigh. A large piece of fascia lata is laid intradurally and secured with sutures along the lesser sphenoid wing. The graft is then spread to cover the frontal fossa and then sutured to the frontal dura. The preserved pericranial flap in the frontal region is turned over the frontal sinus and extended over any defect in the floor of the frontal fossa. Titanium microplates are used here to reattach the bone flap to the cranial vault. The temporal muscle is sutured to the fascia at the lateral orbital rim, and the skin is closed in two layers.

Meningiomas of the Middle Cranial Base. Meningiomas of the middle cranial base involve the sellar and parasellar area. The most frequent are meningiomas of the sphenoid wing, but as mentioned earlier, lateral and middle sphenoid wing meningiomas will not be discussed as skull-base meningiomas since extensive removal of the sphenoid wing extradurally transforms them into convexity meningiomas.

Clinoidal Meningiomas. Clinoidal meningiomas are of three types [20] (Fig. 17.5). Type I originates from the inferior aspect of the anterior clinoid process, which is proximal to the carotid cistern. Thus, the tumor will engulf the carotid artery adhering directly to that adventitia without an interfacing arachnoidal membrane. As the tumor grows, this direct attachment of the vessel wall advances to the carotid bifurcation and along the middle cerebral artery, pushing the arachnoid membrane ahead of it. This anatomic arrangement accounts for the inability of the surgeon to dissect the tumor from the carotid artery and the middle cerebral branches. Type II clinoidal meningiomas originate from the superior or lateral aspect of the anterior clinoid process above the segment of the carotid artery which has already been invested in the arachnoid of the carotid cistern. This is why these tumors are separated from the intracerebral vessels by an arachnoid membrane. This plane allows dissection of the tumor from the vessels even though they may be totally engulfed and narrowed. In type I and type II clinoidal meningiomas, the optic system is separated from the tumor by an arachnoid membrane, making microsurgical dissection of the tumor from these structures possible. Type III clinoidal meningiomas originate at the optic foramen medially to the anterior clinoid. They usually extend into the optic canal and cause visual symptoms early in tumor progression. The arachnoidal membrane investing the carotid artery separates this type of tumor from the vascular structures and makes dissection feasible. However, because these tumors are proximal to the chiasmatic cistern, there may be no arachnoid layer between the optic nerve and the tumor.

Cavernous Sinus Meningiomas. The second type of parasellar meningioma is meningiomas of the cavernous sinus. They are usually of two general types: those that originate in and may be confined to the cavernous sinus and those that invade the cavernous sinus but originate in an adjacent area. Meningiomas originating from the cavernous sinus and confined to it present with extraocular movement disorders and facial paresthesias. Their management is controversial, with options including surgery, radiosurgery, or observation alone.

Meckel's Cave Meningiomas. The third type of parasellar meningiomas is Meckel's cave meningiomas. They usually originate within the cave itself and are rarely confined to it. Patients with these kinds of tumors usually present with facial pain and diplopia. These meningiomas may grow and extend anteriorly into the middle fossa and the cavernous sinus and proceed into the upper clivus and petroclival area. If the extension goes in both directions, it becomes impossible to differentiate these tumors from sphenopetroclival meningiomas.

17.3.5.2 Surgery for Clinoidal and Cavernous Sinus Meningiomas

Clinoidal meningiomas and cavernous sinus meningiomas are best approached through the cranial orbitozygomatic route. The skin incision originates 1 cm in front of the tragus, going behind the hairline up to the superior temporal line on the contralateral side. The cutaneous flap is elevated while preserving the pericranium and the thick areolar tissue. As a subfacial dissection of the temporal muscle is performed to preserve the branches of the facial nerve, an osteotomy of the zygoma is performed using an oscillating saw, and the bone flap is elevated in one piece containing the orbital rim. The orbital roof and the lateral wall of the orbit are then resected in one piece for later reconstruction. The rest of the sphenoid wing is resected, and the anterior clinoid is then drilled using a diamond bit under microscopic magnification and abundant irrigation to avoid thermal injury to the optic nerve. The dura is then opened and the Sylvian fissure exposed and opened widely, identifying the branches of the middle cerebral artery and following it proximally to the carotid bifurcation that is usually either pushed laterally and superiorly by the tumor or engulfed by it in cases of clinoidal meningiomas. The tumor is then debulked using the cavitron ultrasonic aspirator, microscissors and instruments, and suction. The optic apparatus is then identified and preserved, and the optic sheath of the optic nerve is opened and the tumor followed into the optic canal. The carotid rings are opened proximally and distally to permit mobilization of the carotid artery. For tumors involving the cavernous sinus, entering into this area may be either through the medial triangles or through the lateral triangles. Dissection of the tumor progresses in a stepwise fashion beginning by opening the optic nerve sheath longitudinally along the length of the optic canal. The distal dural ring is opened next with the opening extending posteriorly to the ocular motor trigone and thereby also freeing the proximal dural ring and allowing a wide entry into the anterior and superior cavernous sinus space. The carotid artery can be mobilized laterally by releasing it from its proximal and distal dural rings, which then allows entry to the medial cavernous sinus space. Lateral entry into the cavernous sinus begins by an incision beneath the projected course of the third nerve, allowing elevation of the outer dural layer of the lateral wall of the cavernous sinus that is peeled away. The internal carotid artery can be located by dissection between the third and fourth nerves and the first division of the trigeminal nerve; this is Parkinson's triangle. The course of the sixth nerve, which runs lateral to the internal carotid artery and is usually directly opposed to it, is usually parallel but deep to V1. The tumor is removed from the cavernous sinus space using suction bipolar coagulation and microdissection. A plane of cleavage along the carotid artery can usually be developed. Venous bleeding is typically not a problem when the tumor fills the sinus. It may occur as the venous plexus is decompressed during tumor removal. In that event, hemostasis can be obtained by packing the cavernous sinus space with oxidized cellulose or another similar hemostatic agent. In our series [21], total removal of the cavernous sinus meningiomas was possible in 76% of the patients. The major surgical morbidity and mortality rates were 4.8% and 2.4%, respectively. Preoperative cranial nerve deficits improved in 14%, remained unchanged in 80%, and permanently worsened in 6%. Seven patients experienced ten new cranial nerve deficits. Meckel's cave meningiomas are best approached through an extended middle fossa craniotomy with an osteotomy of the zygoma. After performing a resection of the petrous apex, most of the dissection is performed extradurally until Meckel's cave is exposed and the posterior part of the cavernous sinus is entered. The tumor in the posterior part of the cavernous sinus is resected using bipolar coagulation, suction, and microdissection. These patients will usually experience some facial numbness postoperatively, which is temporary in nature.

