CASE REPORT
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PYKNODYSOSTOSIS;
EARLY AND DELAYED CLINICAL MANIFESTATION

DR. A. ODHIAMBO
Oral and Maxillofacial Surgeon and a Radiologist,
Armed Forces Memorial Hospital, Nairobi, Kenya
P. O. Box 456-00202, Nairobi, Kenya

DR. JEREMIAH MOSHY
Oral and Maxillofacial Surgeon,
Muhimbili University of Health and Allied Sciences,
Dar es Salaam, Tanzania.
P.o Box 65014, Dar-Es-Salaam, Tanzania.

DR. W OTIENO
Oral and Maxillofacial Surgeon and a Radiologist,
Armed Forces Memorial Hospital, Nairobi, Kenya
P.o.Box 456-00202, Nairobi, Kenya.

Dr. EN Simon
Oral and Maxillofacial Surgeon,
Muhimbili University of Health and Allied Sciences,
Dar es Salaam, Tanzania.
P.o Box 65014,Dar-Es-Salaam, Tanzania.

Dr. ML Chindia
Professor in Oral and Maxillofacial Surgery,
Nairobi University,
School of Dental Sciences, Nairobi, Kenya.
P.o Box 19676, Nairobi, Kenya.

ABSTRACT... Pyknodysostosis (PKD), also called Maroteaux-Lamy disease or Toulouse-Lautrec syndrome is a rare osteosclerosing skeletal disorder that has an autosomal recessive trait. It is characterized by short stature, brachycephaly, short stubby fingers, open cranial sutures and fontanelles, diffuse osteosclerosis with attendant multiple fractures of long bones and osteomyelitis of the jaw; but with rare visceral manifestations. In this article we present three cases of PKD with diverse classical clinico-radiological features. Worldwide PKD have been reported in 9-months to 55 years but remarkably, we have presented amongst the youngest diagnosed cases, at 8months with visceral manifestations. Understanding early and delayed clinic-radiological manifestations of PKD is very important as accurate diagnosis of PKD avoid misdiagnosing it as hydrocephalous, cleidocranial dysostosis and osteopetrosis as the conditions may resemble each other clinically and radiologically.

Key words: Pyknodysostosis, early, delayed, clinical signs.

INTRODUCTION AND LITERATURE REVIEW

The term Pyknodysostosis (PKD) is derived from Greek, whereby 'pykons' means dense, 'dys' means defect, and 'osteosis' means bone pathology. Maroteaux and Lamy (1962) recognized this condition as an entity in its own right. Previously it was thought to have been a variant of cleidocranial dysostosis, osteopetrosis[1,2,3,4] fluorosis and heavy metal poisoning[5,6] PKD in children is commoner in males than in females, occurring at a ratio of 2:1[7]. It is characterized by short stature[1,8,9] (measuring less than 150cm in adulthood), generalized diffuse osteosclerosis, long bone fractures, hypoplastic clavicles and short stubby fingers[2,8]. Craniofacial features include a large head with frontoparietal bossing, open soft cranial sutures and fontanelles, depressed nasal bridge, beaked nose, obtuse mandibular gonial angle, a high arched grooved palate, maxillary hypoplasia accompanied with relative proptosis, mandibular fractures, osteomyelitis, malpositioned teeth, delayed exfoliation of primary teeth, crossbite, hypercementosis, elongated soft palate precipitating mouth breathing and heavy snoring in addition to periapical cementoma-like lesions in the mandible[2,4,8]. Intraoral features include a grooved or furrowed palate, delayed exfoliation of deciduous teeth but timely eruption of the permanent dentition giving rise to crowding[2,4,9,10] multiple retained teeth, unerupted teeth within follicles and an expanded alveolus[10]. Follicles occasionally get infected leading to chronic suppurative osteomyelitis[10,11,12].

