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Tumors of the Optic Nerve

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Optic nerve glioma.

Optic nerve glioma is a slow-growing tumor that usually occurs more often in children. 30% of patients with this diagnosis also have associated NF1 (neurofibromytaosis type 1) and have a better prognosis.

Malignant gliomas (glioblastomas) are rare and almost always occur in adult men, with a poor prognosis and certain death within one year. Optic nerve gliomas account for about 1% of all intracranial tumors.

About 10% of optic pathway tumors are located within the optic nerve. One third of tumors affect both the optic nerve and the chiasm, another third primarily affects the chiasm itself, and one fourth is localized primarily in the hypothalamus. Only 5% of gliomas are multicentric.

General concepts.

Macroscopically, it is a smooth, fusiform intradural formation with a solid, gelatinous or cystic structure. Despite certain similarities to oligodendrocytes, more careful microscopy, ultrastructural and immunostaining techniques confirmed the presence of low-grade spindle pilocyte (hair-like) astrocytes and glial filaments with the presence of numerous Rosenthal fibers. Other histologic findings include arachnoid hyperplasia and mucous matter. The tumor may arise at the anterior end of the optic nerve and spread posteriorly intracranially or may initially arise from the junction of the optic nerve with the chiasm. Occasionally, glioma from the optic tract or anterior region of the third ventricle may secondary involve the chiasm and optic nerve. About 40% of optic pathway astrocytomas are fibrillary, and 60% are pilocytic. Hypothalamic tumors that have invaded the optic chiasm may present differently, showing signs of local invasion and are histologically not pilocytic in nature, but are similar to other hemispheric gliomas.

Patients with optic pathway gliomas most often present in the first decade with a mean age of 6.5 years, with slowly progressive vision loss, followed by proptosis (although this sequence can sometimes be reversed). Acute vision loss due to tumor hemorrhage is rare. Initial signs and symptoms of malignant gliomas include severe retro-orbital pain, unilateral or bilateral vision loss, and usually massive swelling and hemorrhage of the optic nerve head (disc pallor may also be seen with posterior lesions).

Clinic

Gradual, painless, unilateral proptosis associated with vision loss and afferent pupillary defect is a common presentation. Proptosis is often non-axial, with temporal or inferior dystopia. The head of the optic nerve is initially swollen, but subsequently atrophies. Optociliary collaterals and central retinal vein occlusion are sometimes visible. Intracranial extension to the chiasma or hypothalamus is rare.

The chiasm is affected in approximately half of cases of optic nerve glioma. Intracranial damage may be associated with intracranial hypertension, as well as decreased function of the hypothalamus and pituitary gland.

Computed tomography (CT)

A bone window on a CT scan often reveals widening of the optic nerve canal. Patients with associated NF1 typically have a fusiform dilatation of the optic nerve with a clear margin formed by intact dura. In patients without NF1, the nerve may be more irregular and have some areas of low density.

Magnetic resonance imaging (MRI) diagnostics

MRI often reveals enlargement, kinking, and bending of the optic nerve. The nerve increases in size and acquires a fusiform shape due to the attachment of the dura mater to the periosteum of the optic canal. On T2-weighted images, optic nerve glioma is hyperintense relative to the cerebral cortex and may appear heterogeneous due to cystic degeneration. Gliomas enhance in a variable manner and may show no enhancement at all. MRI may show cystic degeneration if present.

MRI is useful in identifying intracranial extension. It is more sensitive than CT for detecting chiasmatic/hypothalamic tumors. These tumors are typically hypointense on T1-weighted images and hyperintense on T2, as mentioned, and almost always enhance with gadolinium. On T2, a high intensity signal can be seen extending to the lateral geniculate body.

Differential diagnosis

The main differential diagnostic images when imaging shows an enlarged optic nerve are inflammation (neuritis, infection, or pseudotumor), neoplasm, or the result of increased intracranial pressure. Distinguishing inflammatory from neoplastic nerve processes is difficult because both can demonstrate optic nerve enlargement with or without contrast enhancement. Clinical history can then be used to determine the underlying cause. Unilateral involvement, absence of pain with extraocular movements, absence of systemic inflammatory signs at the onset of visual loss, and absence of additional white matter abnormalities or recurrent visual symptoms during the follow-up period may support the diagnosis of optic glioma rather than optic neuritis.

Optic nerve glioma

- Hemangioma, lymphoma, rhabdomyosarcoma, metastases (neuroblastoma,
- leukemia, Ewing's sarcoma), fibrous dysplasia, mucocele of the paranasal sinuses, meningioma, neurofibromatosis

Glioma of the optic nerve and chiasm

- germinoma, sarcoidosis

Optic chiasm glioma with extension to the hypothalamus

- Pituitary adenoma, Craniopharyngioma, Malignant astrocytoma
- Dermoid cyst, chordoma, colloid cyst, fibrous dysplasia, sarcoidosis, histiocytosis X, tuberculous granuloma, hemangloendothelioma

Optic nerve glioma associated with neurofibromatosis type 1. Neurofibromatosis type 1 (NF1) is an autosomal dominant inherited disorder with an estimated incidence of 1:4000. Optic nerve glioma, one of the most significant complications of NF1 in childhood, occurred with an estimated prevalence of 15% (range 1.5–24%). The period of greatest risk for developing symptomatic optic nerve gliomas with NF1 occurs in the first 6 years of life.

Treatment of optic nerve gliomas is controversial. Patients with lack of height, good vision and cosmetic deformity may not require treatment.

For malignant gliomas (glioblastomas), despite treatment including high-dose radiation therapy and chemotherapy, these tumors are usually fatal within 6-12 months.

There are rare reports of spontaneous regression of optic nerve and optic pathway gliomas. Cystic enlargement of lesions associated with sudden vision loss can occur even without true cellular growth. The treatment plan must be carefully individualized for each patient.

The following options may be considered:

1. Observation only for suspected optic nerve glioma, especially if vision is good on the affected side; with close follow-up if radiological features are characteristic of this type of tumor and if the glioma is limited to the orbit. Follow-up examinations and appropriate radiographic studies, preferably MRI, should be carried out at regular intervals. Many patients retain good vision and do not require surgery.
2. Surgical excision in cases of rapid intraorbital tumor growth to isolate the tumor from the optic chiasm and thus prevent chiasmatic invasion. The surgeon must use an intracranial approach to obtain a tumor-free surgical margin. Additional surgical indications may include tumors confined to the orbit with corneal exposure and compromised cosmesis unacceptable to the patient. Removal through an intracranial approach may also be indicated at the time of initial diagnosis or after a short period of observation if the tumor involves the prechiasmatic intracranial portion of the optic nerve. Complete excision is possible if the tumor ends 2-3 mm anterior to the chiasm. Excision may also be necessary if the glioma causes increased intracranial pressure. Excision is rarely used in cases where there is residual vision.
3. Radiation therapy is considered as the only treatment if the tumor cannot be resected (usually involving the chiasm or optic tract) and if symptoms (especially neurological) progress. Postoperative irradiation of the chiasm and optic tract may also be considered if good radiological studies show subsequent tumor growth within the chiasm or if involvement of the chiasm and optic tract is extensive.