Meningiomas of the Posterior Cranial Base. The posterior cranial fossa can harbor a diversified group of meningiomas. Among them are clival, petroclival, sphenopetroclival, jugular foramen, and foramen magnum meningiomas.

Clival/Petroclival Meningiomas. Clival meningiomas originating from the mid-clivus are rare. Typically, they totally encase the basilar artery and its perforators, making them most formidable to expose and dissect. Petroclival meningiomas are, by definition, tumors that originate in the upper two-thirds of the clivus at the petroclival junction medial to the fifth nerve (Fig. 17.6). They often displace the brain stem and the basilar artery to the opposite side. Sphenopetroclival meningiomas are the most extensive of these lesions. They invade the posterior cavernous sinus and grow into the middle and posterior fossa. The bony clivus and the petrous apex are involved, and the sphenoid sinus is invaded. They frequently require an extended perusal approach or a combination of the petrosal and

cranio-orbital zygomatic approaches. Jugular foramen meningiomas are rare. They extend intracranially and extracranially along the lower cranial nerves. They mimic the clinical presentation of glomus jugulare tumors in every aspect. The major morbidity of these lesions stems from paralysis of the lower cranial nerves. Similar to glomus tumors, they are removed through the infratemporal approach.

As mentioned earlier, clival and petroclival meningiomas are resected through the petrosal approach or a total petrosectomy if hearing is completely lost preoperatively. These approaches expose a tumor that extends from the middle fossa to the foramen magnum. It requires only minimal retraction of the cerebellum and temporal lobe. The operative distance to the clivus is shortened by 3 cm, and the surgeon has a direct line of sight to the lesion and the anterior/lateral aspect of the brain stem. The transverse and sigmoid sinuses as well as the vein of Labbé are preserved. The vascular supply to the tumor is interrupted early during the procedure. For petroclival meningiomas, the patient is placed supine with his/her shoulder elevated and his/her head turned 45° away from the side of the tumor. The head is also lowered and tilted towards the opposite side to bring the base of the petrous bone to the highest point of the operative field. The bone flap is carefully elevated, exposing the transverse and sigmoid sinuses. A mastoidectomy is performed exposing the sigmoid sinus and the dura anterior to it, the jugular bulb, the lateral and posterior semicircular canals, and the facial nerve in the fallopian canal. Next, the bone overlying the sinodural angle is removed, exposing the superior petrosal sinus. If hearing is absent, a total labyrinthectomy can be performed at this point, thereby increasing the anterior lateral exposure of the tumor. Then the dura matter is opened along the anterior border of the sigmoid sinus and along the floor of the temporal fossa. The vein of Labbe is identified and protected. The superior petrosal sinus is coagulated and divided, and this division is carried medially through the tentorium, avoiding injury to the trochlear nerve and the superior petrosal vein. Complete sectioning of the tentorium allows the sigmoid sinus along with the cerebellar hemisphere to fall back, thus decreasing the need for retraction. Angling the microscope allows the fourth through twelfth cranial nerves as well as the entire vertebral basilar system and the anterolateral brain stem to be visualized. The cranial nerves of the posterior fossa have a relatively constant relationship to petroclival meningiomas. The trochlear nerve is usually superior and lateral to the tumor, whereas the trigeminal nerve is superior and anterior. The abducens nerve is found anterior and inferior and may be encased by the tumor. The VIIth and VIIIth cranial nerves are posterior and lateral, and the IXth through XIth cranial nerves are inferior. The basilar artery may be displaced posteriorly or to the opposite side, or it may be encased. The posterior cerebellar artery, superior cerebellar artery, AICA, and PICA, are usually posterior and medial to the tumor, but they too may be encased by it. Tumor removal begins with progressive devascularization of the tumor by coagulating and dividing its vascular supply from the tentorium and from its insertion on the petrous pyramid and clivus. The arachnoid over the tumor is opened to allow entry through the capsule and central debulking. As noted above, neurovascular structures may be embedded in the meningioma, requiring that great care be taken, especially when using tools such as the ultrasonic aspirator. The tumor capsule is then dissected free from the surrounding structures, but this must be done gently to avoid hypotension and bradycardia from vagal stimulation. The need to preserve the small perforating arteries of the brain stem and cranial nerves cannot be overemphasized. As for other meningiomas, the point of dural attachment is vaporized and hyperostotic bone removed with a high-speed diamond-tipped drill working under constant irrigation between the cranial nerves. After the dura is closed in a watertight manner, the drilled petrous bone is covered with autologous fat, and the soft tissues are closed in multiple layers.

When the patient has lost hearing preoperatively, a total petrosectomy is done to take advantage of the additional exposure for meningiomas of the clivus-petroclival area and sphenopetroclival area. This technique simply adds a translabyrinthine and transcochlear resection to the petrosal approach.

In patients with a tumor that extends into the middle fossa or anterior cavernous sinus or where the temporal lobe's venous anatomy forbids elevation of the posterior temporal lobe, the petrosal approach is extended anteriorly. The skin incision begins at the zygoma in front of the tragus and extends upward behind the hairline to the superior temporal line. It is then extended posteriorly to circle the ear and continues down behind the mastoid in the neck as described in the petrosal approach. The anterior part of the skin flap is elevated as described in the cranial orbital approach. The initial dissection of soft tissue is similar to that done in the petrosal approach. The superficial temporal artery is preserved. After the bone flap is removed, the temporal

bone is drilled, the dura is opened, and the tentorium is incised as in the petrosal approach. The anterior extension, however, allows the tumor to be exposed and removed from the cavernous sinus, the infratemporal area, and the parasellar area. If necessary, the Sylvian fissure is split, and dissection and tumor removal are done through the transsylvian approach.

Jugular Fossa Meningiomas. Primary meningiomas arising within the jugular fossa have also been reported [22]. Tumors in this location are rare and often have a similar presentation to glomus jugulare tumors. Meningiomas in this location are fraught with more surgical challenges, due to the intimate relationship with the lower cranial nerves. Surgical approaches must be tailored specifically for each patient based on preoperative imaging and intraoperative findings. Radical resection with low cranial nerve morbidity is possible with these lesions [22].

