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Case report

Reconstruction of skull base defects in sphenoid wing dysplasia associated with neurofibromatosis I with titanium mesh

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ABSTRACT

Sphenoid wing dysplasia occurs in 3–7% of patients with neurofibromatosis type 1 (NF1). The typical radiological features are partial or complete absence of the greater wing of the sphenoid. This condition is slowly progressive and may result in temporal lobe herniation into the orbital cavity, producing pulsating exophthalmos and gross facial deformity. Thus, reconstruction of the orbit is important for both cosmetic and functional reasons. Traditional surgical treatment of sphenoid dysplasia involves split bone grafting and repair of the anterior skull base defect. However, several reports have demonstrated complications of graft resorption and recurrence of proptosis and pulsating exopthalmos. In this case series, we present two patients suffering from pulsating exophthalmos due to sphenoid dysplasia. Radiological and MRI studies demonstrated orbital enlargement and complete absence of the greater wing of the sphenoid. Surgical management of these patients involved dural defect repair, and the use of titanium mesh in conjunction with bone graft to act as a barrier between the orbit and the middle cranial fossa. The mesh was fixed by fine screws. Proptosis improved markedly post-operatively and resolved within a few weeks. Ocular pulsation subsided and remained quiescent with at least 1-year follow-up.

1. Introduction

Sphenoid wing dysplasia is relatively rare in the general population and over 50% of the cases are associated with neurofibromatosis type 1 (NF1), a neurocutaneous disorder with an incidence of 1:3000 [1,16,17]. It has been found to occur with a frequency of 3–7% among patients with NF1 [60], co-presenting with clinical features such as cutaneous neurofibromas, café au lait spots, Lisch nodules, axillary and/or inguinal freckling and neural sheath tumors [8]. Sphenoid wing dysplasia may be progressive and may lead to disruption of the orbit, pulsating exophthalmos, and brain herniation into the orbit [7]. In children with NF1-associated sphenoid wing dysplasia, abnormal growth of the skull may lead to severe facial deformity [31].

Whether sphenoid wing dysplasia is congenital as a result of mesodermal maldevelopment or acquired via secondary processes remains controversial, as the specific pathogenesis of the condition remains unclear [21,40]. The typical radiological feature is the presence of a defect in all or part of the greater wing of the sphenoid bone. This is usually accompanied with elevation of the lesser wing of the sphenoid, distortion of the sella and enlargement of the ipsilateral orbit [22,30]. The eye may be enophthalmic or microphthalmic; conversely, if buphthalmos is present, a large eye may be encountered.

The treatment for sphenoid dysplasia depends on the type and severity of the orbital involvement and on the condition of the eye. While repair of bony defects of the orbit and skull base employing a transcranial bone graft was performed as early as 1929 by Dandy [12], only a handful of cases were reported in the literature before 1980, and treatments varied widely [3,12,39,45,46,49,51,54]. With advances in craniofacial surgery during the past three decades, repair of the bony defect in the posterior–superior part of the orbit using a transcranial approach has became a more practiced and standardized therapeutic modality. Bone graft material may be culled from the rib, skull, or iliac crest, and the bone graft is wired, plated, or screwed into the position of the defect [30].

Unfortunately, resorption of bone grafts has been a key limitation in the anterior reconstruction of sphenoid wing dysplasia [23,55,61]. Since then, synthetic material, wires, plates, or soft tissue grafts, as well as a variety of pedicled or free flaps have been advocated for reconstruction of anterior skull base defects [53]. Within the last 10 years, titanium mesh has been advanced as a potential solution to this problem, either used alone [50] or in combination with bone grafts and pericranial flaps [9,53]. A detailed

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Table 1
Summary of all cases of skull base/orbital fibrous dysplasia surgically managed with titanium mesh.

