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RESEARCH ARTICLE

PLEXIFORM NEUROFIBROMA IN A CHILD WITH NEUROFIBROMATOSIS TYPE I: A CASE REPORT.

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Abstract

Introduction:-

Neurofibromatosis Type 1 is a rare autosomal dominant genetic condition[1]; 1 in 3000 subjects, caused by mutation of NF1 gene which is located on chromosome 17 characterised by Cafe au lait macules, axillary freckles tumoral growth along nerves k/a Neurofibromas.[2]

Plexiform neurofibroma is a poorly defined benign tumor of the peripheral nerve sheath which spreads out just under the skin or deeper in the body. Plexiform neurofibromas represent an uncommon variant of NF1(5-15%) [3] in which neurofibromas arise from multiple nerves as bulging & deforming masses involving also connective tissue & skin fold giving appearance of "bags of worms". Its size may greatly vary. Larger tumors are invasive and cause deformities of affected body parts. Surgical removal is the first line of intervention that however can only be partial or subtotal in most cases.[4]

Case study:-

A 10 yrs old child presented to the OPD in Pediatric Surgery with chief complaints of swelling on the left forehead since birth and swelling over right forearm for 3 years. There was no associated h/o pain ,discharge, fever, itching or increase in size of swellings. There was h/o febrile seizures at the age of 2. No significant family history. On clinical examination cystic swelling measuring 1 x 0.8 cm, oval shaped, non tender and mobile, soft in consistency. There was p/o unevenly pigmented brown macules giving the appearance of cafe au lait macules [Fig 1] on various sites. The macules ranged from a few mm to 10 cms in diameter. The borders of the macules were smooth. USG [Fig 2]revealed a well defined hypoechoic, S/C lesion in the frontonasal region with no evidence of vascularity within the mass suggestive of neurofibroma. ExBx of both the swellings were done and sent for histopathological evaluation.

Result:-

Histopathological examination of the Bx of both swellings showed tumor composed of nerve fascicles. Fascicles showed spindle cells with wavy serpentine nuclei with loose myxoid to collagenous stroma. [Fig 3] There was no mitosis or necrosis. A diagnosis of plexiform neurofibroma was given which along with typical

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clinical history and examination of cafe au lait macules lead to the diagnosis of Neurofibromatosis type 1. Currently the patient is doing well and is kept under observation and be reviewed once in every 6 months.

Discussion:-

Plexiform neurofibromas are benign tumors that spread out either just under the skin or deeper in the body, originate from nerve sheath cells and can involve multiple fascicles.The term plexus refers to a combination of interlaced parts or a network. Two types of plexiform neurofibromas have been described : Diffuse type and Nodular Type [1]. The cranial nerves most commonly involved in plexiform neurofibromas are 5^{th}, 9^{th} and 10^{th}[7].

Neurofibromatosis is the term used to describe a group of genetic disorders that primarily affects the cell growth of neural tissues.Atleast eight forms of neurofibromatosis have been recognised , the most common form being neurofibromatosis -1 or von Recklinghausen's disease . Its an autosomal dominant disease caused by a spectrum of mutations in the NF-1 gene. Only 50% of the patients have positive family history and the remaining represent spontaneous mutations.[5,6] This was the case in our patient.

The diagnostic criteria proposed by the National Institutes of Health Consensus Development Conference in 1988 for NF 1 are met if a patient has two or more of the following features :

1. Six or more cafe au lait macules over 5mm in greatest diameter in prepubertal persons and over 15mm in greatest diameter in post pubertal persons.
2. Two or more neurofibromas of any type or one plexiform neurofibroma.
3. Freckling in axillary or inguinal region.
4. Optic glioma
5. Two or more lisch nodules.
6. A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis.
7. A first degree relative (parent, sibling, offspring)with NF 1 based on the above criteria. [7]

Other possible abnormalities that may be seen include central nervous system tumors, macrocephaly, mental defieciency, seizures, short stature and sclerosis. Sexual precocity is seen in 3-5 % of affected children.[1,3,7].

