RESEARCH PAPER | Medical Science | Volume : 3 | Issue : 11 | Nov 2013 | ISSN - 2249-555X

Neurofibromatosis 1with Plexiform Neurofibroma Presenting as Bilateral Ptosis

KEYWORDS: Bilateral Ptosis, Plexiform Neurofibroma, Neurofibromatosis 1

Shachi Jain Taran	Ravindra Kumar	Sonali Jain
Department of Pediatrics, Sri Aurobindo Medical College and PG Institute, Indore	Central Research Laboratory, Sri Aurobindo Medical College and PG Institute, Indore	Department of Radiodiagnosis, Sri Aurobindo Medical College and PG Institute, Indore

ABSTRACT *Here we are describing a case of neurofibromatosis1(NF1) with facial plexiform neurofibroma presenting as bilateral orbital ptosis. The patient had café au lait spots, freckling and plexiform neurofibroma. To the best of our knowledge only one case was reported in literature with bilateral ptosis in plexiform neurofibroma without any systemic features of NF1 from Ireland. No case has been reported with similar condition from India.*

Introduction:
Neurofibromatosis I (Van Recklinghausen disease) is an autosomal dominant disease with incomplete penetrance and variable expression.Its incidence is about 1:3000 live births. Diagnostic criteria include: 1) Six or more cafe-au-lait spots, >5 mm in size in prepubertal and > 15 mm in postpuberal age group; 2) Two or more neurofibromas of any type or one plexiform neurofibroma; 3) Freckling of the axillary or inguinal regions (Crowes sign), 4) Optic glioma; 5) Two or more Lisch nodules; 6) Osseous lesions such as sphenoid dysplasia or thinning of cortex of long bones (with or without pseudoarthrosis); 7) First-degree relative (parent, sibling, offspring) with neurofibromatosisl. Diagnosis is made if two or more criteria are present[1].Plexiform neurofibroma though among one of the criteria of NF1, is itself very significant because of its tendency to grow, turn malignant and producing cosmetic as well as functional problems[2].

Case: A 14 year old male child presented to us with bilateral ptosis and not able to open eyes leading to visual handicap. He was IUGR with birth weight of 1.5 kg and had one month NICU stay. Since then parents noticed swelling over left half of the face involving left upper and lower eyelids.This swelling was growing keeping pace with the growth of the child. There was also very small swelling over right upper eyelid. He also had global developmental delay with all milestones achieved one to one and half year later than normal child. Patient had no history of headache, convulsion and hearing impairment. No other family member was having NF1.

On examination at present the patient was malnourished and stunted with no sign of puberty. General examination shows swelling over left half of face along with both eyelids, freckling over groin, axilla and whole trunk. Four big Café au lait spots measuring 6x4, 3x1, 5x3,3x2 cm size and multiple small café au lait spots of 0.5 to 1 cm were present at various parts of the body.

The swelling of face was extending from left half of nose medially to left pinna laterally, superiorly involving left upper and lower eyelids, right upper eyelid and upper lip, causing disfigurement. The margins of swelling were indistinct, consistency was soft like "bag of worms" as described in literature and overlying skin was hyperpigmented. There was also dimple in the left pinna. There was malocclusion of teeth and persistence of deciduous teeth. There were no neurofibromas, lisch nodules or any bone deformity.

MRI of patient was done which revealed moderate supratentorial hydrocephalous. Rest of brain parenchyma was normal. Sella was enlarged with non-visualization of anterior clinoid processes. Bilateral optic nerves were vertically tortutous but no evidence of tumor was present. There was evidence of retinal detachment of right eye. Ipsilateral lens also appears deformed and displaced. Ill-defined soft tissue thickening was also noted involving bilateral upper eyelids (right side> left side), left cheek, nasal vestibule and upper lip. A relatively defined nodular thickening was also noted in left masticular space.

Patient underwent ptosis-correction surgery in both the eyes, retinal detachment surgery and lensectomy of the right eye. Since parents were not concerned for asthesis and no major functional impairment was present, so further treatment was deffered and decision to keep patient under regular six monthly follow up was taken.

Histopathology of right lid swelling showed a firm nodule measuring 2.5x1x0.5 cm. Hematoxylin and Eosin sections showed features of a plexiform neurofibroma. An epidermoid cyst with heavy infiltration by chronic inflammation was also seen in surrounding soft tissue. No evidence of malignancy seen in the sections studied.

This patient fulfilled three criteria for NF1and probably developed disease due to spontaneous mutation.

Discussion:
Plexiform neurofibromas (PN) are benign peripheral nerve sheath tumors, often involving the trigeminal or upper cervical nerves [2,3]. They are diffuse and elongated fibromas usually seen in only 5-10 percent of patients with NF1 [4]. The histology demonstrates disordered masses of peripheral nerve tissue scattered within collagen matrix. Lesional celsl show positivity for Schwann cell marker S-100. EMA positivity of perineural cells also suggests possibility of plexiform neurofibroma. PN often develop and become physically apparent within the first 2-5 years of life [5]. When present, they are commonly seen on the face and neck. Facial plexiform neurofibromas causing disfigurement appear during the first three years of life if they are to develop at all [1].

