Cleidocranial Dysplasia- A Case Report

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ABSTRACT

Cleidocranial dysplasia is a rare congenital disease. It is characterized by autosomal dominant inheritance pattern which is caused due to mutations in the Cbfa1 gene (Runx2) located on chromosome 6p21. It primarily affects bones which are formedby intra-membranous ossification and have equal sex distribution. It is also known as Marie and Sainton disease, Mutational dysostosis and cleidocrialdysostosis. The skeletal deformities of cleidocranial dysplasia are characterized by partial or complete absence of clavicles, late closure of the fontanels, presence of open skull sutures and multiple wormian bones. This rare syndrome is of utmost importance in dentistry due to presence of multiple supernumerary teeth, facial bones deformities and deranged eruption patterns. We are reporting a classical case of cleidocranial dysplasia in 20 year old patient.

Keywords: *Cleidocranial dysplasia, Marie and Sainton disease, Mutational dysostosis, Cleidocrialdysostosis, Autosomal dominant*

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INTRODUCTION

Cleidocrialdysostosis is a rare congenital defect primarily affecting bones which undergo intra-membranous ossification i.e. calvarial bones and clavicles[1,2,3]. This rare entity follows an autosomal dominant inheritance caused by mutations in the Cbfa1 gene also called Runx2 (Runt related transcription factor 2) located on the short arm of chromosome 6_P21. The Cbfa1 is essential for osteoblast and odontoblast differentiation as well as for bone and tooth formation[4]. In1898, Pierre Marie and Paul sainton were the first to describe this rare anomaly[5]. Since the first report in 1898 more than 1000 cases have been reported in English Literature. Cleidocrialdysostosis is also known as Marie and Sainton disease, Mutational dysostosis and Cleidocranial dysplasia[6]. Cleidocrialdysostosis is a relatively uncommon disorder with a prevalence of 0.5 per 100,000 live births[7]. The skeletal abnormalities commonly include clavicular aplasia or hypoplasia, bell-shaped thorax, enlarged calvaria with frontal bossing and open fontanelles, wormian bones, brachydactyly with hypoplastic distal phalanges, hypoplasia of the pelvis with widened symphysis pubis, enlargement of the frontal and occipital bones supernumerary teeth, delayed eruption of permanent dentition and short stature[8,9]. Shortened or absent nasal bones, paranasal sinus abnormalities, thickening of some segments of the calvaria, small maxillae and delayed union of the mandibular symphysis are less common findings of cleidocranial dysostosis[1,10,11].

Dental findings in cleidocrialdysostosis are characterized by a decreased eruptive force of both primary and permanent dentition, prolonged retention of primary teeth[12] and an increase in odontogenesis leading to an excessive number of supernumerary teeth[13]. The clinical findings of cleidocrialdysostosis although present at birth are often either missed or diagnosed at a much later time. Cleidocrialdysostosis may be identified by family history, excessive mobility of shoulders and radiographic pathognomonic findings of the chest, skull and jaws. Here we are presenting a case of classical case of cleidocrialdysostosis.

CASE REPORT

A 24-year-old patient**(Fig.1)** reported to Department of oral medicine and radiology with presenting complaint of fabrication of prosthesis for missing teeth. The patient had a missing anterior tooth which was causing social embarrassment to him. There was no significant past medical and dental history. The patient had normal gait and posture. He had normal intelligence and well oriented to surroundings. His vitals were normal. There was no sign of pallor, cyanosis and lymphadenopathy noted. He was thin, poorly built and short stature. On extra-oral examination brachycephalic head, frontal bossing, underdeveloped maxilla, depressed nasal bridge**(Fig.1**) was noted with concave facial profile with competent lips**(Fig.2).**

He had shrugged shoulders with more than normal mobility of the shoulder girdle i.e. shoulder could be brought to the midline of chest**(Fig.3).** On intra-oral examination there was missing teeth from right maxillary canine region to left maxillary canine region**(Fig.4)** while mandibular canine and second premolar was missing in left side**(Fig.5)**. There was class III malocclusion with underdeveloped maxilla and prognathic mandible**(Fig.2)**. On the basis of clinical

findings a provisional diagnosis of cleidocranial dysplasia has been suggested. The patient is advised for radiological investigations by panoramic radiograph, PA skull, PA chest, Lateral cephalogram, PA pelvis, hand-wrist radiograph and CT of Head. The panoramic radiograph **(Fig.6)** shows multiple impacted teeth along with supernumerary teeth and rounded gonial angles. PA skull **(Fig.7)** shows widened anterior fontanel and posterior fontanels with presence of wormian bones, top of the metopic suture, sagittal suture and large mandible. PA chest**(Fig.8)** radiograph shows thinning and hypoplasia of the clavicles and bell shaped rib-cage. Lateral cephalogram**(Fig.9)** shows widened anterior and posterior fontanel with presence of wormian bones, nonfusion of saggital, coronal and lambdoid suture of skull bones, persistent metopic sutures and large mandible with impacted teeth and supernumerary teeth. Radiograph of pelvis **(Fig.10)** with both hips shows delayed ossification of bones forming symphysis pubis with diastasis of pubic symphysis, hypoplastic iliac bones, bilateral short femoral neck causing coxavera deformity. Radiograph of both hands**(Fig.11)** shows a bilaterally elongated second metacarpal bone, short hypoplastic distal phalanges of hand bilaterally and pointed terminal tufts. CT of head shows multiple abnormal intra sutural bones are noted typically around lambdoid suture suggestive of wormian bones**(Fig.12).** The saggital suture is widened**(Fig.13)** however coronal suture is fused **(Fig.14)**. Anteriorfontenelle(**Fig.15)** and posterior fontenelle (**Fig.12)** are seen opened up and widened**.** Bilateral zygomatic arch is hypoplastic. The palate is high arched and multiple supernumerary teeth were noted with broad mandible. There was persistent metopic suture with agenesis of frontal sinuses(**Fig.16)**. The nasal bridge is flattened and nasal septum is deviated towards right side with convexity to right with spur formation(**Fig.16)**. There was decreased pneumatization of bilateral mastoid air cells(**Fig.16)**.On the basis of clinical and radiological findings a final diagnosis of cleidocranial dysplasia has been reached.

A multidisciplinary approach has followed involving oral and maxillofacial surgeon, orthodontists and prosthodontics for the management of this patient.

