MARIE - SAINTON SYNDROME - A CASE REPORT OF TWO FAMILIAL CASES

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ABSTRACT

Background: Marie Sainton syndrome is an inherited autosomal dominant disorder characterised by skeletal dysplasia, primarily affecting the development of bones and teeth, caused by mutations in the core binding factor alpha -1 (CBFA-1) gene, also called as RUNX2 (Runt related transcription factor 2) gene located on 6p21 chromosome. It is a very rare condition with incidence of 1 per million individuals. Aim and objectives: To present a case report of affected daughter and father whose diagnosis was made by means of clinical and radiographic findings and to discuss about the clinical features, diagnosis, management and inheritance pattern of the condition. Conclusion: Early diagnosis of CCD is difficult as the craniofacial abnormalities becomes more obvious during adolescence. A multidisciplinary approach is required for management of such manifestations to improve the quality of life of these patients.

INTRODUCTION

Marie - Sainton syndrome, also known as Cleidocranial dysplasia, is a rare polyostotic skeletal dysplasia, primarily affecting the bone undergoing intramembranous ossification. It is a highly polymorphic autosomal dominant skeletal disorder characterised by retarded cranial ossification, open sutures and fontanelles, absent or hypoplastic clavicles, hypoplastic maxilla, supernumerary teeth, short stature and a variety of other skeletal abnormalities. Frontal, parietal and occipital bossing gives the skull a large globular shape with a small face referred to as, ’Arnold face’, named after a Chinese who settled in Africa and changed his name to Arnold.

A member of Runt family of transcription factors, CBFA1 gene (also called as RUNX2) present in chromosome 6p21 is essential for osteoblast differentiation, maturation of chondrocytes, bone and teeth formation. Hence the pathology leads to developmental disorder of mesenchyme and connective tissue with retarded ossification or failure of ossification in some areas. Literature reveals 30-40% of cases appear with no genetic cause. We present a two cases of familial Cleidocranial dysplasia in which father and daughter is affected.

CASE REPORT

CASE 1

A female patient, aged 19 years old, reported to the department of Oral medicine and Radiology, SRM Dental College, Ramapuram with a chief complaint of mobile lower anterior tooth for the past 6months. On probing the history based on patient’s appearance, she reveals no exfoliation of primary teeth since childhood. She also revealed consanguineous marriage between her parents and her father has same appearance as her.

General and physical examination showed short stature, frontal, parietal and occipital bossing (giving skull a globular shape), dropped narrow shoulders, hypertelorism, mid face hypoplasia, wide nasal base, prognathic mandible, long neck, short fingers and toes. The shape of the face was oval, bilaterally symmetrical with competent lips. Intraoral examination reveals multiple retained deciduous teeth (85, 84, 83, 82, 81, 80, 71, 72, 73, 74, 75, 53, 52, 51, 61, 62, 63, 64), permanent teeth (14, 15, 16, 24, 25, 26, 36, 46), root stumps (63, 64, 65), multiple carious teeth (16, 26, 36, 46, 85, 61), crowding of upper lower teeth, high arch palate, reverse bite, pre shedding mobility in 81. Based on he history and clinical findings a provisional diagnosis of Cleidocranial dysplasia and differential diagnosis of idiopathic multiple impacted teeth were given.

Radiographical investigations were carried out. OPG revealed multiple impacted teeth - 11, 12, 13, 17, 18, 21, 22, 23, 27, 28, 31, 32, 33, 34, 35, 37, 38, 41, 42, 43, 44, 45, 47, 48, 31, 32, 33, 34, 35, 37, 38 and impacted supernumerary teeth - 22, 44. Lateral cephalogram reveals frontal, parietal and occipital bossing, open occipital sutures and multiple impacted upper and lower teeth. Anteroposterior view of skull shows open coronal and parietal sutures. Chest radiograph reveals complete absence of clavicles and bell shaped thorax. Hand wrist radiograph reveals thinning of cortex, widening of medullary cavity and slender elongated metacarpals. The
CASE 2
A 52 years old male, father of the above patient was investigated in order to detect the genetic pre-disposition of cleidocranial dysplasia. The patient was conscious, cooperative, oriented, short statured with normal weight and gait. Physical examination showed short stature, parietal bossing, drooping of shoulders, mid face hypoplasia, broad nose, prognathic mandible, short fingers and toes. Intraoral examination showed presence of the following teeth - 47, 46, 45, 44, 43, 42, 41, 31, 32, 33, 34, 35, 36, 37, 11, 13, 14, 15, 16, 17, 22, 23, 24, 25, 28, supernumerary tooth in relation to 23, multiple carious teeth, root stumps in relation to 26 and 38, open and reverse bite. Radiographic investigations were carried out. OPG revealed multiple impacted supernumerary teeth in relation to 31, 41, 32, 33, 34, 43, 14 and 15. Lateral cephalogram revealed frontal and occipital bossing with open occipital sutures. Anteroposterior view reveals open parietal and frontal sutures. Chest radiograph shows hypoplastic clavicles, narrow rib cage, bell shaped thorax and lateral bending of spine. Hand wrist radiograph reveals thinning of cortex, widening of medullary cavity and slender elongated metacarpals.
DISCUSSION
Marie Sainton syndrome or Cleidocranial dysplasia or Cleidocranial dysostosis is a generalised skeletal dysplasia, leading to disturbance in intramembranous and endochondral ossification of the bones especially of cranial and facial skeleton. It is rare autosomal dominant condition with preva- lence one in millions of live births. Being genetic in nature, CCD may pass generation to genera- tion as any other asset. However some autosomal recessive and sporadic cases have also been re- ported.

