Pyle Disease

Subjects: Genetics & Heredity
Contributor: Nora Tang

Pyle disease is a disorder of the bones. Its hallmark feature is an abnormality of the long bones in the arms and legs in which the ends (metaphyses) of the bones are abnormally broad; the shape of the bones resembles a boat oar or paddle.

Keywords: genetic conditions

---

1. Introduction

The broad metaphyses are due to enlargement of the spongy inner layer of bone (trabecular bone). Although trabecular bone is expanded, the dense outermost layer of bone (cortical bone) is thinner than normal. As a result, the bones are fragile and fracture easily. The bone abnormalities in the legs commonly cause knock knees (genu valgum) in affected individuals.

Other bone abnormalities can also occur in Pyle disease. Affected individuals may have widened collar bones (clavicles), ribs, or bones in the fingers and hands. Dental problems are common in Pyle disease, including delayed appearance (eruption) of permanent teeth and misalignment of the top and bottom teeth (malocclusion).

2. Frequency

Pyle disease is thought to be a rare disorder, although its prevalence is unknown. More than 25 cases have been described in the medical literature.

3. Causes

Pyle disease is caused by mutations in the *SFRP4* gene. This gene provides instructions for making a protein that blocks (inhibits) a process called Wnt signaling, which is involved in the development of several tissues and organs throughout the body. In particular, regulation of Wnt signaling by the SFRP4 protein is critical for normal bone development and remodeling. Bone remodeling 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 signaling leads to the bone abnormalities characteristic of Pyle disease.

The Gene Associated with Pyle Disease

- SFRP4

4. Inheritance

Pyle disease is inherited in an autosomal recessive pattern, which means both copies of the *SFRP4* gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene. While they do not develop the condition, they may have mild abnormalities of the long bones.

5. Other Names for This Condition

- metaphyseal dysplasia, Pyle type
- Pyle metaphyseal dysplasia
- Pyle's disease

- Pyle's metaphyseal dysplasia syndrome

References

1. Galada C, Shah H, Shukla A, Girisha KM. A novel sequence variant in SFRP4causing Pyle disease. J Hum Genet. 201 7 Apr;62(5):575-576. doi:10.1038/jhg.2016.166.
2. Haraguchi R, Kitazawa R, Mori K, Tachibana R, Kiyonari H, Imai Y, Abe T,Kitazawa S. sFRP4-dependent Wnt signal mo dulation is critical for bone remodelingduring postnatal development and age-related bone loss. Sci Rep. 2016 Apr27;6: 25198. doi: 10.1038/srep25198.
3. Kiper POS, Saito H, Gori F, Unger S, Hesse E, Yamana K, Kiviranta R, Solban N,Liu J, Brommage R, Boduroglu K, Bo nafé L, Campos-Xavier B, Dikoglu E, Eastell R, Gossiel F, Harshman K, Nishimura G, Girisha KM, Stevenson BJ, Takit a H, RivoltaC, Superti-Furga A, Baron R. Cortical-Bone Fragility--Insights from sFRP4Deficiency in Pyle's Disease. N E ngl J Med. 2016 Jun 30;374(26):2553-2562. doi:10.1056/NEJMoa1509342.
4. Wonkam A, Makubalo N, Roberts T, Chetty M. Pyle metaphyseal dysplasia in anAfrican child: Case report and review o f the literature. S Afr Med J. 2016 May25;106(6 Suppl 1):S110-3. doi: 10.7196/SAMJ.2016.v106i6.11011. Review.