CASE REPORT

Cleidocranial Dysplasia With Encephalomalacia: An Unusual Association

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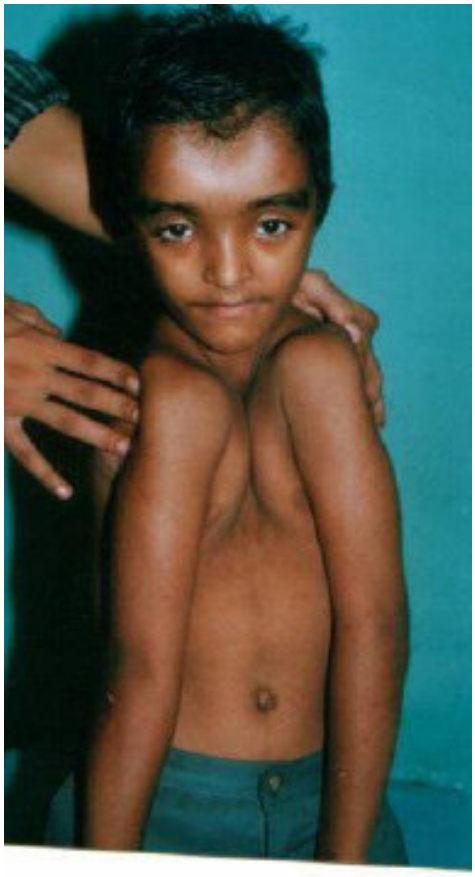
Abstract
We report a new association of familial encephalomalacia of cerebral cortex in a child with cleidocranial dysplasia who presented to us with uncontrolled generalized tonic-clonic seizures.

Keywords: Encephalomalacia, cleidocranial dysplasia

Cleidocranial dysplasia is an autosomal dominant condition with generalized dysplasia of bone; particularly of clavicle and cranium and teeth. This condition was first described by Marie and Santon in a Netherlands (1). Since then over 500 cases have been described in literature with reports of various associations. We report a case of Cleidocranial dysplasia, which had frontal-parietal encephalomalacia and presented to us with refractory seizure.

Case History: A 12-year boy presented with generalized tonic-clonic seizure since the age of 4 years. Seizures were not controlled with a combination of carbamazepine, clobazam and phenobarbitone with maximum allowed dosages. There was no history of neurological deficit or developmental delay. Parent had one other sibling with similar history of seizure. On examination, child had short stature (Height = 120 cm), macrocephaly (head circumference = 59 cm), widely open anterior and posterior fontanels, separated sutures (metopic, coronal, saggital and lambdoid), frontal and parietal bossing, hypertelorism, depressed nasal bridge, drooping of shoulder and narrow chest. The lateral 2/3 of both clavicles was not palpable and both shoulders could apposed in midline (Fig-1). There was history of delayed dentition and caries were present in multiple teeth. Examination of elder brother and mother also showed macrocephaly, open fontanels, sutural diastasis, thick calvarias and wormian bones. Radiograph of chest showed absence of lateral 2/3 of both clavicle and short slanting ribs. Radiograph of skull showed open anterior and posterior fontanels, sutural diastasis, thick calvarium and wormian bones. Skeletal surveys of other parts were normal. CT scan of cranium revealed left frontoparietal encephalomalacia. Patient had no deafness. CT scan of mother was normal whereas that of brother had encephalomalacia of frontal lobe only. Radiographs of mother and brother were similar to patient. A diagnosis of cleidocranial dysplasia with frontoparietal encephalomalacia and refractory seizures was made. Seizures get controlled after addition of valproic acid (60 mg/kg/day). We could not do chromosomal translocation study in this patient because of no availability of this facility at our institute.

Figure-1: Apposition of both shoulders in midline



Discussion: Frontal and parietal bossing, brachycephaly, and persistent open fontanels with late closure of sutures characterize this disorder. The clavicles are either absent or hypoplastic, which leads to abnormally low positioning of shoulders, which can be frequently apposed anteriorly to midline as in our patient. Chest may be narrow with severe kyphoscoliosis and may be an important cause of respiratory distress in later life. Other associated features are late or incomplete development of accessory sinuses, small sphenoid bones, calvarial thickening, wormian bones, depressed nasal bridge, narrow high arched palate, hypertelorism and

and conductive deafness. The primary and secondary dentitions are often delayed, frequently incomplete and misaligned. Supernumerary teeth are common. There may be associated enamel hypoplasia. Proportionate short stature may be observed (2).

There may be associated narrow pubic symphysis, syringomyelia and spina-bifida occulta. Hand anomalies reported include asymmetrical length of finger with long 2nd metacarpal, short and tapering distal phalanges with or without down curving nails (2, 3). Our patient has associated frontoparietal encephalomalacia with same CT finding in other sib, which has not been reported in literature and is most likely cause for refractory seizure in this patient.

Cleidocranial dysplasia is an autosomal dominant disorder with high penetrance. Recently gene for this disorder i.e. Osf2/Cbfa1 has been mapped to chromosome 6p21. The transcription factor, Osf2/Cbfa1 serves as a master gene(4), which regulate osteoblast-specific gene expression. Cbfa1 regulates [illegible]nelial-mesenchymal interactions that controls [illegible]ng morphogenesis and histodifferentiation of [illegible]l enamel organ(5). Other reported genetic [illegible]include micro deletion of chromosome band t(6;18)(p12;24) translocation 12 and pericentric inversion of chromosome 6(6).

Conclusion: Encephalomalacia is an unreported malformation in Cleidocranial dysplasia and may be an important cause of drug resistant seizure in such patients.

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