Parental consanguinity has been identified in more than 30% of the cases as the cause of this autosomal recessive disorder[2,10]. Karyotyping suggests that the gene which determines PKD is located on the short arm of a small acrocentric chromosome probably G-22[2]. It follows mutations in the CTSK gene situated at 1q 21 that codes for cathepsin k lysosomal cysteine protease that is highly expressed in osteoclasts leading to disturbed bone resorption and remodeling[13]. In this article we present three cases of PKD who presented with diverse

classical clinico-radiologic features.

CASE 1

An 8-months-old boy with delayed milestones presented with complaints of apparent head enlargement since birth; mouth breathing and loud snoring for 3 months. Initially the head enlargement did not disturb the child's feeding or sleeping. However, the symptoms worsened and the patient was taken to a nearby hospital where a brain CT-scan revealed features of cerebral atrophy with mild hydrocephalus. The parents were advised on shunting but they opted to seek a second opinion at a referral hospital. The child was a 2nd born in a non-consanguineous family with 1st born being a 6-year-old female who was alive and well. The patient had frontoparietal bone bossing (Fig. 1), copious mucous secretion plugging the nostrils and a hypoplastic mandible.

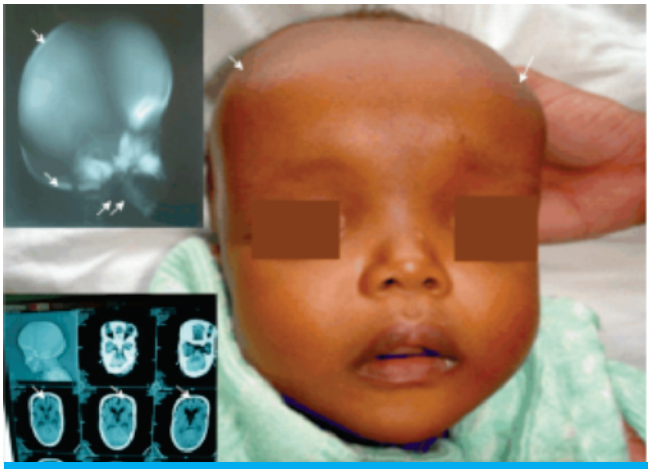

Fig-1 Demonstrates fronto perietal bossing of the bones. Inser, (upper left) the x-ray shows a hyperdense cranial and an obtuse mandibular gonial angle (double arrows) and the CT-scan (lower left inset) shows a rim of cerebrospinal fluid in the lower images; thus discounting hydrocephalus.

The palate was high-arched and V-shaped with the soft palate elongated almost to the posterior pharyngeal wall. The alveolar ridges were enlarged without deciduous teeth clinically present in the mouth at 8 months (Fig. 2). The maxilla was underdeveloped and the head circumference at 48 cm was normal for the age. The anterior and posterior fontanelles were open and pulsatile. The cranial sutures were open and soft to superficial palpation while the chest was pigeon-shaped and had a rachitic rosary. He had a hepatomegally of 4cm below the costal margin and cardiomegally with a rim of pericardial effusion. The infant had decreased nostrils, a depressed nasal bridge and hypertelorism.

The lateral skull X-ray revealed a very dense calvarium, orbital rims and skull base and; wormian bones were also present in the lambdoid suture. Mandibular angles were obtuse and hypoplastic with evident retained ghost-like teeth (Fig.1. Inset).

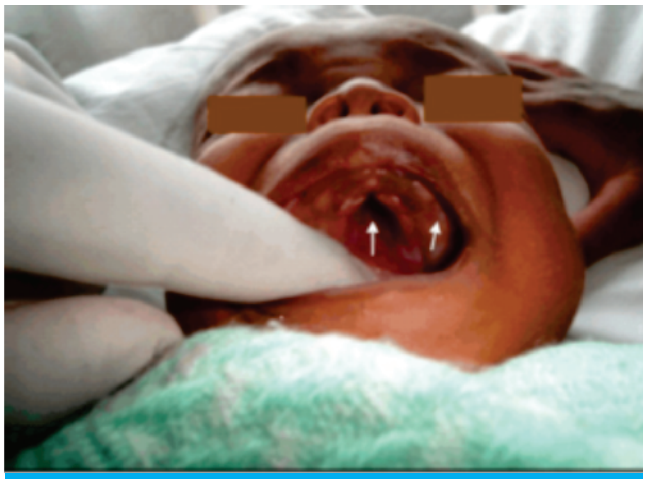

Fig-2. Demonstrates the 8-month-old patients with enlarged alveolar ridge and a high arched v-shaped palate.

