

Character and Semantics of Inflammatory Spine Disease, Calcium Pyrophosphate Deposition Disease and Ligamentous Ossification

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The article by Hajdu et al. (Osteol.Közl.2006.14.19-21.) affords an opportunity to examine the character and semantics of three major phenomenon: Inflammatory spine disease, calcium pyrophosphate deposition disease (CPPD) and ligamentous ossification produced by several different disease processes. The latter, when diffusely present, is often called diffuse idiopathic skeletal hyperostosis (DISH). It is not an articular abnormality, but rather enthesial in character (Resnick 2002, Rothschild 1985, 2002, Rothschild and Martin 2006). Actually, the vertebral centra bridging of inflammatory spine disease is also not an articular abnormality, but rather is an abnormality of the intervertebral disk. Inflammatory spine disease can have an articular component, in the form of zygapophyseal and costovertebral joint erosion and fusion (Resnick 2002, Rothschild and Martin 2006, San Zhang and Rothschild 1993).

When inflammatory spine disease starts at the sacroiliac joints and produces uniform vertebral bridging that proceeds from the lumbosacral spine cephaladly without skip areas, the diagnosis of ankylosing spondylitis can be considered (Resnick 2002). However, ankylosing

spondylitis represents only one variety of a larger disease category, spondyloarthropathy (Resnick 2002, Rothschild and Martin 2005). That category includes ankylosing spondylitis, the arthritis of inflammatory bowel disease, two highly erosive disorders [psoriatic arthritis and reactive arthritis (formerly called Reiter's syndrome)] and an undifferentiated form (Resnick 2002, Rothschild and Martin 2006, Rothschild and Woods 1989).

Examination of the various forms of spondyloarthropathy as population phenomenon reveals 5% of psoriatic arthritis and reactive arthritis have a vertebral appearance indistinguishable from that of ankylosing spondylitis. However, the specific diagnosis of ankylosing spondylitis cannot be made when vertebral disease spares caudal components.

While this may seem a semantic issue, implication of ankylosing spondylitis and the other forms (especially reactive arthritis) are quite different (Resnick 2002). The frequency of reactive arthritis is usually the sequella of infectious agent diarrhea and appears to be a marker for sanitary conditions, increasing in frequency with fecal contamination (Rothschild and Rothschild 1993).

While Hajdu et al. (2006) clearly document the presence of spondyloarthropathy, the presence of skip areas (intervening unaffected areas) precludes the diagnosis of ankylosing spondylitis (Resnick 2002, Rothschild and Martin 2006). Examination of each case reported by Hajdu et al. (2006) is highly instructive:

Case 301, a 25-30 year old male, has bridging of disk spaces, fusion of the right sacroiliac joint and zygapophyseal joint fusion. While the smooth (clearly not ligamentous) right sacroiliac and zygapophyseal joint fusion allow confident diagnosis of spondyloarthropathy (Resnick 2002, Rothschild and Martin 2006, Rothschild and Woods 1989), the disk space bridging illustrates the common challenge of distinguishing the syndesmophytes of inflammatory spine disease from the ligamentous ossi-

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fication of DISH (Resnick 2002). This differential is complicated by tendency to enthesial calcification in spondyloarthropathy (Resnick 2002). Whether this indicates co-occurrence of 2 phenomena or simply the enthesitis of spondyloarthropathy is yet to be clarified. While the bridging at the level of T11-T12 appears ligamentous in figure 1, that at the L4-L5 and L5-S1 levels clearly can be identified to have origin and insertion within the attachment area of the annulus fibrosus, and therefore represents syndesmophytes (Rothschild and Woods 1989).

Rib fusion is more complicated to assess. If fusion occurs through the articular surface, confident diagnosis of spondyloarthropathy is possible (San Zhang and Rothschild 1993). If it is simply through the joint capsule, DISH is perhaps more likely (Resnick 2002). Zygapophyseal fusion is clearly documented in the mid-thoracic region in case 301, where the vertebral centra are missing (at least in the photograph). Figure 1 and the lateral x-ray also illustrate a complication of spondyloarthropathy (Resnick 2002), vertebral fracture at the T11 level.

