



Pulsating Enophthalmos in Neurofibromatosis Type 1

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Abstract

Neurofibromatosis type 1 (NF-1) is a neurocutaneous syndrome with multisystem involvement, especially the central nervous system, eyes, and skin. In this article, we describe a patient with NF-1 with radiologically-imaged sphenoid wing aplasia that led to pulsatile enophthalmos. Although sphenoid wing aplasia in patients with NF-1 frequently occurs as painless pulsatile exophthalmos in clinical practice, as in our case it can rarely present as pulsatile enophthalmos. Globe pulsation occurs as a reflection of intracranial pulsation from direct contact of meningeal structures and globe, secondary to the defect in the posterior orbital wall. The diagnosis is made by the presence of characteristic bone defects on radiological imaging modalities and by the absence of vascular malformations on doppler ultrasonography or computed tomography angiography.

Keywords: Neurofibromatosis type 1, pulsating enophthalmos, sphenoid wing dysgenesis

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Introduction

Neurofibromatosis type 1 (NF-1) is a neurocutaneous syndrome with multisystem involvement, especially the central nervous system, eyes, and skin. It is a disease with autosomal dominant inheritance, seen in 1/3000-4000 births. Besides hamartomas arising in neural crest-derived tissue, other pathologies are seen in mesenchymal tissues. Lisch nodules in the iris, choroidal hamartomas, orbital plexiform neurofibromas, optic gliomas, glaucoma, and orbital bone defects (sphenoid bone dysgenesis) can be seen. Freckling in the inguinal and axillary regions, Cafe au lait spots, scoliosis, vertebral defects and mental problems can be detected systemically [1,2]. However, NF-1 has great importance due to the occurrence of neoplasms such as neurofibromas, central or peripheral nervous system tumors, soft tissue sarcomas, and pheochromocytomas.

Sphenoid bone wing defects are rare conditions and can be seen after surgery depending on the presence of orbital venous malformations. These defects can be seen in 5-10% patients with NF [1]. Cranial or orbital bone disorders occur as a result of the interaction between genetic and developmental factors [2]. Other cranial bone defects may be associated along with sphenoid bone defects [3]. Sphenoid bone wing defects have clinical signs such as a pulsatile exophthalmos, but rarely, as in our case, present as pulsatile enophthalmos. In this report, we will present a patient with NF-1 who had Lisch nodules, choroidal hamartomas and pulsatile enophthalmos due to sphenoid wing dysgenesis.

Case Report

A 20-year-old male was admitted with complaints of low vision and pulsation in the right eye. The current complaints were present since the age of 3, and there was no history of trauma or surgical procedures. He stated that the pulsation in his right eye had become more obvious during exercise. Physical examination showed enophthalmos and synchronized pulsation with the heartbeat in the right eye. Disappearance of enophthalmos was found with forward movement of the globe during the Valsalva maneuver (Figures 1a and 1b). Measurements performed with the Hertel exophthalmometer at 114 mm, determined 16 mm in the right eye, and 18 mm in the left eye. During the Valsalva maneuver measured 18 mm in both eyes. Furthermore, the inter-pupillary distance was 55 mm in primary position, and 60 mm by lateral movement of right-globe about 5 mm on the Valsalva maneuver. Strabismus was not

detected in both eyes on the prism cover test and the Hirschberg test conducted in the primary position. Eye movements were unaffected in all directions. The pupillary light reaction, and intraocular pressure in both eyes was normal. The best corrected visual acuity was 0.05 in the right eye and 10/10 in the left eye. Biomicroscopic exam revealed 2-3 Lisch nodules in the iris of both eyes. Despite a normal ophthalmoscopic examination (Figures 2a and 2b), many patchy hyperreflective lesions were observed (Figures 2c and 2d) within the vascular arcades of both eyes by infrared reflectance imaging performed with a confocal scanning laser ophthalmoscope (SLO) (Heidelberg Retina Angiograph 2, Heidelberg Engineering, Germany). Axial length measurements were 23.70 mm in the right eye, and 24.00 mm in the left eye. A murmur was present in the right eye with a pulse on auscultation. Several Cafe au lait spots, freckling in the axilla and inguinal region were detected on systemic physical examination and thus NF-1 was diagnosed. On electrophysiological studies, visual evoked potentials (VEP) showed reduced amplitudes that confirmed the presence of amblyopia in the right eye. Scotopic and photopic responses in both eyes were in the range of normal latency and amplitude on flash electroretinography. The patient refused to undergo surgery. He was therefore, followed with periodical examinations.