This case also demonstrated dense ribs, hypoplastic lateral ends of the clavicles with extreme ends having been aplastic (Fig.3). There were dense proximal ends of the humera and a healing fracture of the proximal right humerus. Brain ventricles were enlarged but with an apparent rim of CSF along the frontal poles which ruled out hydrocephalus (Fig. 1 inset: CT SCAN). The patient was remarkably short for his age and had delayed milestones. The diagnosis of PKD in this case was made on the basis of clinical and radiological features.

CASE 2

A 40-year-old man presented with persistent pain in the lower posterior left mandible 6 months after he had had a tooth extraction. The patient was of short stature with pronounced bilateral parietal prominences. On craniofacial inspection, the anterior and posterior fontanelles were clinically unossified and there was frontal bossing with mid and lower facial hypoplasia.

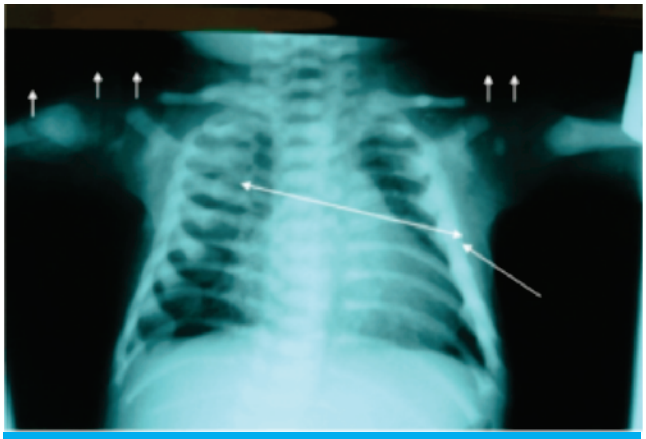

Fig-3. Comprehensively demonstrates classical features including right humerus fracture (single white arrow), bilateral aplastic clavicles (doubles white arrows), cardiomegally (double adged white arrow and a rim of pericardial effusion (long arrow to the left).

Intraoral examination revealed a non-healed extraction socket in a swollen posterior left mandible. Remarkably, the patient had a high-arched palate with tooth crowding in both arches. A lateral view radiograph of the full cranium revealed the typical osteosclerotic features, an obtuse gonial angle, hypoplastic maxillary bone and underpneumatised maxillary sinuses which were characteristic of PKD (Fig. 4)

CASE 3

A 37–years–old man was referred for the evaluation of a persistent cutaneous draining sinus over his left body of the mandible which had manifested 6 months previously (Fig. 5). Notably, the patient had sustained spontaneous upper and lower limb fractures variously (Fig. 5 inset). Craniofacial clinical inspection revealed patent anterior and posterior fontanelles, a high arched palate and tooth crowding in both arches. An orthopantomogragh (Fig. 6) showed generalized tooth hypercementosis with gross features of chronic osteomyelitis in the left body of the mandible characteristic of PKD.

DISCUSSION

Kundu et al[8] and Bathi et al[2] noted that, worldwide PKD has been reported from 9 months to 55 years. Remarkably, we have presented amongst the youngest diagnosed cases, at 8 months with visceral manifestations. The present youngest case had hepatosplenomegaly, cardiomegaly, anaemia, rickets