- Because of debilitating side effects (including mental retardation, growth retardation, optic neuropathy or retinopathy, and secondary tumors in the radiation field), radiation is usually used as a last resort for children who have not yet completed growth and development.

4. Combination chemotherapy using actinomycin D, vincristine, etoposide, bevacizumab, and other drugs has also been reported to be effective in patients with advanced chiasmatic/hypothalamic gliomas. Chemotherapy may delay the need for radiation therapy and thus improve long-term intellectual development and preserve endocrine function in children. However, chemotherapy may also carry a long-term risk of developing blood-borne cancers.

- Regression of optic nerve gliomas has been reported after partial resection, chemotherapy, radiation therapy, or biopsy, and sometimes without any treatment. Other variables, such as genetic, hormonal or vascular factors, have a greater influence on tumor behavior. Most spontaneous regressions of optic nerve glioma have been reported in patients with NF1. Onset of the form

Meningioma of the optic nerve sheath.

Optic nerve sheath meningiomas (ONMS) are rare benign neoplasms arising from the meningothelial cells of the meninges surrounding the optic nerve. The tumor can arise in both the intraorbital and intracanalicular parts of the optic nerve, where there is a meningeal membrane. Primary MOMNs must be differentiated from secondary intracranial meningiomas, which extend into the anterior cranial fossa and involve the optic nerve. Although primary MOSDs are considered benign tumors, they cause slow, progressive vision loss due to

compression of the adjacent optic nerve and its blood supply. This monograph examines primary MOSDs.

Epidemiology and risk factors

Although rare, MON is the second most common primary tumor of the optic nerve and accounts for 1-2% of all meningiomas. They account for a third of primary optic nerve tumors. The incidence of MOSD is highest in adult women in the fourth or fifth decade of life, with women three times more likely than men to be affected. MOSD, however, may rarely occur in children: a review of cases by Dutton found that only 4% of tumors occur in patients under 20 years of age.

Etiology

The etiology of MOSD is not clearly defined and most are idiopathic. Exposure to ionizing radiation has been associated with meningiomas. MORD has also been associated with neurofibromatosis type 2. The most common cytogenetic abnormality found in meningiomas is loss of the long arm of chromosome 22, including the region containing the NF2 gene.[5]

Pathology

MONS consist of a proliferation of meningothelial cells, which are thought to originate from the arachnoid villi of the arachnoid membrane. Macroscopically, they look like rounded formations that compress adjacent tissues with clear boundaries. Typically, MONS grow circumferentially around the optic nerve without invading nerve tissue. They may extend along the length of the nerve and have the ability to invade the intracranial space, in which case involvement of the contralateral optic pathway is of concern. Histologically, MOSD can be one of several types, including syncytial, fibroblastic, transitional, psammomatous (with the presence of psammomatous bodies), secretory, or microcystic. However, these patterns do not carry prognostic information. MONS may rarely exhibit malignant, invasive characteristics along with a higher recurrence rate.

Clinical features

Patients with MOSD may be asymptomatic. Symptomatic patients most often have a gradually progressive, painless loss of monocular vision. Visual acuity at presentation may vary significantly (from 20/20 to no light perception) due to varying levels of awareness of vision loss. Dutton's review found that 24% of patients had finger counting visual acuity or worse, while 45% of patients had visual acuity of 20/40 or better. Signs of optic nerve dysfunction (eg, decreased color vision, visual field loss, ipsilateral relative afferent pupillary defect, and papilledema atrophy/edema) are usually present. Patients may exhibit the classic clinical triad of 1) painless, slowly progressive vision loss, 2) optic atrophy, and 3) so-called “optociliary shunt vessels.” However, the full triad is observed in only a minority of cases. “Optociliary shunt vessels” are collateral vessels formed in response to chronic central retinal vein occlusion (rather than a true shunt) and serve to transfer blood from the retinal venous circulation to the choroidal circulation (ie, retinochoroidal venous collaterals). However, these retinochoroidal venous collaterals are not specific to. In addition, observed in only 30% of patients with orbital, there may also be exophthalmos or deficits in extraocular mobility, depending on the location and size of the tumor. Fundus examination may reveal an initially normal or swollen optic disc, but optic nerve atrophy develops over time

Diagnostic testing

The diagnosis is made clinically and then confirmed using neuroimaging. Although computed tomography (CT) of the head and orbit may show the lesion (especially if it is calcified), magnetic resonance imaging (MRI) of the head and orbit with gadolinium and fat suppression sequences is usually recommended. CT findings include diffuse, tubular lesions with contrast enhancement. Calcifications may also be present within the tumor and are better visible on CT

scans. Gadolinium-enhanced MRI studies of the head and orbit and fat suppression sequences are useful in identifying membrane involvement, and radiographic features are usually so typical that biopsy may not be necessary in the appropriate clinical setting. MRI may demonstrate diffuse tubular thickening of the optic nerve sheath surrounding the optic nerve, often with a characteristic tram-track sign on axial sections or a donut sign on coronal sections. The tumor usually expands homogeneously and vigorously after contrast administration. MRI may also be useful in determining tumor size and assessing intracranial extension. Ga-68 PET/CT has recently been considered as a diagnostic tool for the detection of meningiomas through the use of their somatostatin receptor ligands. Sensitivity and selectivity were found to be 10% higher in detecting primary or recurrent meningiomas compared to MRI, and it demonstrated high potential for predicting tumor growth rate. However, PET is not usually required to diagnose a typical one. Tumor biopsy is not required for diagnosis in typical clinical cases with characteristic radiographic features, and surgery carries a high risk of damage to the optic nerve.

Differential diagnosis

Optic nerve glioma, metastatic disease, leukemic infiltration, neurosarcoidosis, tuberculosis, gummatous syphilis, optic nerve perineuritis, myelin oligodendrocyte glycoprotein (MOG)

Control

Patients with C can be observed if they are asymptomatic and, as a rule, the clinical course and imaging are sufficient to make a diagnosis. Although the lesions are usually histologically benign, symptomatic patients may be offered treatment. Optimal timing of treatment is unclear due to the difficulty of predicting the variable natural history of an individual tumor. Historically, treatment options have included observation, surgical excision, or radiation therapy. A retrospective study by Turbin et al compared visual acuity in patients undergoing observation, surgery, radiation therapy, or a combination of surgery and radiation. All groups of patients had statistically similar initial visual acuity. However, at the end of the follow-up period, only patients who received fractionated external beam radiation treatment alone did not have significantly reduced visual acuity levels. Similarly, Ratnayake et al demonstrated stereotactic radiotherapy as an excellent option with good relative long-term local control. The MRI-based tumor control rate was 100% at 68 months. Additionally, a more recent 2019 retrospective analysis that focused on intensity-modulated radiation therapy demonstrated either stable or improved visual acuity of 81%. The study showed that this method is suitable for stabilizing vision even in patients with severe deficits before treatment. Additionally, many previous studies examining fractionated stereotactic radiotherapy have demonstrated either stable or improved visual field rates of 83.3–100%. These studies, among other things, have shown that radiotherapy can be considered after the decision to intervene has been made, and the goal is usually to prevent further vision loss. Fractionated stereotactic, intensity-modulated, and three-dimensional conformal radiotherapy is generally considered the treatment of choice for symptomatic cases. Stereotactic radiation therapy is well suited for smaller, more well-defined lesions. However, side effects include radiation-induced complications such as secondary radiation retinopathy and optic neuropathy, iritis, cataracts and hypopituitarism.

