

Neurofibromatosis Type 1 with Optic Nerve Glioma: A Case Report

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Abstract: Ocular manifestations are among the criteria included in diagnosing Neurofibromatosis Type 1. Ocular assessments in children with NF1 are important as young children may do not complain of visual impairment until it is advanced. Here in we report a case of Neurofibromatosis Type 1 with optic nerve glioma, in which the diagnosis are aided by imaging; namely B scan and MRI.

Keywords: Neurofibromatosis Type 1, optic glioma, B scan, MRI.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a common inherited disorder with an approximate incidence of 1:3000 [1]. It is an autosomal dominant disorder, with the mutation of a tumor suppressor gene, located on the long arm of chromosome 17q11 [2]. Individuals with NF1 are prone to the development of peripheral (neurofibromas, malignant peripheral nerve sheath tumors) and central (optic pathway glioma, malignant glioma) nervous system tumors. This case report highlights a case of optic glioma in Neurofibromatosis Type 1 which present as asymptomatic tumour that was found on screening neuroimaging.

CASE REPORT

A 10 years old girl was referred from Pediatrics Clinic to Eye Clinic Hospital Kuala Lumpur for eye assessment for Neurofibromatosis Type 1. She was born premature at 34 weeks with birth weight of 2.2kg with no history of retinopathy of prematurity (ROP). She has normal developmental milestone. She is known case of Bronchial Asthma with mild infrequent episodic attack. No epilepsy and no developmental problem such as attention deficit hyperactive disorder or social anxiety disorder. She is the 2nd out of 3 siblings and other siblings are normal. No other family members are having neurofibromatosis type 1.

There was no ocular complain. No presence of eyelid swelling. Parents did not notice of squint or misalignment of the eye. No protrusion of the eyeball and the child has no complain of headache or having problem with gait and balance.

Ocular examination shows best corrected vision for both eyes on first presentation were 6/7.5. Refraction showed low refractive error and the child not requiring glasses. Hirschberg Test was central and no squint noted. No proptosis (Figure 1) and extra ocular muscle movements were normal. Anterior segment examination shows presence of left eye Lisch nodules. Otherwise, the anterior and posterior segment was normal in both eyes. Fundus examination revealed a pink optic disc with a normal cup-disc ratio in both eyes (Figure 2). No nodule or glioma was seen. The macula and the retina were flat.

General examination shows multiple café au lait spots over the body especially on the face, back and extremities (Figure 3). There was also presence of freckles in the axillary and inguinal region. No neuro fibroma lesion noted and there was no bony lesion such as kyphosis or scoliosis or pseudoarthrosis present.

On regular follow up at the age of 12 years old, ocular examination shows that the patient has slight larger pupil on left eye compare to the right eye and retropulsion on the left eye is more resistant compared to the right eye. Fundus examination shows normal disc with no pallor and no choroidal lesion seen.

B scan was then performed, which shows that patient has larger size of optic nerve on the left eye compared to the right eye (Figure 4).

An orbit and brain magnetic resonance imaging (MRI) was subsequently arranged and it shows fusiform enlargement of the left optic nerve involving the intraorbital segment extending into the intracranial

segment displacing the intracavernous Internal Carotid Artery which is consistent with the diagnosis of left optic nerve glioma (Figure 5). There was also presence of signal abnormality in the globus pallidus and left sub thalamus region suggestive of hamartomatous lesion consistent with neurofibromatosis type 1.

This patient was managed conservatively in view stable condition of the optic glioma. On each visit, the visual acuity, RAPD, proptosis, extra ocular muscle movement, the optic nerve characteristic and also the colour vision are monitored. The left eye optic nerve glioma remained stable and patient was subsequently followed up in every six month.

On review during the last follow up, the patient is currently on glasses for low refractive error. Best corrected vision is 6/6 bilaterally. Latest orthoptic assessment shows that she has left eye exotropia but there is presence of fusion and gross stereo acuity. There is no Relative Afferent Pupillary Defect (RAPD) and there is no proptosis. There is presence of left eye Lisch nodules, but other anterior segment structures are normal. Intraocular pressure is normal bilaterally. Optic disc appears pink, without pallor or disc swelling. Macula is clear and retina is flat bilaterally. Colour vision with HRR Plates and D15 were normal in both eyes.