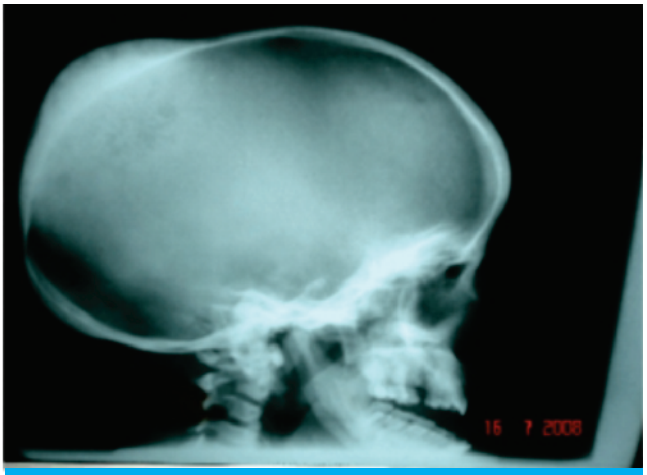

Fig-4. Shows an osteosclerotic calvarium, jaws and shull base; obtuse gonial angle, hypoplastic maxillary bone and underpneumatised maxillary sinuses.

Fig-5. Demonstrates frontal bone bossing, a depressed nasal bridge, hypoplastic malar bones, a cutaneous sinus (white arrow), proptosis and deformed lower limbs (Inset) due to multiple malunited fractures.

and rachitic rosary as was observed by Kundu et al[8].

PKD characteristically presents with transverse diaphyseal fractures of the long bones that heal well. This was obvious in case 3 who had lower limb deformity due to repeated fractures with incomplete management but was coincidentally noted in the infant (case1) as a healing fracture of the right humerus which the mother had no idea had occurred. The infant had not started crawling hence there was a possibility of the fracture having arisen from moderate forces like handling of the

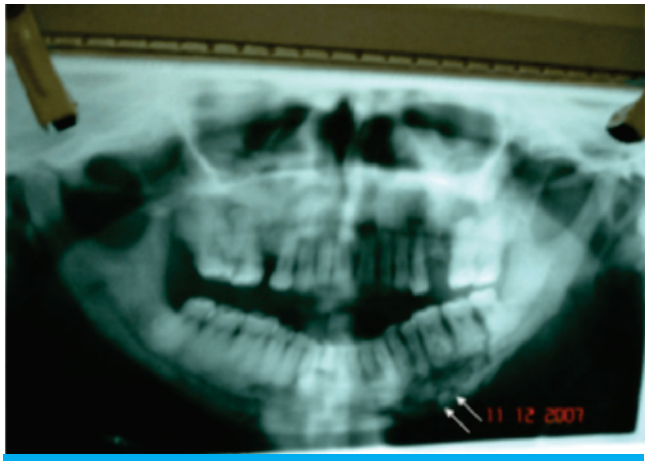

Fig-6. An Orthopantomogram showing gross features of chronic osteomyelitis in the left body of the mandible (white) double arrows). The obtuse gonial angles are evident).

patient by one hand while being strapped at the back of the mother, which is the common practice among Africans in the rural areas. Accurate diagnosis of PKD saved the child from shunting which is frequently done erroneously after misdiagnosing hydrocephalus. A high index of suspicion is necessary whenever a child presents with frontoparietal bone bossing, failure to thrive, short stature but with no features of increased intracranial pressure both clinically and radiologically. Other important features of hydrocephalus may include sunset eyes, engorged cranial veins, turgid fontanelles and sutures and; lack of or a decreasing CSF rim in the cranial subarachnoid space. Under-pneumatization of the maxillary sinus was noted in the three cases though in the infant, the size of the sinus could not be strongly mentioned as a feature the way it had been done by previous authors whose cases were adults since sinuses at this age are under pneumatised. Since the gonial angle, just like the coronoid and mastoid processes, is dependent on muscle activity for its full development, it is improper to stress its obtuse nature in infants as a pathognomonic feature in PKD because at this age it is normally obtuse.

Hypoplasia of the teeth with the ghost-like appearance resembling regional odontodysplasia was noted in case 1 with all the posterior teeth having been hypoplastic and ghost-like. A high-arched grooved hard palate and a long soft palate were present just as reported by Kundu et al[8].

The patient had delayed eruption of primary teeth as was observed by Fleming et al[10].