Proton therapy is another potential treatment option. However, research on the use of proton therapy is limited. Proton therapy may reduce late toxicity due to its ability to provide low scattered doses, a useful quality for treating meningiomas located near the pituitary gland.

Surgery is generally not recommended for eyes with good vision due to the risk of postoperative blindness. Surgery may impair vision due to the shared pial blood supply to the optic nerve. However, surgical excision may be considered in cases of blind eyes with severe exophthalmos or cosmetic deformity or when intracranial extension is at risk, although this event is rare in clinical practice. A recent case report noted complete resolution of visual symptoms and total tumor resection after surgical resection using an endoscopic endonasal approach; some have a morphology (eg, exophytic from the optic nerve sheath) that may be amenable to resection on a

case-by-case basis. Palliative surgery may be further considered for severe vision loss along with disfiguring proptosis.

It has been shown that children have an increased malignant potential compared to adults. Because of the higher rate of intracranial spread, increased complication rates after radiotherapy, and the lack of literature on radiotherapy in studies of pediatric populations, surgical prophylaxis has been suggested as the primary treatment option for children with this condition.

Forecast

The natural history is usually slowly progressive ipsilateral visual loss. However, as noted above, individual speed or progression is highly variable. However, the increased likelihood of positive visual outcome after radiotherapy was associated with good pre-treatment visual acuity.[eleven]The mortality rate is minimal, so any treatment decision (including stereotactic radiotherapy) should include a discussion of risks and benefits. In general, and at our institution, three-dimensional conformal stereotactic intensity-modulated radiotherapy is the treatment of choice for symptomatic

Orbital meningiomas

Meningiomas are usually slow-growing, benign tumors. Primary orbital meningiomas arise within the orbit and include:optic nerve sheath meningiomas(MONS), which are the most common optic nerve sheath tumors, and primary ectopic meningiomas.

Secondary orbital meningiomas arise from the adjacent structures listed below and extend into the orbit through the optic canal or superior orbital fissure: sphenoid wing (SOM), anterior clinoid, cavernous sinus, tuber sella, and olfactory sulcus.

Etiology

Meningiomas are neoplasms arising from arachnoid cells and can occur anywhere arachnoid cells are found. Primary orbital meningiomas arise from meningothelial cells around the optic nerve sheath. Or rarely, ectopia of meningeal tissue in the orbit.

Morbidity

Meningiomas are the most common primary intracranial tumors, accounting for approximately 19% of primary intracranial tumors. However, orbital meningiomas account for only approximately 4-8% of the total number of orbital lesions, with approximately 2-4% being optic nerve sheath meningiomas and 2-4% being secondary orbital meningiomas. Primary ectopic orbital meningiomas are very rare, with few case reports.

The incidence of orbital meningioma is much higher in women compared to men, similar to intracranial meningiomas. The average age of onset for orbital meningiomas is approximately 45 years. However, approximately 7% of ONSM occur in patients younger than 20 years of age and are often more aggressive in the pediatric population.

Risk factors

Although the risk is low with advances in radiation therapy techniques, there are reports of orbital meningioma after radiation therapy. Radiation-induced meningiomas are the most common brain tumors caused by radiation.

Patients withneurofibromatosisType 2 have a mutation in the optic nerve tumor suppressor gene and are predisposed to the development of multiple meningiomas. Deletion of chromosome 22 is found in more than 50% of meningiomas.

There is significant heterogeneity in the histopathology of meningiomas, as can be appreciated above by the several subtypes described in the WHO classification system. In general, whorls of meningothelial cells are present. The cells may be spindle-shaped and separated by fibrous connective tissue. Calcified whorls or psammoma bodies may also be present.

Immunohistochemically, meningiomas are positive for vimentin, which stains mesenchymal tissue. Estrogen and progesterone receptors may also be present, which may explain the growth of meningiomas during pregnancy.

Classification

The World Health Organization has established criteria for classifying meningiomas from benign to malignant based on histological features. According to the latest edition (2007), grade I meningiomas are considered benign and do not have anaplastic features; Grade II meningiomas are defined by the presence of 4+ mitoses per 10 high-power fields (HPF), brain infiltration, and 3 or more of the following: small cell change, increased cellularity, prominent nucleoli, leaf-like growth, or necrosis; and grade III meningiomas have 20+ mitoses per 10 HPF with histological evidence of malignancy.

Table: WHO classification of meningiomas based on histological features	
WHO grade 1 (benign) subtypes include:	Meningiothelial, fibrous (fibroblastic), transitional (mixed), psammomatous, angiomatous, microcytic, secretory, rich in lymphoplasmocytes, metaplastic
WHO grade 2 (anaplastic) subtypes include:	Choroid, clear cell, atypical
WHO grade 3 (malignant) subtypes include:	Papillary, rhabdoid, anaplastic

Orbital meningiomas are most often classified as WHO grade I. The most common orbital subtype was meningothelial, and transitional was the second most common subtype.

Patients may present with the following symptoms, either due to mass effect, compression, or infiltration of the optic nerve. On examination, patients may have exophthalmos, which should be measured with an exophthalmometer, pallor of the optic nerve or papilledema, decreased visual acuity, visual field deficits, globe displacement, limited extraocular movement, or optociliary shunts.vessels.

Symptoms

Patients may experience the following symptoms to varying degrees depending on the severity of the disease and the location of tumor compression/infiltration. Symptoms include vision loss,diplopia, headache and retrobulbar pain.

Diagnostic Imaging

Meningiomas typically appear isodentic to the optic nerve and hyperdense to the brain on CT and will have uniform enhancement on contrast studies. About 20% have calcification. The tramline sign can be seen on axial imaging of the enlarging tumor surrounding the optic nerve. Hyperostosis of the surrounding bones can also be seen. Attention should be paid to canal damage and correlated with clinical examination. On MRI, meningiomas are isointense on T1-weighted images and moderately hyperintense on T2-weighted images. On contrast studies, meningiomas demonstrate homogeneous enhancement. Helpful features include a dural tail (this can be seen in other conditions and is not pathognomonic) and vascular bundles.

Treatment of orbital meningiomas is primarily determined by the patient's symptoms. Patients with visual acuity of 20/50 or better are usually treated conservatively with neuroimaging and ophthalmologic examinations twice a year with visual field testing and color plates. The frequency of neuroimaging and testing may be reduced once the tumor is shown to be stable. Young patients should be examined more often.