Authors	Year	Age	Sex	Etiology	Operative technique	Follow-up	Complications
Friedrich et al.	2003	25	M	Sphenoid wing dysplasia associated with NF1	A modified lateral orbitotomy as revisited by Maroon and Kenderdell was used. However, an anterior curved incision with a lateral extension in the eyebrow was used. After the lateral orbital rim was replaced, fixation was performed with a miniplate (2.0, Mondeal Mini 2000) because intraorbital pressure was suspected to be high. The dura was opened and, the temporal lobe was repositioned and titanium mesh with iliac spongiosa was inserted as an overlay. The procedure was repeated 6 months later. The titanium mesh was found to be turned and most of the transplanted bone had resorbed. A more extended mesh was implanted, and iliac spongiosa was placed on both sides.	7 mos	None
Snyder et al.	1998	30		Sphenoid wing dysplasia in orbital neurofibromatosis	Transcranial bone graft with titanium mesh, orbital translocation	6 mos	Unknown
		2		Sphenoid wing dysplasia in orbital neurofibromatosis	Transcranial bone graft with titanium mesh	6 mos	Unknown
		5		Sphenoid wing dysplasia in orbital neurofibromatosis	Transcranial bone graft with titanium mesh, zygomatic osteotomy; second operation for orbital transcranial bone graft and ptosis correction	15 mos	None
Wu et al.	2008	16	F	Sphenoid wing dysplasia associated with NF1	The patient underwent a right frontotemporal orbital craniotomy. A neuronavigation system was used for guidance. After general anesthesia, the patient's head was positioned and immobilized. No subcutaneous nodules were found in the scalp, and the skull of the entire frontotemporal region was unusually thin with several small bone defects. After gentle retraction of the temporal dura, it became clear that the bone defect was located at the greater wing of the sphenoid and lateral orbital wall. The margins of the bone defect were mapped by the navigator. No superior orbital fissure was observed; however, in the medial wall of the meningocele, the cranial nerves leading to the orbit could be identified. The intraorbital components were decompressed. The titanium mesh was molded and cut based on a stereolithographic model while its margins were smoothed to avoid damaging the dura. Several thick parts of the skull bone around the defect margins that were appropriate for graft fixation were located by the neuronavigator. Then the final graft was secured. After repairing the defect, the orbital rim and bone flap were replaced, and the wound was closed in a standard manner.	30 mos	None

review of the literature reveals five cases of surgical management of sphenoid wing dysplasia with a titanium mesh-based graft (Table 1) [18,55,61].

Here, we present two additional cases of NF1 with dysplasia of the greater sphenoid wing which were treated via a transcranial approach where the skull base defect was closed by titanium mesh. Proptosis and ocular pulsations resolved, and this clinical improvement persisted after 1-year of follow-up.

2. Case reports

2.1. Pre-operative findings

A 21-year-old female presented with right-sided pulsating exophthalmos (Fig. 1a). The degree of exophthalmos was 30 mm by Hertel exophthalmometer and increased with coughing and sneezing. Proptosis was initally noted at age 6 and slowly progressed. Another patient is a 7-year-old male who presented with left-sided pulsating exophthalmos (Fig. 3a). The degree of exophthalmos was 28 mm which also increased with coughing and sneezing. In addition to the forward proptosis, the affected eyes were pushed downward as well. The pre-operative visual acuity was 6/12 in the affected right eye and 6/9 in the left eye for the first patient. In the second patient, visual acuity was 6/36 in the affected left eye and 6/12 on the right. In both patients, the globes of the eye were of the same size. Both patients presented with more than six café au lait spots. Both presented with freckling in the axillary regions.

In both patients, X-ray and CT images revealed hypoplasia of the greater wing of the sphenoid bone, as well as asymmetry of the orbits, sphenoid and ethmoid sinuses (Figs. 2 and 3). MRI scans revealed herniation of the anterior part of the temporal lobe into the orbit, pushing the eye globe forward and downward (Fig. 2). Optic nerve or intracranial mass lesions were not present.