Foramen Magnum Meningiomas. Meningiomas of the craniovertebral junction are either located posteriorly and approached through a laminectomy and suboccipital craniotomy or placed laterally and anteriorly and removed through the transcondylar approach. For the transcondylar approach, the patient is placed in the supine position with the ipsilateral shoulder and back elevated 30–45°. A C-shaped incision begins above the ear and is extended caudally along the edge of the sternocleidomastoid muscle to expose the suboccipital area. The scalp flap is elevated in the subcutaneous plane to the level of the external auditory canal, and next the sternocleidomastoid is detached from the mastoid and retracted inferomedially. Injury to the accessory nerve must be avoided. The lateral mass of C1 is palpated, and the muscles are dissected in a subperiosteal plane from the lamina of the first and second vertebra. Once the inferior oblique muscle is detached, the ventral ramus of the second cervical root is followed medially to the vertebral artery between C1 and C2. The vertebral artery may be transposed medially once the transverse foramen of C1 is opened. A lateral suboccipital craniotomy is fashioned, the sigmoid sinus is skeletonized to the jugular bulb if necessary, and a C1 and C2 laminectomy is performed. The occipital condyle and the lateral mass of C1 are then drilled. Next the dura is incised posterior to the sigmoid sinus with the opening extending inferiorly to the entry of the vertebral artery. The dural incision circumscribes the dural entry of the vertebral artery, allowing its complete mobilization. The uppermost dentate ligament and, if necessary, the posterior C2 nerve root are divided. The accessory nerve is located between the dentate ligament and the posterior spinal nerve root. While the hypoglossal nerve may be either anterior or posterior to the tumor, depending on the tumor's point of origin; if anteriorly placed, it may involve both hypoglossal nerves. The tumor capsule is opened carefully, particular care being taken to avoid injury to the cranial nerves or blood vessels, and debulked. It may be detached from its clival base to decrease the vascularity. Careful separation of the tumor from the medulla and upper cervical spinal cord, the lower cranial nerves, and the vertebral artery may be accomplished by its dissection in the arachnoidal plane surrounding the tumor. The area of dural attachment is removed, as is any hyperostotic bone, and the dura is closed in a watertight manner to prevent CSF leakage. If the entire occipital condyle has been removed, an occipitocervical fusion should be performed. Postoperatively, the patient is managed in either a hard collar or a halo thoracic brace depending on the nature of the fusion construct.

Complete surgical treatment of meningiomas is attempted in all locations of origin. Due to the benign nature of most meningiomas, complete surgical resection offers the patient a cure. Complete resection includes resecting the involved meningeal attachment, dural tail, and areas of hyperostotic bone. Recurrence does happen after incomplete resection. The risk of recurrence decreases with more complete resection [23]. The extent of resection is described by the Simpson grade [23] (Table 17.4).

17.3.5.3 Radiotherapy

External beam radiation seems to be beneficial for aggressive meningiomas such as atypical and malignant meningiomas. To date, very little information exists to support this thesis. Several combined studies found a 58% recurrence rate following gross total

Table 17.4 Simpson grade of surgical resection [23]

Grade I	Macroscopically complete tumor removal with excision of tumor, dural attachment, and abnormal bone
Grade II	Macroscopically complete tumor removal with coagulation of dural attachment
Grade III	Macroscopically complete resection of tumor without resection or coagulation of dural attachment or extradural extension
Grade IV	Subtotal removal of tumor
Grade V	Simple decompression of tumor

resection and a 90% recurrence rate following subtotal resection of malignant meningiomas, which decreased to 36% and 40%, respectively, when surgery was followed by external beam radiation. The recommended radiation dose and target volume for malignant meningiomas average at least 6,000 cGy with a 3- to 4-cm margin. The effectiveness of high radiation doses must be weighed against possible complications. Stereotactic radiosurgery to treat intracranial meningiomas began in the 1960s, and since then it has been used increasingly often. It has been reported that patients with skull-base meningiomas treated with gamma-knife radiosurgery had an 88% control rate of their tumors; however, these series had a mean length of follow-up of less than 5 years [24]. Several series report a growing interest in gamma-knife radiosurgery for the specific treatment of cavernous sinus and other skull-base meningiomas either as primary treatment or following microsurgery. Cranial nerves passing through the cavernous sinus can tolerate radiation doses up to 40 Gy, whereas the optic nerves are considerably more radiosensitive. A recent study in which 88 patients were treated by gamma-knife for skull-base meningiomas found that 12–16 Gy could be tolerated by the optic apparatus if only a short segment is placed at risk. In accordance with this finding, some groups now claim that it is possible to treat some tumors that come as close as 1 mm to the optic chiasm. Three recent studies report 100% tumor control rates, but the follow-up period ranges from 17 to 39 months. Two of these studies report no permanent morbidity. Similarly, good results have been described from gamma-knife treatment of meningiomas involving the foramen magnum and the tentorium.

17.3.5.4 Chemotherapy

Little information is available on the efficacy of traditional antineoplastic agents against either benign or malignant meningiomas. Adjuvant chemotherapy for malignant meningiomas and for recurrences of benign or atypical meningiomas has been administered to a small number of patients, but chemotherapeutic regimens have generally been unsuccessful. Tamoxifen and antiestrogen have been used to treat patients with refractory meningiomas. The success of this treatment is still under investigation; however, preliminary results have been disappointing. This has also been true for mifepristone and RU-486. Recombinant interferon alpha 2b has been used for the treatment of a small number of patients with recurrent, aggressive meningiomas, and the initial reports indicate that it is more effective in traditional chemotherapeutic regimens with lower associated toxicity. Hydroxyurea has been shown to arrest meningioma cell growth in the S-phase of the cell cycle and to induce apoptosis in cell lines from 20 different meningiomas. In one report, use of this medication has been found to have a beneficial effect in treating a small subgroup of patients with recurrent and unresectable meningiomas, but the selection criteria of patients who responded are unclear, and further successful studies using this agent have yet to be published.

17.4 Paragangliomas

Paragangliomas or glomus tumors of the head and neck are tumors that originate from the paraganglia tissue from the extra-adrenal chromaffin cell system and have a close relationship to the arterial and venous structures in the neck and skull base. These tumors are named according to their specific location of origin in the neck and skull base. Tumors that arise from the carotid bifurcation are called carotid body tumors. Glomus jugulare tumors originate from the superior vagal ganglion, while glomus tympanicum tumors arise from the auricular branch of the vagus nerve and glomus intravagalae tumors arise from the inferior vagal ganglion.

