Vertebral changes in ochronosis

Anatomical and radiological study of one case

R. LAGIER AND Š. SIT'AJ
From the Department of Pathology, University of Geneva, Switzerland, and the Rheumatic Diseases Research Centre, Piestany, Czechoslovakia

This discussion of ochronotic spinal changes is based on the post mortem examination of a 50-year-old woman who had been hospitalized for 3 years with schizophrenia and ochronosis. Clinical articular manifestations of ochronosis were present but slight in the limbs, the spine was stiff, and radiography of the vertebral column showed pathognomonic ochronotic changes.

Material and methods
Frontal and sagittal planes of an anterior slice from the lumbar column were studied (T 11071/69); each fragment was x-rayed, decalcified, and embedded in celloidin (paraffin for some small pieces).

Accepted for publication May 17, 1973.

(a) Posterior aspect of slice: intervertebral discs are pigmented and show penetration of bone which may lead to vertebral ankylosing (L1–2), and to marginal bony bridges occasionally incorporating islands of disc (the crater seen in L3 is an artefact)

(b) Anterior view: bony bridges join the vertebrae giving a bamboo aspect. Occasional islands of pigmented cartilage are visible on the surface, especially in spaces L3–4 and L4–5

FIG. 1 Lumbar vertebral slice: L2, 3, and 4 complete, L1 and 5 incomplete.
Sections were studied unstained, and stained with haematoxylin and eosin, van Gieson, or Nile blue (a useful, although non-specific stain for ochronotic pigment (Cooper and Moran, 1957; O'Brien, La Du, and Bunim, 1963)). Calcium deposits in a fragment of intervertebral disc were studied by x-ray diffraction.

Findings

I. INTERVERTEBRAL DISC LESIONS
Macroskopically the discs appeared black (Figs 1(a), 3(a)), but, on microscopic examination, the unstained sections appeared ochre, whence Virchow's term ochronosis. Pigmentation was greatest in the hyaline cartilage joining the vertebral body to the disc (Kleinschmidt, 1922; Putschar, 1966), and decreased through the annulus fibrosus to the nucleus pulposus (Fig. 3(b)).

The fundamental disc architecture was preserved. Even when the nucleus pulposus was obliterated, with fraying of the internal border of the annulus fibrosus on the sides of a split in the centre of the disc, there was no chondrocytic proliferation or fibrocartilaginous remodelling as found in the 'degenerative chondroses' (Fig. 7(a)).

Grossly the discs were hard and brittle. At the margins, occasional sharply pointed splinters of various sizes could be seen microscopically. These splinters were either embedded in a fibrous reaction (Fig. 4) or tightly packed in an osteosclerotic remodelling (Fig. 6), especially in an intervertebral bridge, where islands of pigmented cartilage may remain visible on the surface (Fig. 1b). Segments of disc were sometimes separated from one another by penetrating bone that was occasionally found to weld adjacent vertebrae (Figs 1(a), 5(a)).

The disc fragments were usually surrounded by histiocytes containing phagocytosed ochronotic pigment and some haemosiderin deposits. In the marrow, the histiocytes were numerous in proximity to the fragments, but decreased rapidly at a distance (Fig. 5(b)).

The classic heavy calcareous deposits predominated in the internal zone of the annulus fibrosus (Fig. 7(b)). In corroboration of other observations (Bywaters, Dorling, and Sutor, 1970), x-ray diffraction showed these deposits to be composed of apatite.

II. BONE MODIFICATIONS
Osteogenic remodelling was found secondary to intervertebral disc deterioration, ultimately leading to intervertebral welding and bony bridges (Figs 1(a), 3, 5, 6).

The lamellar structure of the bone attests to the slow activity of the remodelling; the process was slightly more active in contact with the disc fragments, especially between the vertebral bodies (as demon-

Fig. 2 X-ray view of the specimen from Fig. 1, showing disc calcification and marginal bony bridge formation

(a) Anteroposterior view

(b) and (c) Radiographs of sections 1 cm. thick adjacent to the cut surface of the specimen, showing disc calcification and bony bridges more clearly
strated by some signs of aborted erosion, and by some osteoid borders). Rarely, pigmented osteocytes were seen.

