

# Neurofibromatosis Type 1 Associated Unilateral Pediatric Glaucoma and Proptosis—A Case Report

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**N**eurofibromatosis (NF) is a rare condition characterized by hamartomas of neural crest origin. NF is divided into NF type 1 (NF1) and NF type 2 (NF2) based on clinical features. We report a case of a 10-year-old Indian male who presented with NF1 along with unilateral pediatric glaucoma and eye globe enlargement. Pediatric glaucoma association with NF1 further adds rarity the disease.

## Keywords

Neurofibromatosis, pediatric glaucoma, proptosis

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**Compliance with Ethics Guidelines:** Informed consent was received from the parent's of the patient involved in this study. Permission for use of the images was also granted.

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## Case Report

Chief complaint	10-year-old Indian male presented with painless defective vision and left eye globe enlargement of 3 years' duration
History of present illness	10-year-old Indian male presented in our outpatient department with painless defective vision and eye globe enlargement of 3 years' duration. Patient could not previously attend hospital due to his poor socioeconomic status
Ocular history	Patient's mother described his medical history as follows: Patient had a normal face until about 2 years of age, whereafter his mother noticed disfigurement of the left eyelid and the left side of the face. Parents were unable to take him to hospital for treatment. Recently, a medical social worker visited this family and advised them to visit the hospital
Medical history	No history of hypertension and diabetes
Medications	None
Family history	No family history of such disease
Social history	Active, well-adjusted primary school student

## Examination

A 10-year-old Indian male with short stature and skeletal deformities presented. Height 120 cm; blood pressure normal. There were multiple café au lait spots of more than 5 mm on the thorax, abdomen, and back skin (see *Figure 1*). Axillary and inguinal freckling was absent. The left side of the face had hypertrophic deformity due to the plexiform neurofibroma in the maxillary and mandibular region (see *Figure 2C*). The left upper eyelid had an S-shaped deformity and ptosis (see *Figure 2A*). On palpation it felt worm-like, consistent with the plexiform neurofibroma. There was marked proptosis and globe enlargement of the left eye (see *Figure 2B* and *3*). The axial lengths of the right and left eye globe were 22.19 mm and 27.99 mm, respectively. The left eye corneal horizontal and vertical diameters were 13 mm each; the right eye corneal horizontal and vertical diameters were 11 mm each. The best corrected visual acuities of the right and left eye were 20/20 and 20/100, respectively. Extra ocular motility was normal. The right and left pupils were 3 mm and 6 mm, respectively. Afferent pupillary defect was noted in the left eye. Intraocular pressure (IOP) in the right eye and left eye were 12 mmHg and 28 mmHg, respectively. The right eye fundus examination was normal. The left eye fundus examination showed advanced glaucomatous cupping (see *Figure 4*).

## Radiologic investigation

A computed tomography (CT) scan and x-ray of the head and orbit were carried out to investigate a possible optic nerve, orbital, or intracranial involvement.

Figure 1: Images of café au lait spots



A. multiple café au lait spots of >5 mm—thorax skin, abdomen; B. Café au lait spots—back skin; C. Magnified photograph of the café au lait spots.

A skull PA x-ray and lateral view showed an enlarged left orbit with distortion of greater and lesser wings of left sphenoid bone secondary to dysplasia/hyperplasia. The central bony orbit also showed altered to poorly appreciated bony landmarks, thus giving the appearance of bare orbit (bare orbit sign) (see Figure 5).

### Computed tomography brain scan

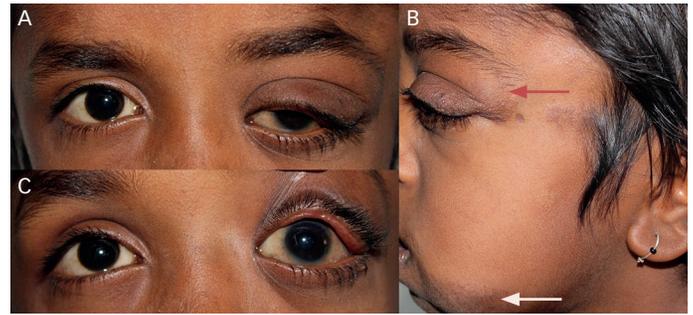
A CT brain scan showed absent to hypoplastic greater wing and, to some extent, lesser wing of left sphenoid bone with resultant direct communication of soft tissues of orbit with the left temporal fossa (see Figure 6).