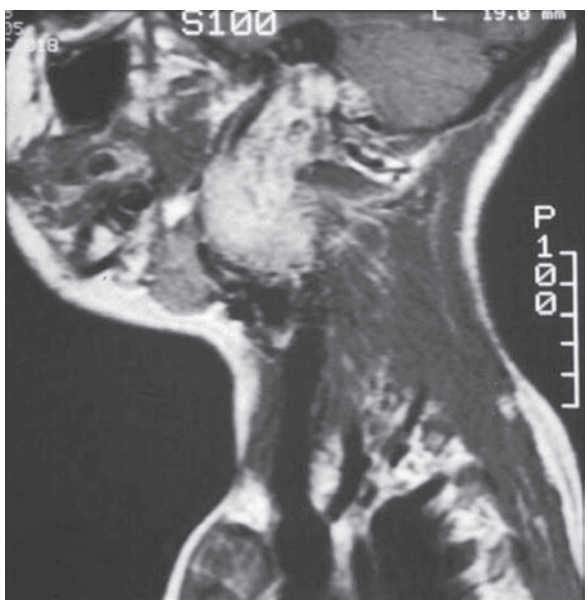

Fig. 17.8 Sagittal MRI demonstrating intravagal paraganglioma

Intravagal paragangliomas often occur lower than glomus jugulare tumors and are differentiated from carotid body tumors by their infiltration of the vagus nerve, and they have no involvement with the carotid body [25] (Fig.17.8). This chapter will focus on glomus jugulare tumors because of their involvement in the skull base and multiple lower cranial nerves.

Glomus jugulare tumors arise from glomus bodies surrounding the jugular bulb. They tend to be very vascular tumors that are usually slowly growing and benign. They invade and destroy the temporal bone, traveling along nerves, arteries, and veins. Often they will invade through the skull base and have an intracranial intradural extension. The intracranial portions can involve the petrous bone, foramen magnum, and clivus.

17.4.1 Epidemiology

Paragangliomas are rare tumors, but they are the second most common tumor involving the temporal bone after vestibular schwannomas, and the most common tumor involving the middle ear. The incidence is ~1 per 1.3 million people per year. They account for < 3% of intracranial tumors, and < 1% of head and neck tumors, and are thus not seen often in neurosurgical practice. Glomus tumors most commonly become symptomatic in the fourth decade of life, but can arise throughout a wide age range. They occur three to six times more commonly in women. Approximately 10% of patients with glomus tumors have paragangliomas in multiple locations, and all patients with suspicion of a glomus tumor should undergo a detailed assessment of other sites. The multiple sites can include any glomus body site in the head, neck, chest, and retroperitoneum. The most common association is the presence of a carotid body tumor along with an ipsilateral glomus jugulare tumor, which occurs in up to 7% of cases. Bilateral glomus jugulare tumors are found in ~2% of patients. These present a more significant treatment challenge due to the risk of lower cranial nerve involvement bilaterally. An autosomal dominant familial form exists that is passed from father to daughter, in which there can be up to a 55% rate of multiple tumors.

Glomus tumors are slow-growing in nature and are often large before becoming clinically evident. There is an average of 3–6 years from time of first symptom to diagnosis.

17.4.2 Symptoms and Clinical Signs

Specific clinical symptoms depend upon the exact location of the tumor, the structures it invades, and the size. The most common presentation is gradual onset of unilateral hearing loss, conductive in nature if the external ear canal is involved, and sensorineural if the hearing apparatus is invaded. Patients with hearing loss often also experience dizziness. Pulsatile tinnitus may be present in highly vascular tumors. Lower cranial nerve involvement produces symptoms of hoarseness, difficulty swallowing, aspiration, shoulder weakness, tongue atrophy, and fasciculation. Cranial nerve paresis is noted in up to 35% of patients. The Xth cranial nerve is invaded most commonly (61%), followed by the VII (54%), the XI (52%), the IX (48%), and least commonly the XII. Larger tumors can produce facial weakness from facial nerve involvement and Horner's syndrome from involvement of the sympathetic chain.

Larger tumors with extensive intracranial extension can cause compression of the brain stem with weakness and sensory deficits, compression of the cerebellum with ataxia and dysmetria, and compression of CSF flow pathways with hydrocephalus and papilledema.

Glomus tumors can secrete low levels of catecholamines manifested by symptoms such as hypertension, excessive perspiration, tachycardia, and headache. Surgical manipulation of these tumors can result in the release of neuropeptides and possibly wide-ranging changes in blood pressure during the operation. Only 1–3% of paragangliomas present with clinical symptoms of catecholamine secretion because detectable symptoms require a high level of catecholamine secretion. Serum catecholamine levels need to rise by four- to fivefold to produce clinical symptoms. Measurement of catecholamine levels in the serum and urine should be a part of the preoperative workup in anyone suspected of having a paraganglioma. Patients with secreting glomus tumors require pre- and intraoperative alpha- and beta-adrenergic blocking medicines.

Serotonin-secreting tumors produce the carcinoid syndrome with bronchoconstriction, abdominal pain, violent headaches, diarrhea, cutaneous flushing, and electrolyte abnormalities. The presence of the carcinoid syndrome is evident by clinical symptomatology, and specific laboratory testing is not required in the absence of symptoms. Octreotide can be used in the preoperative phase for symptomatic relief.

On otologic examination, a pulsatile red mass is often seen behind the tympanic membrane within the middle ear cavity. While this finding is not 100% specific for glomus tumors, the presence of a middle ear pulsatile mass increases the suspicion of this diagnosis.

17.4.3 Diagnostics

Synopsis. The diagnosis of glomus jugulare tumors requires the use of both high-resolution thin-cut CT scanning as well as MRI. Conventional catheter angiography adds information about the vascular nature of the tumor and can also be used to assist in treatment with presurgical embolization. The differential diagnosis of tumors in this location includes schwannoma of lower cranial nerves, meningioma of the jugular tubercle, chordoma, chondrosarcoma, and other temporal bone lesions including cholesteatomas, cholesterol granulomas, and carcinomas.

High-resolution CT scanning is used in the radiographic diagnosis of glomus jugulare tumors. Bone windows can be used to assess the region of the jugular fossa and the bony crest that arises between the carotid artery and the jugular fossa. CT scans also provide detail into areas of bony destruction (Fig. 17.9).

