

# Paleopathologic Evidence for the Evolution of Rheumatoid Arthritis

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**ABSTRACT** A human skeleton recovered from a Sicilian archaeological site and dating from the Hellenistic period (330-210 B.C.) presents a pathological pattern suggesting a transition between ankylosing spondylitis and rheumatoid arthritis, providing evidence in support of the hypothesis that rheumatoid arthritis may have recently evolved out of ankylosing spondylitis.

Rheumatoid arthritis is a generalized inflammatory disease of the connective tissues which affects not only joints, but also can attack tendon sheaths, bursae, and other soft tissues. It is currently a very prevalent disease which, according to conservative estimates, afflicts up to 2% of the adult population (Redford, '69). Curiously, however, convincing evidence of the disease is lacking in the paleopathological literature (Bourke, '67; Short, '74) leading Short ('74) to hypothesize that the disease, as we know it, may be of recent origin. A human skeleton of the Hellenistic period (330-210 B.C.) from Sicily may provide evidence relating to the history and evolution of arthritic diseases.

The skeleton in question is one of two Hellenistic skeletons preserved from the archaeological site of Morgantina, located in Enna province, commune di Aidone, frazione Serra Orlando, map co-ordinate: I G M Fogho 269, NW III, latitude 37°25'50" N, longitude 2°1'37" E. The affected skeleton, from Epytymbion V, area II, trench 4B extension (Sjoquist, '60), is uncatalogued and temporarily housed in a storehouse in Aidone. The other Hellenistic skeleton appears normal.

The affected Hellenistic skeleton presents a pattern of articular disease atypical of any found in either a modern clinical setting or in the paleopathology literature. A combination of traits suggestive of rheumatoid arthritis and ankylosing spondylitis is particularly baffling unless one considers Short's ('74) hypothesis on the evolution of rheumatoid arthritis. Short argues that a search of early

medical writings and the paleopathology literature provides no convincing evidence of rheumatoid arthritis prior to the Seventeenth Century, whereas the great antiquity of gout, degenerative joint disease (DJD, osteoarthritis) and ankylosing spondylitis is well-established. For instance, the latter three are all evident in early Egyptian remains (Snarason, '69). Whereas the absence of any description of symptoms characteristic of rheumatoid arthritis in the early literature could reflect simply a confusion with other diseases, the lack of paleopathologic evidence for rheumatoid arthritis, while, at the same time, evidence of more rare arthritic syndromes is abundant, implies that the disease in its modern form was truly absent. Short suggests that rheumatoid arthritis may have evolved out of ankylosing spondylitis early in the Christian era.

## DESCRIPTION

The Sicilian skeleton, that of a male probably in his fifth or sixth decade at the time of death, displays excellent preservation and relative completeness. Proliferative periarticular osteophytosis resembling DJD affects the distal metacarpals of both thumbs and metacarpals two and three of the right hand. All other hand joints appear normal. Similar degenerative changes affect the distal ulnae bilaterally, albeit more severely on the right side. The right distal radius appears normal; the left is missing. There is reactive bone on both clavicles about the sternoclavicular articulation. Pitting and reactive bone are in



Fig. 1 Periosteal new bone on the ischial tuberosities.



Fig. 2 Left talus and calcaneus showing reactive bone and spur.

evidence on the lateral end of the right clavicle, especially on the superior surface; the lateral end of the left clavicle is missing. A similar combination of pitting and reactive bone affects the superior surface of the right acromion; the left acromion is missing. However, the glenohumeral joints appear normal.

Wavy periosteal new bone covers both ischial tuberosities, but is more exuberant on the right side (fig. 1). Similar reactive bone has been deposited on the spines of both scapulae and on the axial border of the right scapula just below the glenoid surface. Less prolific reactive bone can be detected on the iliac crests and on the left calcaneus around the sustentaculum tali and on the left posterior corner of the left talus (fig. 2).

Cervical vertebrae 2 through 6 are affected

by rather severe osteophytosis of the bodies plus DJD of the right articular facets. Severe osteophytosis also afflicts the lower three thoracic vertebrae and the fourth lumbar; the first three lumbar are less severely affected. The fifth lumbar vertebra was sacralized.

Spur-like exostoses are found on the posterior surface of both calcanei and on both tibial tuberosities. Unilateral spurs are also on the right anterior patella and on the right linea aspera at midshaft.

Several of the upper ribs display an irregular inferior border posteriorly. This unusual morphology, found bilaterally, appears to be sclerotic rather than lytic, yet the cortical bone appears to be no different in texture from normal cortical bone.

Finally, there is evidence of bilateral mild osteoporotic pitting of the five smaller tarsals and mild to moderate cribra orbitalia on the skull.

#### DISCUSSION

The pattern of morbid anatomy presents some features characteristic of DJD, spondylosis, rheumatoid arthritis, and ankylosing spondylitis, but is not typical of any of these. The affected synovial joints individually display sclerosis and osteophytosis characteristic of DJD, but fall into a distributional pattern characteristic of rheumatoid arthritis. There is a definite tendency toward symmetry with involvement of the metacarpophalangeal, wrist, subtalar, and sternoclavicular joints, all atypical of primary DJD, but characteristic of rheumatoid arthritis. Attack of the intervertebral facet joints in the cervical region only is also suggestive of rheumatoid arthritis.

