PYLE’S DISEASE
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PRESENTATION OF CASE
A 10 years old girl presented to us with chief complaint of increasing broadening of upper ends of both legs. There was no other complaint except that she has not lost her milk teeth completely. No positive family history was elicitable. Examination of parents & other two siblings was normal.

On examination she had irregular dentition in the lower jaw. There was broadening of medial ends of both clavicles, upper ends of both humeri, lower ends of both radii, lower ends of both femurs and upper ends of both tibias. Medial ends of ribs were prominent and thickened. Measurements of the body segments revealed that lower segment was relatively longer than normal.

Skeletal survey was done. There was diffuse osteoporosis. The X-ray skull showed mild thickening of the vault and there was lack of pneumatisation of frontal and maxillary sinuses.

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X-ray of the limbs (Figure 3, 4 & 5) showed widened metaphyseal areas with thinned cortices, mild thickened cortex in diaphyseal areas and also mild bowing in the diaphyseal areas (Erlenmeyer-flask deformity).

The haematological and biochemical investigations were all normal. Chromosomal study was also undertaken in this case. A study of the karyotypes of these cells showed them to be pseudolipid. In the group C there was an extra chromosome while in group B there was monosomy of chromosome 15. These two abnormalities were found in every karyotype of this patient. (Figure 6). However specific gene study was not done in this case.

**CLINICAL DIAGNOSIS**  
Metaphyseal Dysplasia.

**DIFFERENTIAL DIAGNOSIS**  
- Craniotubular Dysplasias (Cranio Metaphyseal Dysplasia)  
- Gaucher Disease  
- Osteopetrosis  
- Thalassemia  
- Niemann-Pick Disease  
- Schwartz-Lelek Syndrome  
- Lead Poisoning  
- Chronic Leukaemia  
- Engelmann Disease

**PATHOLOGICAL DISCUSSION**  
Metaphyseal dysplasia, also known as Pyle’s disease, Pyle’s syndrome, Pyle-Cohn syndrome, and Bakwin-Krida syndrome is a very rare disorder in which the outer part of the shafts of long bones is thinner than normal and there is increased risk of fractures. Only 30 cases have been reported in literature so far. It is characterized by defect in metaphyseal remodelling that leads to grossly widened metaphyses of long bones with marked cortical thinning and osteoporosis (Erlenmeyer-flask deformity).

The earliest case was reported by Edwin Pyle in 1931. He reported a 5-year-old child with bony deformities in skull and limbs. The patient had marked knock knee deformity, long bones of arms and legs were enlarged at the ends. These enlargements of bones were neither painful nor tender. He postulated a failure of bone resorption as the pathophysiological basis of disease, which would lead to superimposition of several layers of under modelled bone at the metaphyseal segment.¹

Bakwin and Krida they also reported in 1937 studied the same patient and corroborated the findings. Also reported about the sister of this patient who was also suffering from metaphyseal dysplasia.² Gorlin et al in 1970 presented a strong case for segregating it from cranio-metaphyseal dysplasia.³

The aetiology has however still not been established i.e. whether it is familial, autosomal recessive or because of consanguinity.⁴,⁵ Its casual genetic mutation is still unknown, probably caused by mutations in SFRP4 (secreted Frizzled Related Protein 4) gene. This gene provides instructions for making a protein that blocks a process called WNT signalling, which is involved in the development of
several tissues and organs throughout the body. In particular, regulation of WNT signalling by the SFRP4 protein is critical for normal bone development and remodelling. Bone remodelling is a normal process in which old bone is broken down and new bone is created to replace it. Mutations in the SFRP4 gene are thought to prevent the production of functional SFRP4 protein. The resulting dysregulation of WNT signalling leads to the bone abnormalities characteristics of Pyle’s disease.

It is characterized by defect in metaphyseal remodelling that leads to grossly widened metaphysis of long bones with marked cortical thinning & osteoporosis. Most patients present with mild genu valgum & unable to fully extend the elbows. Patients may present with dental caries, mandibular prognathism, spinal alignment problems. Our patient also had malocclusion of teeth. Disproportionate limb lengthening was noticed in our case as longer lower segment. Mental development, physical development are usually normal as is seen in our case.

Neeraj Gupta et al (2008) reported a case of 12-year-old child in which they also did bone densitometer which was suggestive of osteoporosis. Diego et al also reported case of two female siblings, daughters of consanguineous parents. Laboratory tests showed no other relevant findings as is in our case.

**DISCUSSION OF MANAGEMENT**

As the patient was asymptomatic, no surgical intervention was done. Any corrective surgery for deformities shall be undertaken when needed.

**FINAL DIAGNOSIS**

Pyle’s Disease.

**REFERENCES**