MRI scans are useful for assessing the soft-tissue component of glomus tumors. These tumors show heterogeneous intensity on both T1- and T2-weighted

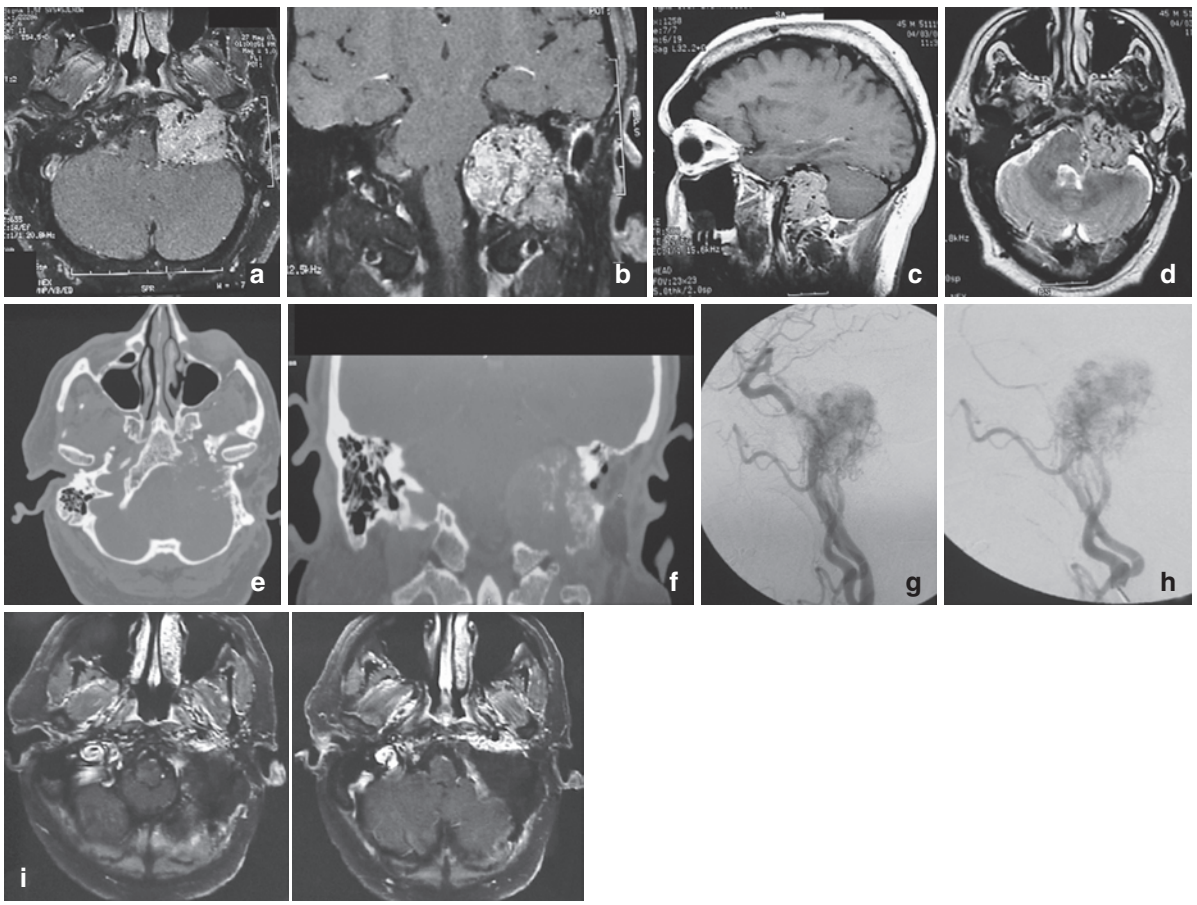

Fig. 17.9 (**a**–**i**) Imaging of glomus jugulare tumors from one patient. (**a**–**c**) Preoperative postcontrast T1 imaging of glomus jugulare tumor in axial, coronal, and sagittal planes demonstrating heterogeneous contrast enhancement. (**d**) T2 MRI of glomus tumor demonstrating serpiginous dark regions corresponding to large flow voids. (**e**, **f**) CT scan in the axial plane and coronal reconstruction demonstrating bony destruction of the skull base. External carotid artery (**g**) and vertebral artery (**h**) angiogram in a patient with a glomus jugulare tumor demonstrating large tumor blush and high vascularity. (**i**) Postoperative MRI from the same patient showing radical resection of tumor