This disease involves mutation in Run related transcription factor -2 (RUNX-2) otherwise called as core binding factor A1 (CBFA1) gene on chromosome 6p21, which controls every stages of matura- tion of both osteoblasts and odontoblasts. This results in delayed maturation of tooth and bone in RUNX2 deficient tissues. Literature reveals that dental maturation of CCD subjects is retarded by 4years. Specific tests for the RUNX2 gene (sequence analysis, deletion/duplication analysis) were not performed in our case because of patient’s financial situation and keeping in consideration that 30 - 40% of clinical diagnoses are not genetic supported.

The main clinical features of CCD recognised in childhood include short stature, delayed closure of frontanelles, frontal - parietal bossing, abnormal dental development including multiple retained deciduous teeth and delayed eruption of permanent teeth, long neck, drooping of shoulders and ex- cessive mobility of shoulder girdle. The clinical spectrum varies even within families and ranges from mild cases with only dental abnormalities to severe cases with pronounced skeletal deformi- ties.

Distinctive radiographic features include aplasia (10%) or hypoplasia of clavicles, delayed ossifica- tion of skull and pelvic bones, open sagittal and coronal sutures, multiple wormian bones in the lambdoid and coronal suture regions, hypoplastic, thin or discontinuous zygoma, downward bend-ing of zygomatic arch, hypoplastic or absent nasal bones, abnormally small or absent maxillary si- nuses, narrow ascending ramus of mandible with nearly parallel anterior and posterior borders, ab- normally slender and pointed coronoid process with abnormal distal curvature and coarse trabecular pattern and multiple impacted permanent and supernumerary teeth, narrow bell shaped thorax, scol-iosis, etc. Craniofacial features reveals brachycephaly type of head, frontal bossing, mid face hy- poplasia, depressed nasal bridge and prognathic mandible.

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<tr>
<th>CLINICAL / RADIOGRAPHIC FEATURES</th>
<th>DAUGHTER</th>
<th>FATHER</th>
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<tr>
<td>Short stature</td>
<td>X</td>
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<tr>
<td>Narrow chest</td>
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<td>Frontal bossing</td>
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<td>Mid face hypoplasia</td>
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<td>Brachycephaly</td>
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<td>Clavicular aplasia</td>
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<td>Clavicular hypoplasia</td>
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<td>Retention of primary teeth</td>
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<td>Delayed eruption of permanent teeth</td>
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<td>Multiple impacted permanent and supernumerary teeth</td>
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<td>Short fingers and toes</td>
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<td>Short terminal phalanges</td>
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Complications of CCD include gene valgum, pes planus, recurrent sinusitis, upper respiratory tract infections, breathing difficulties, ear infections, hearing loss, dental caries, osteomyelitis of jaws, etc., Managing and treating dental and craniofacial manifestations is challenging and requires proper planning to attain successful results. An interdisciplinary approach including a pedodontist, or- thodontist, oral surgeon and prosthodontist is recommended. Extraction of retained primary and su- pernumerary teeth, surgical exposure of impacted permanent teeth with orthodontic guided eruption is preferred in adolescent patients. In adults, dental implants and fixed prostheses are the preferred therapeutic measures in cases requiring multiple extractions of teeth. Open anterior frontanelles, sutures can be corrected by cranioplasty using bone cement. After growth completion, mid face deficit can be corrected by orthognatic surgery.

According to Chin-Yun Pan et al., 500 independent cases of CCD has been reported in the literature with 80 of those containing gene analysis. Specific test for RUNX2 gene was not performed in our patient because of her financial situation and considering the fact that 30-40% of the clinicaldiag noses are not genetic supported.

DIFFERENTIAL DIAGNOSIS
Mandibuloacral dysplasia is an autosomal recessive disorder caused by mutations in genes LMNA or ZMPSTE24. The disorder is characterised by short stature, delayed closure of cranial sutures, hypoplastic mandible, dental crowding, clavicular dysplasia, sparse hair (some may even develop alopecia) and progressive stiffness of joints. Radiographic findings reveals acrosteodesplasia of fingers and toes, delayed ossification of carpal bones and hypoplastic roots of teeth.
Pycnodysostosis or Marteaux Lamy syndrome presents with similar features as CCD including dwarfism, osteopetrosis, short terminal phalanges, open cranial sutures and fontanelles.

Crane heise syndrome can be considered as one of the differential diagnoses of CCD which is characterised by large head, poorly mineralised calvarium, dysplastic low set ears, hypoplastic clavicles, agenesis of cervical vertebrae, genital hypoplasia, cleft lip and palate.

CDAGS syndrome (Craniosynostosis, anal anomalies and porokeratosis) is characterised by premature closure of sutures, delayed closure of fontanelles, cranial defects, hypoplastic clavicles, genitourinary and anal malformations and skin eruptions.

Hypophosphatasia is caused by very low activity of alkaline phosphatase in serum and tissues. The condition is characterised by poorly mineralised cranium, open sutures, short ribs and narrow thorax.

With respect to OPG findings, differential diagnoses of Gardner’s syndrome, Peutz Jegher syndrome, osteopetrosis, Zimmerman Laban syndrome, Noonan syndrome, Chondroectodermal dysplasia, hemifacial atrophy, hypothyroidism, hypopituitarism, cherubism, cleft palate, gingival fibromatosis, etc., can also be considered as all these conditions are associated with multiple impact-ed teeth.

CONCLUSION
Timely recognition of the condition and counselling the patients with hereditary risk factors are mandatory. Although CCD is associated with various skeletal abnormalities, these patients visit dental clinics only when they require treatment for dental and orofacial problems. Therefore, dentists have essential roles in identifying CCD and planning and implementing a multidisciplinary therapeutic management aimed at improving quality of life in patients with this condition.

REFERENCES
11. Radhika Verma, MK Jindal. Familial Cleidocranial Dysplasia.10.5005/jp-journals-10005-1055