Often, overlying hyperpigmentation ("giant café-au-lait spot") or hypertrichosis can be seen [6].

PN cause significant morbidity as they are diffuse, nodular and grow along the length of a nerve involving multiple nerve branches and plexi [7]. These tumours intrude the surrounding soft tissue and there is evidence of bony hypertrophy in some instances [7]. Their growth rate is highly variable.There may be periods of rapid growth, particularly in adolescence, followed by periods of relative inactivity.In patients with NF-I

Volume : 3 | Issue : 11 | Nov 2013 | ISSN - 2249-555X

there is a propensity for the neurofibromas to undergo malignant transformation (5% cases) at a higher rate than that observed for comparable tumors in the general population. This is especially true for plexiform neurofibromas.

Removal of benign plexiform neurofibromas is frequently very difficult due to encroachment of the tumor on surrounding structures and nerves and its inherent vascular nature. Life threatening hemorrhage can occur, particularly with facial plexiform neurofibromas. There are few case reports mentioning use of CO2 laser and cryoassisted surgery in literature. A number of agents (including farnesyl transferase inhibitors, antiangiogenesis drugs and fibroblast inhibitors) are being used in clinical trials to assess their therapeutic effect on growth of plexiform neurofibromas[8,9]. Currently, there is insufficient evidence to support the use of any of these drugs in patients with symptomatic plexiform neurofibromas and surgery remains mainstay of treatment for the tumors causing significant disfigurement or functional impairment [10].

Our case is unusual because of presence of bilateral ptosis which is very rare phenomenon and to the best of our knowledge no case has been reported with bilateral ptosis with systemic neurofibromatosis.

Legends to figure:

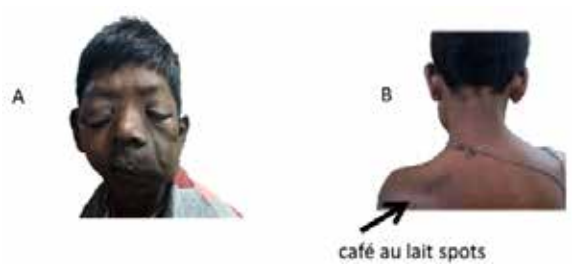

Figure 1
A: Clinical picture of patient showing plexiform neurofibroma with bilateral ptosis

B:Café au lait spots and freckling on the back of patient

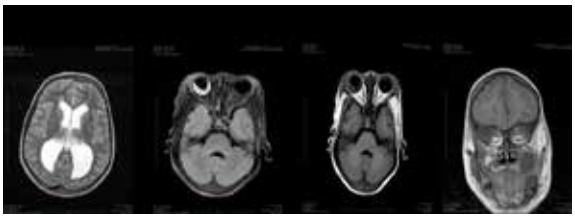

Figure 2:
A: T_2W Axial image showing moderate dilations of supratentorial ventricles.

B & C: Axial FLAIR and T_1W images showing retinal detachment of right eye with subretinal either proteinacious fluid or hematoma and nodular thickening of both upper eyelids

D: T_1W Corona limage showing nodular soft tissue signal in left masticator space

REFERENCE

1. Ferner RE, Huson SM, Thomas N, Moss C, Willshaw H, Evans DG, Upadhyaya M, Towers R, Gleeson M, Steiger C, Kirby A. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. J Med Genet. 2007 Feb;44(2):81-8. | 2. Kumar SS, Kumar DM, Thirunavukuarasu R. Diffuse plexiform neurofibroma.Indian J Surg. 2010 Jul;72(Suppl 1):363-4 | 3. Ghalayani P, Saberi Z, Sardari F. Neurofibromatosis type I (von Recklinghausen's disease): A family case report and literature review.Dent Res J (Isfahan). 2012 Jul;9(4):483-8. | 4. Hassan I, Keen A, Shah PA. Facial Plexiform Neurofibromatosis In A Patient With Neurofibromatosis Type1: A Case ReportOur Dermatol Online. 2012; 3(1): 24-27 | 5. Khachemoune A, Al Aboud K, Al Hawsawi K. Diffuse plexiform neurofibroma in a 13-year-old girl. Dermatol Online J. 2003; 9(5): 23 | 6. Korf B R. Diagnostic outcome in children with multiple café au lait spots. Pediatrics. 1992;90(6):924-7. | 7. Korf BR. Plexiform neurofibromas. Am J Med Genet 1999; 89: 31-37 | 8. Packer R J, Gutmann D H, Rubenstein A, Viskochil D, Zimmerman R A, Verzina G, Small J, Korf B. Plexiform neurofibromas in NF1: toward biologic-based therapy. Neurology. 2002;58(10):1461-70. | 9. Widemann BC, Salzer WL, Arceci RJ, Blaney SM, Fox E, End D, et al. Phase I trial and pharmacokinetic study of the farnesyl transferase inhibitor tipifarnib in children with refractory solid tumors or neurofibromatosis type I and plexiform neurofibromas. J ClinOncol. 2006 Jan 20;24(3):507-16. | 10. Wise JB, Patel SG, Shah JP. Management issues in massive pediatric facial plexiform neurofibroma withneurofibromatosis type 1. Head Neck. 2002 Feb;24(2):207-11.