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RESEARCH ARTICLE

MELNICK NEEDLE SYNDROME: A RARE CASE REPORT AND REVIEW.

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Abstract

Introduction:-

Melnick-Needles Syndrome is a rare inherited disorder characterized by skeletal dysplasia, typical facial appearances, and a large cranium with open fontanelles. We report a female patient with Melnick-Needles Syndrome, with typical radiographic and biochemical investigations along with a genetic confirmation.

Inheritance:-

Melnick Needles Syndrome (MNS) is a hereditary skeletal dysplasia involving most of the bones, first reported in 1966. A primary biochemical defect in collagen synthesis is hypothesized to be at fault. Clinical features, including a typical facies, combined with characteristic radiographic features make its diagnosis relatively secure.

Melnick and Needles (1966) described families that contained multiple cases in multiple generations of a severe congenital bone disorder characterized by typical facies (exophthalmos, full cheeks, micrognathia and malalignment of teeth), flaring of the metaphyses of long bones, s-like curvature of bones of legs, irregular constrictions in the ribs, and sclerosis of base of skull, open fontanels. Male-to-male transmission was thought to have occurred in 1 instance. **In males, the disorder is nearly always lethal in infancy. Lifespan of female patients might not be affected**

Osteodysplasty' was the term suggested by Coste et al. (1968), who described an affected 58-year-old woman. Bone disease was recognized in infancy when she began to walk. Normal childbirth was impossible because of contracted pelvis. Osteoarthritis of the lumbar spine and hips gave much pain. Her height was normal. Striking facies comprised frog-like eyes, high forehead, full red cheeks, and receding chin. X-rays showed curved long bones, tortuous ribboned ribs, and deformed clavicles, scapula, and pelvis.

Kristiansen et al. (2002) reported 2 severely affected girls with Melnick-Needles syndrome and their mildly affected mother. They analyzed the X-chromosome inactivation pattern in this family to determine if it was related to the variable phenotype. A very skewed inactivation pattern was observed in the blood from both the mildly affected

mother and one of her daughters, whereas a highly skewed inactivation pattern in buccal smear DNA was observed in the mother only. X inactivation, therefore, did not explain the variable phenotype in this family.

Melnick-Needles syndrome is an X-linked dominant disorder. Most cases described are in females. Nyhan and Sakati (1976) described a family with 4 affected females in 3 successive generations. Von Oeyen et al. (1982) found a sex ratio of 21 females and 3 males in reported cases. Melnick (1982) studied 4 additional families in the United States; in two, 3 generations were affected and in the other two, 2 generations. The Melnick-Needles syndrome had been assumed to be an autosomal dominant disorder. However, Gorlin and Knier (1982) analyzed reported families with restudy of some. Melnick had reexamined the male 'cases' in the kindred he reported in 1966 and found them in fact to be normal. In all, Gorlin and Knier (1982) found 23 patients in 15 pedigrees. Most cases were sporadic and may represent new mutations. In only 3 pedigrees was there transmission from one generation to the next, always female to female.

Case report:-

A 50 year old female reported to the department with c/o pain in left lower back tooth region for the past 6 months. H/o pain for the past 6 months which was of intermittent nature. H/o pain and h/o pus discharge from left lower facial region since 2 months, which had increased after a left lower tooth extraction before one month, and had reduced since one week.

Family history revealed that the patient was the youngest among four. Her mother had given birth to 2 males, who were still born, her elder sister was apparently normal and she had a few special features. H/o similar features exhibited by the patient's great grandmother.

She was short, obese, moderately nourished. She had Increased upper/lower segment ratio, broad face, frontal bossing, ocular hypertelorism, broader nasal bridge and snubby nose, double chin, forcibly competent lips (fig 1). Extra orally, (fig 2) there was a sinus opening along the left inferior border of mandible with superficial scab formation and a surrounding area of erythema with no active drainage of pus. The length of hands was normal with short stubby fingers, short nails, Mild kyphosis of spine was evident, legs were shorter and were present with apparent bowing below the knee joint causing leg length discrepancy. There was presence of palpable Right and Left Submandibular lymph nodes measuring approx 1x1.5 cm in dimension which are tender on palpation and movable. Intra orally, narrow maxillary and mandibular arch was evident, she had multiple missing teeth, root stumps and presence of central area of clefting involving the hard palate, soft palate and uvula (fig 3). There was also a non healing extraction socket in relation to 37.