Coronal reformatted bone window images of the anterior skull base showed absent sphenoid wings (see Figure 7).

There was mild abnormal dilatation of the left lateral ventricle with square box appearance of frontal horn. The rest of the ventricles appear unremarkable. No obvious periventricular ooze was seen. There was small curvilinear cerebrospinal fluid density, extra axial cystic lesion seen anterior to left temporal lobe without mass effect, or midline shift consistent with arachnoid cyst (see Figure 8).

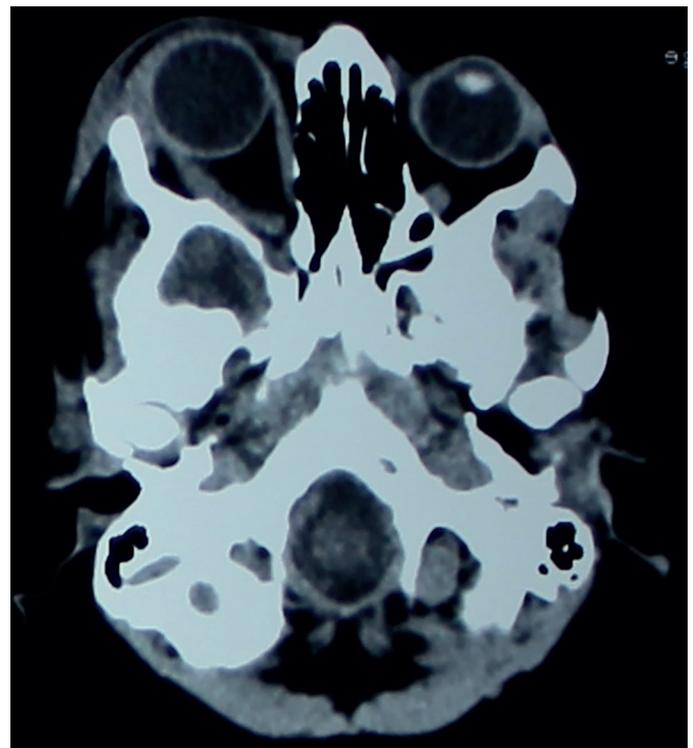
There was gross left proptosis with a relatively enlarged left globe; however, the left globe was normal in shape and attenuation. Ill-defined extra conal soft tissue was noted in the left orbit. Therefore, it was considered that the presence of a neurofibroma was causing proptosis of the left eye globe. Three-dimensional (3D) CT volume rendered technology images of the skull showed an enlarged left orbit with deficient postero-superior wall of the left orbit consistent with absent to hypoplastic sphenoid wing (see Figure 9).

Figure 2: Examination images



A. S-shaped deformity and ptosis caused by plexiform neurofibroma of the left upper eyelid; B. Showing proptosis and globe enlargement of the left eye; C. Upper arrow indicates plexiform neurofibroma of the left upper eyelid; Lower arrow indicates hypertrophic deformity due to the plexiform neurofibroma in the maxillary region.

Figure 3: Computed tomography scan



Computed tomography scan axial cut showing proptosis and globe enlargement of the left eye.

These findings of sphenoid wing dysplasia, dilated lateral ventricle, left exophthalmos, and ill-defined soft tissue in left orbit were consistent with neurofibromatosis (NF) type I.

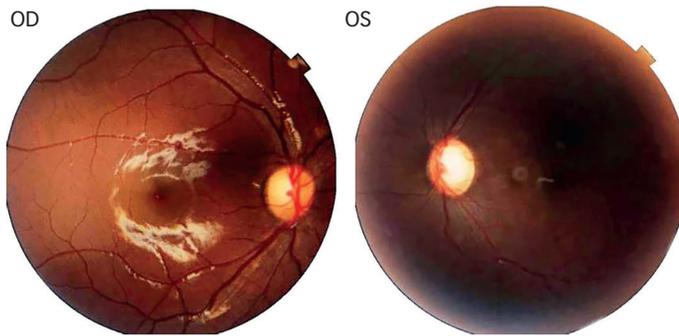
### Management

Left eye trabeculectomy with 0.04% Mitomycin C applications with releasable sutures was performed under general anesthesia. Post-trabeculectomy IOP readings were consistently in the normal range on Day 1, 7, 30, and 90.