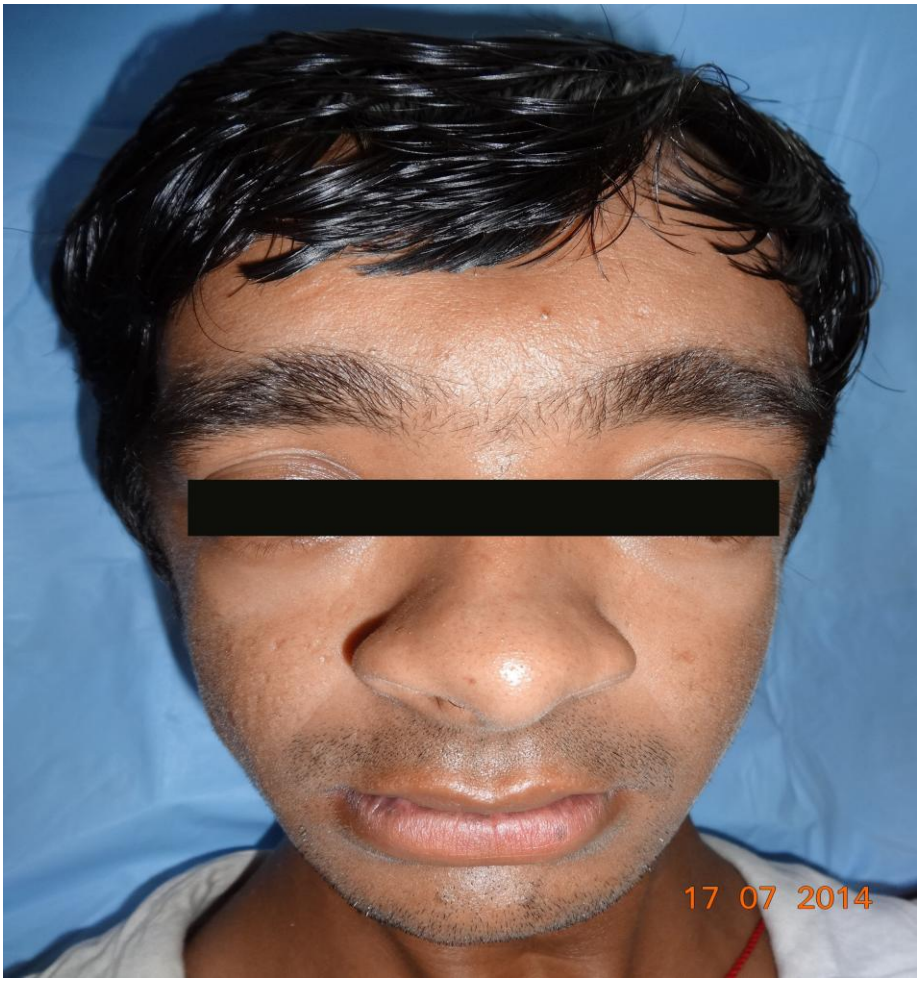

Fig. 1: Profile photograph of patient showing brachycephalic head, frontal bossing, underdeveloped maxilla and depressed nasal bridge

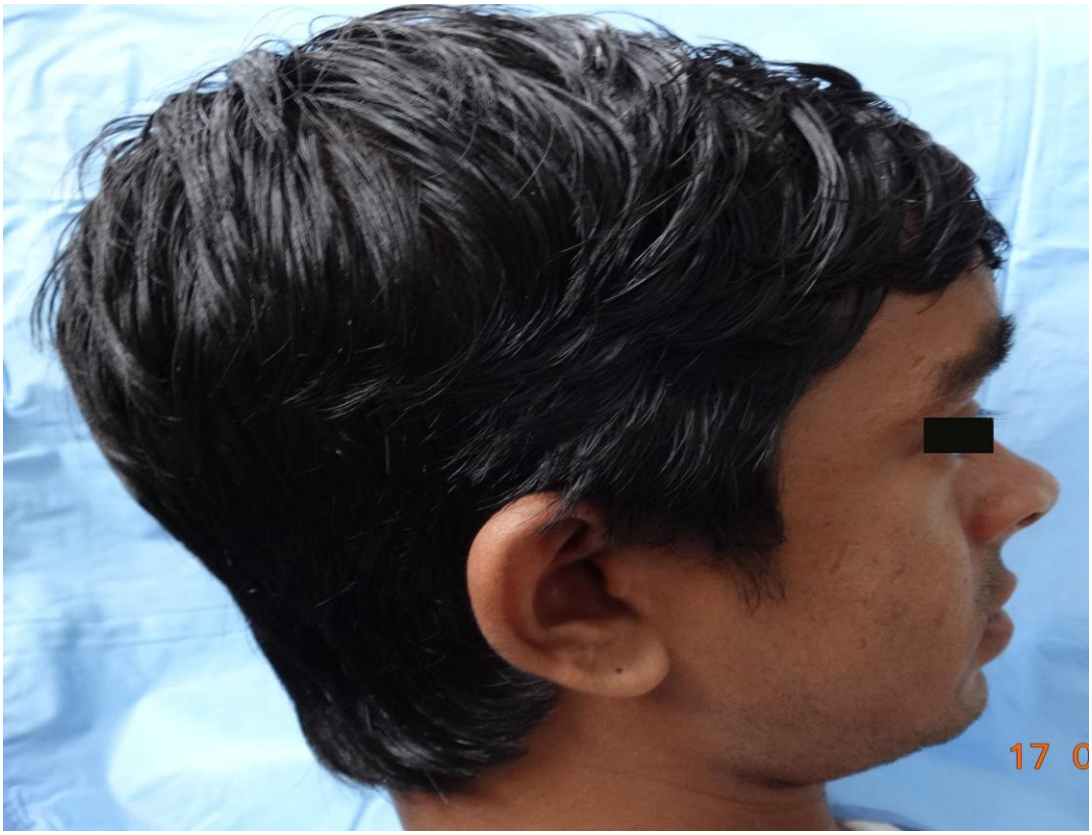

Fig. 2:Lateral view of patient showing concave facial profile with competent lips