Further from the discal lesions, there was moderate osteoporosis (Červeňanský, Šit’aj, and Urbánek, 1959; Klaus, Křížek, and Vranešič, 1961; Kolář and Křížek, 1968; Louyot, Gaucher, and Montet, 1967), but no abnormal endosteal remodelling. On the whole, the marrow was haemopoietic, and was fibrous only in the immediate vicinity of the deteriorated discs.

Slight subperiosteal deposits of pigment were exceptionally observed near a disc, but, with the exception of some exposed parts of the discs, the anterior surface of the vertebral column appeared to be unpigmented (Fig. 1(b)). The rare segments of ligament present in the specimen were unpigmented.

Discussion
Clinical and radiological manifestations of spinal ochronosis, brought about by the slow impregnation of the discs by homogentisic acid, usually begin in the third decade (Louyot and others, 1967; Šit’aj, 1963), about 10 years before the appearance of peripheral manifestations. Radiological and post mortem observations show that the entire spine may be involved, but that the earliest manifestations are usually lumbar. This early predilection may be related to the multiple and complex forces to which the spine is submitted. The articular manifestations of an otherwise generalized ochronotic impregnation, thus would seem to depend on local mechanical conditions.

The discal deterioration of ochronosis differs from that of the vertebral ‘degenerative chondroses’, often seen with ageing or consequent upon mechanical disorders. Ochronotic disc deterioration is due to a brittleness comparable to that observed in the cartilage, or fibro-cartilage, of an ochronotic diarthrodial joint (Lagier, Boussina, Taillard, Sasfavian, Chafizadeh, and Fallet, 1971; Lichtenstein and Kaplan, 1954; Putschar, 1966).

The disc fragments thus formed, provoke a reaction in adjacent connective tissue identical to

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**FIG. 3 Lumbar disc L2–3**

(a) Macroscopic view, showing discs invaded by bone, both centrally and by marginal bridges. Surface of celloidin-embedded specimen. × 1·3

(b) Unstained histological section. Pigment confined to disc, and most pronounced in cartilaginous plate between intervertebral body and annulus fibrosus. × 1·9

(c) Haematoxylin and eosin stain better demonstrates the bony bridges, on the right, in association with a segment of longitudinal ligament. × 1·9

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However, this ligament may be pigmented (Lichtenstein and Kaplan, 1954) as well as other vertebral ligaments (Kleinschmidt, 1922). Inconstant impregnation of ligaments in ochronotic hips and knees has also been observed.

Polydical deterioration, accompanied by bone remodelling, explains the clinical manifestations observed in vertebral ochronosis: slow onset, discrete pain, spinal stiffening, loss of physiological curves, and decrease in height (O'Brien and others, 1963). It also explains the occasional discal ruptures provoking a radicular syndrome, which may require surgery (McCollum and Odom, 1965). Disc ruptures are much more frequent in males than females.

RADIOLOGY

In ochronosis, a series of non-specific bone lesions brings about a complete remodelling of the vertebral column. When such lesions are associated with calcifications of the discs, the radiological picture is highly suggestive and practically pathognomonic of vertebral ochronosis, whereas changes in the peripheral joints alone are non-specific (Fig. 2).

(A) Calcium deposits, similar to those in the annulus fibrosus, have also been found in the pubic symphysis (Sit'aj, 1963), in the helix of the external ear (Mueller, Sorensen, Strandjord, and Kappas, 1965; Pomeranz, Friedman, and Tunick, 1944; Thompson, 1957), and in costal cartilage (Cooper and Moran, 1957). They have not been observed in diarthrodial articulations. Since this disc calcification is composed of apatite, and appears to be secondary in origin, it may be considered to be dystrophic calcification. Nevertheless, it must be distinguished from other dystrophic disc calcifications which are more common, but topographically more limited, generally to the centre of the discs. Nor should such deposits be confused with the deposits chondrocalcinosis, which are smaller, more peripheral, and crystallographically different, although chondrocalcinosis may be seen in ochronotic patients.

