Pre-ankylosing spondylitis

Histopathological report

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Pasion, E. G., and Goodfellow, J. W. (1975). *Annals of the Rheumatic Diseases*, 34, 92. Pre-ankylosing spondylitis. Histopathological report. A novel explanation for the natural history of joint destruction in the early phase of ankylosing spondylitis is proposed on the basis of the clinical history, x-ray appearance, operative findings, and histopathology of a young patient believed to be suffering from the peripheral form of this disease.

Seldom has there been any mention in the literature of the histopathology of the early stages of ankylosing spondylitis, for study has been hampered by the fact that being a nonfatal disease material from the early stages is difficult to obtain.

Several papers have been published about the histopathology of ankylosing spondylitis but none of the cases presented were early in the chronological sense. The generally accepted description (Cruickshank, 1951, 1960) can be summarized in the following quotation, 'The disease apparently begins in the synovial tissue as a subacute or chronic inflammation, associated with proliferation, producing an excessive number of villi with a thickened lining of synovial cells. Proliferation also occurs over the surface of the articular cartilage and other intra-articular structures. Granulation tissue is formed which destroys the cartilage and later penetrates the underlying bone. Opposing layers of this granulation tissue frequently become adherent and, as the inflammation subsides, firm fibrous ankylosis is established. In this disease, the ankylosis usually becomes bony. These features are similar to those seen in rheumatoid arthritis and are the basis for the current opinion that ankylosing spondylitis is a variant of rheumatoid arthritis' (Cruickshank, 1951). The same author, writing in 1960, made no fundamental changes to these views of the histopathology of the disease, a description which accords in general with that of other authors (Rutishauser and Jacqueline, 1955).

Bywaters (1968) described the joint pathology in a patient who died in the pre-ankylosing stage of the disease. In addition to changes similar to those above, he reported buds of granulation tissue penetrating the articular cartilage of the femoral head *from beneath* the cartilage. He specifically distinguished this kind of articular cartilage destruction from

within from the familiar process of destruction from without by migrating pannus. He formulated a hypothesis saying that the '... disease is some change in cartilage, or some change in the body's reactions to cartilage, whereby the latter becomes an

FIG. 1 Showing the appearance of the hip at the time of operation

FIG. 2 *The femoral head on dislocating the hip joint revealing the smooth shiny surface with apparently intact articular cartilage*

active auto-immune target, so that it gets invaded either at the margin where it joins normal connective tissue or where the normal bony layer protecting it from marrow blood vessels becomes deficient'.

A case history is presented of a patient in whom a peripheral type of ankylosing spondylitis was diagnosed and from whom biopsy material became available. This material strongly suggests to us a quite different pathological process from that described by Cruickshank and is consistent with the hypothesis formulated by Bywaters.

Case history

The patient, a girl of 16, first attended the rheumatology clinic in September 1966 with swelling of the left knee, raised ESR, and negative slide latex test. There was no relevant family history or any serious illness in the past. A biopsy showed congestion with proliferation of lining cells in the synovial membrane.

In July 1967 she began to complain of pain in both hips. Flexion deformity of about 10° was found on both sides with limited range of motion. X-rays of the hips showed marked reduction of the joint space and revealed early erosion of the sacroiliac joints. In view of these findings and a chest expansion of $7/8$ ", a diagnosis of ankylosing spondylitis was made.

Later, a synovial biopsy of the left hip confirmed the appearance of a nonspecific chronic inflammation, similar to the biopsy specimen from the left knee. A synovectomy was subsequently performed on the left hip with good initial relief of pain.

In September 1967 she had severe pain in the right hip and a cup arthroplasty was performed in October 1967. Unfortunately, there is no note of the state of the articular

FIG. 3 *Appearance of synovium showing the granulation tissue and nonspecific inflammatory reaction in the stratum synoviale. $\times 146$*

cartilage at that time and the biopsy material refers solely to the synovium.

In May 1968 she came under the care of J.W.G. at the Nuffield Orthopaedic Centre. Her left hip had now deteriorated and a cup arthroplasty was performed on that side. Fig. 1 shows the x-ray appearance of this hip at the time of the operation. The operative findings were a surprise and will be described in more detail.

On opening the capsule of the hip, the synovium did not appear thickened or inflamed—nor was there free fluid in the joint. On dislocating the hip a smooth shiny femoral head completely covered with apparently intact articular cartilage was revealed (Fig. 2). In contrast, the

acetabulum was entirely devoid of articular cartilage—presenting the appearance of raw and bleeding bone.