The goals of surgery for orbital meningiomas include long-term tumor control, restoration of optic and cranial nerve function, and prevention of cosmetic defects. Surgical intervention for ONSM is usually performed in cases of intracranial extension of the optic chiasm or in patients with a blind eye and severe disfiguring exophthalmos. The treatment of orbital meningiomas

involves a multidisciplinary team that includes an oculoplastic surgeon and a neurosurgeon. Surgical resection or removal of secondary orbital meningiomas is determined by the location of the tumor and associated symptoms. Complete surgical resection is often not possible due to the involvement of delicate structures, and patients with orbital meningiomas often require periodic surgery to remove the tumor. Marinello et al indicate that visual function in patients with OOS mainly depends on the presence and degree of compression of the optic nerve at the entrance or within the optic canal. They emphasize that decompression of the optic canal is important to reduce compression of the optic nerve. Studies show that about 75% of patients have stable or improved visual acuity after surgery. Improvement in visual acuity has been reported to range from 30 to 50%. Proptosis improves in 85-90% of patients after surgery.

Radiation therapy. Recent evidence suggests that radiotherapy should be considered prior to surgery in patients with significant symptoms of ONSM. The optic nerve and chiasma are the most sensitive structures in this area, even compared to the adjacent cranial nerves. With single-dose radiosurgery, optic nerve damage has been shown to be dose dependent, with very low rates of optic neuropathy at doses <10 Gy and up to 78% of cases at doses >15 Gy. The incidence of optic chiasm and nerve injury is extremely low with fractionated therapy to a total dose of <60 Gy, provided the fractionated dose is <2 Gy.

A study by Turbin et al. compared the visual outcomes of four treatment groups in patients with ONSM: radiation alone, surgery alone, radiation and surgery and observation. Radiation therapy alone produced the best visual outcome, and the authors recommend fractionated radiotherapy at a dose of 50–55 Gy as initial treatment for patients with ONSM.[14]. Similarly, it is believed that additional radiation therapy to residual tumor after surgical resection may improve outcomes by reducing recurrence and stabilizing or reducing tumor size. A study by Peele et al. showed no recurrence in 42 patients treated with radiation therapy during a 4-year follow-up period after subtotal resection or tumor recurrence. In the nonirradiated group, recurrence occurred in 42% of patients with subtotal resection of the primary tumor.

Some tumors that are benign on initial histologic analysis may undergo malignant transformation after radiation therapy and may then become clinically much more aggressive with rapid growth and regrowth after surgical removal of the tumor.

Postoperative complications include trigeminal hypoesthesia, oculomotor nerve palsy, andfacial paralysis. Ocular complications associated with radiation therapy includeradiation retinopathy, iritis, cataracts and retinal vascular occlusion.

Forecast

Relapse rates range from 17% to 42%. Recurrence rates are lower in patients with radiation therapy after surgery. However, this also depends on the WHO grade of the tumor.

Orbital schwannoma

Orbital schwannoma (OS) is a rare type of peripheral nerve sheath tumor with variable clinical presentation. Orbital schwannomas usually affect the head and neck and are rarely found within the orbit. Other tumor types in this family include neurofibromas and malignant fibromas, which are more commonly seen in patients with neurofibromatosis (NF). Orbital involvement occurs in 11-28% of patients with NF-1 or a family history of NF, but the risk of developing orbital schwannoma specifically in these populations is 1.5%. Benign schwannomas usually present between the 2nd and 6th decades of life, and no racial association has been identified. These tumors rarely undergo malignant transformation. Differences in tumor size and location often pose unique therapeutic challenges.

Etiology

Schwannomas result from hyperplasia of myelin-producing Schwann cells. The molecular etiology of this hyperplasia is not fully understood, but with knowledge of the pathology of

neurofibromatosis it has become clearer. In NF-1, biallelic loss of the tumor suppressor gene neurofibromin on 17q11.2 results in uncontrolled Ras gene signaling, promoting Schwann cell hyperplasia. In NF-2, loss of the merlin gene (22q11.2) also contributes to Schwann hyperplasia. These tumors typically affect cranial sensory nerves, primarily V1 and less commonly V2, cranial nerves in the orbit, and those innervating the extraocular muscles. In addition, schwannomas with infiltration of the ciliary body, choroid, iris, sclera, and posterior ciliary nerve were observed inside the orbit. In rare cases, the optic nerve is involved, which is associated with the autonomic perivascular nerves surrounding the nerve sheath.

Orbital schwannomas present insidiously with gradual, nonpulsatile exophthalmos and sometimes eyelid edema. Most of these tumors infiltrate the upper quadrant, causing inferiorly displaced proptosis or frank hypoglobus. When presenting late, patients may experience double vision, limited eye movement, decreased visual acuity, and symptoms of optic nerve compression, including scotomas, dyschromatopsia, and impaired contrast sensitivity. Depending on which nerve is affected, patients may experience pain or paresthesia in the area of the nerve. In severe cases, there may be a palpable orbital mass. Schwannomas rarely involve bilateral orbital involvement, with only one case reported.

Differential diagnosis

The differential diagnosis includes other types of OS, including neurofibromas or malignant OS, meningioma, cavernous hemangioma, lymphangioma, fibrous histiocytoma, lymphoma, dermoid cyst, hemangiopericytoma, pleomorphic lacrimal gland adenoma. It is almost impossible to distinguish these tumors based on clinical examination alone.

Imaging is extremely useful for detection and evaluation, but some tumors will be difficult to distinguish and will require pathology. Imaging should focus on size, location, distribution, and growth rate, especially if serial imaging is used.

There are several imaging modalities for evaluating and monitoring orbital schwannoma. Computed tomography (CT) is optimal for assessing bone erosions and planning surgery, while magnetic resonance imaging (MRI) characterizes swelling and damage to adjacent soft tissue structures.

CT

On CT, orbital schwannomas appear as smooth, round, elongated, and homogeneous lesions with a density similar to extraocular muscle. In addition, CT can reveal calcification in primary tumors. They have strong enhancement with CT contrast. These are smooth, well-defined tumors that take the shape of a cavity and grow along the orbital axis. Orbital schwannomas have a more oval or fusiform shape compared to other schwannomas. They are typically extraconal, whereas other lesions, such as hemangiomas, are often intraconal. Schwannomas have a tendency to invade through the superior orbital fissure compared to meningiomas. In addition, CT will reveal their characteristic extension into the bone without erosion of fissures, which occurs less frequently with neurofibromas.

MRI

Schwannomas typically have hypointense signals on T1 and hyperintense signals on T2. MRI can reveal both homogeneous and heterogeneous enhancement and correlate with tumor histology and morphology. Antoni A areas are intermediate in intensity with T1 and T2, but Antoni B areas are hypointense on T1 and hyperintense on T2. There is no contrast enhancement, but approximately 41% of schwannomas may have cystic degeneration—these areas may correlate with those of Anthony W. MRI can distinguish schwannoma from lymphoma because lymphoma has intermediate T2 and molds around adjacent structures, whereas schwannomas invade and deform neighborhood. Dermoid cysts are similar in shape but are T1 hyperintense and do not contain gadolinium enhancement. (160) Solitary fibrous tumors are similar in intensity and location on T1 and T2, but dynamic contrast-enhanced MRI can be

used to distinguish them. On dynamic contrast MRI, solitary fibrous tumors will have a smoother washout curve due to their highly cellular stroma, whereas schwannomas exhibit a washout plateau due to the heterogeneous and loose arrangement of cells. Dynamic MRI enhancement will allow differentiation of cavernous hemangiomas, as cavernous hemangiomas will show progressive enhancement on later images.