Fig- 1: No proptosis

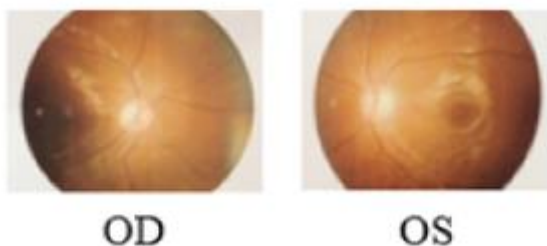


Fig-2: Fundus Photo of normal disc with no disc edema or pallor and no choroidal lesion seen bilaterally



Fig-3.1: Frontal view with café au lait spots on the face



Fig-3.2: Café au lait spots on the back



Fig-3.3: Café au lait spots on the arm



Fig- 3.4: Café au lait spots on the leg

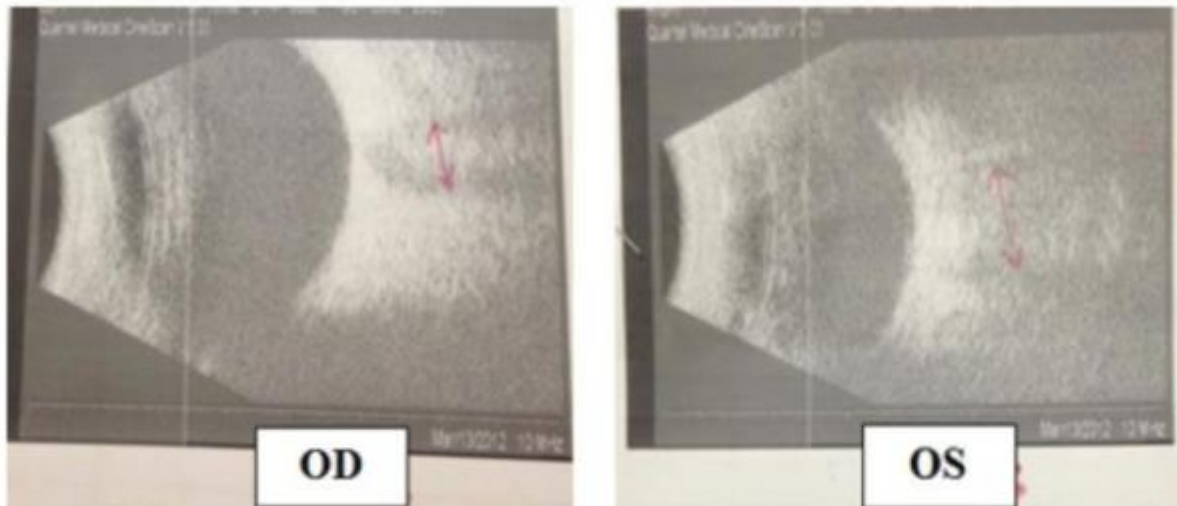


Fig-4:B scan shows patient has larger size of optic nerve on the left eye compared to the right eye

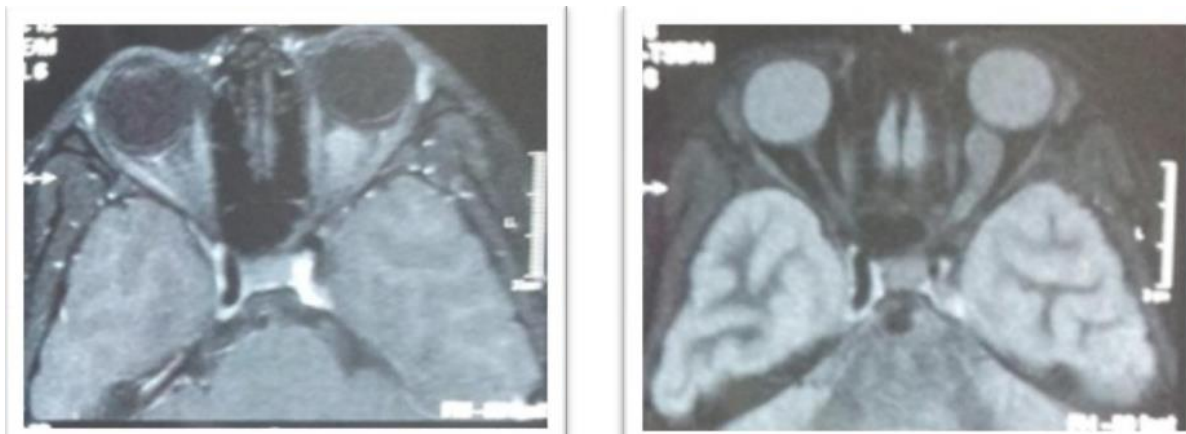


Fig-5: MRI shows fusiform enlargement of the left optic nerve

DISCUSSIONS

Neurofibromatosis type 1 (NF1) is a common disorder of phacomatoses that arises secondary to mutations in the tumor suppressor gene, NF1 which is located in the long arm of chromosome 17 (17q11.2). It is an autosomal dominant pattern of inheritance but the disease can also emerge as the result of a sporadic new mutation. It affects both sexes equally. Similar to other autosomal dominant cancer predisposition syndromes, people with NF1 start life with a germ line mutation in one copy of the NF1 tumor suppressor gene; however, tumors require somatic (acquired) inactivation of the remaining functional NF1 allele, leading to complete loss of NF1 expression in specific cell types [2].