The patient in discussion fulfilled two of the above criteria ; he had numerous cafe au lait macules and two plexiform neurofibromas.

The classical cafı au lait macule is said to have a smoother border when associated with neurofibromatosis than those seen in the *McCune-Albright syndrome* . It has been accepted that any patient with six or more cafı au lait macules greater than 15 mm in diameter is likely to have neurofibromatosis until proven otherwise. Whitehouse D. in 1966 modified this for children to five or more spots greater than 5 mm in diameter. Less than 1% of healthy children may have three or more of such macules, although 1 to 2 cafı au lait macules are encountered in healthy individuals without any signs of the disease. Although most individuals who develop neurofibromatosis are not born with cafı au lait macules, these may develop during the first three years of life, prompting patients to seek medical attention for their child. [8]

Roughly 20-30% of patients with neurofibromatosis have axillary freckling, known as Crowe's sign. Both axillary freckling and inguinal freckling may develop during puberty. Areas of freckling and regions of hypertrichosis occasionally overlay plexiform neurofibromas. This freckling is not seen in patients without neurofibromatosis. Nodules (Lisch nodules) and cafı au lait macules of the iris bilaterally have been described as characteristic of neurofibromatosis in ophthalmological literature.[1,8]

Oral manifestations may occur in as high as 72% of the cases. The most common reported finding is enlargement of fungiform papillae seen in about 50% of all affected patients. However, the specificity of these findings for neurofibromatosis is unknown. Macroglossia is also known to occur. Only about 25% of the patients may show solitary or multiple oral neurofibromas. The tongue, lips, palate, buccal mucosa, gingiva and floor of the mouth are involved [5,6,7,9] . In contrast, our case did not show any of these oral manifestations.

Radiographic manifestations of neurofibromatosis, especially in children, have been reviewed comprehensively. These include macrocranium, macroencephaly, cervical kyphosis, bony dysplasia, sclerosis, enlarged acoustic canal and bowing, and pseudoarthrosis, especially of the tibia. Oral radiographic findings may include enlargement of the mandibular foramen, enlargement and branching of the mandibular canal, increased bone density, concavity of the medial surface of the ramus, increased dimension of the coronoid notch and cyst like lesions [5,7]. Our case did not show any of these manifestations.

Neurofibromas are composed of Schwann cells, fibroblasts, mast cells and vascular components. Histologically the neurofibromas occurring in neurofibromatosis show the same features as solitary neurofibromas except that usually no distinct margin is found between the neurofibroma and surrounding tissue [8]. On microscopy plexiform neurofibromas have a loose myxoid background with a low cellularity. They consist of poorly organized mixture of nerve fibrils with extensive interlacing of the nerve tissue. Small axons may be seen among the proliferating Schwann cells and perineural cells. These distorted masses of myxomatous peripheral nerve are still contained within perineurium and surrounded by neurofibroma. The tumor is immunoreactive for S-100 protein. [5,10]

Surgery is the mainstay of treatment but in case of plexiform neurofibromas it is not a cure because of location and invasive nature which prevent complete resection. They tend to recur.[1,6]

There is no specific therapy for NF1. The treatment is towards management of complications and genetic counselling of parents.