The present cases were all males enhancing Wolfgang's report7 that PKD was commoner in males than females. However, no parental consanguinity was volunteered in our cases as had been reported by Bathi et al[2] and Fleming et al[10]. In the developing world, PKD leads to lower limb deformity because of repeated diaphyseal fractures which are hardly treated due to lack of facilities and resources. Since the fractures heal rapidly, patients tend to ignore the deformities despite their severity. Discharging sinuses occur in the jaws because of poor blood supply due to hypercementosis and hyperdense bones. Follicles of impacted teeth may also get infected leading to discharging sinuses or chronic suppurative osteomyelitis. However, to date no cystic lesions or bone tumors have been reported in association with follicles of impacted teeth in PKD.

The differential diagnosis of PKD includes cleidocranial dysostosis and osteopetrosis. Notably, cleidocranial dysostosis presents with a normal height, bone texture, gonial angles and the absence of diffuse oteosclerosis. Osteopetrosis may present with stunted growth, a dense skull base, diffuse oteosclerosis, multiple fractures and malunion. The hands, feet, clavicles, gonial angles, maxilla and skull vault are normal. Management of PKD is multidisciplinary: supportive treatment includes the management of anaemia, recurrent infections, failure to thrive, hypocalcaemia, fractures of bones and diverse dental ailments.

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REFERENCES

1. Agarwal T, Kirubakaran C, Sridhar G. **Pyknodysostosis: A Report of two Siblings with Unusual Manifestations.** Annals of Tropical Paeditrics: International Child Health

1999: 19:301-305.

2. Bathi RJ, Masur VN. **Pyknodysostosis – A report of two Cases with a brief Review of the Literature.** Int. J. Oral Maxillofacial Surg 2000: 29: 439-442.

3. Beighton P, Horan FH. **A Review of the Osteopetrosis.** Postgraduate Med. Journal 1997: 53:507-516.

4. Jones CM, Rennie JS, Blinkhorn AS. **Pyknodysostosis. A review of Reported Dental Abnormalities and Report of Dental findings in two Cases.** Br. Dent. J 1988: 164: 218-220.

5. Ronald BJG, Sandra KF, Karen IN, Paul SC, Thomas PN. **The Infant Skull: A Vault of Information.** Radiographics 2004: 24: 507-522.

6. Thomas B, Elias-Jones AC, Sridhar av. **A New born Twin with Unusual Chest Radiography.** Postgraduate Medical J 2006: 82:180-181.

7. Wolfgang D. Radiology Review Manual, 6th Ed. New Delhi. Wolters Kluwer Health (India) Pvt. Ltd. 2007. pp149-150.

8. Kundu ZS, Marya KM, Magu S, Rohilla S, Yadav V. **Radiological quiz-Musculoskeletal.** Indian J. Radiol Imaging 2002: 12:435-436.

9. Singh AR, Kair A, Anand NK, Singh JR. **Pyknodysostosis: Visceral Manifestations and Simian Crease.** The Indian J. of Pediatrics 2004: 71: 453-455.

10. Fleming KW, Barest G, Sakai O. **Dental and Facial Bone Abnormalities in Pyknodysostosis: CT Scan Findings.** American J. of Neuroradiology 2007: 28:132-134.

11. Alibhai ZA, Matee MIN, Chindia ML, Moshy J. **Presentation and Management of Chronic Osteomyelitis in an African Patient with Pycnodysostosis.** Oral Diseases 1999: 5:87-89.

12. Dimitrakopoulos T, Magopoulos C, Katipodi T: **Mandibular Osteomyelitis in a patient with Pyknodysostosis: A case report of a 50 yrs Misdiagnosis.** J. of Oral and Maxillofacial Surgery 2007: 65:580-585.

13. Gelb BD, Guo-Ping S, Chapman HA, Desnick RJ. **Pycnodysostosis, a lysosomal Disease caused by Cathepsin k Deficiency.** Science 1996: 273: 1236-1238.

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Correspondence Address:
Dr. Jeremiah Moshy,
P. O. Box 65014,
Dar-Es-Salaam, Tanzania.
jeremiahmoshy@yahoo.com

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"Adopt the pace of nature: her secret is patience."

(Ralph Waldo Emerson)