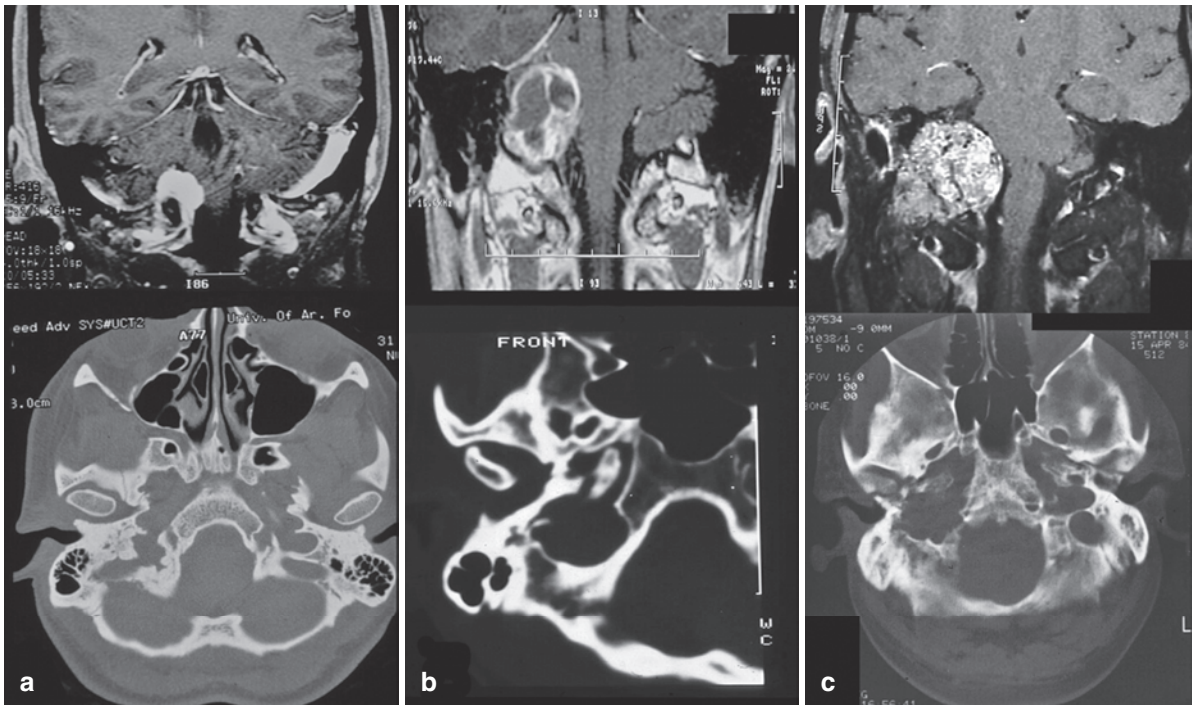

Fig. 17.10 (**a**–**c**) Comparison imaging of different tumors within the jugular fossa. (**a**) MRI and CT of jugular foramen meningioma demonstrating features of homogeneous contrast enhancement, presence of a dural tail, and hyperostosis of the jugular tubercle. (**b**) MRI and CT of jugular foramen schwannoma demonstrating presence of large cyst, dumbbell shape, and sclerosis of bone. (**c**) Glomus jugulare tumor demonstrating heterogeneous contrast enhancement, serpiginous flow voids, and bony destruction on CT

images. The highly vascular nature of paragangliomas creates serpiginous areas of vascular signal void throughout the tumor (Fig. 17.9). This is most evident in tumors >2 cm in diameter. This appearance of a tumor in the jugular fossa is often diagnostic of glomus jugulare tumors. Glomus tumors show strong contrast enhancement after the administration of gadolinium. MRI can be useful in assessing the intracranial intradural extension as well as extension into the neck. It is also possible to investigate the relationships of the tumor to arterial and venous vascular structures with MRI.

Conventional catheter angiography has a role both in the diagnosis and treatment of glomus tumors. Angiograms provide information about the blood supply to the tumor and the involvement of the internal carotid artery. Branches of the external carotid artery, specifically the ascending pharyngeal artery and the occipital artery, usually provide the main blood supply to glomus jugulare tumors, and a dense tumor stain is often seen with angiography in these tumors. Tumors that extend intracranially can recruit blood supply from the internal carotid and vertebral arteries (Fig. 17.9). Angiography is also helpful to identify the presence of multiple glomus tumors in a patient.

The differential diagnosis of tumors within the jugular foramen includes paragangliomas, meningiomas, and schwannomas. The differences among these tumors can often be seen on preoperative radiographic imaging (Fig. 17.10). Meningiomas often enhance intensely with contrast, have a dural tail, and cause hyperostosis of underlying bone (Fig. 17.10a). Schwannomas are often cystic and cause sclerotic changes in bone (Fig. 17.10b). Finally, glomus tumors show serpiginous flow voids and cause lytic destruction of bone (Fig. 17.10c). Preoperative diagnostic evaluation looking for these characteristics may be extremely helpful for surgical planning.

17.4.4 Staging and Classification

Synopsis. There have been many different classification schemes for glomus tumors in the literature. The first classification system was proposed in 1962 by

Table 17.5 Fisch classification of glomus tumors [26]

Class A: Glomus tympanicum. No evidence of bony erosion, tumor confined to the tympanum
Class B: Glomus hypotympanicum. Tumors arise from the hypotympanum with intact cortical bone over the jugular bulb
Class C: Glomus jugulare. Tumors erode the bone over the jugular bulb
C1: Involves the carotid foramen only
C2: Vertical segment of the carotid canal involved
C3: Horizontal segment of the carotid canal involved
C4: Foramen lacerum and cavernous sinus involved
Class D: Intracranial extension of tumor
De1: Intracranial extradural extension up to 2 cm
De2: Intracranial extradural extension > 2 cm
Di1: Intracranial intradural extension up to 2 cm
Di2: Intracranial intradural extension > 2 cm

Table 17.6 Glasscock-Jackson classification of glomus tumors [27]

Type	Physical findings
Glomus jugulare:	
I	Tumor within jugular bulb, middle ear, and mastoid
II	Tumor extending beneath internal auditory canal
III	Tumor extending to petrous apex
IV	Tumor extending into clivus, infratemporal fossa
Glomus tympanicum:	
I	Small mass limited to promontory
II	Tumor filling middle ear
III	Tumor filling middle ear, extending to mastoid
IV	Tumor filling middle ear, extending to mastoid or through tympanic membrane, filling external auditory canal, may extend anterior to interior carotid artery

Table 17.7 Al-Mefty criteria for complex glomus tumor [28]

Giant size
Multiple locations (bilateral, ipsilateral)
Malignant
Catecholamine-secreting (plasma catecholamine levels increased fourfold)
Association with other lesions (adrenal tumor, intracranial aneurysm, etc.)
Previous treatment with adverse outcome that increases risk of surgery (sacrifice of carotid artery, postradiation, postoperative deficits, complications of embolization)

Alford and Guilford. This system took into account the patient's symptoms, physical findings, radiographic findings, and neurological exam. Later classification systems by Fisch [26] and then by Glasscock and Jackson [27] consider anatomical location, tumor extension, and size and are used more frequently today.

The pathological evaluation is uniform for paragangliomas. There are few pathological criteria that can distinguish between benign and malignant tumors. The designation of malignant or benign is based on the clinical course as opposed to histological features of the tumors.

Fisch proposed a classification system of glomus tumors, taking into account the extent of temporal bone erosion, carotid artery involvement, and intracranial extension [26]. Tumors with intracranial extension are classified in class D. These tumors are further divided into those with extradural (De) and those with intradural (Di) extension (Table 17.5).

Glasscock and Jackson proposed a classification system that divided glomus tumors into glomus tympanic and glomus jugulare locations [27]. Table 17.6 gives the classification for glomus jugulare tumors. Types 2–4 can have intracranial extension.

Patel et al. in 1994 considered brain stem compression and vascular encasement as more important factors than size of intradural extension alone, as these factors displayed more prognostic value.

