LESSON OF THE MONTH

Painted black

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A 65 year old patient attended our hospital because of painful degenerative arthritis of the left hip joint. Chronic low back pain was a concomitant complaint. For this she had been treated elsewhere under the diagnosis ankylosing spondylitis. Coincidentally, she mentioned that she had had unpleasant dark stains in her underwear since childhood, which became more intense after washing. Her two sisters and the youngest daughter of one of them had the same complaints. General inspection showed black pigmentation in both sclera (fig 1). The radiographs of the lumbar spine showed degeneration of the discs with narrowing of the space and dense calcification of the remaining disc material. The radiological appearance resembled a “bamboo spine” (fig 2). Routine laboratory investigations showed no abnormalities.

During hip replacement surgery the synovia and the cartilage of the femoral head were stained black. Histological examination of cartilage and the synovium showed in both a histiocyte fibrous reaction with pigmented macrophages. The postoperative course was uneventful.

DISCUSSION

Alkaptonuria is an autosomal recessive inborn error of metabolism. The incidence varies between 0.1 and 1 per million, with a higher prevalence in areas with a large degree of consanguinity.^{1–3} The enzyme homogentisic acid oxidase, which is normally present in liver and kidney and is responsible for the total turnover of homogentisic acid (HGA) in

Figure 1 Black pigmentation in sclera of the patient.

Figure 2 Radiograph of the lumbar spine of the patient. Notice the bamboo spine appearance without osteophytes and calcification of the intervertebral ligaments.

maleylacetic acid in the phenylalanine-tyrosine catabolism, is deficient. As a result HGA is excreted in large volumes in urine and sweat. If urine containing HGA stands for some time, it turns dark as the acid is oxidised to a melanine-like product. Urine and sweat containing HGA also causes dark stains in clothes. Alkaline agents, like soap, increase the process of polymerisation making the stains even more intense. Other sites in which HGA may accumulate are cartilage, tendons, sclerae, skin, and the intima of large vessels. Virchow used the term ochronosis in 1866 for the deposition of the oxidised HGA in these collagen tissues.⁴

The striking clinical feature of ochronosis is the pigmentation of the sclerae and auricles,⁵ which becomes noticeable after the age of 30. Peripheral ochronotic arthropathy is common in the larger joints.³ Deposition in the articular cartilage leads to brittleness and fragmentation, causing a non-specific synovitis. The correct diagnosis is usually made around the age of 40. Ochronotic arthropathy is clinically and radiologically not distinguishable from other forms of degenerative osteoarthritis, except for the lumbar spine. The first clinical symptom in lumbar spondylar ochronosis is usually progressive lower back pain and stiffness. Eventually, there is a complete rigidity with dissolution of the lumbar lordosis and thoracic kyphosis. The clinical picture resembles ankylosing spondylitis. Pathognomonic for ochronosis is the radiological presentation of multiple narrowed discs with linear calcifications.⁶ Little osteophyte formation and minimal calcification of the

intervertebral ligaments are present. The “bamboo spine” appearance can be imitated by severe bony bridge formation (pseudosyndesmophytes). Differentiation from ankylosing spondylitis can be difficult because of these pseudosyndesmophytes, but fusion of the sacroiliac joints generally does not occur in ochronosis. During operation, cartilage and synovia appear coal black. The synovial fluid is speckled with particles, fragments of pigmented cartilage and calcium pyrophosphate dihydrate crystals, giving it a ground pepper appearance.

At present, there is no treatment for this enzyme deficiency. In the past, high doses of ascorbic acid were prescribe to prevent deposition of the ochronotic pigment in collagen tissue.⁷ This, unfortunately, cannot prevent progression of the disease. A lifelong diet, low in phenylalanine is hardly feasible because phenylalanine is an essential amino acid and, although this sort of diet can diminish the secretion of HGA, it has no effect on the course of the disease.⁸ Treatment options are only supportive. Finally, arthroplasty of the hip, knee, or shoulder joint is often inevitable.

THE LESSONS

- A bamboo spine appearance of the lumbar spine on radiographs without osteophytes, and calcification of the intervertebral ligaments should arouse suspicion of alkaptonuria.
- Patients with black pigmentation in sclerae or auricles, or both, should be asked about unpleasant stains in their underwear.
- There is no treatment for alkaptonuria, except supportive measures.

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