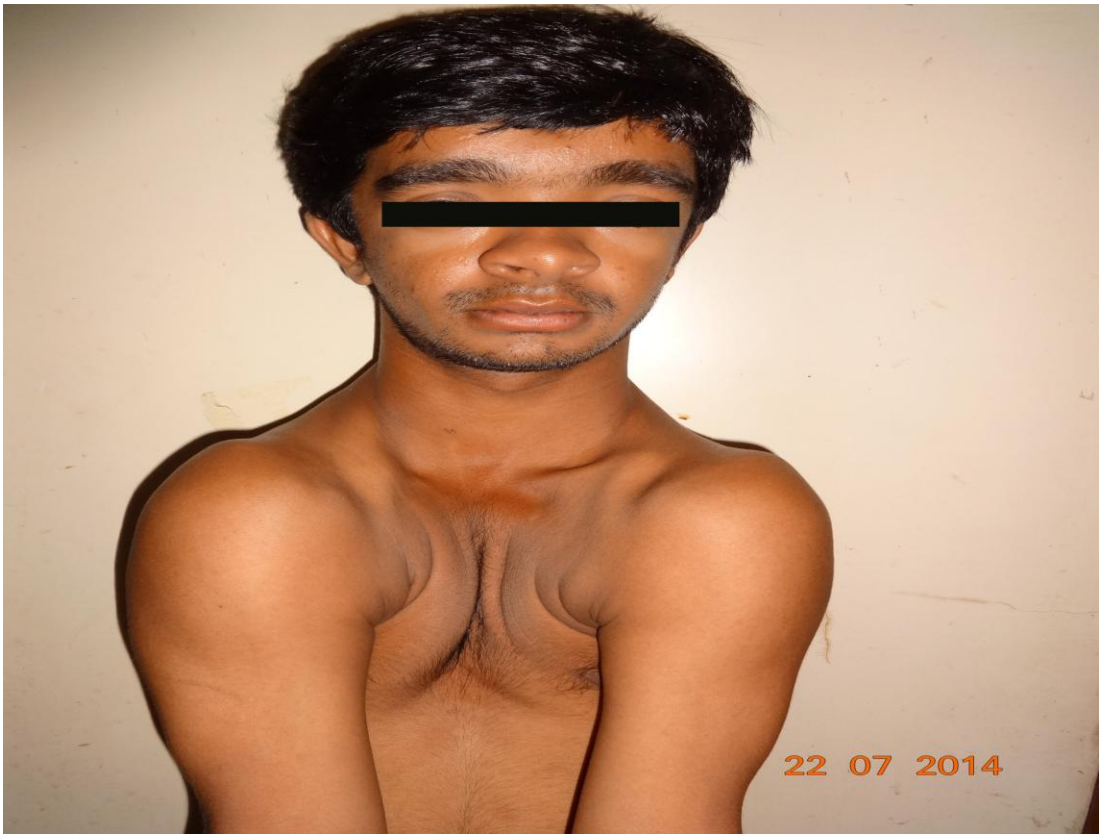

Fig. 3: Frontal view of patient showing shrugged shoulders with more than normal mobility of the shoulder girdle i.e. shoulder could be brought to the midline of chest

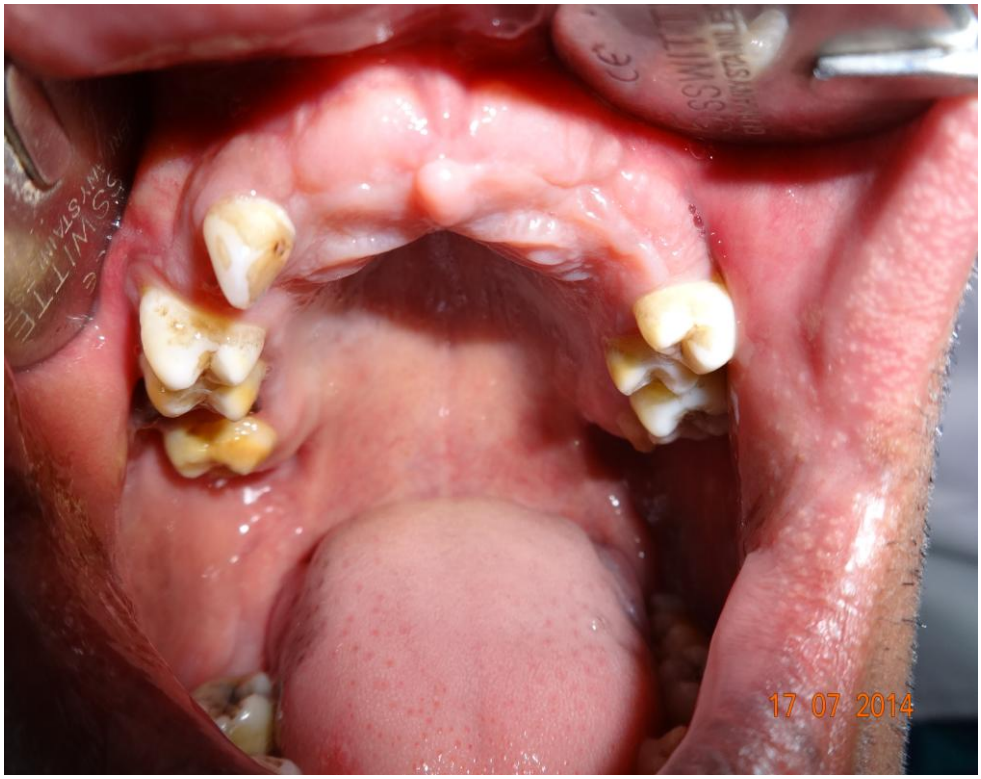

Fig. 4: Intra-oral view showing missing teeth from right maxillary canine to left maxillary canine region

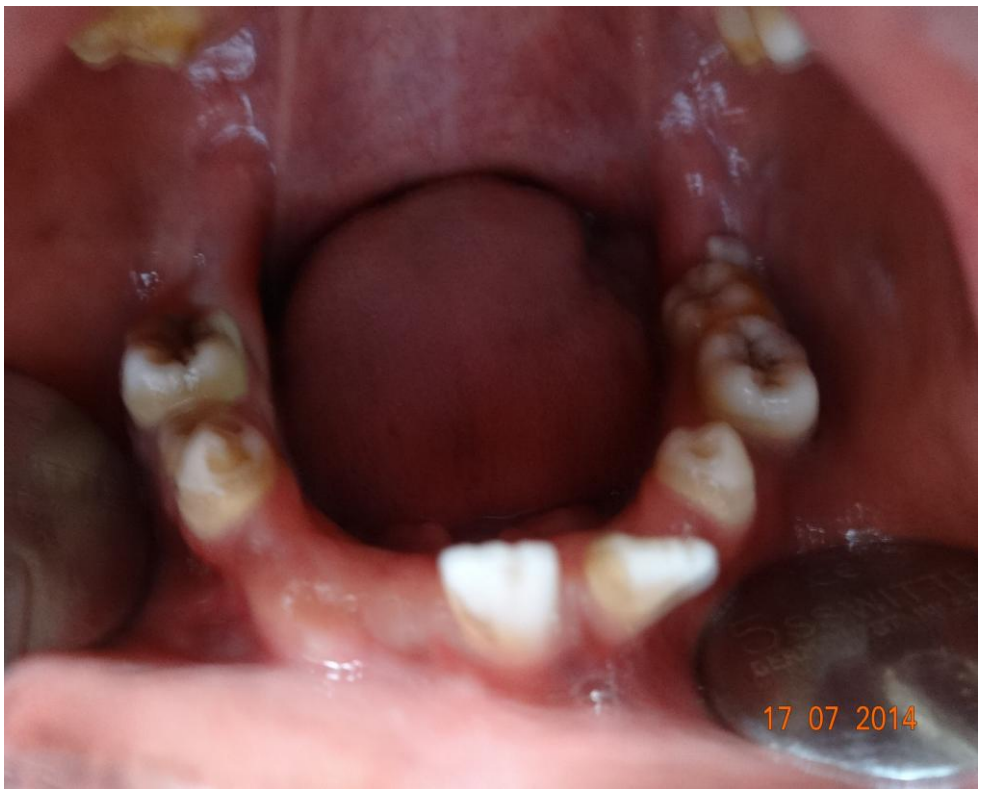

Fig. 5: Intra-oral view showingmissing mandibular canine and second premolar in left side