### Discussion

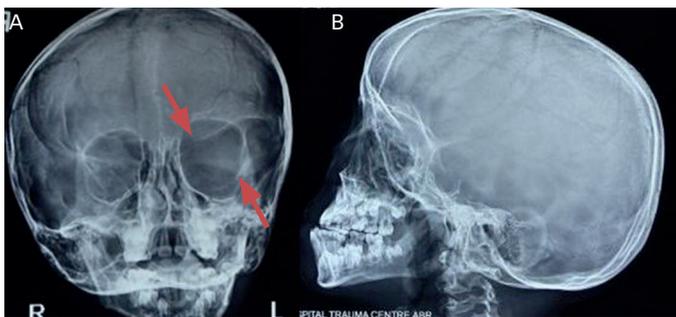
NF is a rare condition characterized by hamartomas of neural crest origin. The prevalence of NF1 is about one in 3,500 live births.<sup>1</sup> The transmission

Figure 4: Fundus examination



OD fundus photo is normal; OS fundus photo showing advanced glaucomatous cupping.

Figure 5: X-ray images



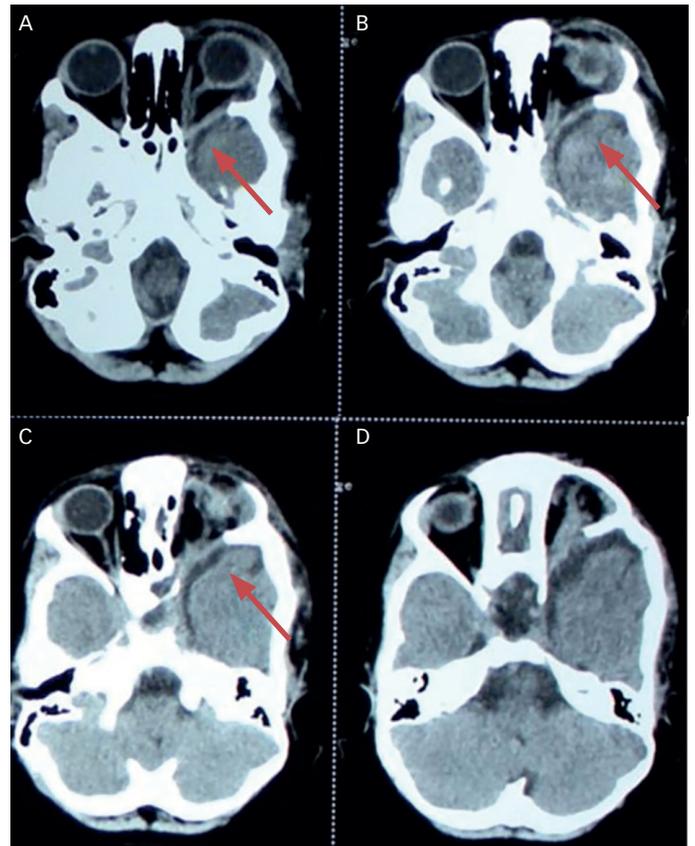
A. X-ray PA; B. Lateral view showing enlarged left orbit with distortion of greater and lesser wings of left sphenoid bone secondary to dysplasia/hyperplasia.

modality is autosomal dominant; however, approximately 50% of cases are caused by spontaneous mutations, and there is considerable variability of expression between affected families. Diagnosis is usually performed clinically and is based on specific diagnostic criteria. NF is divided into type 1 (NF1 or von Recklinghausen syndrome) and type 2 (NF2, acoustic NF, or central NF).

