Neurofibromatosis Type 1 Associated with Two Rare Features—Cavernous Haemangioma of Forehead and Hamartomas in Globus Pallidus

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Abstract: Neurofibromatosis Type 1 is a disorder which is autosomal dominant in inheritance, due to deletion or inactivation of the NF gene in the pericentromeric region of chromosome 17. The incidence is about 1 in 3000. Very rarely neurofibromatosis 1 can be associated with cavernous haemangioma or arteriovenous malformation. It is also found that hamartomas in Globus Pallidus is rare. Here we are presenting a case of neurofibromatosis Type 1 with cavernous haemangioma face. The case is presented for its rare association and also the rare site of the hamartoma in the brain.

Key words: Neurofibromatosis Type 1, Cavernous haemangioma

INTRODUCTION

Neurofibromatosis is a complex disease with neuroectodermal abnormalities. This autosomal dominant disease shows a penetrance of about 80%. (It may be accompanied by cerebrovascular complications, mainly stenosis or aneurysms and rarely vertebral arteriovenous fistulas and malformations. (2) One report has mentioned a cavernous angioma in the liver (3) and a recent case report mentions an association of Sturge Weber syndrome with this condition (4).

On imaging the brain multiple hamartomas are sometimes found in this condition in the cortex and periventricular area. Various neural tumours are also reported to be associated with the disease.

Prenatal and pre symptomatic diagnosis in suspected cases of familial neurofibromatosis 1, can be done with genetic-linkage studies with DNA markers but it is not useful in sporadic cases [1].

Case Report: A 9 year old male child born of non consanguineous marriage reported to us with a swelling on the forehead on the right side of the face which was slightly above the skin, slightly hyperpigmented with reddish hue and was diagnosed as haemangioma. He also had multiple café au lait spots, around 16 in number, most of it over 5mm, on his face, trunk and extremities. His systemic examination was normal. Ophthalmological examination revealed multiple Lisch nodules in the iris. His blood count, peripheral smear study and urine analysis were normal.

MRI brain without IV contrast administration with Fast spin echo, Gradient echo and Inversion recovery techniques PD/FSE T2W and FLAIR axial; FSW T2W, SPGR Coronal sections, T1W Sagittals showed bilateral symmetrical well demarcated T2/flair hyperintensities in Globus Pallidus, dentate nucleus and cerebral peduncles (Right > Left). The lesions were hypointense on T1 and not restricted in DW1. No mass effect. MRS revealed normal NAA peak and normal ratios.

There was a diffuse signal intensities involving the periorbital deep subcutaneous tissue on the right side extending to the temporal muscle of thickness upto 1 cm. No intracranial extension. This was diagnosed as Cavernous Haemangioma in right peri orbital region.

Biochemical results were Serum pyruvate was 0.32 mmol/L (normal 0.03-0.10), Serum Ferritin (CLIA) was 25.9 ng/ml (normal 22-322), Serum Lactate (Turbidimetry) was 12.6 mg/dl (normal 4.5-19.8). Serum Ceruloplasmin was 0.41 g/L (normal 0.2-0.6), 24 hours urinary copper excretion was 43 micrograms/24 hours (normal 15-60).
DISCUSSION

This child satisfies the criteria for Neurofibromatosis type 1 (Von Recklinghausen disease or peripheral neurofibromatosis) since he has around 16 café-au-lait spots most of which is more than or equal to 5mm in size and also multiple Lisch nodules in his iris [2]. Lisch nodules were more seen in younger patients than were neurofibromas and these nodules are useful in diagnosing neurofibromatosis. Multiple Lisch nodules, are specific for neurofibromatosis [3]. This satisfies two major criteria.

Simple Cavernous angioma alone, without other organ involvement is rare in neurofibromatosis. In this case investigations like MRI, USS abdomen does not reveal any visceral haemangiomas.

There were multiple hyper intense lesions in the MRI which can be attributed to hamartomas associated with neurofibromatosis. But to our surprise, it was there in Globus Pallidus, Dentate Nucleus (predominantly Grey matter nuclei) which is rare site for hamartoma to occur. Mitochondrial disorders and Wilsons disease were considered as differential diagnosis. They were ruled out by the biochemical tests which showed normal serum pyruvate, lactate, Ferritin and ceruloplasmin. 24 hours urinary copper excretion was normal which ruled out Wilsons disease.

CT brain did not show any calcifications. MRS was also normal ruling out other granulomas.

The Hamartomas may be attributed to neurofibromatosis, even though the sites where hamartomas are seen usually are cerebral peduncles, cortex and periventricular areas.

The association between Neurofibromatosis and vascular manifestations were reported earlier in very few cases like intrasellar (pituitary) cavernous angioma, hemangiopericytoma-like arrangement with gaping blood vessels, renal angiomyolipoma in three different cases [4-6]. Cutaneous cavernous hemangioma associated with a hemangioma of the liver and NF1 was also reported in one 3 year old girl [7]. Neurofibromatosis type I may also be accompanied by cerebrovascular complications, mainly stenosis or aneurysms and more rarely vertebral arteriovenous fistulas and malformations [3].

The child and the family were counseled regarding the possible inheritance of the disease and was advised yearly ophthalmological assessment, regular BP check up. Orthopedic follow up.

REFERENCES

