Pyle disease (metaphyseal dysplasia)

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Pyle disease is an innocuous autosomal recessive disorder in which mild clinical manifestations contrast with the radiological appearances of gross metaphyseal undermodelling. The disorder was first reported by Pyle* in 1931¹ as "a case of unusual bone development", when he documented a boy aged five years who presented with knock knees. This child and his affected sister were restudied by Bakwin and Krida,² who designated the disorder 'familial metaphyseal dysplasia'. Semantic confusion with craniometaphyseal dysplasia arose, but this issue was clarified when Gorlin *et al*^{3,4} emphasised the separate status of these entities.

The term 'metaphyseal dysplasia' was used in the 1983 Paris Nomenclature and, in deference to popular convention, the eponym Pyle was added in brackets. About 20 cases of Pyle disease can be recognised in published reports and these are listed in the table.

Clinical features (fig 1)

The most frequent clinical feature is genu valgum, usually of mild degree. The elbows lack full extension and widening of the lower femora and clavicles may be palpable. The bones are sometimes fragile.

FIG 1 The face and habitus are normal except for genu valgum and widening of the transverse diameter of the knees.

TABLE Published reports of Pyle disease.

References	Patients	Country of origin
1	Male aged 5	USA
5	Male	Germany
2	Pyle's patient and sister aged 8	USA (Irish-American)
6	Brother and sister aged 33 and 34	USA
7	Brother and sister aged 53 and 46	USA
8	Female	Germany
9	Brother and sister aged 18 and 38	South Africa (English)
10	Male	France
11	Two brothers	India
4	Brothers aged 47 and 49	USA
12	Brother and sister	Italy
13	Female aged 54*	France
14	Male and female aged 20 and 24, distantly related*	South Africa (Afrikaner)

*Parental consanguinity.

*Edwin Pyle (1891-1961) studied medicine at the Columbia University College of Physicians and Surgeons, New York. He was an orthopaedic surgeon at Waterbury Hospital, Connecticut, USA, when he delineated the disorder which now bears his name.

but fracturing is not usually a significant problem. Carious teeth, mandibular prognathism, spinal malalignment, and disproportionate limb lengthening are inconsistent manifestations. Cranial nerve compression and dyshaemopoiesis do not occur and intelligence, general health, height, and physique are normal.

Radiological features (figs 2 to 6)

Radiographically, the metaphyses of the tubular

bones show massive expansion which extends into their shafts. The cortices are thin and the affected portions of the skeleton are radiolucent. These changes are most evident in the distal regions of the femora, but all limb and digital bones are involved. In the skull, the calvarium and base may be mildly sclerotic, and the vertebrae sometimes show minimal platyspondyly. The medial portions of the clavicles and the sternal ends of the ribs are widened, as are the pubic and ischial bones of the pelvis.

FIG 2 Patchy sclerosis of the calvarium and base, with poor pneumatisation of the mastoid air cells.

FIG 3 The clavicles show marked medial expansion.

FIG 4 The proximal portion of the humerus is very undermodelled.

FIG 5 The femora exhibit gross Erlenmeyer flask deformities and marked cortical thinning.

FIG 6 The proximal portion of the tibia is flared and the cortex is thin.

Differential diagnosis

Pyle disease is unlike any other disorder and diagnosis is not difficult. In particular, the truly remarkable metaphyseal expansion sets Pyle disease apart from the craniotubular bone dysplasias and other disorders which manifest an Erlenmeyer flask malformation of the femur. The autosomal dominant form of craniometaphyseal dysplasia, with which Pyle disease has been confused, can be differentiated in terms of the mode of inheritance, lesser metaphyseal widening, and greater cranial sclerosis. The rare autosomal recessive type of craniometaphyseal dysplasia is characterised by very severe craniofacial abnormalities, stunted stature, and mild metaphyseal changes.

Management

Persons with Pyle disease are often asymptomatic, but genu valgum and the sequelae of fractures may

require orthopaedic intervention. Orthodontic measures may be necessary for the dental abnormalities.

Genetics

Autosomal recessive inheritance is well established. Affected sibs and parental consanguinity have been reported by several authors, as shown in the table. The clinically asymptomatic heterozygote may have minor disturbances of modelling of the tubular bones.

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References

- ¹ Pyle E. A case of unusual bone development. *J Bone Joint Surg (Am)* 1931;**13**:874–6.
- ² Bakwin H, Krida A. Familial metaphyseal dysplasia. *Am J Dis Child* 1937;**53**:1521–7.
- ³ Gorlin RJ, Spranger J, Koszalka MF. Genetic craniotubular bone dysplasias and hyperostoses; a critical analysis. *Birth Defects* 1969;**5**(4):79–95.
- ⁴ Gorlin RJ, Koszalka MF, Spranger J. Pyle's disease (familial metaphyseal dysplasia). *J Bone Joint Surg (Am)* 1970;**52**:347–53.
- ⁵ Cohn M. Konstitutionelle Hyperspongiosierung des Skeletts mit partiellem Riesnwuchs. *Fortschr Roentgenstr* 1933;**47**:293–7.
- ⁶ Hermel MB, Gershon-Cohen J, Jones DT. Familial metaphyseal dysplasia. *AJR* 1953;**70**:413–21.
- ⁷ Feld H, Switzer RA, Dexter MW, Langer EM. Familial metaphyseal dysplasia. *Radiology* 1954;**65**:206–12.
- ⁸ Reviglio GM. Rara osteopatia da turbe dell'accrescimento osseo. Malattia di Pyle. *Minerva Med* 1954;**1**:418–22.
- ⁹ Komins C. Familial metaphyseal dysplasia (Pyle's disease). *Br J Radiol* 1954;**27**:670–5.
- ¹⁰ Forestier J, Guillemot R. La maladie de Camurati-Engelmann. *Rev Rhum Mal Osteoartic* 1956;**23**:222–7.
- ¹¹ Daniel A. Pyle's disease. *Indian J Radiol* 1960;**14**:126–31.
- ¹² Tognolo P, Manaresi C. La displasia metafisaria famigliare. *Arch Putti Chir Organi Mov* 1964;**19**:58–62.
- ¹³ Mabilie JP, Benoit JP, Castera D. Dysplasie métaphysaire de Pyle. *Ann Radiol (Paris)* 1973;**16**:273–8.
- ¹⁴ Heselson NG, Raad MS, Hamersma H, Cremin B, Beighton P. The radiological manifestations of metaphyseal dysplasia (Pyle disease). *Br J Radiol* 1979;**52**:431–40.
- ¹⁵ Beighton P, Cremin B. *Sclerosing bone dysplasias*. Berlin: Springer-Verlag, 1980.

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