Orbitotemporal Neurofibromatosis: Classification and Treatment

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ABSTRACT  Purpose: To review the clinical findings in orbitotemporal neurofibromatosis and discuss treatment options. Clinical features, histopathologic characteristics, and treatment options are reviewed. Methods: A Medline literature search from 1966 to 2004 was performed, using the key words: orbitotemporal neurofibromatosis, orbitopalpebral neurofibromatosis, orbitofacial neurofibromatosis, cranio-orbital neurofibromatosis, cranio-orbital-temporal neurofibromatosis, and the pertinent literature was reviewed. Additionally, our experience with two patients is reported. The surgical procedures are discussed. Conclusion: The management of orbitotemporal neurofibromatosis is challenging. The planned surgical approach and extent of resection depend on the severity of the orbital soft tissue and bony involvement and on the visual potential. Ultimately, orbital exenteration may be needed for rehabilitation and cosmesis.

KEYWORDS  Orbitotemporal neurofibromatosis; orbitopalpebral neurofibromatosis; orbitofacial neurofibromatosis; cranio-orbital neurofibromatosis; cranio-orbital-temporal neurofibromatosis

INTRODUCTION

Neurofibromatosis type 1 is an autosomal dominant disorder with an incidence of approximately 1 in 3000 live births (Ricardi, 1981). The patient may develop grossly disfiguring neurofibromas of the orbital, temporal and facial region, also known as orbitotemporal neurofibromatosis (Jackson et al., 1993). The neurofibroma arises from proliferation of the multiple cellular elements in peripheral nerves (Grabb et al., 1980). Although benign histologically, these hamartomas can be disfiguring in their relentless growth (Park et al., 2002). In the literature, orbitotemporal neurofibromatosis (OTNF) is the term most commonly used; however, it has also been reported under several different names, including orbitopalpebral neurofibromatosis (Marchac, 1984; Morax et al., 1988), orbitofacial neurofibromatosis (Van der Meulen et al., 1982), cranio-orbital neurofibromatosis (Poole, 1989), and cranio-orbital-temporal neurofibromatosis (Havlik & Boaz, 1998).

The onset of OTNF begins in childhood. The child presents with upper eyelid swelling, which eventually progresses to a mechanical blepharoptosis with
an immobile upper lid, and ultimately, amblyopia (Jackson et al., 1983). The neurofibroma may extend into the subcutaneous tissue with swelling of the temple, forehead, or midface. Extraocular muscles may be directly involved, resulting in lack of conjugate eye movement (Morax et al., 1988). There are associated symptoms of ocular irritation, pain and epiphora (Jackson et al., 1983, 1993; Marchac, 1984; Morax et al., 1988). Progression of OTNF results in severely disfiguring proptosis, a downward displacement of the globe and lateral canthus, and compromised visual acuity.

The characteristic skeletal abnormality in OTNF is the absence of the greater wing of the sphenoid, which may be partial or complete, allowing communication between the middle cranial fossa and the orbit. This defect results from widening of the superior orbital fissure and loss of the adjacent bone of the greater and lesser sphenoid (Poole, 1989). The temporal lobe of the brain may herniate into the orbit causing pulsating exophthalmos. Less frequently, the orbital contents may herniate into the middle cranial fossa causing enophthalmos (Jackson et al., 1993). Intracranial lesions may include glioma of the optic nerve and arachnoid cysts, causing headaches and seizures (Marchac, 1984). Intraorbital neurofibromas result in eventual bony orbit enlargement with hypoplasia of the supraorbital and infraorbital rims, zygoma hypoplasia, and orbital floor depression (Jackson et al., 1993). The skull x-ray typically shows an enlarged, egg-shaped bony orbit (Henderson, 1994).

The treatment of OTNF is difficult. We report our experience with OTNF to illustrate the clinical findings and the surgical approaches used in their correction.

**CASE REPORTS**

**Patient 1**

A 6-year-old girl presented with right upper lid blepharoptosis and amblyopia. She had neurofibromatosis type 1 with multiple café-au-lait spots, Lisch nodules, and blepharoptosis of her right eye since birth. At age 2, she underwent right anterior orbitotomy for debulking of her orbital neurofibroma and right ptosis repair. At 6 years of age she had recurrent right upper lid mechanical ptosis from expansion of her neurofibromas (Fig. 1A). Ocular examination revealed best corrected visual acuity of 20/80 in the right eye and 20/20 in the fellow eye. Margin reflex distance 1 was −1 mm right eye, +3 mm left eye. Levator function was 9 mm on the right side and 16 mm on the left side. After debulking and levator resection, the patient had improved visual acuity and ptosis correction (Fig. 1B).
right eye, 13 mm left eye. Her right globe was displaced 4 mm inferiorly. Cycloplegic refraction revealed anisometropic astigmatism with $-0.75 + 3.50 \times 120$ right eye and $+0.75 + 0.75 \times 070$ left eye. There was prominent right temporal swelling with no bony involvement. Her visually significant right blepharoptosis was obscuring her visual axis, causing superior visual field deficits and worsening amblyopia. We performed a right anterior orbitotomy with tumor debulking and levator resection. She has been followed for 2 years without recurrence (Fig. 1B).