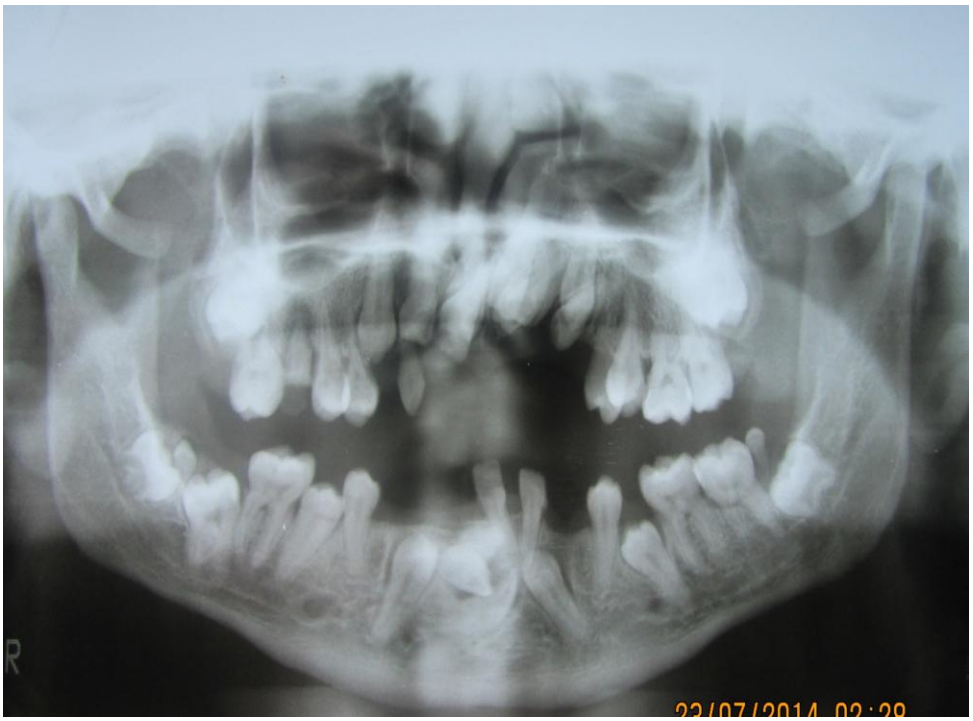

Fig. 6: Orthopantomogram showing multiple impacted teeth along with supernumerary teeth and rounded gonial angles

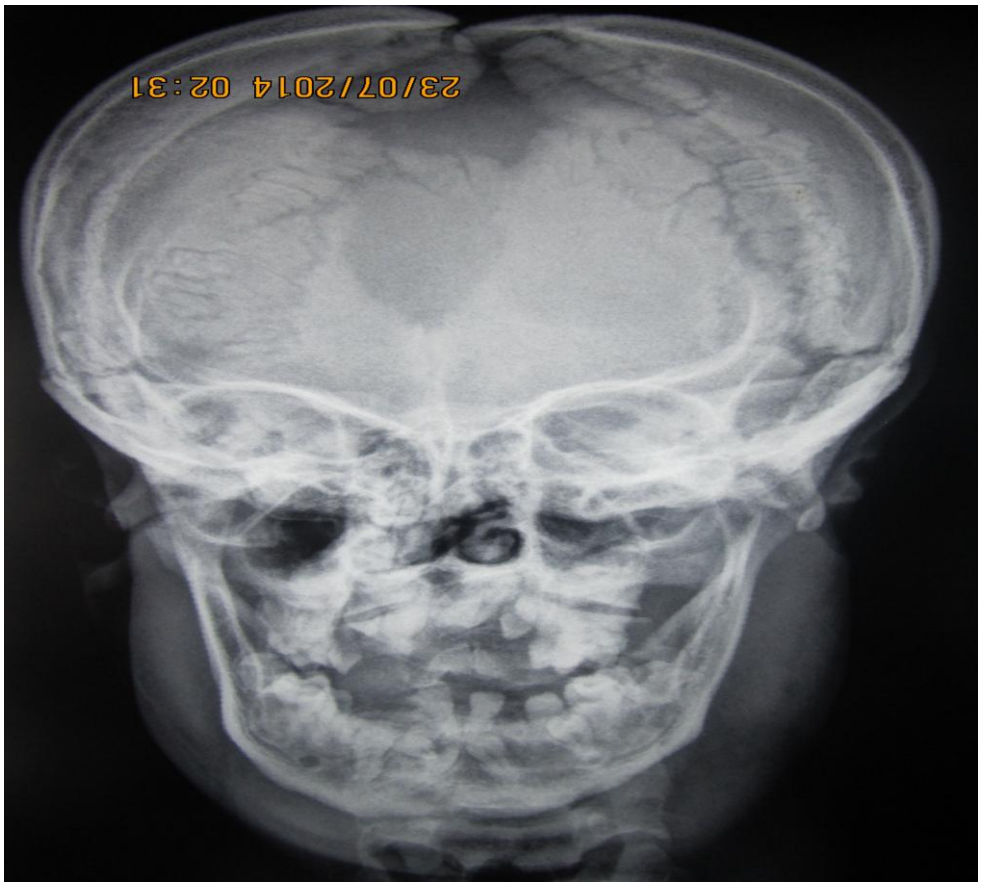

Fig. 7: **PA skull showing widened anterior fontanel and posterior fontanels with presence of wormian bones, top of the metopic suture, sagittal suture and large mandible**

