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CASE SERIES

A Case Series on Ocular and Systemic Manifestations in Neurofibromatosis Type 1

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Abstract

This case series presents five patients diagnosed with Neurofibromatosis Type 1 (NF 1), each exhibiting a range of ocular and systemic manifestations. Ocular findings included Lisch nodules in all patients, with three demonstrating choroidal abnormalities and one presenting with pulsatile proptosis secondary to sphenoid wing dysplasia. Additional features included a plexiform neurofibroma of the eyelid, café- au- lait spots, pseudo arthrosis of the tibia, neurofibroma nodules, and positive family history. In several cases, ophthalmic features were the initial clue prompting further systemic evaluation and eventual diagnosis of NF 1. This series highlights the critical role of comprehensive eye examination in the early detection of NF 1 and underscores the need for multidisciplinary collaboration in the management of this multisystem disorder.

Keywords: Café-Au-Lait Spots, Choroidal Abnormalities, Lisch Nodules, Neurofibromatosis Type 1, Plexiform Neurofibroma, Pseudo Arthrosis, Pulsatile Proptosis, Sphenoid Wing Dysplasia, Ocular Manifestations

1. Introduction

Neurofibromatosis Type 1 (NF1) is a common autosomal dominant neurocutaneous disorder caused by mutations in the NF1 gene located on chromosome 17[1]. It affects multiple organ systems including the skin, bones, nervous system, and eyes. The clinical spectrum of NF1 is broad and variable, even among members of the same family[1]. The diagnosis is primarily clinical, based on the NIH diagnostic criteria, which include characteristic cutaneous, neurological, skeletal, and ophthalmic signs[2].

Ophthalmic features, particularly Lisch nodules, choroidal hamartomas, and orbital involvement such as sphenoid wing dysplasia, are not only diagnostically significant but may also be the earliest manifestations of the disease[3-5]. These ocular signs are often detectable before systemic involvement becomes clinically evident. Therefore, ophthalmologists play a crucial role in the early diagnosis and multidisciplinary management of NF[3-5].

2. Aim and Objectives

To describe the ocular manifestations in patients with Neurofibromatosis Type 1.
To correlate ocular findings with systemic features.

3. Review of Literature

Friedman JM. J Child Neurol. 1999[1]- This landmark review outlines the clinical spectrum and natural history of NF 1. It highlights the NIH diagnostic criteria and describes the typical onset and progression of café-au-lait spots, neurofibromas, skeletal deformities, and Lisch nodules. It emphasizes the need for early diagnosis and lifelong surveillance due to the progressive and variable nature of the disease.

Legius *et al*., Neurology. 2021[2]- Legius *et al*., revised the diagnostic criteria for NF1 and legius syndrome, incorporating genetic testing and refined clinical features to improve early and accurate diagnosis, and to differentiate NF 1 from legius syndrome.

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Midena *et al.*, (2025)[5] conducted a large pediatric cohort study (n=237) to evaluate ocular signs in NF 1. At baseline, they found optic pathway gliomas (20.7%), Lisch nodules (43.5%), choroidal abnormalities (46.8%), and retinal vascular abnormalities (6.8%). During follow-up, new cases were observed in 6.4% (OPG), 22.4% (LNs), 21.4% (CAs), and 5.4% (RVAs), with mean onset around 6–7 years of age. Importantly, development of new ocular signs after 7 years was rare. The study also showed that Lisch nodules and choroidal abnormalities arise independently, supporting their recognition as distinct diagnostic criteria, and suggested that truncating NF 1 variants may be linked with a higher ocular disease burden. This work highlights the critical window of early childhood for ocular surveillance in NF 1.

Parrozzani R *et al.*, Br J Ophthalmol. 2015[4]- This study demonstrates that choroidal nodules are highly prevalent in NF 1 patients and can be better detected using near-infrared reflectance imaging. It proposes these lesions as a potential new diagnostic criterion in children, particularly when Lisch nodules are absent. This imaging modality may allow earlier and non-invasive diagnosis.

4. Material and Methods

Study location: Single centre tertiary hospital in South India

- ✓ Study design : prospective
- ✓ Sample size : 5
- ✓ Study period: 1 year

Data collected,

1. Demographic data
2. BCVA
3. Underlying systemic illness
4. Ophthalmic examination
5. Slitlamp examination
6. General and systemic examination
7. Fundus photography
8. CT /MRI Brain/orbit.

