CLEIDOCRANIAL DYSPLASIA, NEUROFIBROMATOSIS TYPE-I WITH FRONTAL LOBE GLIOMA

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INTRODUCTION

Cleidocranial Dysplasia is a benign hereditary condition, inherited as an autosomal dominant. The disease has considerable variation of expression. Thirty percent of the cases are due to spontaneous mutation [1]. The gene responsible for cleidocranial dysplasia is a transcription factor in gene and is termed CBFA-I.

Neurofibromatosis type-I represents 90% of NF cases. Prevalence is 1 in 4000 persons, 50% are new mutations, 30% are AD inherited. The NF – I gene has been identified and lies on chromosome 17 q 11.2.

CASE REPORT

This eight years old girl, third daughter of consanguinous parents presented with frontal headache, vomiting and deteriorating school performance for the last five months. She had grown slowly since early childhood but had otherwise remained healthy and active until the onset of her symptoms five months ago. Her headache had worsened with time and was often accompanied by vomiting. Vomiting was non-projectile and usually associated with nausea. According to her mother, she did not have any permanent teeth yet and most of her primary dentition was still intact. On examination she was found to have height and weight below the third centiles. Head circumference was appropriate for age. She had frontal bossing but no other facial dysmorphism. Multiple café-au-lait spots were noticed randomly distributed over her trunk and extremities (fig 1,2) All of these were well above 1.5 cm in the longest diameter. Further search revealed axillary freckling which was more marked on the right side. She could painlessly approximate both shoulders in front of the chest (fig 3). This uncanny flexibility had also been noticed by her parents previously. Ophthalmologic examination was done which revealed papilledema. No iris Lisch nodules or visual field defects were detected. Her blood pressure was normal for age

The girl fulfilled NIH criteria for neurofibromatosis type I. Papilledema was provisionally attributed to hydrocephalus due to aqueductal stenosis or cerebral glioma, both conditions being well known associations of NF-I. Cleidocranial dysplasia was also strongly suspected and indeed quickly confirmed by an x-ray chest which revealed a small rudimentary clavicle on the right side and absent clavicle on the left (Fig 4). Wormian bones on x-ray skull (Fig 5) further strengthened the diagnosis. CT scan brain with contrast enhancement was urgently arranged. It showed an irregular mixed density mass in left frontal lobe with extensive perifocal vasogenic edema and mass effect showing faint patchy contrast enhancement. CT findings were highly suggestive of a glioma (Fig 6).

The girl underwent a percutaneous biopsy which confirmed the tumour to be a glioma. Tumour resection was carried out followed by radiotherapy. The girl made uneventful recovery except for slightly slurred speech and consistently low scores at IQ tests especially in the visuospatial tests. She is on three monthly follow-up.

DISCUSSION

This girl had coexistent neurofibromatosis type I and cleidocranial

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dysplasia, conditions not previously known to be associated.

Neurofibromatosis type I have an incidence of 1:4000 worldwide and affect all ethnic groups. The diagnosis of this autosomal dominant disorder is clinical and depends on finding any two of the following seven criteria (NIH criteria) [2] (a) Six or more café-au-lait macules over 5 mm in greatest diameter in prepubertal individuals and over 15 mm in greatest diameter in postpubertal individuals. (b) Axillary or inguinal freckling consisting of multiple hyperpigmented areas 2-3 mm in diameter. (c) Two or more iris Lisch nodules best seen on slit lamp examination. (d) Two or more neurofibromas or one plexiform neurofibroma. (e) A distinctive osseous lesion such as sphenoid dysplasia or cortical thinning of long bones with or without pseudoarthrosis. (f) Optic glioma (g) A first degree relative with NF-I whose diagnosis was based on the above criteria.

Neurologic complications are responsible for significant morbidity in patients with NF-I. These range from learning disabilities, complex partial and generalized seizures and hydrocephalus due to aqueductal stenosis , tumors of the CNS like optic glioma, gliomatosis cerebri, astrocytomas, meningiomas and neurilemmomas. Hypertension is a common accompaniment of NF-I.

There is no specific therapy for NF-I. However search for other affected family members, genetic counseling and periodic examinations for early detection of treatable complications are the major responsibilities of the physician caring for these patients.