Al-Mefty et al. consider a subset of glomus tumors as "complex" [28]. These complex tumors fulfill one or more of the following criteria: giant size, multiple locations (bilateral or ipsilateral), malignant, catecholamine secreting, association with other lesions (adrenal tumor), and previous treatment with adverse outcome (sacrifice of carotid artery, prior radiation, postoperative deficits, complications of embolization) (Table 17.7). These factors increase the risks associated with surgical resection.

Glomus tumors in all anatomical locations have a similar pathological appearance. They demonstrate clusters of epithelioid cells (chief cells) within a vascular stroma background. The background stroma contains many capillary-sized vessels. The histopathology does not correlate with clinical behavior. There are no pathological features associated with malignant behavior. The designation of malignant or benign is a factor of the patients' clinical course. Malignant behavior is associated with fast growth with aggressive bony erosion and invasion. Often these patients will have associated anemia, early distant metastases, and rapid progression to death.

17.4.5 Treatment

Synopsis. Surgical resection of glomus tumors has historically been associated with high morbidity and

mortality rates. With newer skull base techniques and improved preoperative embolization possibilities, surgery for these tumors is possible with decreased morbidity and mortality, and it has become possible to achieve long-term disease control [28]. Surgical planning must be tailored for each patient based on the location, extension, and invasion from the tumor. Preoperative endovascular embolization has taken on a critical role in the surgical treatment of these tumors. Glomus tumors have been considered radioresistant in the past, but newer studies using radiosurgery for these lesions have proven promising. Treatment planning is essential for patients with multiple tumors, especially in patients with bilateral tumors. These patients present a particular management challenge as bilateral lower cranial nerve deficits are associated with high morbidity.

17.4.5.1 Surgery

With advances in skull base surgical techniques, intraoperative cranial nerve monitoring, intraoperative frameless stereotactic navigation systems, and expertise, surgical resection of glomus tumors has become feasible with decreased morbidity and mortality. Complete surgical resection can produce a cure from this disease. The specific surgical approach is tailored for each patient depending on the location of the tumor, extent of bony invasion, the patient's clinical condition, and pre-existing neurological deficits. Multiple steps are essential for safe surgery of glomus tumors: (1) proximal and distal control of the internal carotid artery, (2) coagulation/ligation of feeding arteries, (3) proximal control of the sigmoid sinus, (4) identification and preservation of the cranial nerves, (5) reconstruction to prevent CSF leak and infection. The intracranial and extracranial aspects of the tumor are exposed together, allowing single-stage resection of the entire tumor (Fig. 17.11). Preservation of the lower cranial nerves can be accomplished with intrabulbar dissection (Fig. 17.12), but this technique is not effective in cases of tumor invasion through the outer venous wall or invasion of the actual cranial nerves. Preservation of the internal carotid artery is achieved by careful dissection under microscopic visualization. A cleavage plane is usually discovered between the tumor and arterial adventitia. Carotid sacrifice and bypass are seldom warranted. Surgery for glomus tumors should be similar to surgery for arteriovenous malformations due to the high vascularity and arteriovenous shunting through the tumor. Venous ligation is delayed until the end of the procedure, after feeding vessels are coagulated and ligated.

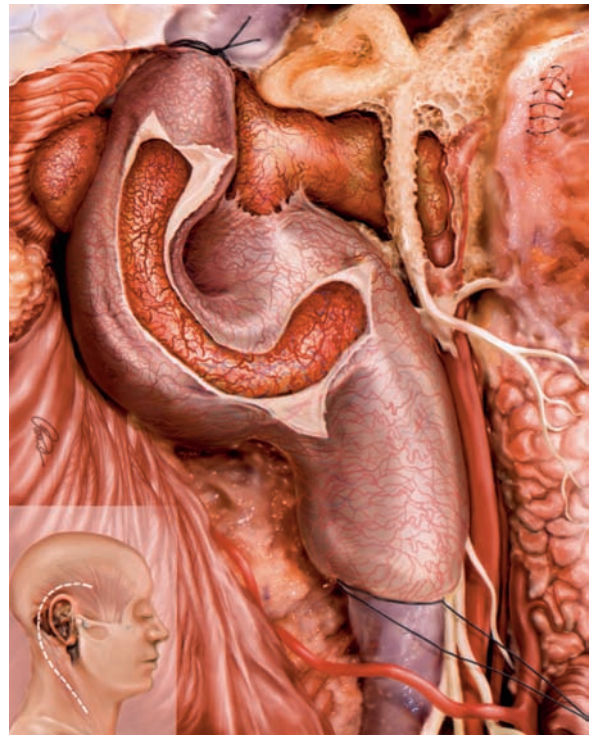

Fig. 17.11 Surgical exposure of glomus jugulare tumors demonstrating complete tumor exposure and isolation prior to resection through the postauricular incision (*inset*). This illustration demonstrates ligation of the sigmoid sinus and jugular vein. The facial nerve is maintained within its bony canal to decrease the risk of facial weakness (from [28])

Intraoperative neurophysiologic monitoring of cranial nerves correlates with improved outcome in skull base surgery. This fact is especially true for tumors within the jugular foramen. Monitoring of electroencephalography (EEG) and somatosensory evoked potentials (SSEP) is complemented by cranial nerve monitoring. Specifically for tumors in this anatomical location, monitoring of cranial nerve VII, brain stem auditory evoked potentials, and cranial nerves IX, X, XI, XII is an essential part of a surgeon's armamentarium.

Recent surgical results demonstrate that with the combination of skull base surgical techniques, preoperative embolization, intraoperative neurophysiologic monitoring, and surgical expertise, safe and complete