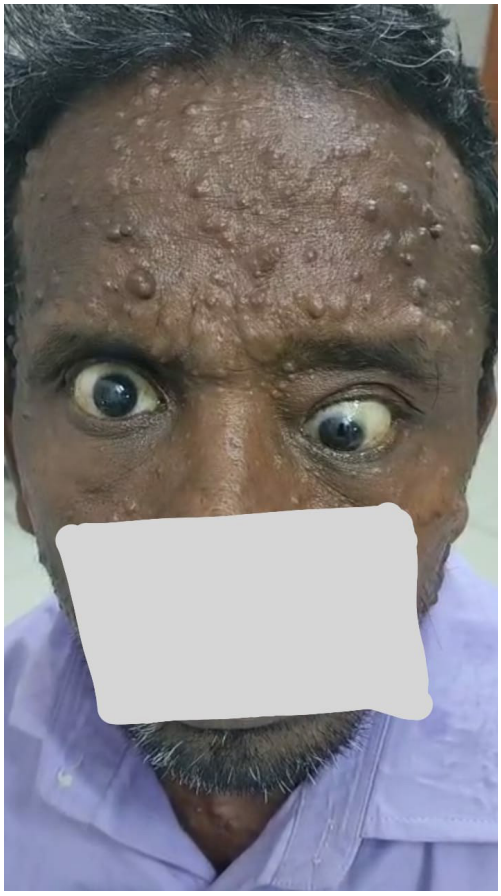
5. Results (Including Observations)

Five patients diagnosed with Neurofibromatosis Type 1 (NF 1) were included in this series. The age at presentation ranged from 3 to 46 years (mean 16.6 years) with three females and two males as mentioned in the table 1.

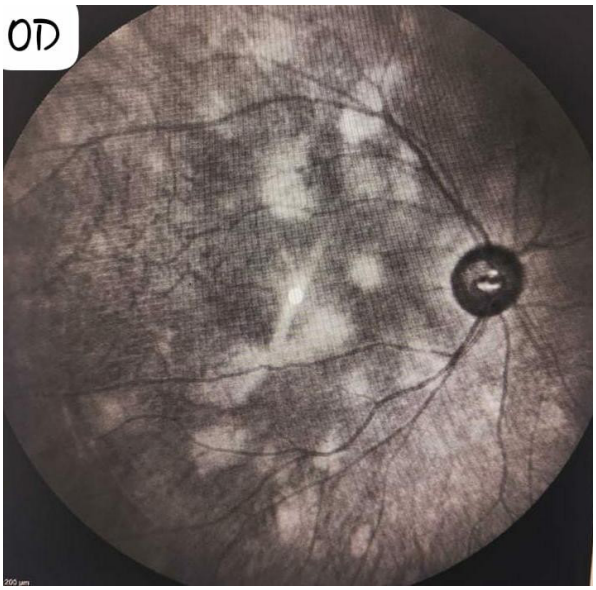
5.1 Ocular Manifestations

All patients (100%) had Lisch nodules (Figure 7), which represented the most consistent finding. Choroidal abnormalities (Figure 2 and 3) were detected in three patients (60%), and pulsatile proptosis (Figure 1) due to sphenoid wing dysplasia (Figure 6) was observed in one patient (20%). A plexiform neurofibroma of the eyelid causing ptosis (Figure 5) was noted in one patient (20%). Best-corrected visual acuity was normal in four patients, while one patient with sphenoid wing dysplasia showed mild visual impairment.

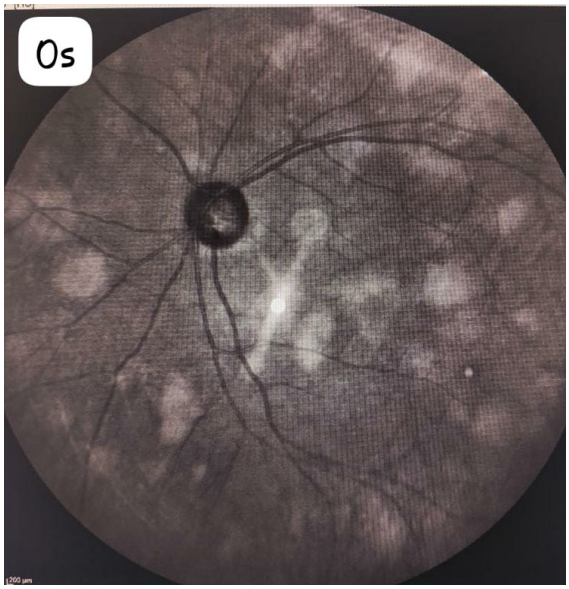
Systemic manifestations:
Two patients (40%) had café- au-lait spots (Figure 8), two (40%) demonstrated cutaneous neurofibroma nodules (Figure 1), and one patient (20%) had pseudo arthrosis of the tibia (Figure 4). A positive family history was reported in one case (20%).