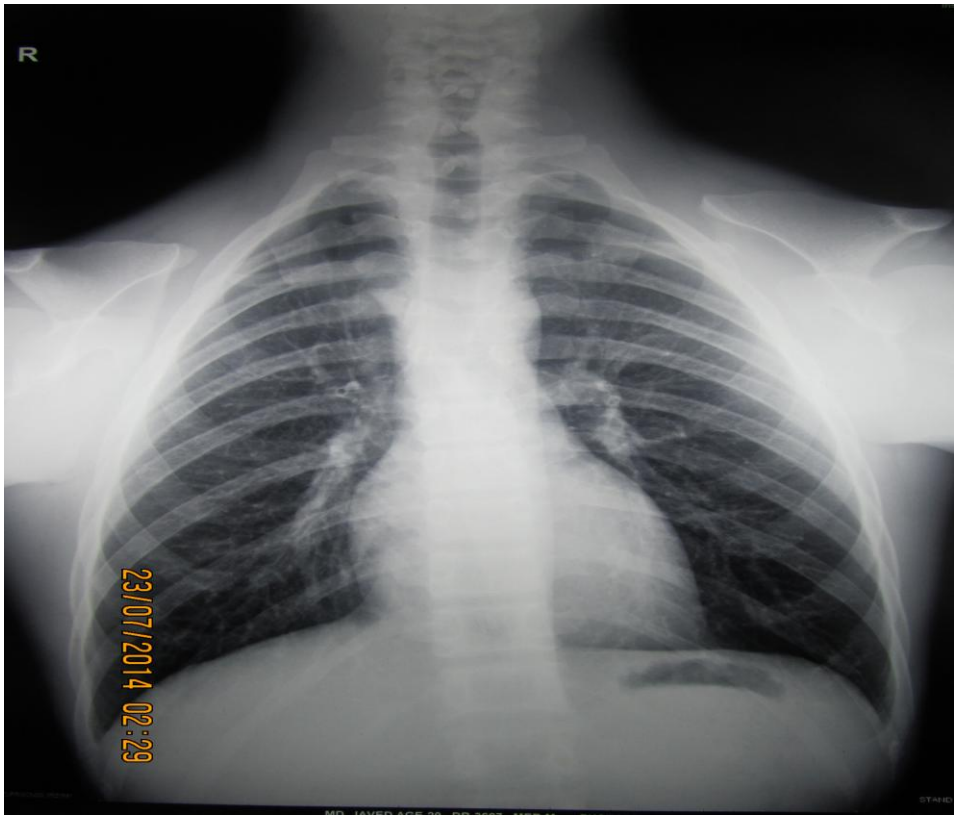

Fig. 8: PA **Chest radiograph showing thinning and hypoplasia of the clavicles and bell shaped rib-cage**

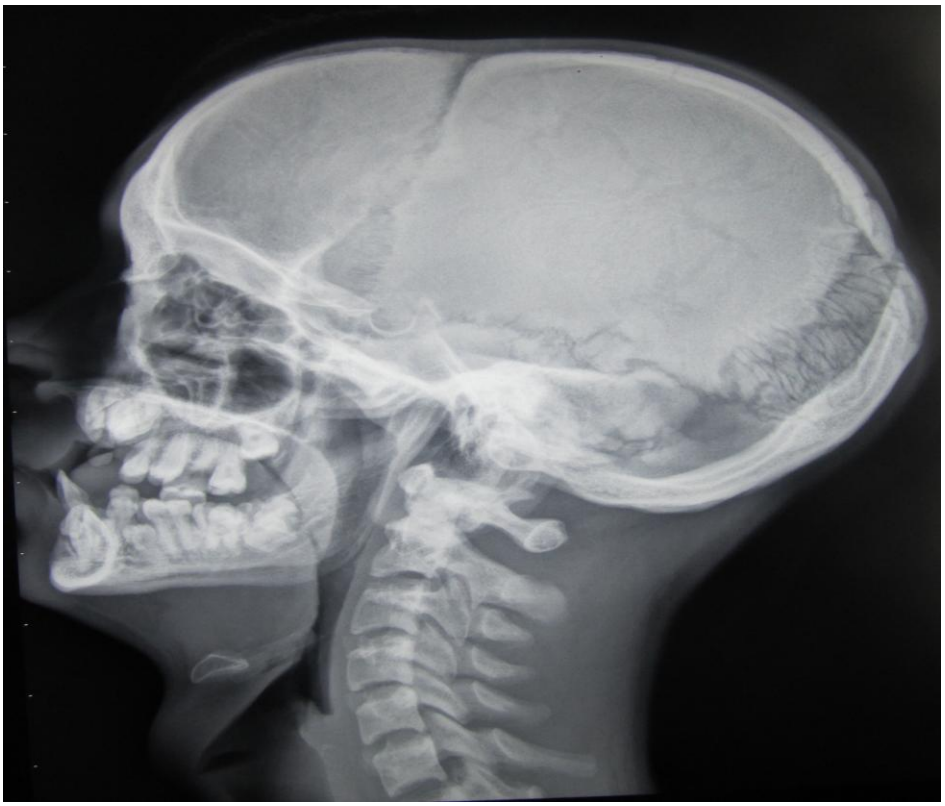

Fig.9:**Lateral ceph showing widened anterior and posterior fontanel with presence of wormian bones, nonfusion of saggital,coronal and lambdoid suture of skull bones, persistent metopic sutures and large mandible with impacted teeth and supernumerary teeth**

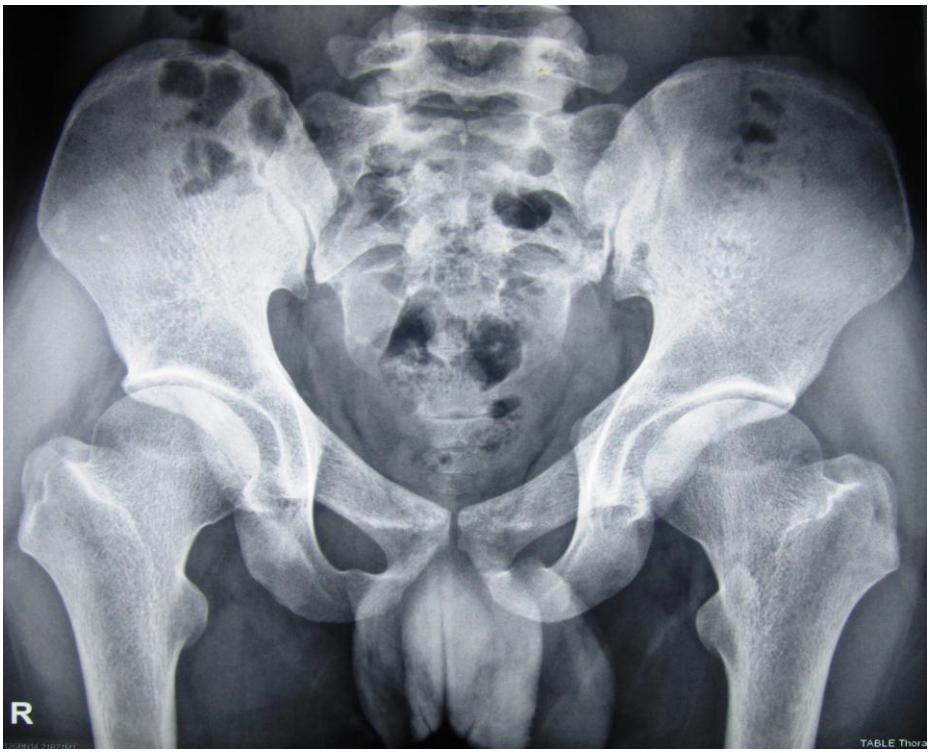

Fig. 10: PA Radiograph of pelvis with both hips showing delayed ossification of bones forming symphysis pubis with diastasis of pubic symphysis, hypoplastic iliac bones, bilateral short femoral neck causing coxavera deformity