2.2. Operative technique and findings

A large frontotemporal craniotomy was performed after tarsorrhaphy to protect the cornea. The bone was very thin and nearly

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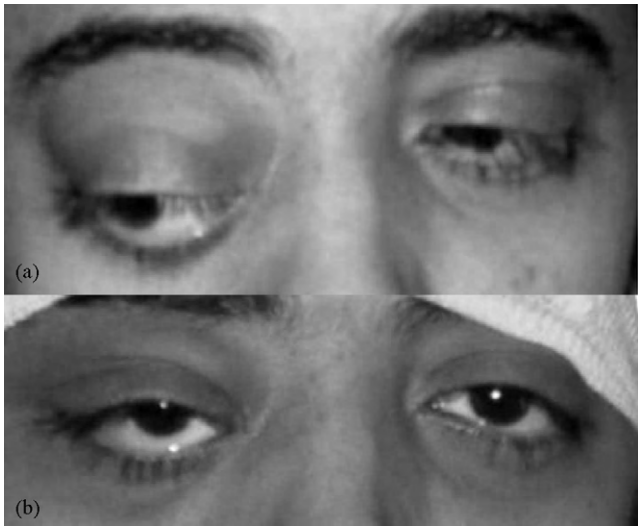

Fig. 1. Case 1: (a) Pre-operative picture showing forward and downward protrusion of the right eye and (b) post-operative picture showing resolution of proptosis with residual ptosis.

absent in the depth of the temporal fossa. The dura over the temporal lobe was fused with the periorbita. To expose the temporal lobe, a dural incision was made 1 cm lateral to its adhesion to the periorbita. The CSF space was found to be enlarged with thickened leptomeningeal coverings. The brain was gliotic. The fibrotic temporal lobe, occupying the retro-orbital space, was excised. No tumor tissue was found in the palpebrae, orbit, temporal region, or skull base. The periorbita was left intact to protect the orbital structures. A pericranial flap was obtained and was sutured to the free end of the temporal dura. The other end of the pericranial flap was sutured to the periorbita. Further re-enforcement of the pericranial flap was achieved by Duragen synthetic dural graft (Integra LifeSciences Corporation) to prevent CSF leak (Fig. 4).

The absent greater wing of sphenoid created a skull base defect. In the first case, the defect was triangular and approximately 4 cm at its widest part. In the second case, the defect was oval in the place of the orbital roof and lateral wall (Fig. 3). Titanium mesh was tailored intraoperatively to follow the curvatures of the anterior and middle cranial fossae and to close the defect by acting as a barrier between the orbital cavity and the cranium (Fig. 4). The titanium mesh was fixed in situ by screws—anteriorly in the orbital plate of the frontal bone and posteriorly in the petrous part of the temporal bone. The osteoplasic flap was closed in layers and an extradural drain was inserted.

2.3. Post-operative course

Peri-operatively, there were no complications. Both patients experienced full regression of proptosis—12 mm in the first case (Fig. 1b) and 10 mm in the second. There was no pulsation of the eyeballs. Eyelid edema and proptosis resolved within a few weeks. Extraoccular movements were normal and visual acuity remained at baseline for both patients at follow-up of 1 year.

3. Discussion

Neurofibromatosis type 1, formerly known as von Recklinghausen disease and caused by mutations in the NF1 tumor suppressor gene located on chromosome 17q11.2, is one of the most commonly inherited autosomal dominant disorders [27,59]. Though more than 50% of cases are spontaneous, 80% of inherited cases are of paternal origin [8]. Although café au lait spots, freckling, and cutaneous neurofibromas are the most frequent clinical signs in NF1 patients, neurofibromatosis may affect a wide range of organ systems including the skin, eye, skeleton, cardiovascular system,

