Disorders associated with osteopoikilosis

5 different lesions in a family

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Submitted 02-07-09. Accepted 02-10-19

ABSTRACT Although osteopoikilosis is generally considered an accidental finding, several developmental dysplasias coexisting with this disorder have been reported. However, all authors have mentioned only one coexisting finding, and most of them are case reports. We report a family in whom various members had osteopoikilosis with 5 different associated lesions. We suggest that osteopoikilosis is a bone manifestation of a generalized fibroproliferative or stenosing disease.

Osteopoikilosis is the term used to describe discrete spherical areas of increased bone density, 2–10 mm in diameter, in the metaphyses and epiphyses of the long bones, carpus, tarsus and membranous bones, such as the pelvis and scapulae (Green et al. 1962, Walpole and Manners 1990). The etiology and pathogenesis remain obscure (Green et al. 1962, Szabo 1971), but an autosomal, dominant inheritance with variable penetrance has been found (Schorr et al. 1972, Kobus et al. 1989, Benli et al. 1992, Günal et al. 1993). Several developmental dysplasias coexisting with osteopoikilosis have been reported during the last 30 years (Resnick and Niwayama 1971, Schorr et al. 1972, Verbov 1977, Mindell et al. 1978, Weisz 1982, Ayling and Evans 1988, Kobus et al. 1989, Grimer et al. 1989, Chigira et al. 1991, Günal et al. 1993, Butkus et al. 1997, Havıtçıoglu et al. 1998). In particular, the associations with dacryocystitis (Gunal-Seber-Basaran syndrome) and dermatofibrosis (Buschke-Ollendorff syndrome) have been accepted as different syndromes (McKusick 1994, Birth Disorders Information Directory, Orphanet, http://orphanet.infobiogen.fr). However, all authors have reported only 1 coexisting lesion. Schnur et al. (1994) described a case with spinal stenosis and otosclerosis . We report a family of osteopoikilosis with 5 different coexisting lesions.

Patients

A 39-year-old man was hospitalized with low back pain. Radiographs revealed small spherical areas of increased density in both proximal femora (Figure 1), and further examinations showed similar lesions in the elbow and wrist. 11 of his relatives had similar lesions.

We examined 17 members of the family with special reference to osteopoikilosis and the disorders reported to be associated with osteopoikilosis.

Results

11/17 members of the proband's family had osteopoikilosis. Their mean age was 41 (5–81) years. The pedigree of the family was consistent with an autosomal dominant inheritance (Figure 2).

The sclerotic lesions were commonest in the wrist (n = 14), pelvis and proximal femora (n = 10), metacarpals (n = 9), tarsal bones (n = 5), and distal humerus (n = 3). They were bilateral, except in 2 patients who had unilateral lesions.

7 members of the family had associated lesions. 4 cases (II: 1, II: 2, II: 5, III: 3) had dermatofibrosis lenticularis, 2 (III: 1, III: 2) had spinal stenosis

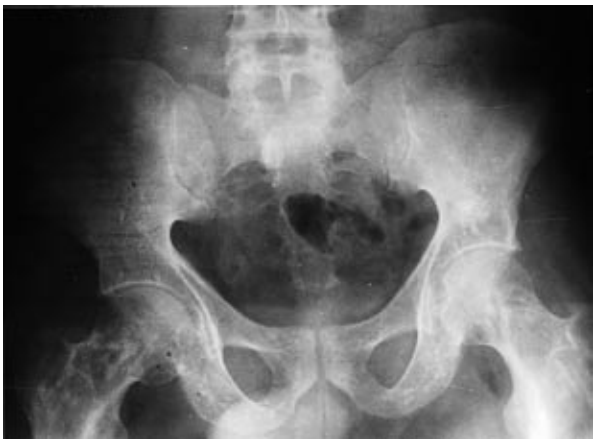

Figure 1. The proband with osteopoikilotic lesions in both proximal femora

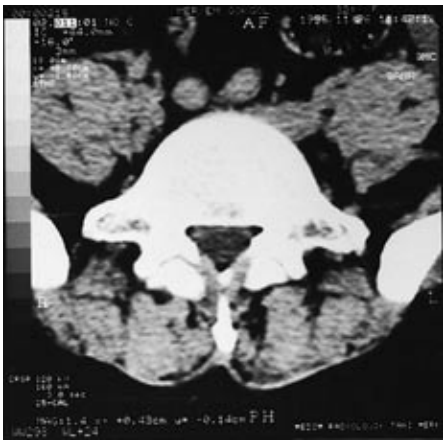

Figure 3. Case III: 1, spinal stenosis.