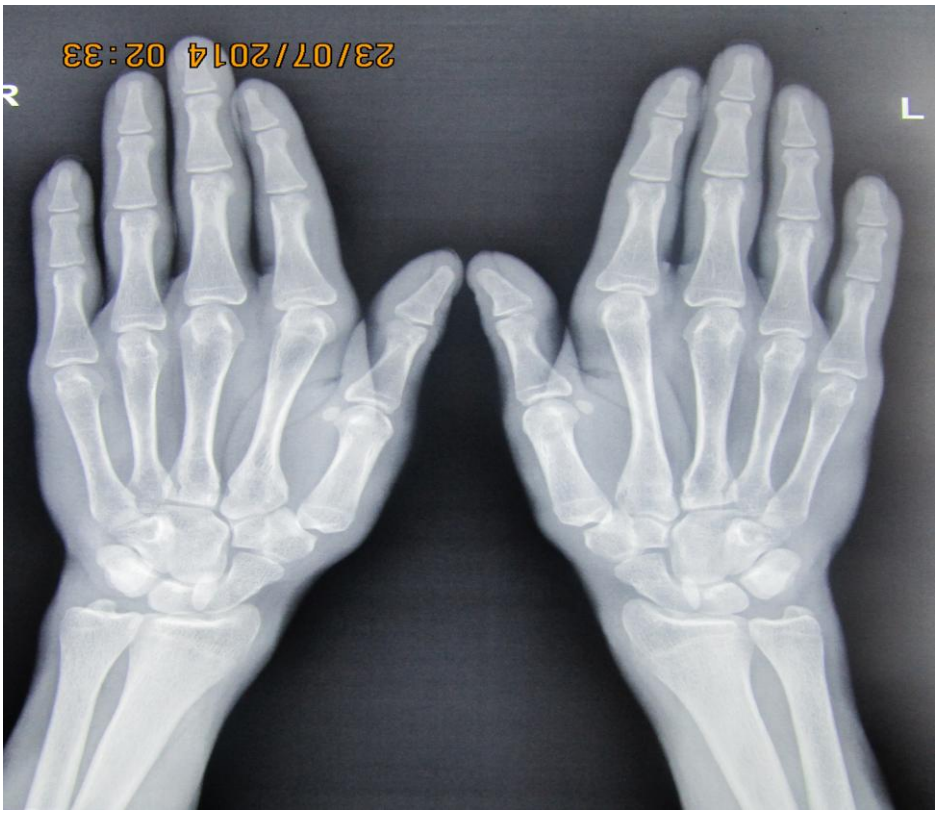

Fig. 11: Radiograph of both hands showing a bilaterally elongated second metacarpal bone, short hypoplastic distal phalanges of hand bilaterally and pointed terminal tufts

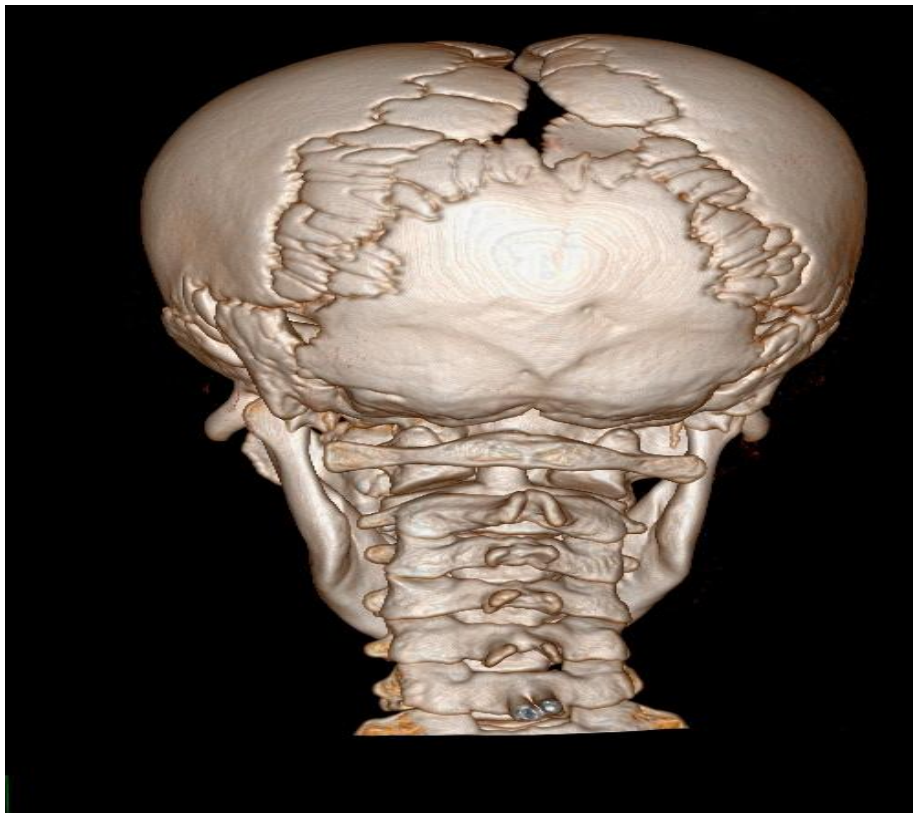

Fig.12: 3D CT showing multiple abnormal intra sutural bones typically around lambdoid suture suggestive of wormian bones and opened up and widened posterior fontenelle

