

Kleebattchadel

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Abstract- Kleebattschadel (clover leaf shaped skull) is a rare and severe form of craniosynostosis occurring due to various syndromic and non syndromic etiologies(1). One among them is Pfeiffer syndrome, a rare inherited disorder that associates craniosynostosis, broad and deviated thumbs and big toes, and partial syndactyly on hands and feet caused due to FGFR gene mutations.

Index Terms- Kleebattscadel, Pfeifer syndrome, craniosynostosis

I. INTRODUCTION

22 days old neonate first born of non consanguineous parentage with a normal antenatal and birth history was admitted with complaints of swelling and outward protrusion of right eye from birth. The baby also had umbilical discharge, poor feeding and irritability for the past two days. On examination baby had no weight gain since birth but vital functions were stable. Clinically baby had fused sutures with closed fontanelles, Subluxation of right eyeball with severe chemosis, Lagophthalmos and exposure keratitis in the left eye.



Figure 1: photo showing proptosis

A detailed physical examination revealed a Midline palatal groove, Low set ears, mid facial hypoplasia, Ankylosed elbow, large thumb and a prominent toes. The baby had umbilical discharge but no indurations. Systemic examination was normal.



Figure 2 :photo showing large toe

Investigations revealed a normal septic workup, liver and renal function tests. Ultrasound abdomen was normal and karyotyping revealed a normal 46 XY pattern. X ray of the skull showed clover leaf shaped skull bone appearance.

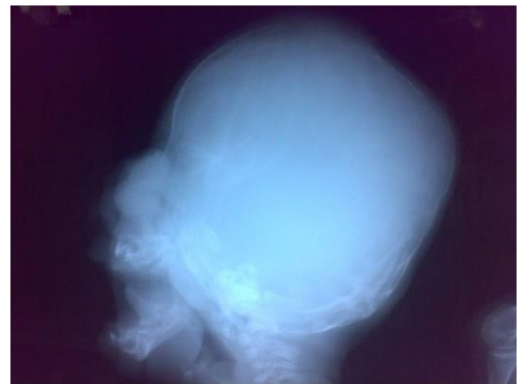


Figure 3: x ray showing clover shaped skull

CT SKULL showed Fusion of all sutures, prominent lateral ventricles. Also the pits on surface of the skull suggestive raised Intra Cranial Tension.

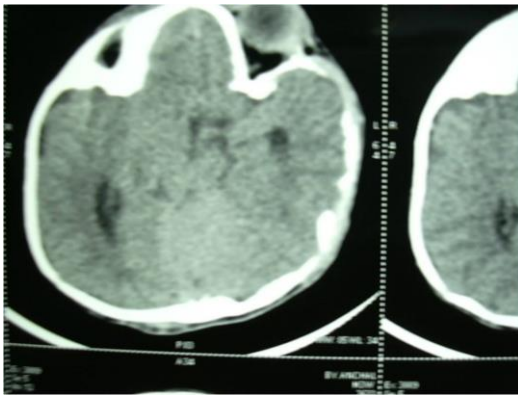


Figure 4 CT showing fused cranial bones

The above physical and radiological features fitted with Pfeiffer syndrome type 2, one of the causes for Kleeblattschädel (clover shaped skull). Type 2 Pfeiffer consists of cloverleaf skull, extreme proptosis, finger and toe abnormalities, elbow ankylosis or synostosis, developmental delay and neurological complications.

The child was treated with antibiotics till cultures were sterile. Ophthalmology opinion was obtained who advised evisceration for right eye and median tarsorrhaphy for left eye. Child was established feeds well and is now on weight monitoring for neuro surgical intervention for fused sutures.

II. DISCUSSION

The cloverleaf skull, or Kleeblattschädel, is a rare skull deformity resulting from premature fusion of multiple cranial sutures and characterized by a trilobar skull with bossing of the forehead, temporal bulging, and a flat posterior skull. The Kleeblattschädel anomaly has been reported to occur in patients with both syndromic and nonsyndromic forms of craniosynostosis. The causes of Kleeblattschädel are Crouzon syndrome, Apert syndrome, Carpenter syndrome, Osteoglyphonic dysplasia, Chromosomal duplication of 13,15q, Amniotic band anomalies, Bilateral subtemporal decompression, Beare-Stevenson cutis gyratum, Campomelic dysplasia, COH syndrome, Pfeiffer syndrome, Say pozanski syndrome and Thanatophoric dysplasia(2).