The dystrophic calcification of ochronosis, which extensively involves multiple discs, forms radiological images which, alone, evoke the diagnosis. For this reason, ochronosis was considered to be frequent in ancient Egypt (Simon and Zorab, 1961; Wells and Maxwell, 1962); however, the calcifications often seen in the published radiographs of mummies appear more homogeneous and are not associated with narrowing of interspaces, nor with adjacent bone remodelling. It is presumed that such calcifications are an artefact of the embalming process (Gray, 1967). This aspect of paleopathology is discussed elsewhere (Gardner and Griffin, 1971).

(B) Vertebral dislocation and narrowing of interspaces may occur at different levels due to multiple disc deterioration. The splits in the centre of

**Fig. 4** Histological detail of lumbar disc L2-3, left border. Fragments of deteriorated disc are imprisoned in the connective tissue remodelling deep to the longitudinal ligament and, deeper, in the newly formed intervertebral bone. x 6-5.
the discs explain the vacuum phenomenon image, the observation of which, at several levels, strongly suggests the diagnosis of ochronosis. This phenomenon seems constant and occurs relatively early in course of the disease (Kostka, Sít’aj, and Niepel, 1965).

(C) Ossification of the discs explains occasional radiological obliteration of the vertebral interspaces and formation of marginal intervertebral bridges.

**DIFFERENTIAL DIAGNOSIS AND TERMINOLOGY**

Radiography of the vertebral column may permit the diagnosis of ochronosis, corroborated by the finding of alcaptonuria, often previously unsuspected. An analysis of the differential diagnoses is thus less important in practice than in theory.

When the vertebrae are not welded, deterioration of the discs provokes a condensation remodelling of the vertebral surfaces with small lipping marginal osteophytes (Ott, 1956). This intervertebral arthrotic remodelling may be distinguished from that of 'degenerative chondrosis' by the overall x-ray image, and above all, by histological differences. This process should not be considered a 'degenerative rheumatism', at least, if the usual meaning of the term is to be preserved.

In the presence of marginal spurs or intervertebral bridges, the distinction should be made between those of ochronosis and those of spondylosis or of ankylosing vertebral hyperostosis (Forestier and Lagier, 1971). In ochronosis, the bony overgrowths are thinner, and there is no thoracic preference. The radiographical presence of several diffusely calcified discs is virtually diagnostic. In addition, even though spondylotic osteophytes may be present, in ochronosis, an intervertebral osteoarthritic
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Fig. 6 Aspects of the anterior border of marginal ankylosis in L2-3 (left lateral sagittal plane). The bone bridges the pigmented disc and incorporates an isolated fragment of disc.

remodelling or welding can also be found. For these reasons, the term spondylosis is not applicable in ochronotic spinal disease, as it does not encompass the entire anatomical picture.

The intervertebral bridges create a 'bamboo spine' image, resembling ankylosing spondylitis; this diagnosis should be considered, especially when x-ray changes in the hip, knee, and shoulder, are comparable to those of a chronic inflammatory rheumatism, and the more so if the pubic symphysis or sacro-iliac joints are narrowed or welded, and if the intervertebral articular facets show interspace narrowing possibly associated with erosions, or even with bony ankylosis (Uebermuth, 1928; Pomeranz and others, 1941; Ott, 1956; Brocher, 1966). The sacro-iliac joint is usually not eroded or welded in ochronosis, Again, disc calcifications strongly suggest ochronosis and homogentisic aciduria is a constant finding in this disease. We thus think that the term 'ochronotic ankylosing spondylitis' should be abandoned.

A purely descriptive term, such as 'ochronotic spondylopathy' would seem preferable to avoid confusion in terminology.

Summary
A radiological and pathological study of a case of ochronotic spondylopathy is presented.
The principal observation was pigment impregnation of the intervertebral discs, resulting in brittleness, calcification, and an osteogenic reaction which may give rise to intervertebral bridges and/or welding of the vertebral bodies.

The radiological picture of ochronotic spondylopathy is practically pathognomonic, and should not be confused with vertebral osteoarthrosis, spondylopathy, ankylosing vertebral hyperostosis, or (especially) ankylosing spondylitis.

We thank Mrs. Ketty Sapounova who prepared the histological sections. This study was supported in part by a grant from the Commission Fédérale des Maladies Rhumatismales, Bern, Switzerland.

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