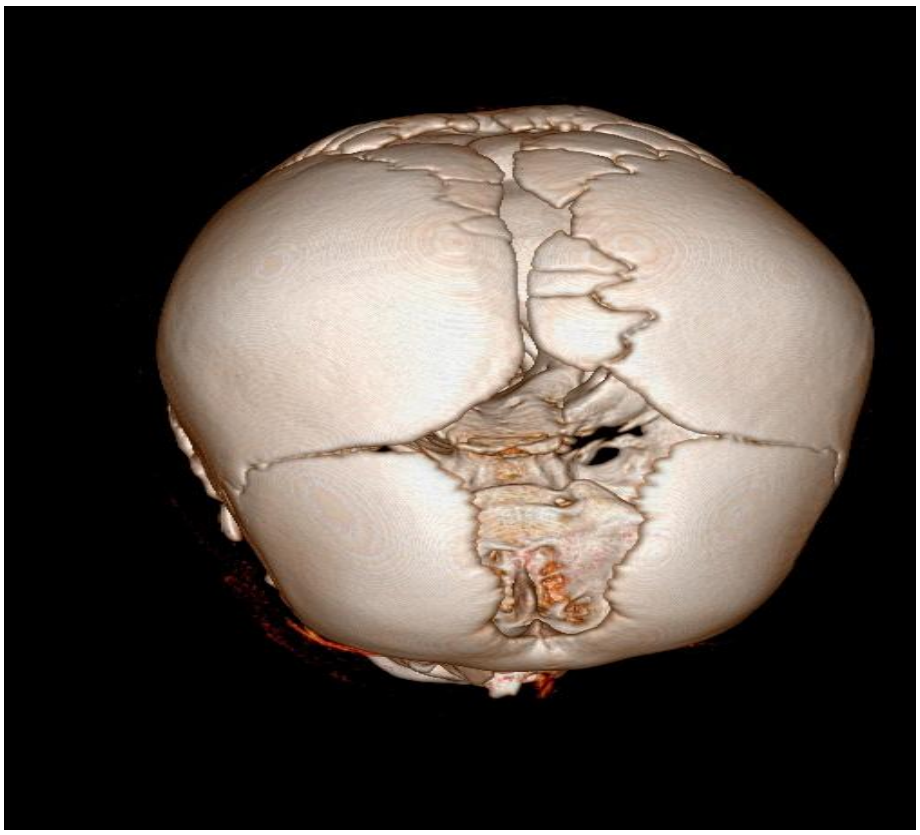

Fig.13: 3D CT showing the widened saggital suture

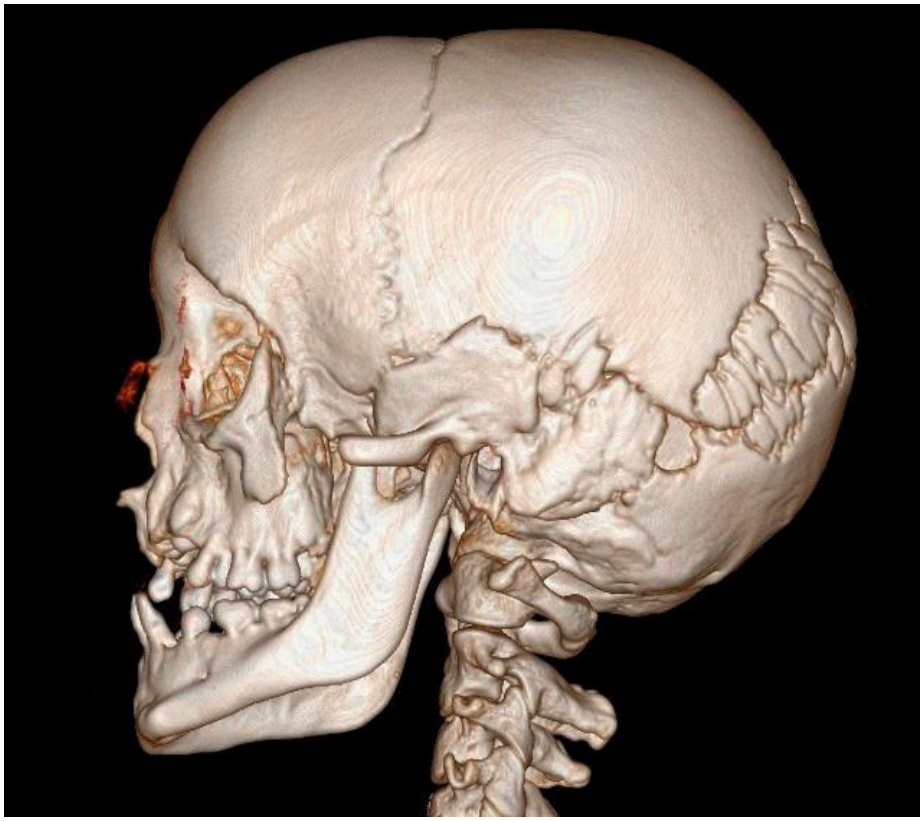

Fig.14:3D CT showing fused coronal suture

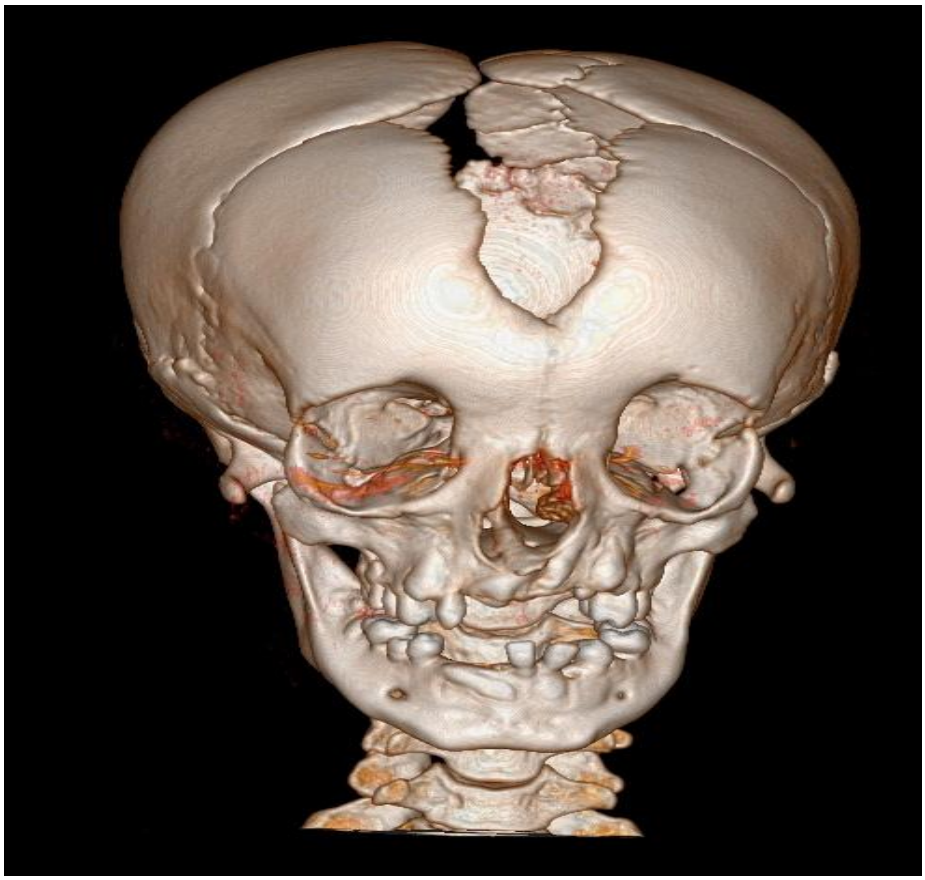

Fig.15: Anterior fontenelleare seen opened up and widened

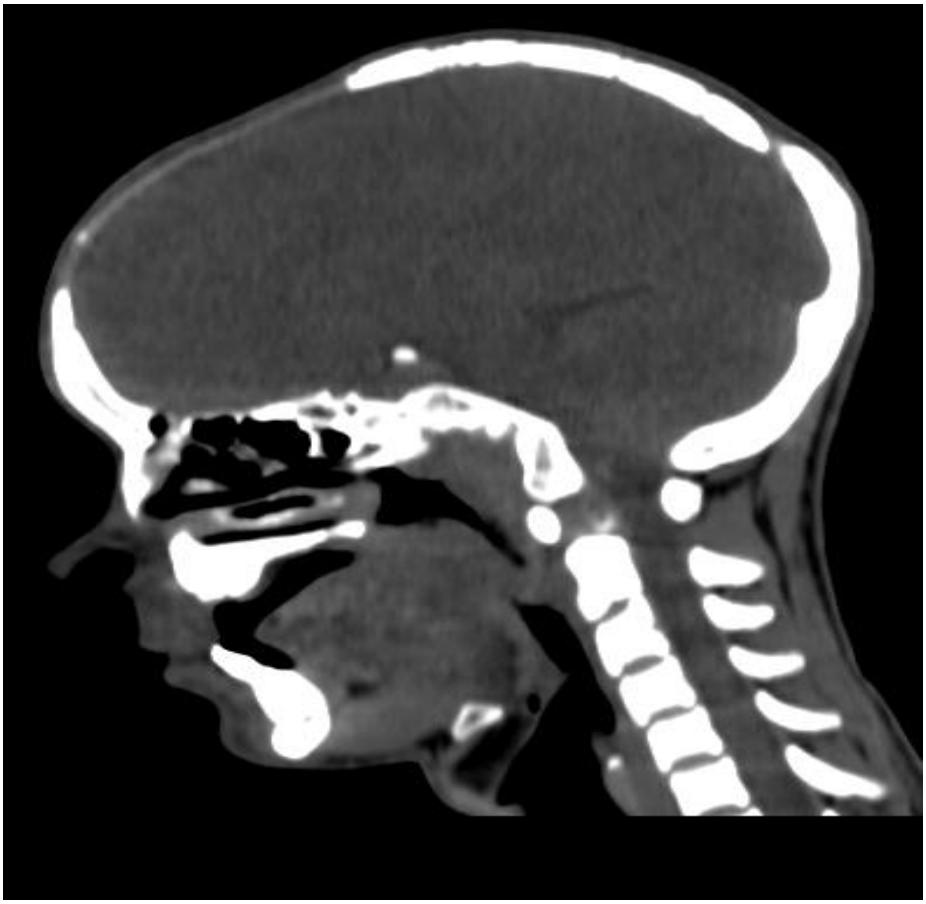

Fig.16: The sagital CT There was persistent metopic suture with agenesis of frontal sinuses. The nasal bridge is flattened and nasal septum is deviated towards right side with convexity to right with spur formation. There was decreased pneumatization of bilateral mastoid air cells

DISCUSSION

Cleidocranial dysplasia is an autosomal dominant polymorphic skeletal disorder primarily affecting bones formed by intramembranous ossification with variable expressivities. Cleidocranial dysplasia results from mutation in the transcription factor Runx2/Cbfa1 located on chromosome 6p21[14]. It is characterized by retarded cranial ossification, patent sutures and fontanelles, supernumerary teeth, short stature and a number of other skeletal abnormalities[15]. Cleidocranialdysplasia is first described by Marie and Sainton in 1898. It is also known as Marie-Sainton disease, mutationaldysostosis, and cleidocranial dysostosis[16]. The first case of clavicular defects was reported by Martin in 1765. Another case with both clavicles and the skull affected was reported in 1871 by Scheuthauer. In 1897 Marie and Sainton coined the descriptive term cleidocranialdysostosis. It is a rare disorder with a prevalence of 0.5 per 100000 live births[17]. Due to generalized involvement of bone the term dysostois is replaced by dysplasia[18].Cleidocranial dysplasia primarily involves the bones derived from endochondral and intramembranous ossification like cranium and clavicles[19]. The oral manifestations of cleidocranial dysplasia are delayed exfoliation of primary teeth, delayed eruption of permanent, multiple impactions of the permanent teeth, multiple impacted supernumerary teeth, class III skeletal malocclusion and bilateral posterior crossbite[20,21]. Dental anomalies are very characteristic of cleidocranial dysplasia and found in almost all cases frequently. The multiple supernumerary teeth (up to 30 