Following clinical examination we conducted a radiological survey.

OPG (fig 4): The entire maxillofacial complex appeared hypoplastic, with presence of generalised horizontal bone loss extending approx 4 mm below CEJ of all teeth. Presence of multiple radiopaque sclerotic bony mass evident along the periapical aspect of 34, 35, 36, 37, 46 that is outlined by a faint radiopaque sclerotic border. The inferior border of mandible was irregular, with obtuse mandibular angle bilaterally. Presence of generalised reduction in the width of the body of mandible, and the inferior alveolar canal cannot be traced in the right side. In the left side the superio inferior width is compromised causing downward displacement of the inferior alveolar canal. In right side: Complete loss of condylar process and sigmoid notch. In left side: thinning of head and neck of condylar process with wide sigmoid notch. Partial loss of ramus of mandible in right side.The cervical vertebra exhibit increased radiodensity with bone within bone pattern.(Rugger Jersey sign)and there is elongation of styloid process bilaterally.

HAND WRIST RADIOGRAPH (fig 5):- PA view: Exhibits increased radiodensity of Radius, Ulna and the metacarpels and carpels bilaterally. There is generalised hypoplasia of distal phalanges except the 4^{th} finger in left hand and mild cortical thickening of all bones. Presence of increased sclerosis and thickening of the terminal portion of ulna causing a bulbous calcified bone mass suggestive of Malunion? and Improper callus formation. The scapholunate space is significantly decreased bilaterally.

CHEST PA view:- (fig 9) Reveals sclerosis of ribs along with few exhibiting radiolucent fracture lines in relation to 1^{st} and 2^{nd} rib bilaterally. The R and L clavicle appear hypoplastic and are present with comminuted fractures with displaced fragments. The medial portion of left clavicle is present with irregular sclerotic radiodense mass suggestive of malunion. A faint radiolucent line is present in the right 1^{st} and 2^{nd} rib suggestive of undisplaced anterior rib fracture.

SKULL PA view:- (fig 6) The mesiodistal width of the skull is increased causing increased size of the vault. Mild hydrocephalus evident along with presence of widespread homogenous areas of radiodensity along with incomplete closure of the anterior fontanel and cranial sutures. It also reveals hypoplastic maxillofacial complex, with discontinuity along the right lower border of mandible. Aplasia of frontal and maxillary sinus. Discontinuity present along the right zygomatic arch causing mild displacement.