**Patient 2**

An 8-year-old boy presented with disfiguring proptosis of the left eye. He had neurofibromatosis type 1 with multiple café-au-lait spots and proptosis of his left eye since birth. Later, he developed a pulsatile exophthalmos due to absence of the left greater sphenoid wing with temporal lobe and arachnoid cyst herniation into the orbit. At age 2, he underwent craniotomy with tumor debulking and sphenoid wing reconstruction in collaboration with neurosurgery. Further tumor growth required tumor debulking with temporal bone contouring and orbital reconstructions at ages 4 and 7. At 8 years of age, he had disfiguring proptosis of the left eye from recurrence of his neurofibromas (Fig. 2A). Ocular examination revealed best corrected visual acuity of 20/400 in the left eye and 20/25 in the fellow eye. The left eye had proptosis of 20 mm. He had downward displacement of his left globe, downward displacement of his medial and lateral canthi, upper eyelid mechanical ptosis with 0 mm levator function, prominent left temporal swelling, exposure keratopathy of the left eye, and limitation of extraocular movement in the left eye. The unsightly facial and orbital appearance was a psychosocial concern for the patient and his parents, with limited potential for visual recovery and satisfactory cosmesis. In collaboration with neurosurgery, we performed a craniotomy and left orbital exenteration with bone excision and orbit reconstruction, with placement of preserved skin grafts (Fig. 2B). Histopathology of the exenteration specimen revealed multiple enlarged nerve bundles in the superior eyelid and orbit (Fig. 3).

**DISCUSSION**

The treatment of OTNF is frustrating to both patient and surgeon. Due to the extensive, diffuse soft tissue infiltration and lack of encapsulation, complete excision
FIGURE 3 Exenteration specimen of patient 2 reveals multiple enlarged nerve bundles in the superior orbit and intraconal space (A, H&E × 1) as well as similar structures in the upper eyelid protruding into the superior fornix (B, H&E × 20). These neurofibromas are composed of cells with elongated, spindle shaped nuclei and fine wavy immature collagen fibers, so called “maiden hair” (C, H&E × 400).

of the neurofibroma is virtually impossible (Grabb et al., 1980). The patient and surgeon are often faced with multiple tumor recurrence followed by multiple subtotal excisions. Cosmetic deformity occurs from the tumor’s relentless growth.

Most surgeons recommend that surgery be done at an early age in an attempt to avoid orbital deformity, to preserve eye function by maintaining everything as anatomically correct as possible, and to prevent functional problems of eyelid ptosis and consequent blindness (Jackson et al., 1993). In 2–16% of cases, orbital neurofibromas may undergo malignant transformation (Grabb et al., 1980). Most cases, however, are benign growths with aggressive tumor infiltration. Resection should be as complete as possible with preservation of function if possible. The planned surgical approach and extent of resection depend on the severity of the orbital soft tissue and bony involvement and on the visual potential (Table 1). Jackson et al. (1993) originally proposed classifying patients into three groups, which require different approaches to treatment:

1. Orbital soft tissue involvement with a seeing eye
2. Orbital soft tissue and significant bony involvement with a seeing eye
3. Orbital soft tissue and significant bony involvement with a blind, malpositioned eye.

When the orbital neurofibromas only involve soft tissues, surgery is performed to remove the bulk of the lesion. Only the rare, well-circumscribed neurofibromas can be removed intact through an anterolateral orbitotomy (Krohel et al., 1985). However, the more common plexiform neurofibroma has diffuse soft tissue infiltration which makes complete resection difficult. Orbital neurofibroma debulking is done via an anterior, lateral or anterolateral orbitotomy. If blepharoptosis results in amblyopia, concomitant levator resection should be conservative (Marchac, 1984). Disfiguring facial neurofibromas require radical resection and reconstruction in an attempt to limit recurrence. Conservative, partial excision leads to subsequent recurrences. In cases when only partial resection was possible, Park et al. (2002) introduced the technique of netting the remaining tumor with Teflon mesh. The Teflon mesh serves to suspend the drooping soft tissue and substitute for the destroyed
subcutaneous tissue. Whether the mesh compression serves to suppress regrowth or forces the growth of the tumor to a less resistant region remains to be investigated. Recently, soft-tissue, periorbital deformities of orbitotemporal neurofibromatosis have been classified by Lee et al. (2004). These include: brow ptosis, upper lid infiltration with ptosis, lower lid infiltration, lateral canthal disinsertion, and conjunctival and lacrimal gland infiltration.

When neurofibromas involve both orbital soft tissue and the bony wall, the defect in the greater sphenoid wing causes pulsating proptosis. An intracranial approach provides superior exposure and visualization for tumor debulking and posterolateral orbital wall reconstruction. The oculofacial plastic or orbital surgeon collaborates with a neurosurgeon in performing a transcranial orbitotomy with a bilateral frontal bone flap approach as first described by Marchac (1984). Briefly, a bicoronal incision is made and a bilateral frontal bone flap is elevated. The dura is dissected from the orbital contents and the herniated temporal lobe is reduced back into the middle cranial fossa via intracranial exposure. The periorbita is incised to allow orbital fat to fill the enlarged orbital cavity. If upper eyelid ptosis is present, it is addressed at a later date to avoid corneal exposure and to allow for a more precise adjustment after swelling subsides (Marchac, 1984; Morax et al., 1988). Many surgeons perform a two-stage operation, with intracranial and intraorbital debulking with elevation of the globe and canthopexies in the first stage, and subcutaneous debulking with reconstructive surgery on the upper eyelid, face, and temple in the second stage (Henderson, 1994).