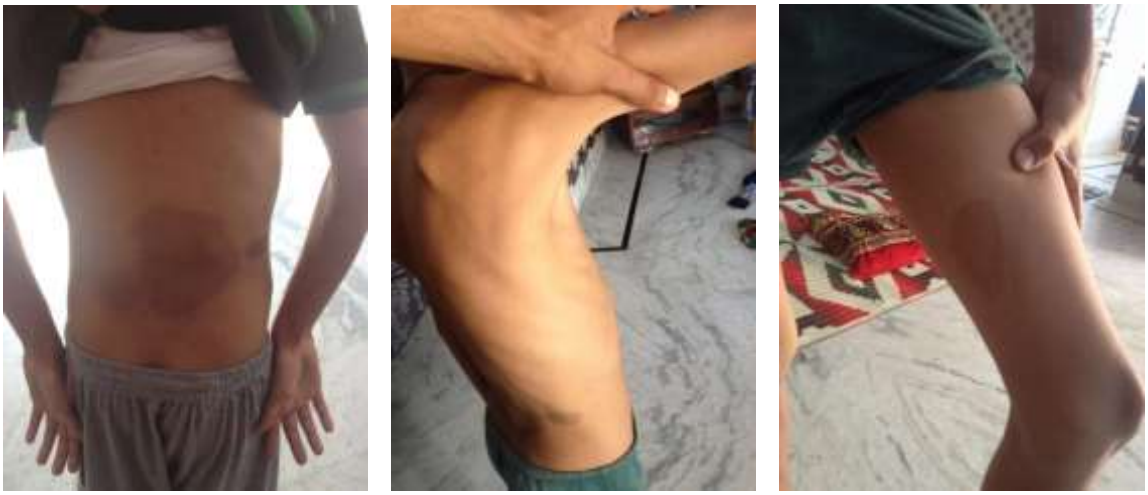

Fig. 1:- Cafe au lait macules at multiple sites

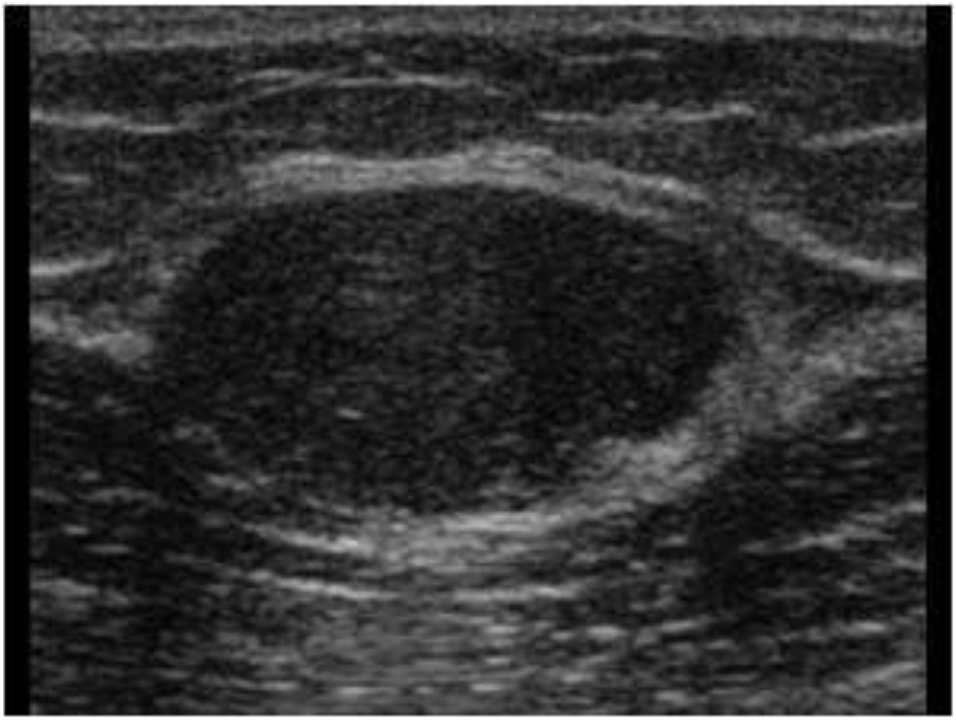

Fig 2:- USG showing a well defined hypoechoic lesion with no evidence of vascularity.