Figure 1. (a) Eye view in the normal position (b) Eye view during the Valsalva maneuver



Figure 2. (a and b) Fundoscopic view of both eyes (c and d) Hyperreflective choroidal hamartomas in infrared reflectance imaging of both macula.

The patient underwent cranial Computed Tomography, Computed Tomography Angiography (CTA) and Magnetic Resonance Imaging (MRI) for further evaluation. There was no vascular pathology on cranial CTA. However, the greater and the lesser wing of the sphenoid bone was absent on the right side (Figures 3a, 3b and 3c). Enlargement of the middle cranial fossa, herniation of the dural structures and extra-axial cerebrospinal fluid (CSF) space into the right

orbital region through the bony defect were the additional findings. MRI findings are similar to CTA findings. Optic nerve, extraocular muscles, and Zinn ring were in the normal configuration but orbital fat tissue was atrophic. Herniated meningeal structures that filled with BOS, which is cause of pulsations, were observed to be in contact with the back part of the globe. The extra-axial CSF space around the right cerebral hemisphere was wider than the left side. Contrast-enhanced MRI sequences showed no mass and vascular lesion on the side of the bony defect. The dural structures were thick on the affected side when compared to the opposite side (Figures 3d, 3e and 3f). Both the MRI and the CTA images showed that the right ethmoid sinus and the right side of the cavernous sinus were hypoplastic. The pituitary gland was displaced to the left side of the sella turcica because of a mass-like effect of the wide CSF space. Additionally, a few hyperintense foci in the supratentorial white matter were noted on FLAIR and T2W images without any contrast enhancement that could support the presence of hamartomas. Orbital fat tissue, on B-mode USG, was less dense and reduced in thickness when compared to the left eye, without evidence of vascular flow on doppler USG.

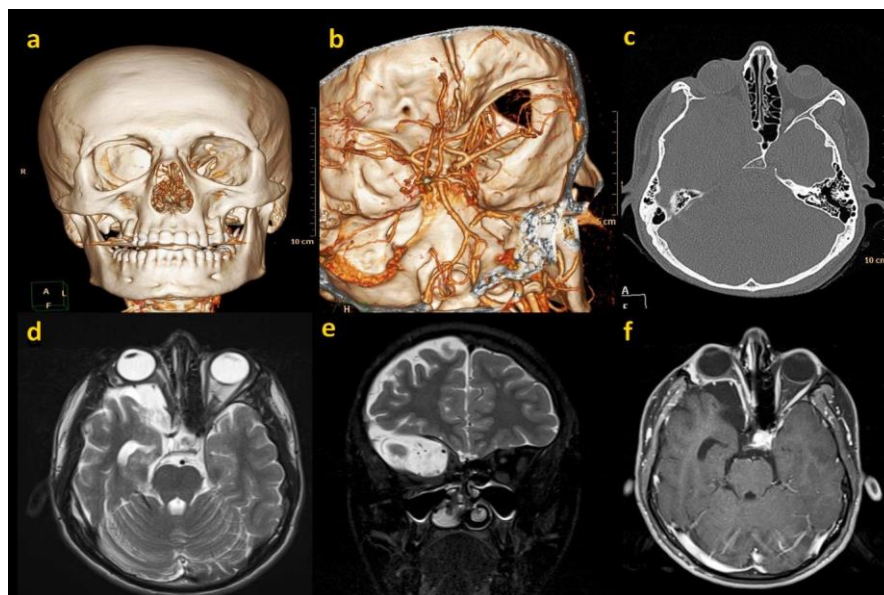


Figure 3. (a, b and c) An absent greater and lesser wing of the sphenoid bone were seen on 3D Volume Rendering CTA and axial CT images. There was no vascular lesion seen on the 3D Volume Rendering CTA. (d and e) Herniation of the dural structures and CSF space into the right orbital region through the bony defect is seen on axial and coronal T2W images. (f) Note the thickened and enhanced dural structures and absence of a mass lesion on contrast-enhanced axial FS T1W image.

Discussion

Enophthalmos is a backward movement of the eyeball on the anterior-posterior axis in the orbital cavity. Globe location within the orbital fossa may vary depending on age, sex, and ethnicity. Three different pathological mechanisms contribute to the development of enophthalmos and include orbital expansion (post-traumatic orbital wall fractures, sphenoid bone wing agenesis, orbital varices, and maxillary sinus agenesis), reduction of orbital contents (age-related fat atrophy, orbital varices, radiotherapy, lipodystrophy, linear scleroderma, hemifacial atrophy, after trauma/surgery) and contraction of the orbital contents (fibrosis or tumors) [4].