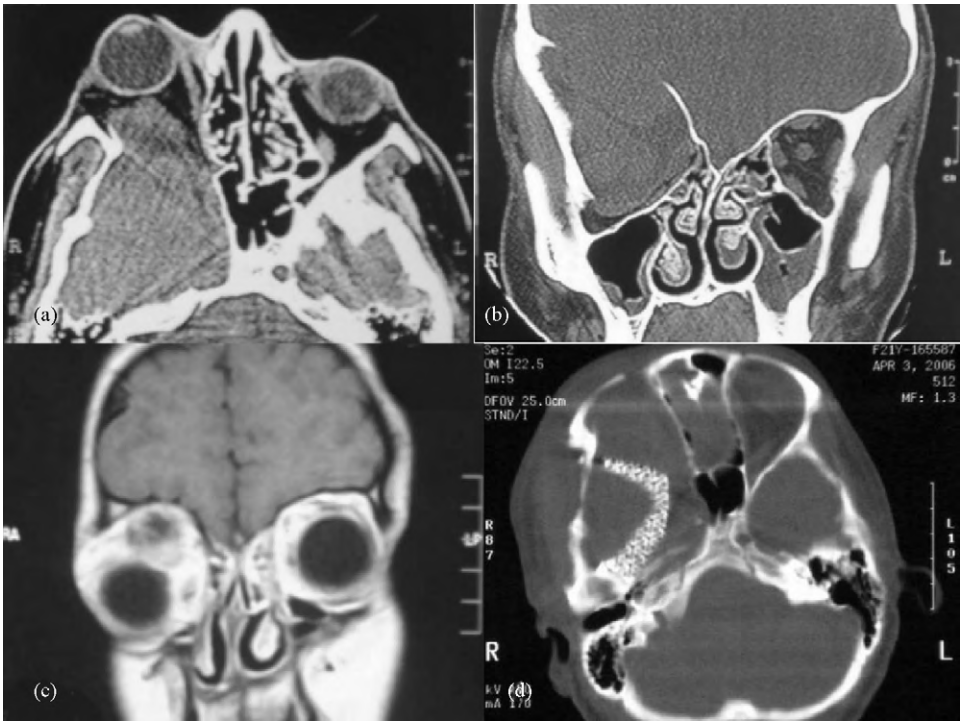

Fig. 2. Case 1: (a) Axial CT of orbits showing absence of the right greater wing of sphenoid. The temporal lobe is herniating into the orbit pushing the eye forward. (b) Coronal head CT reveals right temporal lobe herniation into the orbit. The orbital floor is displaced downwards and the ethmoid bone is displaced medially. (c) Coronal MRI showing the severe downward and outward deviation of the eye. (d) Post-operative head CT scan showing the reconstruction of the posterior wall of the orbit and the greater wing of the sphenoid bone.

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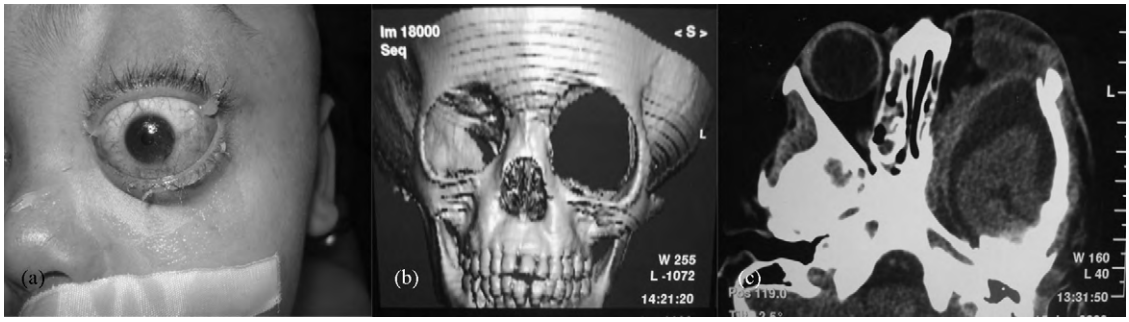

Fig. 3. Case 2: (a) Pre-operative picture showing forward and downward protrusion of the left eye. (b) Coronal head CT scan revealing the absence of the sphenoid wing and the orbital roof. (c) Axial CT showing the absence of left greater wing of sphenoid with temporal lobe herniation into the orbit pushing the eye forward.

endocrine system, and central nervous system [63]. Osseous manifestations have been reported in approximately half of patients with NF1 [11,26]. The most common skeletal anomalies include scoliosis, absence of the greater sphenoid wing, tibial pseudarthrosis, short stature, spinal meningocele, and macrocephaly [8].

Though much work has been attempted to link the molecular biology of NF1 to its clinical manifestations, much remains unclear. It is known that neurofibromin, the gene product of NF1, is a GTPase activating protein and potent down-regulator of Ras proteins [35]. In mice, neurofibromin expression begins in embryonic day 11 and is expressed in a variety of tissues, including the developing central nervous system, heart, lung, liver, stomach, and dorsal root ganglia [19,25,28,41]. While neurofibromin expression in osteoblasts during embryogenesis has not been conclusively demonstrated, adult mouse chondrocytes, osteoblasts, and osteoclasts express neurofibromin in vivo [19,37,62]. Reduced or loss of function in NF1 causes a dose-dependent elevation in Ras activity, which in turn activates a number of signaling events such as the MAPK pathway and PI3K pathway, affecting different patterns of cellular proliferation and differentiation in different tissues [4,43].