NF1 is diagnosed by presence of at least 2 of these criteria (criteria elaborated by United States National Institute of Health) [3]:

1. 6 or more café au lait spots that are larger than 5mm in greatest diameter in pre pubertal individual (size larger than 15mm in post pubertal individual)
2. Freckles in the axillary or inguinal region
3. 2 or more neuro fibroma of any type or 1 plexiform neuro fibroma
4. Optic nerve glioma
5. 2 or more Lisch nodule (iris hamartomas)
6. Distinctive osseous lesion such as kyphoscoliosis, malformation of the facial bones (eg sphenoid dysplasia) or pseudoarthrosis (bowing of the long bone with a tendency to fracture)
7. A first degree relative (parent, sibling or offspring) with NF1 by the above criteria

Other than the features mentioned in the diagnostic criteria, NF1 also associated with pheochromocytoma, aneurysms of cerebral and renal arteries, epilepsy, learning difficulties [4] and it also predispose the affected person to malignant cancers in central nervous system, lung, breast, colon and liver in later life [5]. This make NF1 need multidiscipline approach and management.

Ocular assessment in children with NF1 is important because NF1 is known to be associated with multiple ocular problems such as glaucoma, choroidal nevi and retinal astrocytoma, on top of the Lisch Nodule and optic glioma.

Optic glioma is present in 15-20% of patients with NF1 [6]. Studies suggest a distinct female preponderance in patients with NF1 [7]. Listernick *et al.*; studied a group of 227 children with NF1 and found that 67% (22/33) of patients with optic nerve glioma were female [8]. NF1 is most commonly present in the first decade of life. The median age of onset is

approximately 5 years old, with over 80% of patients younger than 15 years of age.

Most papers reported that optic nerve glioma in NF1 tend to have indolent course with symptomatic lesions only occur in 1-5% of the patients [9]. Patients typically present with decreased visual acuity, which may worsen with growth of the glioma within the optic pathway nerves. Other signs include optic disc edema, pallor, atrophy, relative afferent pupillary defect, decreased color vision, pupil dysfunction, visual field defects, ocular motility problems, and proptosis [10].

Optic nerve glioma in NF1 is typically limited to the optic nerve without chiasmal involvement, which can occur uni or bilaterally. However, sometime the natural history of optic glioma in NF1 is almost impossible to predict. If the tumor extend to the hypothalamus, endocrinopathies such as accelerated growth and precocious puberty may manifest. Hypothalamic lesions can cause hydrocephalus, which may have a significant impact on morbidity and 15-year mortality rates approach 50% [10].

Suma Ganesh *et al* reported a case of 3 year old girl who presented with left eye loss of vision and strabismus. Her best-corrected vision in the right eye was 20/40 (N9) and in the left eye was counting fingers at one foot. A brain magnetic resonance imaging (MRI) was performed and showed a fusiform enlargement of the left optic nerve with a thickened right optic nerve. The optic chiasma showed enhancement extending to involve the optic tracts bilaterally. Posteriorly non-enhancing altered signals appearing hyper intense were seen along the optic radiations. A diagnosis of NF-1 with bilateral optic pathway glioma - pilocytic astrocytoma was made. This case was treated with radical radiotherapy. On post radiotherapy follow-up, visual acuity in the right eye was 20/40 and in the left eye was no perception of light. The fundus examination showed disc pallor both eyes, left eye more than right [11].

Vasudha Gupta *et al.*; also reported another case of 3 year old girl who presented with left eye poor vision (<20/400) and left eye proptosis 3mm, in which the dilated fundus examination of the left eye disclosed a large mass from the optic nerve head which is associated with sub retinal fluid. There was neovascularisation at the optic disc as well as superior retinal haemorrhage. The child received chemotherapy (vinblastine) over a period of 70 weeks and the tumor regressed in which on the last follow up (16 months post diagnosis) the left optic nerve head was pale and atrophic and BCVA no light perception in the affected eye [12].

Early age of symptom onset (less than one year) is associated with a likelihood of progression. Progression after the age of 12 years is uncommon, but some patients may still lose their vision in adolescence, highlighting the need for careful monitoring of vision in these children until they reach adulthood. For this patient, close observation is the mainstay of the management at current moment. Given the stable nature of optic glioma in this case, active surveillance can be a reasonable option. Progression of the disease as indicated by progressive proptosis, visual deterioration, visual field loss and sign of intracranial extension with radiographic progression need to be watched out which might advocate treatment, which aimed to halt further progression. Most importantly, treatments are indicated to save life as intracranial extension and progression is a poor prognostic factor and the leading cause of death in optic nerve glioma in NF1 [13].

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