B-scan ultrasonography can be used for rapid assessment, follow-up, or progression of schwannomas. On ultrasound they appear as round, well-defined, hard lesions with a reflective surface. They may also appear as heterogeneous or cystic lesions with different tissue surfaces that influence signal intensity. Acoustic depressions on ultrasound suggest the presence of intratumoral hemorrhage.

Most schwannomas are described as "common," but there are four additional histologic variants: cellular, melanotic, plexiform, and neuroblastoma. All subtypes stain strongly for S-100, a protein found in neural crest-derived cells. Type 4 collagen staining reveals pericellular collagen deposition. In addition, schwannomas stain positive for SOX10, p16, and neurofibromin but negative for epidermal growth factor receptor. In the orbit, most schwannomas are of the conventional variety, followed by the cellular variety; other variants are very rare in orbit. Regular and cellular subtypes are identified by their fibrous smooth capsule of perineurium of neural origin. The melanotic subtype has a thin fibrous shell, but the capsule is poorly visible and may be lobulated in the plexiform variant. Smaller schwannomas grow eccentrically from the parent nerve. A larger schwannoma may outgrow the brain nerve but, unlike a neurofibroma, will not infiltrate diffusely. On light microscopy, schwannomas have a biphasic histologic morphology with variable patches of patterns. Anthony A patterns are hypercellular with tufts and tufts of compact spindle cells containing indistinguishable cytoplasmic borders running parallel along their long axis. In addition, Antoni A patterns have Verocay bodies, which are nuclear regions surrounded by clusters of elongated spindle cell nuclei arranged in palisades. Periodic acid-Schiff stain and immunoperoxidase assay for laminin are strongly positive, demonstrating that each cell forms a basement membrane. There may be mitoses, but they will not be aggressive. Anthony B phases are hypocellular and less organized. Anthony B patterns have vacuolated cells arranged in sheets in a myxoid or microcystic matrix. This pattern has small, irregular, hyalinized vessels surrounded by inflammatory foamy histiocytes and collagen fibers.

- Unlike the common subtype, cellular schwannoma has minimal or absent Anthony B tissue pattern with cells that are tightly packed into fascicles. They may look like Anthony A, but have poorly formed Verokai bodies. Cells may also show atypia and an increased number of mitoses, raising suspicion for malignancy. Neoplasms of smooth muscle should also be considered and distinguished from cellular schwannomas by immunostaining for smooth muscle actin. The plexiform subtype is similar to the regular subtype because it contains a true capsule and a population of cell types. However, it arises from nerve plexuses or ganglion fascicles of palisaded spindle cells surrounding the original nerve. Plexiform schwannomas are characterized by more Antoni patterns of type A compared to type B. They may be confused with a sarcoma due to their high cellularity, but without mitotic activity, atypia, and necrosis with strong S-100 immunostaining, they are unlikely to be so.
- Melanotic subtypes are extremely rare tumors, and only in one case do they involve the orbit. Melanotic contains various pigments and dyes for HMB-45 and Melan-A. Pigmentation is most pronounced in melanophages. They may be difficult to distinguish from malignant melanoma, but must be based on histomorphology, cytoarchitecture, and features of malignancy.
- Neuroblastoma is also extremely rare, with only one orbital case reported. A distinctive feature is the "giant rosette", a central eosinophilic collagen core surrounded by small round or oval cells with hyperchromic nuclei. There are few or no malignant signs.

Immunohistochemical staining was similar to normal but negative for synaptophysin CD99 and neuron-specific enolase.

- Cystic schwannoma is a type of regular schwannoma but has degenerative microcystic and myxoid areas that coalesce to form a macrocyst visible under low power microscopy.
- Ancient schwannomas occur in conventional and cellular subtypes that degenerate over time and include microcystic changes, hemorrhage, and calcification. They have cellular atypia and pleomorphism, leading to confusion with sarcoma. But the absence of mitotic figures, areas A and B, and a positive S-100 result distinguishes it from sarcoma.

The primary treatment for orbital schwannoma is excision, ideally preserving the integrity of the capsule. Numerous surgical approaches have been described. Most schwannomas occupy the superior orbit, requiring an anterior orbitotomy through an incision in the crease of the upper eyelid or a subglabellar incision. Lateral orbitotomy can be performed for superolateral tumors.

Inferior or medial lesions require inferior transconjunctival incisions. Relatively anterior medial tumors can be accessed through a transcaruncular incision. Tumors of the posterior medial wall near the orbital apex can be accessed through an endoscopic endonasal approach. If a schwannoma involves the superior orbital fissure, a pterional extradural approach is recommended, providing adequate access to the superior posterior orbit, superior orbital fissure, and optic canal. Regardless of the approach chosen, the surgeon must differentiate the nerve as sensory from motor before sacrificing it. This can be avoided by microsurgery or careful dissection of the capsule. Tumors can be treated by debulking using serial imaging to monitor tumor progression.

Radiation therapy:

Radiation treatment for schwannomas is evolving. Early studies noted complications of optic neuropathy. Fractionated radiation can treat smaller tumors to reduce radiation exposure, but unfortunately the optic nerve can withstand the same radiation doses as the tumor. Optic neuropathy has been reported in reports with as little as 8-12 doses of gray. However, radiation therapy is warranted to assist in the surgical treatment of tumors in compact areas with important adjacent neurovascular bundles. Recently, stereotactic gamma knife therapy has been used. One study showed tumor size reduction or stability with Gamma Knife therapy. Single-dose Gamma Knife treatment is not recommended for apical schwannomas due to the potential for damage to the optic nerve and associated visual field defects and loss of visual acuity. Instead, multiple gamma knife therapy is indicated for orbital schwannomas; one study showed tumor stability or shrinkage in 6/7 patients, and two of them had decreased vision. This technique can be used to treat small, inoperable, inaccessible, or benign postoperative schwannomas. This is an alternative to extraction, but indications vary and are not established.

If resection is not possible, osseous or fatty orbital decompression may be a suitable alternative to improve the patient's quality of life. This is especially true for apical schwannomas, where compression of the optic nerve may occur due to the compact location. Two studies demonstrated that decompression was beneficial in cases with slow-growing apical tumors and reliable follow-up. This option is indicated for benign, slow-growing schwannomas in elderly patients with intact vision, rapidly developing clinical deterioration, absence of malignancy, and consent to serial imaging after the procedure. Side effects include diplopia, hypoglobus, and enophthalmos, rarely.