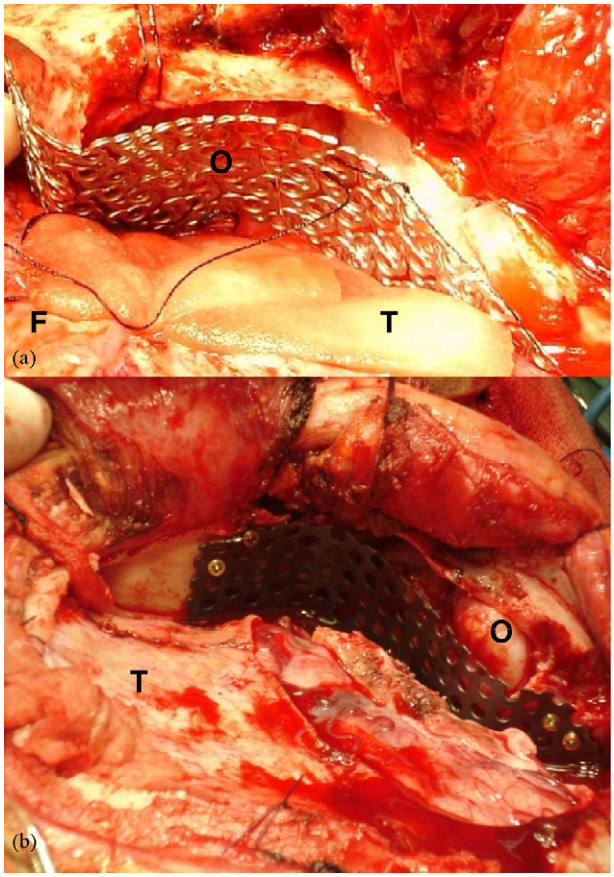

Fig. 4. Intraoperative views through frontotemporal approach. (a) Case 1: Synthetic dural replacement used to repair the dural defect along with titanium mesh used to reconstruct the absent sphenoid wing. (b) Case 2: Titanium mesh is used to separate the middle cranial fossa from the orbit. F: frontal lobe; O: orbit; T: temporal lobe.

As a tumor suppressor gene, some have argued that the phenotypic manifestations of NF1 insufficiency occur mainly as a result of loss of heterozygosity. Indeed, homozygous null NF1 mice proved embryonic lethal, and heterozygous NF1 mice showed no reduction in early survival or any human-like NF1 deficiency states [5,29]. Importantly, conditional knock-out NF1 mice developed dysfunctional and malformed limbs [36], which included abnormal joints and bones, and in humans, double-inactivation of NF1 has also been found in pseudarthrosis tissue specifically [58]. In addition, homozygous loss of function in NF1 has also been implicated in the development of neurofibromas and neurofibrosarcomas in humans [44,56].

Despite the clear evidence for neurofibromin's role in skeletogenesis bone homeostasis, how these molecular findings translate into a clinical phenotype is still unclear. One hypothesis for the pathogenesis of skull base defects in NF1 patients attributes the osseous defect to abnormal NF1-haploinsufficient bone remodeling in the presence of external pressure, usually via an adjacent mass or an increased intracranial pressure [23,48]. These masses may include plexiform neurofibroma [15,27,32,56,60], meningocele [2,11,12], or other soft tissue masses. This type of progressive osseous erosion as a secondary process has been directly documented by CT imaging. Macfarlane et al. used serial CTs to demonstrate progressive destruction of the greater sphenoid wing associated with an enlarging orbital soft tissue mass in a child with NF1 [40]. The authors hypothesized that the tumor caused expansion of the superior orbital fissure, dural herniation, and subsequent bone erosion from localized CSF pressure. Similarly, Jacquemin et al. reviewed orbital abnormalities in 24 patients, and found focal decalcification/remodeling of orbital walls adjacent to plexiform neurofibromas in 18 patients and enlargement of cranial foramina resulting from tumor infiltration of sensory nerves in 16 [31,32]. The authors attributed the expansion of the middle cranial fossa into the posterior orbit, enlargement of the orbital rim, bone erosion and decalcification, and enlargement of the cranial foramina to the effect of these adjacent masses. Along these lines, some authors have speculated that sphenoidal dysplasia in some patients with NF1 may result from dural ectasia of the trigeminal nerve [6].