supernumerary teeth reported in some cases) are one of the most striking features of cleidocranial dysplasia. Early diagnosis and removal of supernumerary teeth is highly recommended to avoid impedance in normal eruption of permanent teeth[21]. There is delayed root development in permanent dentition and a lessened but not entirely absent eruptive potential[22]. The failure in tooth eruption may be due to the absence of cellular cementum and excessive amount of acellularcementum of the roots of the affected teeth[23]. The skull base is dysplastic with stunted growth characterized by increased skull width leading to brachycephaly and hypertelorism which are usually associated with frontal and biparietal bone bossing[21]. Brachycephaly and hypertelorismoccur due to delayed closure of anterior fontanel and metopic sutures and reduced growth of dysplastic skull base[24]. In 10% of cases clavicles are completely absent however in other cases can clavicles shows variable degrees of

underdevelopment[25]. A diagnosis of cleidocranial dysplasia is usually based on the clinical and radiological examinations. The panoramic radiograph usually shows multiple unerupted teeth in both the jaws. Skull radiograph (lateral view) demonstrates open skull sutures, delayed closure of fontanels and multiple wormian bones. The chest radiograph (PA View) usually shows the clavicular hypoplasia and bell shaped rib-cage along with poorly formed paranasal sinuses and zygomatic complex[26]. The differential diagnosis of cleidocranial dysplasia includes Apert syndrome, Dubowitz syndrome, Russell-silver syndrome, Down's syndrome and Crouzon syndrome[27]. The complications associated withcleidocranial dysplasia is pesplanus, genu valgum, shoulder and hip dislocation, recurrent sinusitis, upper airway complications, recurrent ear infection, hearing loss, dental caries, osteomyelitis of the mandible or maxilla, respiratory distress in early infancy[28]**.** Treatment of clediocranial dysplasia involves a multidisciplinary approach which is focused on correction of skeletal deficiencies, dentofacial deformity and correction of malocclusion and extraction of supernumerary teeth.

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