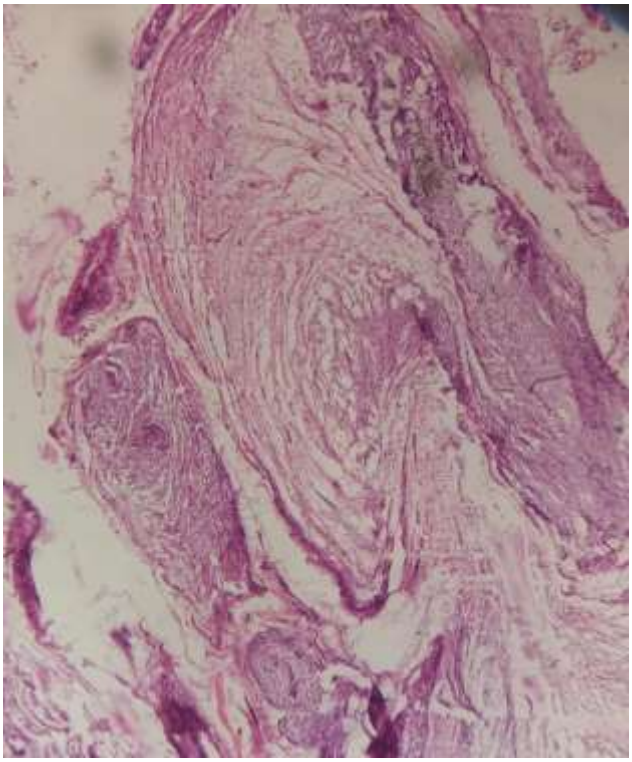

Fig.3:- Histopathological picture of plexiform neurofibroma showing bundles of concentric nerve fibres with areas of myxoid changes.

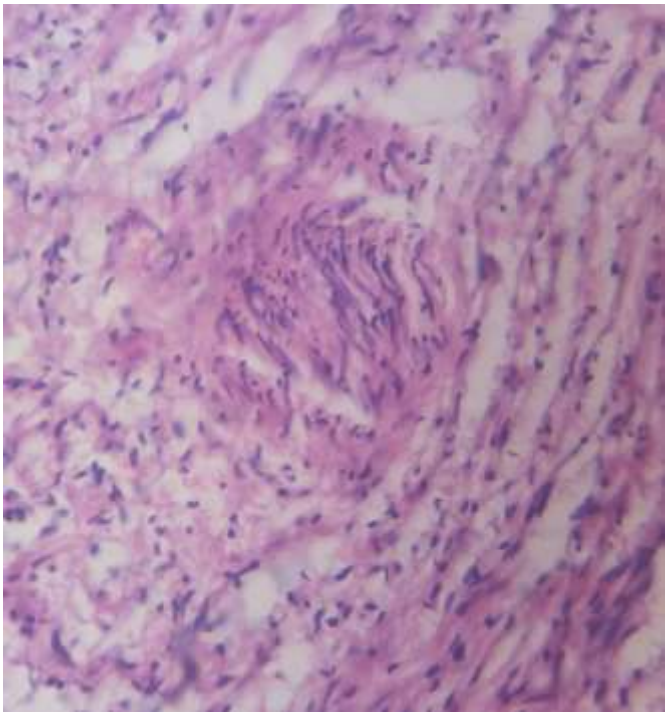

Fig.:- Nerve Fascicles showing spindled cells with wavy serpentine nuclei.

Conclusion:-

Plexiform Neurofibromas remain a devastating manifestation of NF1. Although characteristically benign, plexiform neurofibromas can cause pain, disfigurement & more importantly may turn malignant. There appears to be no clear correlation between any two of the multiple features associated with NF-1.This makes it difficult to accurately predict the process of the disease in a person. The one salient feature found in all cases of NF-1 is its progressive nature .Thus the general trend in each case is towards worsening of the disease.Therefore there should be early diagnosis of condition & alerting the patient towards future complications. Long term follow up is mandatory. Psychological counselling along with instilling of self confidence in such patients can possibly reduce their suffering and help them improve their quality of life.

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