HISTOLOGY

Synovium

There was a fibrinous exudate on the synovial surface with granulation tissue and a nonspecific inflammatory reaction in the stratum synoviale. Haemosiderin pigment was present in the synovium (Fig. 3).

Cartilage

Histology confirmed the macroscopical observation that the surface of the cartilage was smooth and intact (Fig. 4).

FIG. 4 *Showing the articular cartilage which is smooth and intact without any pannus evident on the surface and no evidence of chondrocyte proliferation. $\times 76$*

FIG. 5 Polarized light examination of the cartilage showing the complete and intact tangential layer of surface fibres. $\times 55$

No pannus was to be found, nor was there any evidence of chondrocyte proliferation.

Polarized light examination of the cartilage showed that the fibrous structure was normal and in particular that the tangential layer of surface fibres was complete (Fig. 5).

By contrast there was an intense vascular proliferation in the bone end-plate with numerous tufts of vascular fibrous tissue penetrating into the calcified zone of the cartilage (Fig. 6). In some areas the cartilage seemed to rest upon an almost complete sheet of granulation tissue (Fig. 7).

Discussion

(1) The clinical diagnosis in this patient was that of ankylosing spondylitis of the peripheral kind (Hart and Robinson, 1959). The patient has been under the continued supervision of Dr. A. G. S. Hill at the Oxford Regional Rheumatic Diseases Research

FIG. 6 (a) Showing the intense vascular proliferation in the bone end-plate with numerous tufts of vascular fibrous tissue penetrating into the calcified zone of the cartilage. (b) High power view of (a). $\times 50$

6(a)

6(b)

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FIG. 7 *In some areas the cartilage seemed to rest upon a sheet of granulation tissue. $\times 53$*

Centre at Stoke Mandeville from 1966 to 1974, and there has been no reason in the light of later experience to alter the clinical diagnosis. The eventual obliteration of the sacroiliac joints (Fig. 8) lends support to the diagnosis. Although sacroiliitis is not specific for ankylosing spondylitis (Calabro and Maltz, 1970), since it has occasionally been observed in juvenile rheumatoid arthritis (Calabro and Marchesano, 1968), psoriatic arthritis (Dixon and Lience, 1961), Reiter's syndrome (Good, 1965), and arthritis associated with ulcerative colitis (Wright and Watkinson, 1965), these conditions had all been ruled out in the differential diagnosis. The absence of joint changes in the spine by no means excludes the diagnosis of ankylosing spondylitis in women (Hart and Robinson, 1959).

(2) The findings at surgery in the left hip strongly suggested that the pathological process at work in this case was quite different from the disease process

FIG. 8 *X-ray showing the obliteration of the sacroiliac joints*

of rheumatoid arthritis. We suppose that the fundamental destructive lesion was an inflammatory disorder of the immediate subchondral bone. Granulation tissue formed *deep* to the cartilage eroded the bone end-plate and invaded the calcified zone of the cartilage. Since the nutrition of mature articular cartilage comes from its synovial surface, this infiltration in the subchondral region did not destroy the overlying cartilage—nor did it cause a proliferative reaction within it. We think that the process had reached this stage of development in the femoral head at the time of surgery.

Since the articular cartilage is attached to the bone by the implantation of its vertical collagen fibres into the calcified zone (Fig. 9), it follows that a destructive lesion like that described above would eventually allow the cartilage to break free. We suggest that the appearance of the acetabulum at surgery was the result of this eventual shedding of its lining cartilage—exposing to view the inflamed and congested subchondral bone.

(3) Although we believe that in this case the effective lesion was in the subchondral bone, we have also to recognize that a synovitis was present in the three joints of this patient submitted to biopsy. However, the histological appearances do not allow us to accept that the cartilage was eroded from its synovial surface—as must have been the case were the synovial inflammation itself the prime lesion. Note also that the x-rays of the hip show no evidence of the peripheral erosion indicative of such a process.

(4) The most distinctive feature of the natural history of ankylosing spondylitis is—as its name suggests—the strong proclivity to develop bony ankylosis. If the pathological process in this disease is the one we describe above then this tendency to bony ankylosis as an end result is explained. Had this process in our patient been allowed to progress on the femoral head to the stage achieved in the acetabulum, an ideal circumstance for ankylosis would have existed.

FIG. 9 Showing a normal hip joint cartilage. $\times 40$

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