Eighty-five percent of patients with NF suffer from NF1. The genetic defect in NF1 is almost always a mutation in the neurofibromin gene on chromosome 17 (17q11.2). Neurofibromin normally functions to downregulate the p21 ras oncogene. Loss of the neurofibromin tumor suppressor function leads to the proliferation of neural tumors. The most common features of the disease include multiple neural tumors (neurofibromas) on the skin or within the body, pigmented skin lesions (i.e. café au lait spots), and Lisch nodules (pigmented iris hamartomas). Only 10% of NF patients have NF2, which is associated with bilateral acoustic neuromas or schwannomas. The defect in NF2 is on chromosome 22q. In addition to acoustic neuromas, NF2 patients frequently have ependymomas of the spinal cord or multiple meningiomas. Clinical diagnosis of NF1 requires two or more clinical features (see Figure 10).<sup>2</sup>

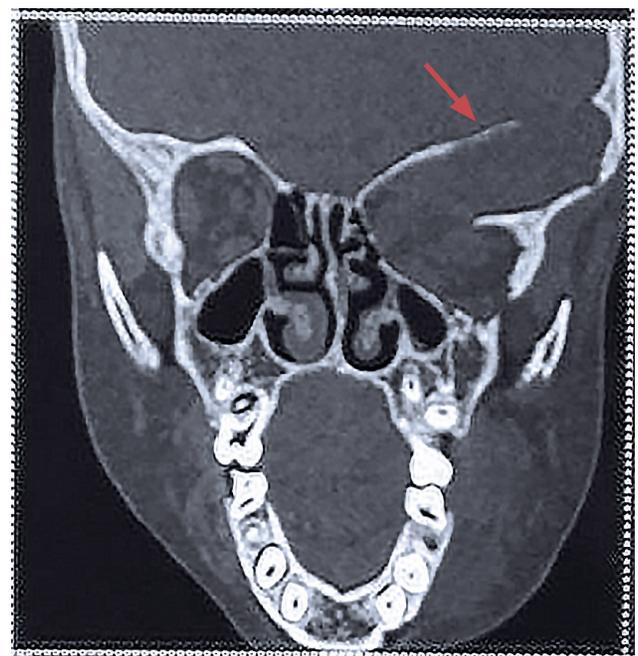
Our case had the following clinical features of NF1 criteria: The patient had more than six café au lait spots (>5 mm in diameter) on the thorax, abdomen, and back of the body;<sup>2</sup> plexiform neurofibroma of the left eyelid causing S-shaped deformity and ptosis;<sup>3</sup> plexiform neurofibroma of the left side of the face caused hemifacial deformity;<sup>4</sup> and sphenoidbone dysplasia was seen in x-ray and CT scan.

Figure 6: Computed tomography scan



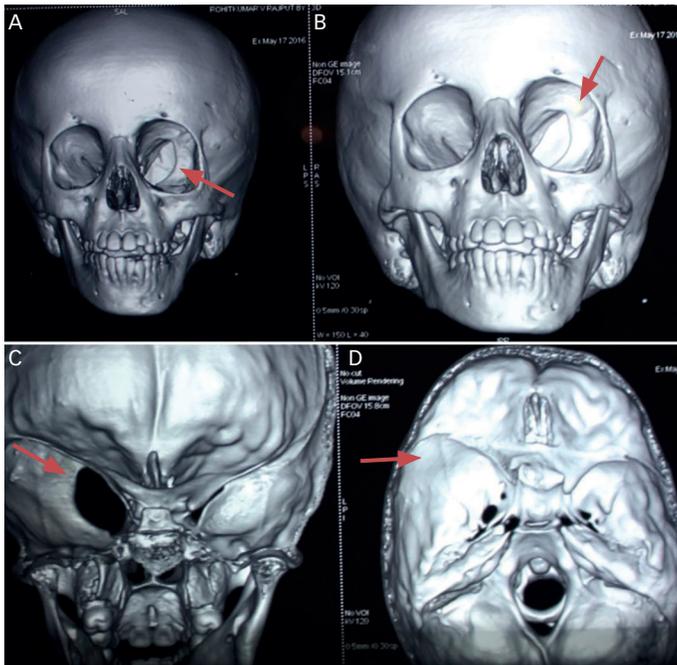
A–D: Serial axial sections of the brain and skull base at orbital level show ill-defined soft tissue in the extra conal compartment of the left orbit, absent or hypoplastic left sphenoid wing, and resultant free communication of orbit and middle cranial fossa structures.

Figure 7: Coronal reformatted bone window images



Coronal reformatted bone window images of the anterior skull base show absent sphenoid wing on the left side (arrow).