Medical support

In case of relapse and malignant transformation, long-term observation is required. After obtaining stable MRI images for several years, patients can be followed up annually or biannually.

Forecast

After complete surgical excision, the prognosis is generally good with a very low risk of recurrence. In one report it was observed that visual acuity did not deteriorate in 19/22 and 22/22 patients, and almost half of them had limited eye movement after surgery, which improved over time. In addition, few of these patients had chronic ptosis and fixed mydriasis. In the absence of neurofibromatosis, a small number of schwannomas recur after complete excision.

Meningioma of the sphenoid wing

Meningiomas of the sphenoid wings are slow-growing tumors arising from the outer epithelial cells of the arachnoid membrane. They are the most common tumor of the intracranial space with spread to the orbit

Morbidity

The annual incidence of symptomatic meningiomas is approximately 2 cases per 100,000 people. Anterior skull base meningiomas account for 40% of all intracranial meningiomas, and sphenoid wing meningiomas account for 11–20% of intracranial meningiomas. Meningiomas of the wing of the sphenoid bone with secondary invasion into the orbit are rare.

Meningiomas of the sphenoid wing are classified as either globoid tumors with a nodular shape or as a plaque-like tumor, which is flat and extends along the entire sphenoid ridge. Depending on the location, spherical tumors are divided into 3 groups: internal (medial), median and lateral (pterional). Medial wedge meningiomas have higher morbidity, mortality, and recurrence rates compared with other meningiomas due to their involvement of the anterior visual pathways, anterior intracranial arteries, and cavernous sinus.

Etiology

Meningiomas of the sphenoid wings are slow-growing tumors arising from the outer epithelial cells of the arachnoid membrane.

There are currently no specific environmental risk factors.

Genetically, the most well characterized and common alteration is loss of the NF2 gene (NF2) on chromosome 22q. NF2 encodes a tumor suppressor known as merlin. Approximately 60% of sporadic meningiomas have been found to have mutations in NF2. Meningiomas may also be associated with other genetic syndromes, such as Gorlin and Rubinstein-Taybi syndromes, but the association is not as strong as with NF2.

System associations

Meningiomas can be multiple, especially if associated with neurofibromatosis type 2 (NF2).

General pathology and classification

The appearance of sphenoid wing meningioma specimens has significant pathological variations. Many variants occur, including secretory, microcystic, clear cell, lymphoplasmacytic-rich, chordoid, atypical, malignant, papillary, and anaplastic variants. In general, the typical pathological features found in most meningiomas are whorls of meningothelial cells consisting of epithelioid type cells with eosinophilic cytoplasm and ovoid nuclei with or without vacuoles or pseudoinclusions. Meningiomas may contain calcium deposits in the center of whorls of cells called psammoma bodies. Figures 1 and 2 show typical examples of histopathological specimens of meningiomas.

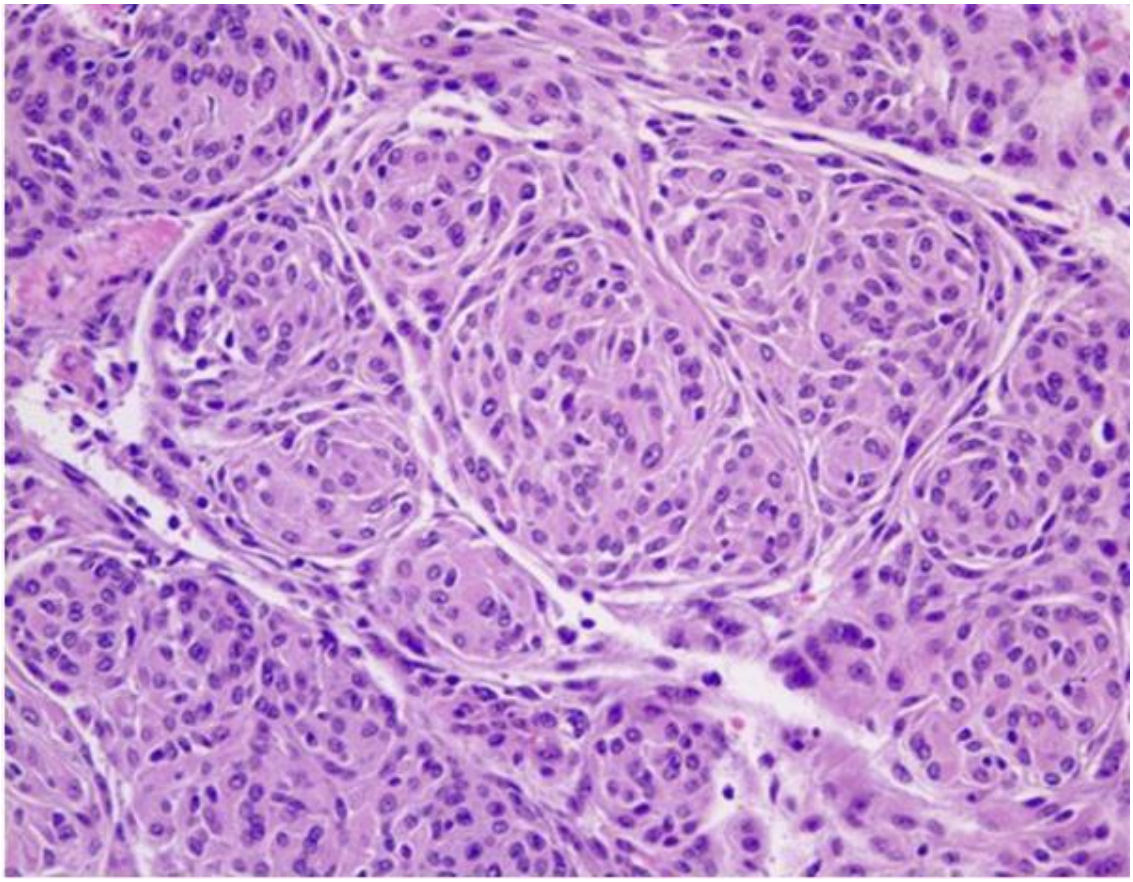


FIGURE 1: Meningioma of the sphenoid wing (H&E, 20x). The image shows whorls of meningothelial cells consisting of epithelioid-type soft cells with eosinophilic cytoplasm located in a syncytium. The nuclei are oval with vacuoles and pseudoinclusions.