Patients with severe soft tissue and bony involvement due to OTNF may have poor vision from dense amblyopia, immobile or complete blepharoptosis, or intraocular neurofibromas (Jackson et al., 1983). The desire to preserve the eye in these patients has often led to incomplete resections with relentlessly progressive recurrences and a disfiguring cosmetic result that are almost always a disappointment. If a large tumor is stable without progression or if an enlarging OTNF disfigurement does not cause significant psychosocial concerns for the patient, then observation is a prudent option. However, if an unsightly facial and orbital appearance causes major psychosocial distress to the patient, and if the eye has poor visual potential, then orbital exenteration is a viable option and often produces the best cosmetic results, according to case reports by Jackson et al. (1983), Poole (1989), and Van der Meulen et al. (1982). Although exenteration for an essentially benign tumor is extreme, it may greatly reduce future progression and reduce the possibility of future malignant transformation, particularly in patients who have a blind, malpositioned eye (Jackson et al., 1983).

For exenteration and reconstruction of the absent greater sphenoid wing, Jackson et al. (1983) described an operation where only an orbital approach was necessary. First, the plexiform tumor involving the face, temple, and eyelid is removed. The eyelid skin is preserved and is later used to cover the interior of the reconstructed orbit. Next, an exenteration of all orbital contents is performed. The herniated temporal lobe is

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**TABLE 1** Orbitotemporal neurofibromatosis: classification and treatment.

<table>
<thead>
<tr>
<th>Orbital soft-tissue involvement with a seeing eye</th>
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<tbody>
<tr>
<td>Debulk tumor</td>
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<tr>
<td>Consider mesh</td>
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<tr>
<td>Conservative blepharoptosis repair</td>
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<tr>
<td>Debulk tumor</td>
</tr>
<tr>
<td>Reduce orbital contents into orbit and intracranial contents into middle cranial fossa via intracranial approach</td>
</tr>
<tr>
<td>Cover bony defect with frontal bone flap</td>
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<tr>
<td>Enlarge orbit volume with osteotomies to accommodate enlarged orbital soft tissue mass</td>
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<tr>
<td>Elevate the canthal ligaments and build up the floor to elevate the globe</td>
</tr>
<tr>
<td>Conservative blepharoptosis repair at a later date</td>
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<tr>
<td>Debulk tumor by exenteration</td>
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<tr>
<td>Reduce intracranial contents into the middle cranial fossa via orbital approach</td>
</tr>
<tr>
<td>Cover bony defect with split-rib bone graft</td>
</tr>
<tr>
<td>Reduce orbit volume and adjust orbit position with osteotomies and bone grafts for symmetry</td>
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<tr>
<td>Fit orbital prosthesis</td>
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the orbit. The lateral orbital wall is shifted further laterally by another osteotomy to increase the volume of the orbital space to accommodate the increased orbital bulk from the residual tumor. The floor is elevated, utilizing bone graft taken from the vault to counteract the downward globe displacement. The canthal ligaments are elevated and fixed using transnasal canthopexy and transbony wire to address the downward canthi displacement. The periorbita is incised to allow orbital fat to fill the defect of the roof and posterior wall of
reduced back into the middle cranial fossa via an orbital approach. The defect in the greater sphenoid wing can be reconstructed with split-rib bone grafts by this orbital approach. The greatly enlarged orbit is reduced in size and volume: the floor is elevated using osteotomies to reposition the inferolateral orbital rim supranasally while inlay bone grafts further reduce orbit size and volume by filling the supraorbital rim and building up the posterior orbital wall. Later, an orbital prosthesis is fit.

These craniofacial operations should not be taken lightly. There is a rather high complication rate compared to other intracranial craniofacial operations (Poole, 1989). Neurofibroma-infiltrated tissues are very vascular and bleed heavily during excision. Wound healing is slow. Complications may include excessive bleeding at surgery, delayed hematoma, cerebral edema, recurrence of pulsating proptosis, and medial canthal and lateral canthal redisplacement (Marchac, 1984; Poole, 1989). Again, if a large tumor is stable without progression or if an enlarging OTNF disfigurement does not cause significant psychosocial distress for the patient, then conservative treatment with observation is a prudent option.

CONCLUSION

The management of orbitotemporal neurofibromatosis is challenging. The planned surgical approach and extent of resection depend on the severity of the orbital soft tissue and bony involvement and on the visual potential. If there is any useful vision, the eye should be preserved. However, if the eye has poor visual potential and the fellow eye is healthy, orbital exenteration may limit disfiguring and destructive regrowth and provide the best cosmetic result.

REFERENCES


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