Case 416, a 50-60 year old male, has overgrowth of bone illustrated at the elbow. A portion of the overgrowth near the radial aspect of the distal humerus appears ligamentous/enthesial. The proximal ulna illustrates marginal bone over-growth, suggestive of osteoarthritis. However, the ulnar aspect of the distal humerus illustrates a ridge of the type typically seen with calcium pyrophosphate deposition disease (CPPD) (Rothschild and Martin 2006, Rothschild et al. 1990). The illustrated fused metacarpals have a crumbled distal appearance, characteristic of CPPD (Rothschild and Martin 2006, Rothschild et al. 1990). The metatarsal-tarsal fusion has effaced bony margins. While this appearance may be compatible with direct infection, it could also represent a peripheral manifestation of spondyloarthropathy (Resnick 2002, Rothschild and Martin 2006, Rothschild and Woods 1989). Because the latter only affects axial joints in 40% of afflicted individuals (despite the category name), radiologic examination would be required to resolve that question.

Case 11, a 20-40 year old male has vertebral osteophytes characteristic of spondylosis deformans, sometimes miscalled osteoarthritis (Rothschild 2005). While osteophytes occur in both, osteoarthritis is a disease of joints, not disk spaces (Resnick 2002, Rothschild and Martin 2006). Additionally present is anterior longitudinal ligament ossification and clearly enthesial costovertebral fusion, characteristic of DISH (Rothschild 2002). However, DISH is usually a disease of older individuals. While it can rarely affect an individual this young, hypervitaminosis A must also be considered (Rothschild 2002, Rothschild and Martin 2006). Histologically, the latter has disorganized architecture (Rothschild and Martin 2006). That contrasts with presence of normal Haversian systems in DISH.

Case 16, a 35-40 year old male, has vertebral bridging that on x-ray is clearly documented as involving both the

annulus fibrosus and the anterior longitudinal ligament. Vertebral compression is noted in several of the illustrated vertebrae. Without illustration, it is unclear if the reported metacarpal phalangeal joint fusion was articular (and therefore a manifestation of spondyloarthropathy) or enthesial (DISH).

Hajdu et al. (2006) very nicely document the background of age prediction from examination of skeletons, although ethnic background can be a confounding factor (Hoppa 2000, Schmidt 2004). However, validated criteria are available for recognition of spondyloarthropathy (Rothschild and Martin 2006, Rothschild and Rothschild 1993, Rothschild and Woods 1989, 1991). Brothwell (1963) hypothesized as to skeletal recognition of disease. Subsequent population-based criteria have been developed from examination of clinically-diagnosed individuals (Rothschild and Martin 2006, Rothschild and Woods 1989, 1991).

Medicine and anthropology share a common language, often quite disparate in meaning (Rothschild and Martin 2006). Collaboration is critical if misinterpretation is to be avoided. It also allows more up to date literature access for both.

Spondyloarthropathy is a category of disease. Distinguishing among the varieties can be approached by examination of exclusion criteria. Ankylosing spondyloarthropathy and inflammatory bowel disease produce symmetrical vertebral fusion, proceeding from lumbosacral to cervical spine. Presence of skip areas and asymmetry rule out those diagnoses (Resnick 2002, Rothschild and Martin 2006). The vertebral bridging in ankylosing spondylitis and inflammatory bowel disease is marginal in distribution, starting from the vertebral endplate margin, while those of reactive arthritis, psoriatic arthritis and undifferentiated spondyloarthropathy can also take their origins from a more (vertebral) central, non-marginal area. Presence of non-marginal syndesmophytes rules out ankylosing spondylitis and inflammatory bowel disease as the variety of spondyloarthropathy present.

Given the implications of reactive arthritis for assessment of ancient sanitary conditions (Rothschild and Rothschild 1993), it would be of interest to know the denominator for the population. Of course, interpretation will be tempered by the long period of cemetery usage — possibly camouflaging periods of significant fecal contamination.