Figures 1. (LE) Pulsating proptosis.



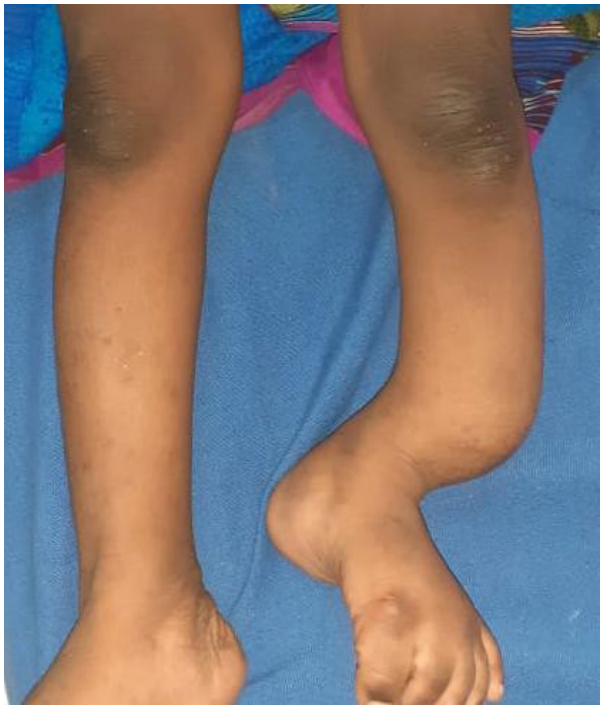
Figures 2. (RE) Choroidal abnormalities.



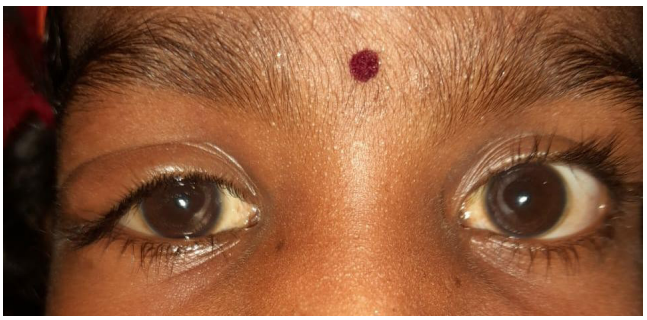
Figures 3. (LE) Choroidal abnormalities

Diagnostic contribution of ocular features:
In three patients, ocular findings such as Lisch nodules, choroidal changes, and eyelid neurofibroma were the initial clinical clue leading to further systemic evaluation and confirmation of NF 1.

Overall observation:
All five patients satisfied the NIH diagnostic criteria for NF1. Ophthalmic imaging, including slit- lamp examination, multicolor fundus imaging, and neuro



Figures 4. Left leg deformity with pseudoarthrosis of tibia.



Figures 5. (RE) S shaped lid deformity.

imaging, played a pivotal role in establishing the diagnosis and guiding systemic evaluation.

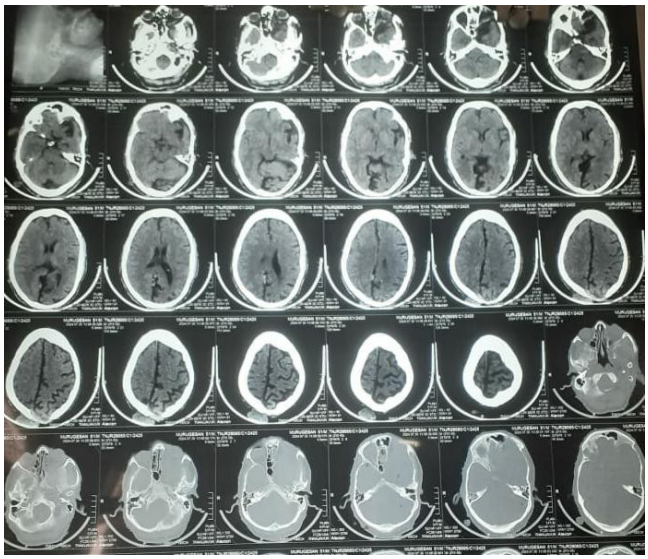
6. Discussion

All five patients met NIH diagnostic criteria. Lisch nodules, present in all cases, were the most consistent ocular finding. Three had choroidal abnormalities visualized via multicolor imaging. Sphenoid wing dysplasia with pulsatile proptosis was a rare but notable finding in one patient. One had plexiform neurofibroma of the eyelid, a hallmark feature.