Cleidocranial dysplasia is another autosomal dominant disorder characterized by drooping shoulders easily approximated in the midline in front of the chest, frontal bossing, open fontanelles, mild short stature and dental anomalies. They have small and angular face. This condition is relatively

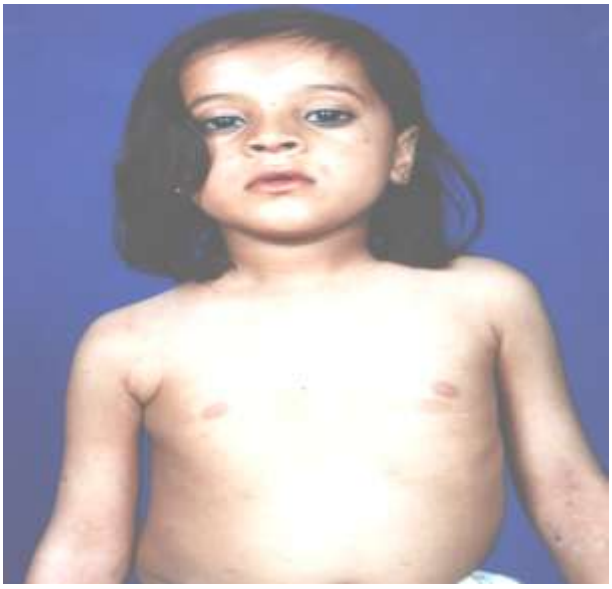

Fig. 1: Multiple café-au-lait spots seen on the face, chest, abdomen and upper limbs.

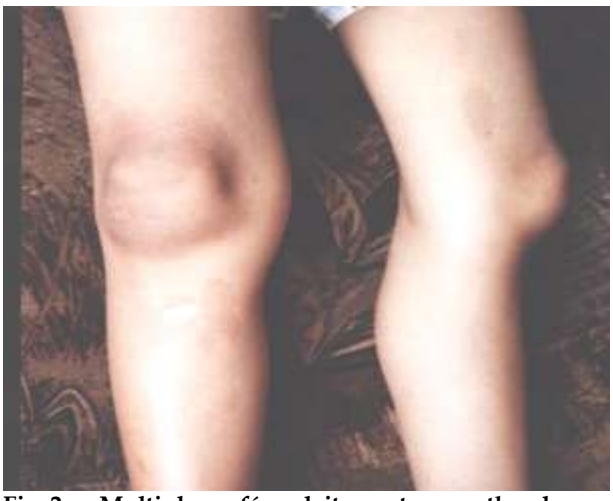

Fig. 2: Multiple café-au-lait spots on the lower limbs.

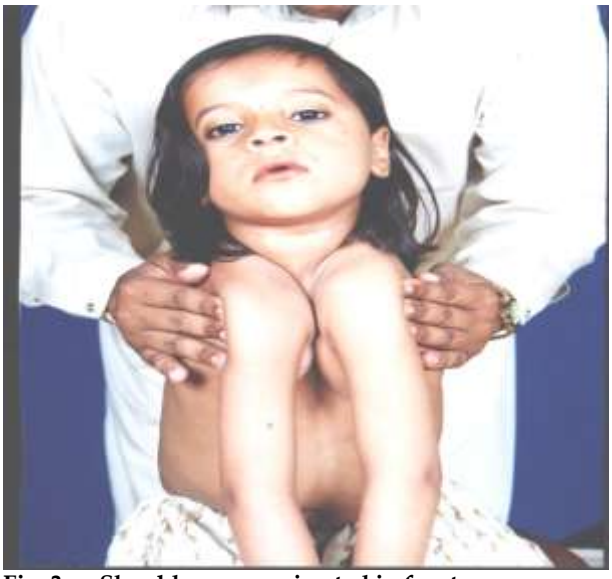

Fig. 3: Shoulders approximated in front.

benign and treatment aims at orthopaedic and dental correction.

Radiological changes are widespread and usually bilateral [3, 4]

Clavicles: may be absent, total [10 %] or partial. Outer, inner or central defects may occur. Scapulae are small and high with small glenoid fossae.

Thorax: is narrow and bell shaped Ribs may be short, supernumerary or bifid. Vertebral bodies may retain infantile biconvex shape.

Skull: Mineralisation is delayed. Cleft high arched palate. Facial bones are small but mandible is of normal size. Fontanellaes remain open. Sutures are widened. Bodies of sphenoid are hypoplastic. Many wormian bones are seen. Frontal and parietal bossing. Basilar Invagination is seen. Persistent metopic suture. Notch in posterior margin of foramen magnum.

Pelvis: Imperfect ossification of pubic bones. Congenital coxa vara. Iliac wings are hypoplastic.