This explanation cannot be used to explain the orbitosphenoid defects in our patients due to the lack of soft tissue masses noted intraoperatively. In fact, others have also noted the surgical or radiographic absence of tumor contiguous with osseous lesions of the skull where pressure-induced osteolysis cannot be attributed as

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a cause of sphenoid dysplasia [13,20,26,33]. Moreover, some have observed that even where tumor is found adjacent to the sphenoid wing, the bone does not show irregular resorption as would be expected of an erosive tumor, and others have pointed out that this replacement of the sphenoid bone with tumor should still result in a barrier, which is unable to account for the pulsating exopthlamos frequently found in NF1 patients [23,40]. Coupled with the observation that many cases of orbitosphenoid defects are present at birth and the spatial localization of these lesions are almost always in the posterior–superior orbit, a second theory on the origin of skeletal anomalies in patients with NF1 hypothesizes that they are malformations arising from defective mesodermal and neuroectodermal development [26]. Nevertheless, this hypothesis is imperfect as well, as it cannot explain the reason why these lesions are frequently unilateral, and why the sphenoid bone is preferentially affected compared to other skull bones.

Regardless of the pathogenesis of sphenoid dysplasia, its surgical treatment and repair is complicated by the fact that NF1 patients exhibit recalcitrant bone repair [52]. This is seen in the high rate of pseudoarthrosis seen in NF-1 patients undergoing scoliosis correction spinal fusions (from 15 to 31%) [10]. Moreover, surgery on congenital pseudarthrosis of the tibia – involving physical excision of abnormal bone tissue followed by fixation with an intramedullary rod or external device – may require multiple revision surgeries [14,34,57]. Even then, limb function may remain compromised, and unfortunately, amputation is not uncommon. In NF1 patients with sphenoid dysplasia, those who have undergone traditional split bone grafting have suffered from bone resorption, graft displacement, and resulting recurrence of pulsating exophthalmos [23,47,55]. Ex vivo experiments have also confirmed these clinical findings, as pseudarthrotic tissue cultured from patients was found to be osteoclastogenic, and in vitro experiments have shown reduced vascularity or vascular thickening to play a role in pseudarthrosis as well [24,38].

As a result, surgical correction of sphenoid dysplasia can be difficult. Surgical goal includes dural closure and restoration of the barrier between the middle cranial fossa and the orbital cavity. This can be performed through an intracranial approach [42,47], although in some cases a lateral orbital approach may be employed [18]. The intracranial approach affords easier retraction of the frontal and temporal lobes for dural separation from the periorbita, while allowing for better exposure to the bony defect and preservation of the optic nerve [7]. The intracranial approach also allows for excision of herniated gliotic temporal lobe tissue and dural grafting. Titanium mesh is easily shaped to mimic the contour of the anterior and middle cranial fossae floor for skull base defect reconstruction as this eliminates the possibility of bone resorption and help prevent recurrence of herniation and proptosis.

Titanium mesh does carry a higher risk of infection. Nonetheless, it has been successfully used in reconstruction of large anterior cranial base defects after tumor resection or trauma successfully [2,53].

4. Conclusion

In this case report, we present two patients who underwent surgical correction of NF1-associated sphenoid wing dysplasia with titanium mesh reconstruction. The condition was treated via a cranial approach where the herniated temporal lobe was retracted from the orbit and its gliotic tip was excised. This procedure corrected the proptosis and pulsating exophthalmos without the chance of bone resorption and recurrence of symptoms. Titanium mesh reconstruction is a safe surgical option for patients with symptomatic sphenoid dysplasia.

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