The role of ophthalmic imaging—including slit lamp, multicolor fundus, OCT, CT orbit, and UBM—was

Table 1. Shows demographic profile, clinical features, ocular and systemic findings of all patients

Caseno	1	2	3	4	5
Age	46	10	3	11	13
Sex	Male	Female	Female	Male	Female
Presenting complaints	Protrusion of left eye	Drooping of right upperlid	Leg deformity in left side (Figure 4)	Routine school screening	Routine school screening
Clinical features	Left eye pulsating proptosis (Figure 1),, BE) lisch nodule, multiple cutaneous neurofibroma (Figure 1)	Lisch nodule, Plexiform neurofibroma in right upperlid (Figure 5), family history of NF 1	Lisch nodule in both eye, multiple cafe-au- lait spots (Figure 8)	Lisch nodule in both eyes, multiple neurofibroma nodule	Lisch nodule in both eyes, cafe- au- lait spots
Investigations	Fundus- BE) choroidal abnormalities (Figure 2 and 3). CT brain - sphenoid wing dysplasia in left side (Figure 6)	Other systemic examination normal	Imaging of left leg - pseudo arthrosis of tibia (Figure 4)	Fundus - BE) choroidal abnormalities	Fundus - BE) choroidal abnormalities



Figures 6. CT brain showing left sphenoid wing dysplasia.

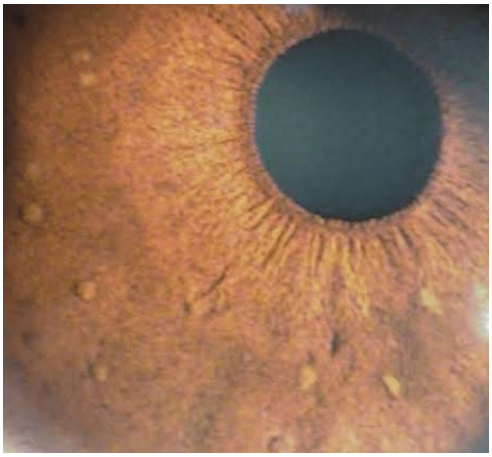
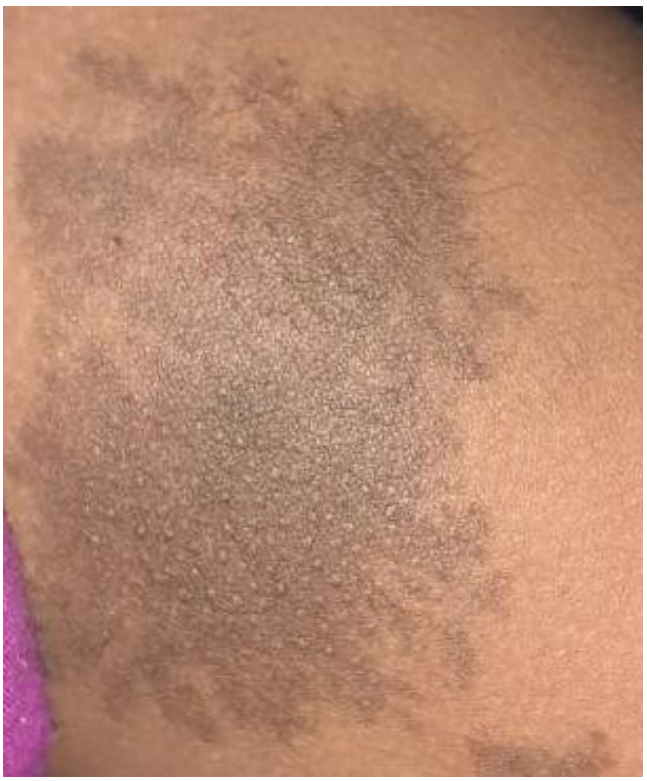


Figure 7. Slit lamp examination - lisch nodule.



Figures 8. Cafe - au -lait spot.

critical in diagnosis and management. Early detection led to systemic screening and confirmation of NF 1 in all cases.

7. Summary and Conclusion

Ocular findings are often the earliest and most accessible signs of NF1. Their recognition facilitates

early systemic screening and multidisciplinary care. This series underlines the ophthalmologist's role in NF1 diagnosis and management.

8. References

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