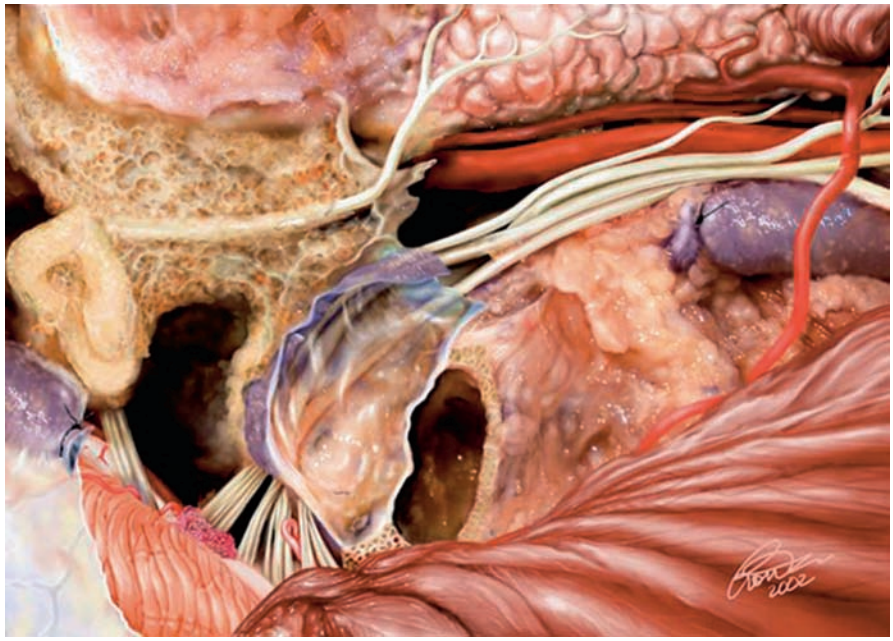

Fig. 17.12 Illustration demonstrating intrabulbar resection of tumor used to preserve the lower cranial nerves within the jugular foramen. The medial and anterior walls of the jugular bulb are kept intact to prevent manipulation of these nerves (from [28])

resection of glomus tumors is achieved. Al-Mefty et al. examined the surgical results in 28 patients with "complex" glomus jugulare tumors [28]. Gross total resection was achieved in 86% of patients. There was no mortality and minimal morbidity, with few new permanent cranial nerve deficits. CSF leak and infection were reported surgical complications.

While the surgical approach is similar for other tumors within the jugular foramen [29], surgical planning is crucial in patients with paragangliomas as many patients will harbor multiple tumors. Preoperative evaluation is particularly important in patients with bilateral glomus tumors. In this patient population (10% of all patients), surgical goals and plans must be modified to prevent bilateral lower cranial nerve deficits. Specifically, care must be taken in the dissection of the facial nerve. Leaving a thin rim of bone on the nerve and proceeding with dissection with transposition of the facial nerve decrease the risk of facial paresis postoperatively. Additionally, the surgeon avoids closing the external auditory canal to prevent loss of conductive hearing. Most importantly, intrabulbar dissection is crucial to prevent lower cranial nerve injury. Unfortunately, this dissection technique does not work when the tumor has infiltrated the posterior wall of the jugular bulb or has penetrated the cranial nerves.

Surgery on patients with catecholamine-secreting tumors presents further challenges. Manipulation of the tumor during surgery can cause release of the catecholamines, causing wide swings in blood pressure and hypertensive crisis. Preoperative planning with the anesthesiologist is required to perform surgery safely. The secreted catecholamines can be counteracted with α- and β-adrenergic blockade. It is crucial that α-blockade be started before β-blockade to prevent hypertensive crisis.

17.4.5.2 Radiation

Historically, glomus tumors have been considered to be radioresistant. Within the last 10 years, radiosurgery with gamma-knife or LINAC systems has been used more frequently for glomus tumors. Recent results have shown promising results with glomus tumors that are within the treatment size limit for radiosurgery [30]. Treatment of these tumors with radiosurgery is safe, with a 8.5% rate of cranial neuropathy and a 2.1% rate of permanent morbidity. Tumor growth was controlled in ~98% of patients, although only 36% had a decrease in the size of the tumor. With these promising results, radiosurgical treatment of glomus tumors is likely to become more common. Longer term follow-up is required to assess growth rates over time with radiosurgery. The advantages of surgery include complete removal of tumor and alleviation of mass effect.

Surgical resection is also able to treat tumors that are larger than the size limits of radiosurgery. Thus, surgical resection remains the treatment of choice for patients who desire complete removal and immediate cure of tumor, for large and giant tumors, for tumors with brain stem compression or significant intracranial extension, and for tumors with severe vascular encasement. Radiosurgery may have indications for residual tumors after surgical resection, and for elderly patients with small tumors.

17.4.5.3 Chemotherapy

There are currently no reports of chemotherapy regimens beneficial in the treatment of benign paragangliomas. There are a few studies using chemotherapy in the treatment of patients with malignant glomus tumors, but there are no accepted treatment regimens for this disease.

17.4.5.4 Embolization

Increasing endovascular technologies have improved the ability to perform superselective catheterization of feeding arteries to embolize glomus tumors. Recent advances in catheter systems, newer embolic materials, and improved quality of imaging allow for safer embolization procedures. Preoperative embolization techniques allow devascularization of the tumor prior to surgical manipulation. Due to the highly vascular nature of these tumors, preoperative embolization decreases subsequent blood loss during surgery, and thus makes surgery safer. The common feeding arteries are the ascending pharyngeal artery, other external carotid artery branches, and in large tumors the internal carotid artery and vertebrobasilar system. Embolization is indicated for large or complex tumors.

There are risks associated with embolization. Strokes may be caused by catheter manipulation or reflux of embolic material into the internal carotid artery system. Often there is significant arterial shunting from the external carotid system to the internal carotid and vertebrobasilar systems through the large vascular channels within the tumor, allowing embolic material to enter vessels supplying the brain. Cranial nerve palsies are also possible, as the embolized arteries often supply the lower cranial nerves. Due to these significant possible complications of embolization, the treating surgeon requires careful patient selection for this procedure. Small tumors without significant intracranial extension often do not require preoperative embolization.

17.4.6 Prognosis/Quality of Life

The prognosis for benign glomus tumors depends mostly on the cranial neuropathies caused by the tumor itself and on the treatment of the tumor. Gross total resection is possible in up to 88% of tumors and up to 86% of complex tumors. Gross total resection offers a cure from the disease in benign forms of paragangliomas. Malignant tumors result in rapid recurrence, metastasis, and death within a short time.

Lower cranial nerve deficits can alter the patient's quality of life after treatment for glomus tumors. Most patients present with some form of lower cranial neuropathy caused by the tumor itself. Treatment of these tumors may increase the cranial nerve deficits, in the form of facial weakness, hearing loss, difficulty swallowing, aspiration, hoarseness, and tongue weakness. Additional procedures such as medialization of the vocal cords may be necessary, and a few patients require tracheostomy and gastrostomy. Intrabulbar dissection techniques are used to minimize such deficits. Surgical planning is required in patients with bilateral tumors, as bilateral cranial neuropathies cause significantly higher morbidity. In these patients, subtotal resection and adjuvant radiosurgery for residual tumor may be the best treatment option.

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