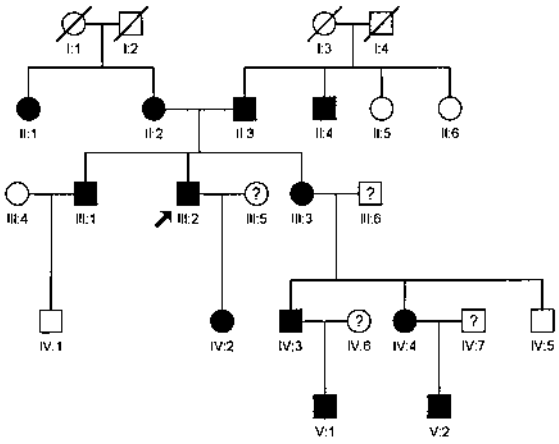

Figure 2. Pedigree of the family. The arrow indicates the proband.

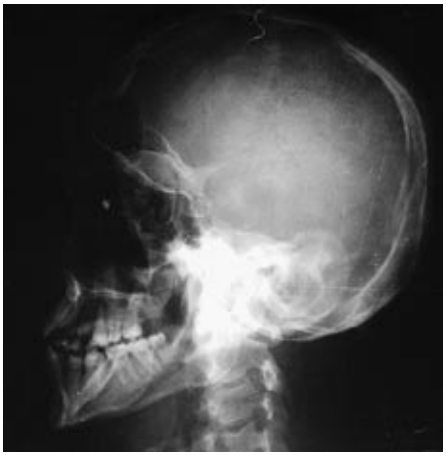

Figure 4. Case II: 2, dacryocystography showing stenosis of the lacrimal canal.

(Figure 3), 1 (II: 2) had dacryocystitis (Figure 4) and 1 (II: 6) had a peptic ulcer and a keloid in the abdominal region.

Discussion

In the last 30 years, various developmental malformations have been reported to be associated with osteopoikilosis, including: 1) coarctation of the aorta, double ureter, pubert as praecox, urogenital defects, growth abnormalities, peptic ulcer, diabetes mellitus at the endodermal strata level (Schorr et al. 1972, Weisz 1982, Ayling and Evans 1988, Kobus et al. 1989); 2) arthritis, exostoses, osteitis condensans ilii, melorheostosis, spinal stenosis, dacryocystitis, giant cell tumor, fibrous dysplasia, chondrosarcoma, osteosarcoma, synovial chondromatosis at the mesodermal level (Green et al. 1962, Resnick and Niwayama 1971, Mindell et al. 1978, Weisz 1982, Ayling and Evans 1988, Grimer et al. 1989, Kobus et al. 1989, Chigira et al. 1991, Günal et al. 1993, Butkus et al. 1997, Havıtçıoglu et al. 1998); and 3) facial abnormalities, hare lip, dental abnormalities, dermatofibrosis lenticularis disseminata, keloid formation, plantar and palmar keratomas at the ectodermal level (Schorr et al. 1972, Verbov 1977, Weisz 1982, Ayling and Evans 1988, Kobus et al. 1989).

So far as we know, this is the first family to be reported with 5 different associated lesions (dermatofibrosis lenticularis, dacryocystitis, spinal stenosis, peptic ulcer and keloid formation). This indicates that osteopoikilosis is associated with

fibroproliferation, and not with some unique disorders.

From the pathoanatomical point of view, osteopoikilosis is caused by condensation of cancellous bone (Havıtçıoglu et al. 1998). The lesions appear to be metabolically active; they become denser with time, but later their size may change or they may disappear (Chigira et al. 1991). The precise origin of these abnormal areas is disputed, but they appear to represent foci of deranged differentiation in cancellous bone (Verbov 1977, Ayling and Evans 1988). The associated lesions of osteopoikilosis show similar patterns: proliferation of metabolically active fibroblasts is involved in the pathogenesis of dermatofibrosis lenticularis or keloid formation (Verbov 1977), while stenosis of the contents of the lacrimal sac or the spinal canal is a prerequisite for the development of dacryocystitis or spinal stenosis (Duke-Elder 1974, Weisz 1982).

There are also some other important features in the present family. One member of the family (Figure 2, II: 2) has dacryocystitis and dermatofibrosis lenticularis in association with osteopoikilosis. To our knowledge, she is the second in the literature, after the case of Schnur et al. (1994), to have two associations. A review of the literature showed only 1 report of spinal stenosis (Weisz 1982) and dacryocystitis (Günal et al. 1993) in association with osteopoikilosis. Our study also adds new cases with such associations (Figure 2, III: 1, III: 2, II: 2).

On the other hand, although we detected 2 lesions associated with osteopoikilosis in 2 members of the family (Figure 2, II: 5, II: 6), a careful examination of the radiographs of these cases revealed no signs of osteopoikilosis. This is probably due to disappearance of the lesions with age.

The present family clearly shows the association of osteopoikilosis with fibroproliferative or stenosing lesions, not with a unique disease phenotype. We suggest that if osteopoikilosis or any associated lesions are detected in a patient, members of their family should be screened for other lesions since some of them carry the risk of malignant transformation (Mindell et al. 1978, Ayling and Evans 1988, Grimer et al. 1989, Havıtçıoglu et al. 1998).

This study was supported by funds from Xenon Bioresearch Inc.

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