Figure 8: Scan image



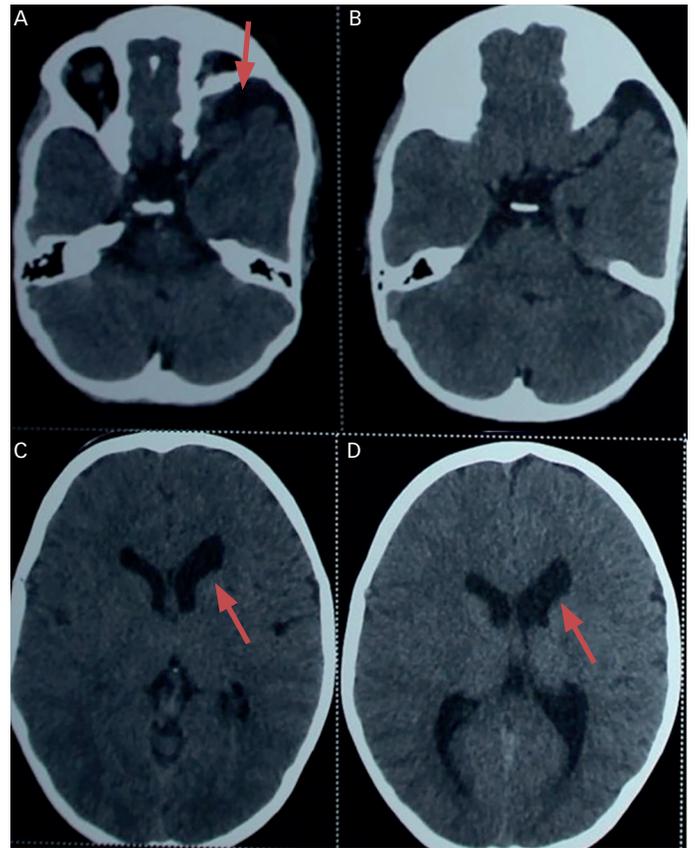
A–B: There was small curvilinear cerebrospinal fluid density, extra axial cystic lesion seen anterior to left temporal lobe without mass effect or midline shift consistent with arachnoid cyst; C–D. Mild abnormal dilatation of left lateral ventricle with square box appearance of frontal horn.

Although Lisch nodules are common findings in NF1 they were absent in our case. Axillary freckles were also absent.

The right eye was normal. Left eye corneal horizontal and vertical diameters were 13 mm each. The right eye corneal horizontal and vertical diameters were 11 mm each. The axial lengths of the right and left eye globe were 22.19 mm and 27.99 mm, respectively. The left eye had advanced glaucomatous optic atrophy. Morales et al. found that globe enlargement was most severe when associated with glaucoma but also present on the side with orbito–facial involvement in patients without glaucoma. The presence of neurofibroma may induce globe enlargement on the affected side in orbito–facial NF1.<sup>3</sup>

Glaucoma has been reported in 1/300 NF1 patients.<sup>4</sup> Recent studies have made a distinction between NF1 patients with or without orbital–facial involvement—such as plexiform palpebral neurofibroma—and a finding of glaucoma was seen in 23% of the patients with orbital–facial NF1.<sup>3</sup> Asymmetric globe enlargement in ipsilateral orbital–facial NF1 was found in patients with glaucoma, with axial lengths ranging from 26 to 36 mm; the difference in the contralateral unaffected eye was

Figure 9: Computed tomography images



A–D Computed tomography volume rendered technology images of skull showing defect of sphenoid wing (absent/hypoplastic) at postero-superior wall of left orbit giving bare orbit sign.

Figure 10: Clinical diagnosis of neurofibromatosis type 1

- Clinical diagnosis of NF1 requires two or more of the following:
- Six or more café au lait spots (>5 mm in diameter for prepubertal children and >15 mm in postpubertal patients)
  - A plexiform neurofibroma (or two or more neurofibromas of any type)
  - Crowe sign (multiple freckles in the axillary or inguinal region)
  - Optic nerve 'glioma'
  - Two or more Lisch nodules
  - Sphenoid dysplasia, cortical thinning in long bones, or other distinctive osseous lesion
  - A first-degree relative with confirmed NF1

4–6 mm.<sup>3,4</sup> In our case, the left eye globe was asymmetrically enlarged; the difference in the contralateral unaffected eye was 5.8 mm. □

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