The presence of enophthalmos may be clinically noted as an asymmetric view between the two eyes. Hertel exophthalmometer and radiological imaging techniques such as CT, MRI and USG may be helpful in the diagnosis and evaluation of enophthalmos. While CT scan may demonstrate the bony structure, MRI may reveal additional information about the soft tissue surrounding the globe [4]. Doppler USG can assist in the detection of vascular disorders [5].

Intraorbital masses or sphenoorbital meningoencephalocele in patients with NF-1 may cause exophthalmos. But in some NF-1 patients, the superior orbital fissure may expand due to sphenoid bone defects. As a result of this, an increase in the orbital volume in conjunction with an enlarged orbital space related to a larger middle cranial fossa may cause enophthalmos [6,7]. However, enophthalmos has been reported in some cases depending on the increase in orbital volume. The orbital volume increase can be seen due to infratemporal fossa herniation of the orbital fat tissue that causes expansion of the inferior orbital fissure [8]. In addition, some authors showed a relationship between enophthalmos and orbital fat tissue atrophy [6,9]. Ye et al. reported a NF-1 patient presenting with an unusually rapid enophthalmos during thoracocentesis of intrathoracic meningocele that presumed to be hydrothorax. In this case, they concluded that enophthalmos had evolved as a result of protrusion of the orbital structures through sphenoid bone wing defects due to a sudden decrease in intracranial pressure during thoracocentesis [10].

As in our case, in patients with NF-1, pulsation of the eye may be the only symptom, and may rarely be clinically evident as pulsatile enophthalmos [7]. Globe pulsations occur as a result of intracranial pulse waves that are transmitted to the eye and the orbital structures due to large

defects in the orbital wall [5]. During the Valsalva maneuver, as a result of decreased venous return, globe pulsations may lead to the disappearance of enophthalmos as in the present case, and even to exophthalmos, which is directly reflective of intracranial pressure. Therefore, the differential diagnosis is required especially with orbital varices that present as enophthalmos. Orbital varices are expansions that occur generally in the superior ophthalmic vein. In such cases, the Valsalva maneuver causes an increase in venous pressure, although this may sometimes be more apparent as proptosis. When dilate vein is empty or when they present in combination with orbital wall bone defects or orbital fat tissue atrophy, there are signs of pulsatile enophthalmos [4,11,12]. Moreover in the literature, in a patient who has no signs of NF-1 with an orbital mass, pulsatile enophthalmos has been reported depending on the presence of sphenoid bone defects [6]. Orbital venous malformations can also lead to progressive enophthalmos and must be remembered in the differential diagnosis in patients with enophthalmos. In these cases, CT findings of a phlebolith suggest the presence of a venous malformation [13].

In patients with NF, hamartomas can be seen in tissues of neural crest origin including the eye. Yasunari et al., in their study of 33 patients, revealed that all patients have hamartomas by using infrared monochromatic light with confocal SLO that were not detected on fundoscopic examination, and have claimed that hamartomas should be included in the diagnostic criteria of NF [14]. The choroidal abnormalities that are specific to NF-1 are most frequently observed within the vascular arcade, and their numbers increase with age [15]. As in our patients, fundus appears normal under conventional ophthalmoscopic examination and on fundus autofluorescence imaging while choroidal hamartomas are easily noted with infrared reflectance or infrared fluorescence imaging methods. In addition, fundoscopic examinations can reveal optic atrophy (glioma or dependent hydrocephalus), glaucomatous pitting, choroidal nevus and melanoma in NF.

Although there is no complete cure for neurofibromatosis due to the pattern of inheritance, genetic counseling should be offered to patients. In children, NF-1 should be evaluated with a complete ophthalmologic and neurological examination. They should be regularly monitored with imaging techniques as optic gliomas may develop. Due to the higher incidence of strabismus, glaucoma and refractive defects in these patients, children who have not completed their visual development are at greater risk. Orbital plexiform neurofibromas

should be monitored since amblyopia may develop depending on the presence of mechanical ptosis; surgical excision should be performed if necessary. A sphenoid wing reconstruction with autologous bone grafts or titanium materials is a technique that may provide cosmetic and functional improvement in patients with a temporal lobe herniation and pulsatile exophthalmos or in patients with NF-1 who have orbital bone defects.

Conclusion

Although sphenoid wing aplasia in patients with NF-1 occurs frequently as painless pulsatile exophthalmos in clinical practice, it can rarely occur as pulsatile enophthalmos. Transmission of the intracranial pulse waves to the orbital content is seen as a globe pulsation due to a defect in the posterior orbital wall. The diagnosis is made by the presence of characteristic bone defects using radiological imaging modalities, and with the absence of vascular malformations on doppler USG or CTA.

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