Secondary DJD may develop in joints previously subject to rheumatoid disease, especially if the joint continues to be used (Jaffe, '72; Greenfield, '75; Short et al., '57). In practice this condition may be difficult to distinguish from primary DJD, especially if a single large joint is involved (Jaffe, '72). However, secondary DJD is found in locations which would be considered atypical for primary DJD (Martel, '72).

The osteophytosis of the vertebral bodies is morphologically typical of spondylosis and definitely not typical of ankylosing spondylitis. Moreover, there is no destruction of the sacroiliac joints, which is prerequisite for a diagnosis of ankylosing spondylitis. Instead, the joint margins show only mild lipping.

Spondylosis is a normal concomitant to aging, and in this case may have been aggravated by the fusion of the fifth lumbar and first sacral vertebrae. It is likely to be of independent etiology from the peripheral arthritis.

On the other hand, there is a pathological pattern highly suggestive of ankylosing spondylitis. In this disease there is a distinctive appearance of periosteal new bone at sites of muscle attachments at points of stress (Greenfield, '75; Cook, '69) which tends to be bilaterally symmetrical, whereas similar reactions in psoriatic arthritis and Reiter's syndrome are likely to be asymmetric (Jensen and Steinbach, '77). The initially irregular new bone is particularly common on the ischial tuberosities, iliac crests, and calcanei. Although periosteal new bone is common in ankylosing spondylitis, it is very rare and minimal when it does occur in rheumatoid arthritis (Dilson et al., '62). That the periosteal new bone may derive from an infection distinct from that affecting the joints is possible, but the distinctive appearance and location of the lesions, so typical of only ankylosing spondylitis, makes this unlikely. The reactive bone on both ends of the clavicles also suggests ankylosing spondylitis, which in the extremities may produce minimal to moderate subperiosteal bone adjacent to affected joints (Martel, '72). In fact, periarticular erosions may be superficial with frequent reactive sclerosis and bone apposition in the glenohumeral, acromioclavicular and sternoclavicular joints (Martel, '72; Engleman and Engleman, '77).

Spur formation on the posterior heels is known to occur in both ankylosing spondylitis and rheumatoid arthritis (Dilsen et al., '62), and is probably a reflection of tenosynovitis. Since tenosynovitis is a common feature of rheumatoid arthritis, spur formation at points of tendinous attachment around the knee may be explicable.

The strange morphology of the posterior ribs and the cribra orbitalia may be unrelated to the other skeletal lesions. However, rheumatoid arthritis has been known to involve the posterior portion of the upper ribs bilaterally (Greenfield, '75; Martel and Dixon, '64) as well as the axial border of the scapula, but the lesions are characteristically erosive and involve the upper margins. Here again the Hellenistic skeleton shows sclerosis whereas modern rheumatoid arthritis shows lysis. It

is possible that the cribra orbitalia may reflect an anemia which usually develops in rheumatoid arthritis and has been considered its most common nonarticular feature (Jaffe, '72). However, cribra orbitalia is believed to result from hyperplasia of the bone marrow in response to anemia. Since the anemia of rheumatoid arthritis is hypoplastic, the cribra orbitalia in this case is more likely due to another form of anemia.

#### CONCLUSIONS

A majority of current medical opinion holds that rheumatoid arthritis and ankylosing spondylitis are two diseases. Among other points of distinction rheumatoid arthritis afflicts two or three females for every male, whereas ankylosing spondylitis displays an overwhelming preference for males. Yet the similarities between the two are such that for many years ankylosing spondylitis was considered to be a variant expression of rheumatoid arthritis. The etiology of both diseases remains obscure.

One interpretation of the Sicilian skeleton is that it represents a stage in the evolution of rheumatoid arthritis out of the parent disease, ankylosing spondylitis. At that time the disease expressed its predilection for attacking the peripheral rather than axial joints, while retaining the ability to evoke a primarily sclerotic rather than lytic bone response and also retaining the tendency to provoke periostitis at sites of musculotendinous attachments. A detailed description of the evolutionary process and the time span involved cannot be gleaned from the study of a single skeleton. I would submit, however, that the skeletal pathology represents a transitional form, that is, that it represents some temporal phase in the evolutionary process. One might expect a great deal of variability in early rheumatoid disease owing both to temporal differences and to a certain variable human response to a single pathological process.

As Short ('74) has pointed out, the possibility of a recent origin for rheumatoid arthritis is of more than simple historical interest; it would support epidemiological studies (Bennett and Burch, '68) in suggesting that there are undiscovered environmental causative factors. In any case, the pattern of systemic arthritic disease affecting the Hellenistic skeleton is unlike any seen today,

implying that the pathogenesis of arthritic diseases has not remained unaltered throughout human history.

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