Fig 1: profile picture

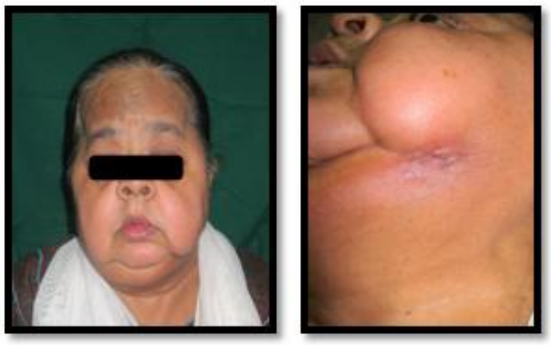


Fig 2: EXTRA ORAL FEATURES

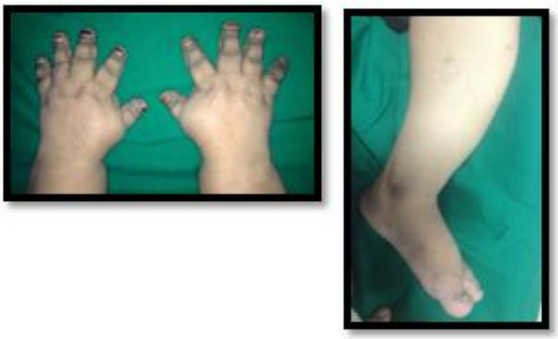


Fig 3: INTRA ORAL FEATURES

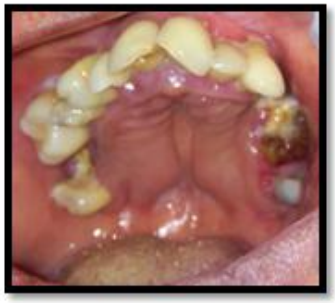


Fig 4: OPG

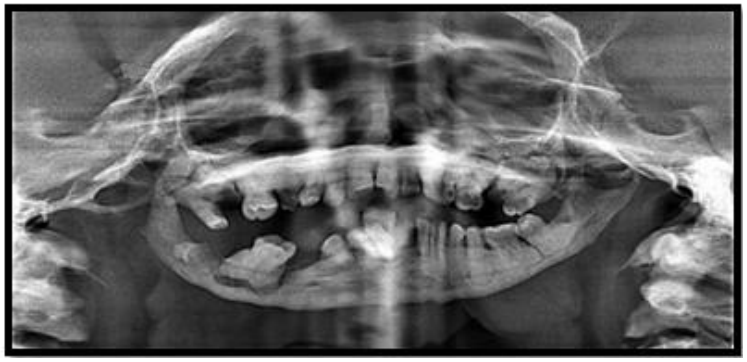


Fig 5: HAND WRIST

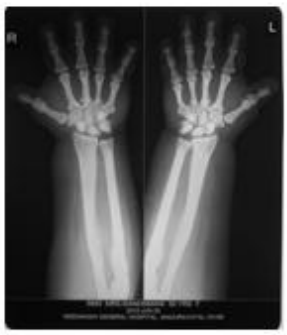


Fig 6: PA SKULL

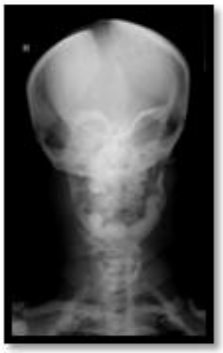


Fig 7: LATERAL SKULL

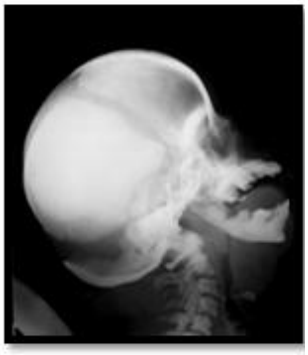


Fig 8: 3D SKULL

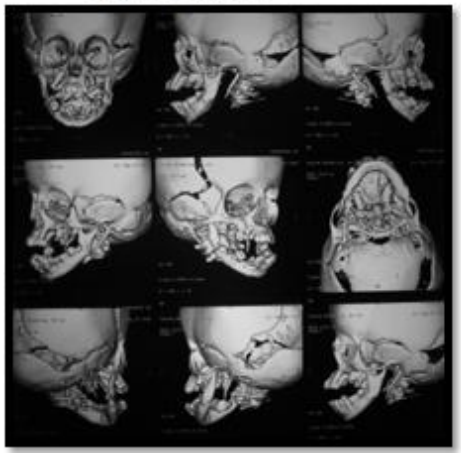
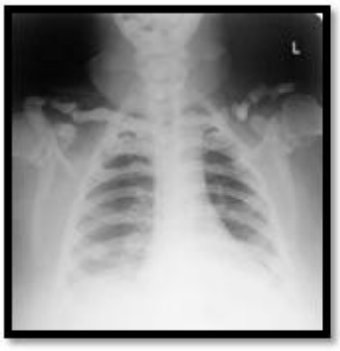


Fig 9: CHEST RADIOGRAPH



SKULL : LATERAL view:- (fig 7) Reveals increased cortical thickening of the frontal and occipital regions, with open anterior and posterior fontanels giving the occipital region a "Cut bone" defect. There is increased radiodensity of the vault and also "double density" due to overlapping of the frontal and parietal bones. Complete aplasia of the frontal and maxillary sinuses is evident. The cervical vertebra exhibit sclerotic changes and give a "bone in bone "appearance.