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Response to the suggestions of prof. Rothschild and prof. Sebes

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In their paper on inflammatory spine disease, calcium pyrophosphate deposition disease (CPPD) and ligamentous ossification, Professors Rothschild and Sebes have commented on cases discussed in a previous publication of ours (HAJDU et al., 2006). They suggested extending investigations aimed at distinguishing between various lesions and proposed alternative underlying disorders in individual cases. Having considered their propositions and guidance, we have re-evaluated the cases described previously in detail. The following is a concise summary of this re-review.

Tomb N° 301. According to our diagnosis, the male individual (deceased at the age of 25 to 30 years) had seronegative spondyloarthropathy – spondylitis ankylopoetica (SA) in particular. Professors Rothschild and Sebes agreed that this case might have suffered from a disorder belonging to the category of spondyloarthropathies; in view of certain criteria, however, they refuted our diagnosis and suggested the possibility of Reiter's syndrome (reactive arthritis [RA]), psoriatic arthritis (PA), or an undifferentiated form of seronegative spondyloarthropathy. Taking the diagnostic criteria of these disorders into account, we have concluded that none of the typical features of RA – i.e. enthesopathy of the calcaneus (AUFDERHEIDE, RODRIGEZ-MARTIN, 1998), periosteal neoossification on the long bones of the hands and feet, erosions with neoossification commonly seen in the joints of the feet (ROGERS & WALDRON,

1995) – could be found. PA is ruled out by several factors: cervical spine was not involved and neither arthritis mutilans, nor 'pencil & cup' lesions could be ascertained (ROGERS & WALDRON, 1995). Enthesopathy of the calcaneus was not observed either (AUFDERHEIDE, RODRIGEZ-MARTIN, 1998). In consideration of the above, the possibility of RA and PA can be ruled out with high certainty. Re-reviewing the case according to the guidance contributed by Professors Rothschild and Sebes suggests an undifferentiated form of seronegative spondyloarthropathies as the most likely diagnosis.

Tomb N° 416 contained the skeleton of a male individual deceased at the age of 50 to 60 years, who had osteoarthritis according to our diagnosis. Professors Rothschild and Sebes extended diagnostic options to suspected CPPD (calcium pyrophosphate deposition disease). As evidenced by the literature, the latter disorder is mono- or oligoarticular in 95 per cent of cases (AUFDERHEIDE, RODRIGEZ-MARTIN, 1998). Although only a couple of bones were suitable for analysis, arthrosis was ascertained on the acromion of the scapula, as well as on the acromial surface of the clavicle, in addition to the changes described in our article. Therefore, it is reasonable to conclude that the majority of available bones were afflicted by disease. Furthermore, we insist that all the abnormalities detected on the bones constituting the elbow joint resulted from arthrosis – including neoossification of enthesiopathic origin on both humeral epi-

condyli. On the other hand, the comments and suggestions of Professors Rothschild and Sebes on the bones of the foot cannot be disregarded. In keeping with their advice, these bones will be submitted to radiologic examination to identify the true underlying cause among the options suggested.

Tomb N° 11. We have diagnosed DISH in the case of this male individual who had deceased at the age between 20 and 40 years. As it has been mentioned also in our article, DISH pre-dominantly afflicts individuals over the age of 50, whereas it is uncommon in younger age groups (ROTHSCHILD, 2002). In view of the young age of this case, Professors Rothschild and Sebes suggested hypervitaminosis A. This is a welcome suggestion and we shall undertake pertinent analyses to examine the possibility of this condition. Nevertheless, it must be noted that the age of the deceased was specified in a rather wide range between 20 and 40 years of age. This is explained by the fact that within the methodology suitable for estimating biological age, techniques designed for narrowing the tentative age range were either inapplicable, or shifted the age at death towards the upper limit of the range specified. Unfortunately, the influence of the underlying disorder on age determination could not be ruled out with certainty.

Tomb N° 16. Despite his relatively young age of 35 to 40 years, this male had DISH, beyond doubt. Readers are reminded that - as referred to in our article - this case has

been discussed already in a brief, but richly illustrated case report (BERNERT et al., 2003).

Finally, we would like to express our thanks to Professor Bruce Rothschild and to Professor Jenő Sebes for their honoring attention to, as well as their useful comments on our work. We are indebted to the editorial staff of the journal *Osteologiai Közlemények* for publishing our paper and subsequently, this response.

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