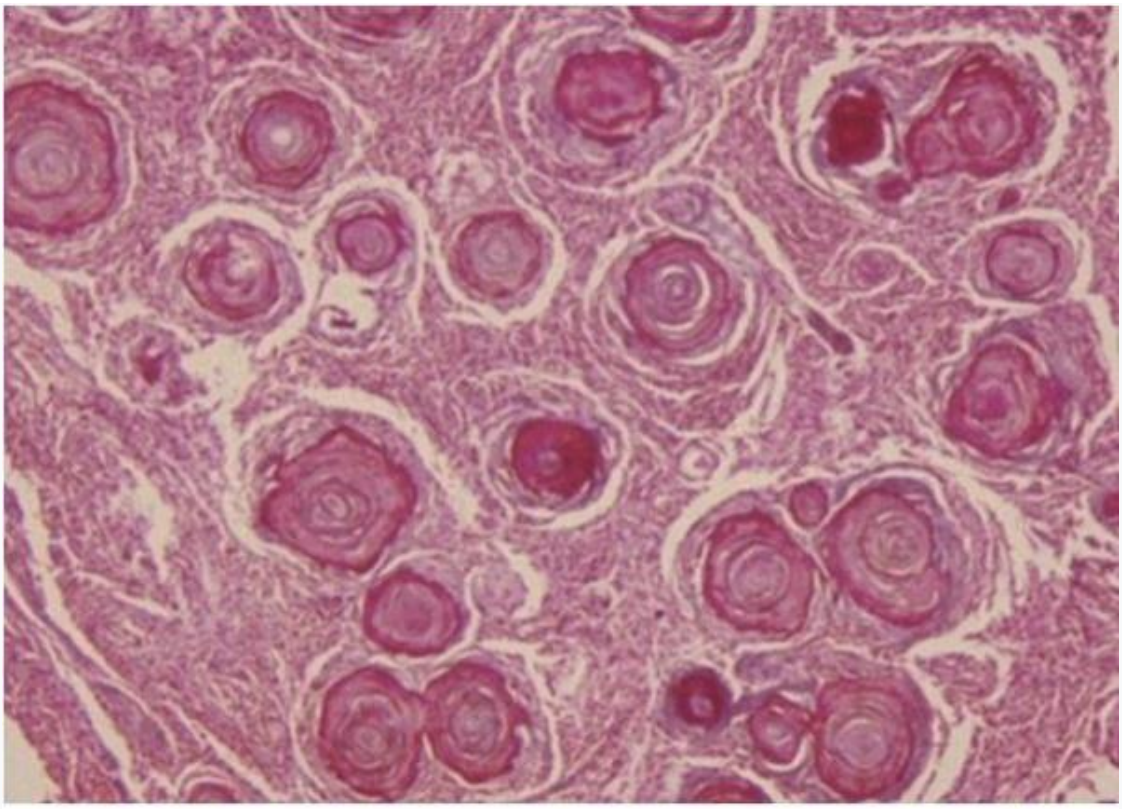


FIGURE 2: Localized psammomatous meningioma of the sphenoid wing, stained with H&E (20x). The image demonstrates diffuse psammoma calcifications often found in the center of meningothelial whorls.

The pathological and clinical classification of meningiomas is based on the WHO classification system for brain tumors.

WHO grade I - includes secretory, microcystic, clear cell, lymphoplasmocyte-rich and chordoid variants. Despite invasion into adjacent bone structures, grade I meningiomas do not invade the brain parenchyma.

WHO grade II – includes an atypical variant. This type of meningioma is characterized by frequent mitoses and an increased nuclear-cytoplasmic ratio.

WHO grade III/IV - includes malignant, papillary and anaplastic variants. This type of meningioma is characterized by even more mitosis, necrosis, and invasion of the brain parenchyma.

In a large retrospective study of 1663 patients undergoing surgery for meningioma, 90% were WHO grade I benign tumors and 10% were atypical or anaplastic variants, WHO grade II or III.

Clinical features

Ophthalmological manifestations of sphenoid wing meningioma vary depending on the location of the primary tumor. The tumor may spread from the intracranial space into the orbit through the bone, superior orbital fissure, or cavernous sinus. They may present with progressive symptoms of orbital or temporal fossa formation, including temporal fullness, proptosis, globe displacement, ptosis, and impaired extraocular motility. Tumors near the sella or optic nerve can cause visual field defects, swelling, or atrophy of the optic disc. Eyelid edema and chemosis are also common. The average age of onset is 50 years, with higher incidence among women and Caucasians.

Figure 3: A 48-year-old woman with bilateral exophthalmos (left greater than right), temporal fullness, upper eyelid steatoblepharon, and conjunctival injection secondary to a large sphenoid wing meningioma involving the left orbit and cavernous sinus.

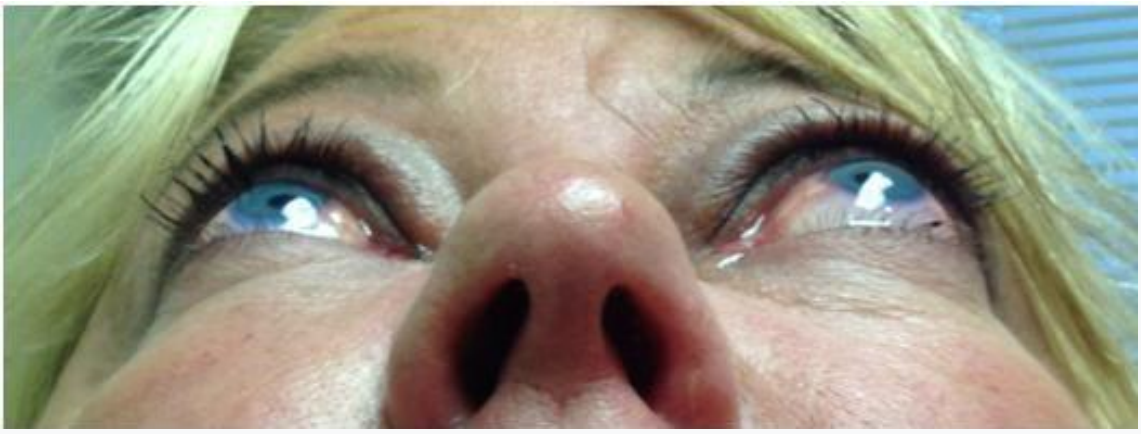
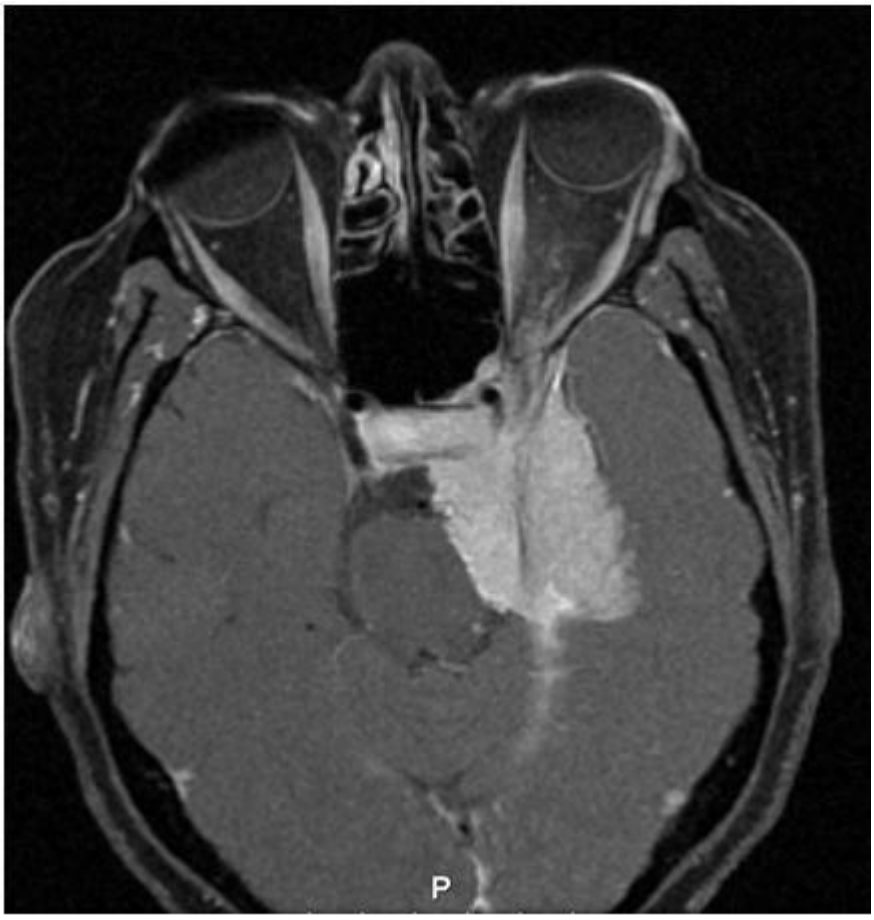