Transcranial view:- Reveals, elongated styloid process superimposing onto the body of mandible. Presence of discontinuity in the right lower border of mandibular body complete loss of right condylar head and sigmoid notch. The inferior alveolar nerve cannot be traced. Decreased intervertebral disk space between C2 and C3

Pelvic girdle:- Exhibits increased radiodensity of the crest of Ilium. Presence of radiolucent fracture lines evident in the right superior ramus of pubis and bilateral ischial tuberosity region. The fracture line in the left superior ramus is present with a cloud like callus formation around it. Fractures involving the middle third and superior third of the right and left femur evident which are present with a cloud like callus formation bilaterally along with increased radio density suggestive of malunion. Reduced cortical width of femur bilaterally with dense pattern of trabeculae giving it a "Ground glass " appearance in Right side. Coxavalga of right femur head and coxavara of left femur head(due to malunion)

3D CT SKULL:- (fig 8) Same osseous features were confirmed in 3D imaging- with visible open fontanelles, cranial sutures and elongated styloid processes.

The positive radiological features gave us a hint to perform a few blood investigations which revealed

Routine blood values:- Hb%, RBC, WBC, BT, CT, DC: within normal limits RBS: 371 mg/dl, Serum Alkaline phosphatase: 108 IU/L (50yrs- 39- 100 IU/L), VITAMIN D: 15.64 ng/ml (<20 ng/ml= deficiency), CALCIUM: 9.3 mg/dl, Serum Acid Phosphatase: 1.9 IU/L (0- 0.8 IU/L), Parathyroid Hormone: 96.59 pg/ml (14.0- 72.0 pg/ml).

Taking into account all the positive clinical features, and striking radiological features and lab investigatory findings, we arrived at a final diagnosis of Melnick Needle Syndrome.

Discussion:-

First described in 1966 by John Melnick and Carl Needles, Melnick-Needles Syndrome is a rare X-linked dominant syndrome characterized by generalized bone dysplasia, a relatively large cranium, and typical facial appearances [1, 3].

Individuals with MNS have a particular facial appearance with prominent, widely-spaced eyes, full cheeks, small facial bones, and an unusually small lower jaw (micrognathia). The skull may be slow to develop and the way in which affected individuals bring their teeth together (bite) may be abnormal.The upper arms and the last bones in the fingers (distal phalanges) may be shorter than normal [2, 3, 4]. One of the short bones of the arm (radius) and of the leg (fibula) may be bowed. The distal ends of the long bone of the arm (humerus) and of the two short bones of the leg (tibia, fibula) may be flared. The connection between the long bone of the leg (femur) and the hip may be misaligned (coxa valga), producing an unusual walking pattern (gait).Occasionally, dislocation of the hip may occur. Other abnormalities may also be noted. Congenital heart defects and high blood pressure in the lungs have also been reported in those with MNS, which was ruled out in our patient[4,7].

Individuals with MNS may develop osteoarthritis of the back and/or hip in later years. The shape of the pelvis in females may make normal childbirth difficult. Those affected may be unusually susceptible to respiratory infections. Intellectual development is normal in individuals with this condition.MNS is more severe and lethal in males. Abnormalities seen in affected males include bulging eyes, protrusion of internal organs through the abdominal wall (omphalocele) and major skeletal abnormalities.

The differential diagnosis of Melnick-Neddles syndrome includes Frontometaphyseal dysplasia[2], Otopalatodigital type II syndrome and Serpentine fibulae associated with polycistic kidneys and other anomalies because of some similar radiological and clinical findings.[1,2]

Conclusion:-

Melnick-Needles Syndrome is a rare disease with multiple manifestations. The case illustrates the need for knowledge about the clinical, radiological and hematological features to arrive at a diagnosis which in turn necessitates the dental management protocol and their possible complications in such conditions.

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