Pfeiffer syndrome affects about 1 in 100,000 individuals. A craniosynostosis in association with short, broad thumbs and big toes are the major diagnostic clues for Pfeiffer syndrome. Patients have premature fusion of the coronal and lambdoid sutures and occasionally of the sagittal sutures, leading to an abnormal skull shape. There is a characteristic facial appearance: disproportionally wide head with flat occiput, full high forehead, underdeveloped midface with receded cheekbones (midfacial hypoplasia), a small nose with low nasal bridge and widely spaced eyes (ocular hypertelorism). Patients often show prominence of the eyes (ocular proptosis) due to very shallow orbits.

The thumbs and big toes are short and broad. There is a typical deviation of thumbs and great toes away from the other digits and webbing (syndactyly) of the second and third fingers and toes. Additional abnormalities may include mental

retardation, aqueductal stenosis with ensuing hydrocephaly, cerebellar and brain stem herniation, low-set ears, external auditory canal stenosis or atresia, recurrent ear infections, and infrequently, internal anomalies such as hydronephrosis, pelvic kidneys and hypoplastic gallbladder. Visual abnormalities may be a feature, either primary, due to the proptosis or secondary, due to increased intracranial pressure.

Patients with Pfeiffer syndrome may manifest upper airway obstruction related to midface hypoplasia and secondary nasal obstruction; tracheal anomalies have been infrequently reported. Based on the severity of the phenotype, the Pfeiffer syndrome has been divided into three clinical subtypes(3) :

- Type 1 Pfeiffer or "classic" Pfeiffer syndrome involves individuals with mild manifestations including brachycephaly, midface hypoplasia, and finger and toes abnormalities. It is associated with normal neurological and intellectual development, and generally has a good outcome.

- Type 2 consists of trilobated skull deformity (cloverleaf skull), extreme proptosis, finger and toes abnormalities, elbow ankylosis or synostosis, developmental delay and neurological complications. The cloverleaf skull can cause limited brain growth, and the extreme proptosis can cause severe visual impairments.

- Type 3 is similar to type 2 but without the cloverleaf skull. The absence of cloverleaf skull in type 3 can make the diagnosis difficult to establish. Types 2 and 3 have occurred only in sporadic cases, and have an increased risk for early death due to severe neurological compromise and respiratory problems(4).

Mutations in the fibroblast growth factor receptor (*FGFR*) genes cause Pfeiffer syndrome: *FGFR1* (on chromosome 8p11.2-p11) and *FGFR2* (on chromosome 10q26) Type 1. Pfeiffer syndrome is caused by mutations in either the *FGFR1* or *FGFR2* gene. Types 2 and 3 are caused by mutations in the *FGFR2* gene. Mutations in *FGFR1* therefore usually give a milder phenotype(5).

The main differential diagnosis includes the syndromes that are characterized by craniosynostosis (Apert, Carpenter, Crouzon, isolated cloverleaf skull, and Thanatophoric dysplasia). Interestingly, mutations in the same *FGFR*(either *FGFR1*, *FGFR2* or *FGFR3*) can result in different craniosynostosis syndromes, thus implicating a common pathologic mechanism with *FGFR* gain of function in Pfeiffer, Apert, Muenke, and Beare-Stevenson syndromes. Pfeiffer syndrome and Apert syndrome are noteworthy for some similarities but the two disorders are nosologically and genetically distinct. Crouzon syndrome is phenotypically similar to Pfeiffer syndrome but lacking the hand and foot anomalies. Phenotypic overlap occurs with Muenke syndrome, which is caused by a specific *FGFR3* mutation. Sometimes Pfeiffer syndrome has been confused with Saethre-Chotzen and Jackson-Weiss syndromes, since broad toes may occur in both.

Pfeiffer syndrome is an autosomal dominantly inherited disorder meaning that children of a person with Pfeiffer have a 50% chance of inheriting the syndrome. Recommendations for the evaluation of parents of a proband with an apparent *de novo* mutation include clinical, radiographic and molecular genetic evaluation.

The primary treatment of craniofacial abnormalities associated with craniosynostosis is surgical reconstruction that

usually requires a series of staged procedures. In the first year of life the synostotic sutures of the skull are released. In syndromic craniosynostosis the first surgery is often as early as at three months of age. The aim of this surgery is decompression of the brain and remodeling of the skull, and if necessary, elongation and expansion of the bony orbits [10]. As the child grows, skull remodeling may be required. Early treatment may reduce the risk for secondary complications such as hydrocephaly. In a second stage, midfacial surgery is performed to reduce the exophthalmos and the midfacial hypoplasia.

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