Figure 4: 48-year-old woman with bilateral exophthalmos (left more than right), temporal fullness, upper eyelid steatoblepharon, and conjunctival injection secondary to a large sphenoid wing meningioma involving the left orbit and cavernous sinus

Diagnostic Imaging

Imaging of sphenoid wing meningiomas demonstrates a thick, homogeneous tumor bed with relative preservation of anatomical structures. Tumors grow slowly and tend to conform to structures and cause compression rather than tissue invasion. The average annual growth rate of meningiomas is 1–3 mm per year. On CT, meningiomas are isoattenuating to slightly hyperattenuating and demonstrate homogeneous and intense enhancement after administration of iodinated contrast. On MR images, T1- and T2-weighted sequences have different signal intensities but enhance intensely and uniformly after gadolinium administration. They are also prone to hyperostosis and calcification, which can be seen on CT or MRI. Additionally, the presence of dural extension (also known as dural tail) helps differentiate meningioma from fibrous dysplasia.



Treatments for sphenoid wing meningioma include observation, surgery, radiation therapy, and chemotherapy. Early surgery is often preferred for younger patients and healthy older patients, while observation is usually preferred for asymptomatic older patients with multiple medical problems[12].

Operation

Meningioma resection has long been considered the primary and definitive treatment for meningioma. Surgery for sphenoid wing meningiomas is difficult due to their complex intracranial, intraosseous, and intraorbital growth pattern, which brings them into close proximity to major nerves and arteries. The advantages of this approach include: immediate removal of the lesion, rapid reduction of intracranial mass effect, and the ability to make an accurate pathological diagnosis. Surgery is usually performed using multistage procedures that take advantage of different approaches (eg, endoscopic endonasal surgery for lesions of the anterior skull base). This technique can minimize complications associated with resection of the entire tumor in one operation. The total resection rate is approximately 50%. Surgical complications range from 1 to 18%. The five-year disease-free survival rate for WHO grade I

meningiomas is 88%. A study of 53 patients with microsurgically treated meningiomas of the sphenoid wing revealed that deliberate incomplete resection of the tumor has a beneficial effect on postoperative quality of life, primarily due to the exclusion of neurological defects. In these cases of incomplete tumor resection, postoperative radiotherapy or radiation therapy is considered beneficial. Other factors that improve postoperative quality of life in patients with sphenoid wing meningiomas undergoing microvascular surgery are poor blood supply and lack of tumor adhesion to adjacent structures.

Radiation therapy

Radiation therapy is widely used in the treatment of sphenoid wing meningiomas. In the past, radiation therapy was only used for malignant meningomas or for relapses. Improvements in radiation therapy technology have changed this paradigm. Treatment decisions are made individually and multimodally, using both surgery and radiation therapy for patients with symptomatic tumors. Various radiation treatment options for sphenoid wing meningioma include: stereotactic radiosurgery, fractionated stereotactic radiation therapy (FSRT), intensity-modulated radiation therapy (IMRT), and particle radiation therapy (also known as proton beam). In stereotactic radiosurgery, all radiation is directed to the tumor in one fraction, while in FSRT and IMRT the dose is given in multiple fractions over time. The main difference between FSRT and IMRT is that IMRT can treat more complex shapes and larger tumors because it improves the radiation's ability to conform to the tumor margin and minimizes damage to important normal structures. Clinically, radiosurgery is a safe alternative to resection of skull base meningioma in patients who are not good candidates for surgery; however, there are limitations for tumors in close proximity to critical and radiosensitive structures. FSRT and IMRT are usually used when the tumor is around radiosensitive structures such as the optic nerve or chiasm. For radiotherapy in general, local control rates of 92–100% have been reported. The incidence of permanent neurological deficit ranges from 1.6% to 9.8%. After radiation therapy, tumor volume decreases by 33% after 2 years and by 36% after 3 years.

Chemotherapy

Chemotherapy is also used to treat advanced, recurrent, or inoperable meningiomas. Many agents have been tried, including typical cytotoxic agents and mifepristone. In general, chemotherapy does not play a significant role in the treatment of meningioma, as there is usually significant systemic toxicity with little or no tumor regression. Combination chemotherapy with hydroxyurea is currently being evaluated. Inhibition of angiogenesis has become one of the key mechanisms in the treatment of meningiomas, as they are highly vascular tumors. In vitro studies using targeted molecular therapies against PDGF (platelet-derived growth factor), VEGF (vascular endothelial growth factor), EGF (epidermal growth factor) and MAPK (MAP kinase) appear promising in recurrent meningioma.

Treatment Summary

All treatment modalities can play a role in the treatment of sphenoid wing meningioma. In a review article published by Coombs et al, they proposed a relative general standard of care for the treatment of skull base meningiomas. Figure 6 presents a proposed decision tree for the treatment of skull base meningiomas. The flowchart describes consideration of surgery and/or radiation therapy in the presence of symptoms, tissue compression, exophthalmos, or cavernous sinus infiltration. In the absence of symptoms or signs, observation may be appropriate.

Forecast

In general, the malignancy rate of skull base meningiomas (including sphenoid wing meningomas) is low. In a large retrospective study of 1663 patients operated on for menigioma, 90% were benign (WHO Grade I) and only 10% were atypical or anaplastic (WHO Grade II or III). The main risk factors for higher WHO grade were location outside the skull base (OR 1.7) and age >= 65 years (OR 1.5). Male sex also conferred a twofold risk of the higher WHO score.

Recurrence-free survival for WHO grade I meningioma with surgery, radiation therapy or combination treatment is almost 90%. Morbidity varies after therapy, with rates of permanent neurological deficit ranging from 1.6-9.8%. The morbidity of the tumor and therapeutic interventions depends on the location of the tumor and its proximity to vital neurological and ocular structures.

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