Teeth: Maxillae are small, teeth are crowded. Failure of eruption of secondary teeth. Supernumerary teeth (upto 13) which may even be displaced into the orbit. Cement formation is deficient.

Hands: Anomalies of the hand are very common. Second and 5th metacarpals are long with short middle phalanges and supernumerary ossification centres at their bases. Cone epiphyses and phalangeal tapering may be seen. Nails are abnormal [5].

Associations: Short fibulae, congenital pseudoarthrosis of the femur, genu valgum, obliquity of the articular space of ankle joint.

CONCLUSION

The lack of positive family history in this patient both for NF-1 and CCD indicates

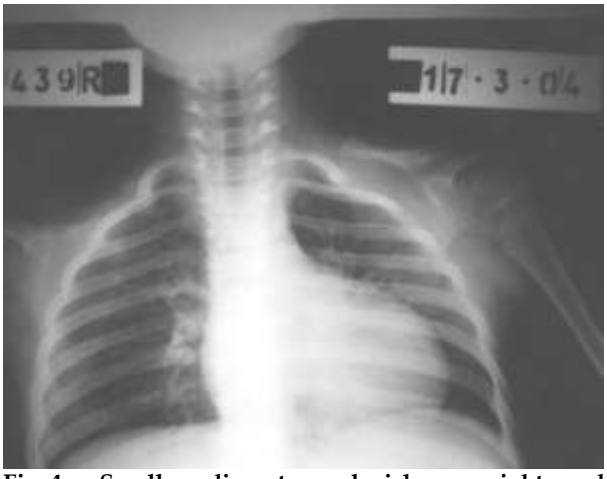

Fig. 4: Small rudimentary clavicle on right and absent clavicle on left.

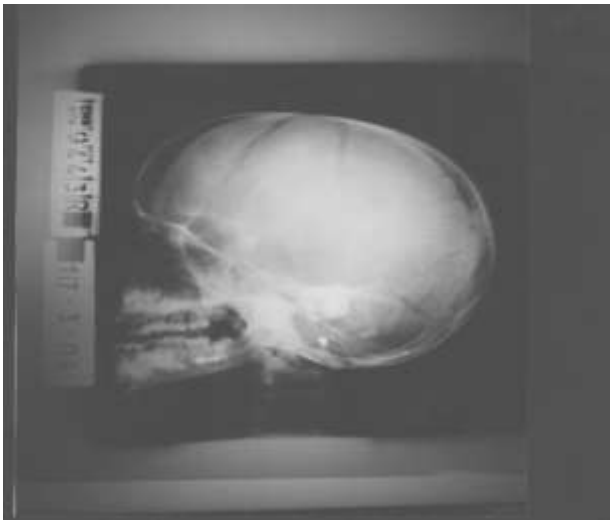

Fig. 5: Skull lateral view showing multiple wormian bones.

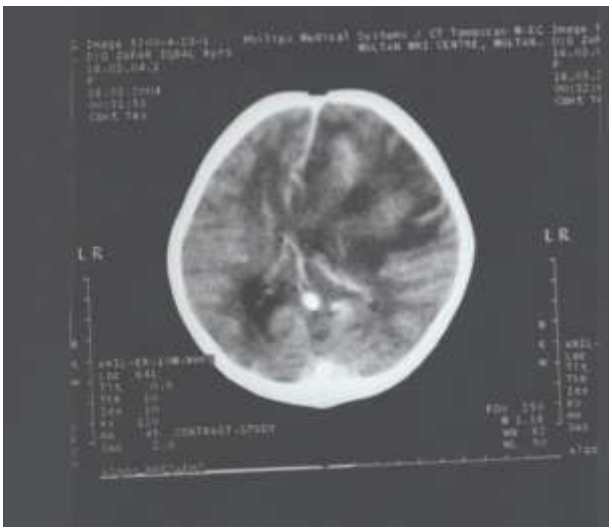

Fig. 6: Contrast enhanced CT scan brain showing mixed density mass in left frontal lobe with mass effect. It shows patchy enhancement and extensive perifocal vasogenic oedema.

spontaneous mutation as the apparent causative process. The defective genes responsible for these disorders are not linked geographically or in any other way to each other. This is the first case reporting neurofibromatosis type I and cleidocranial dysplasia in the same patient not described in over lap syndromes. Finding the reason for the occurrence of these two disorders together other than by sheer chance is yet another riddle for the geneticist to solve.

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