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PROBABLE CASES OF SKELETAL INFECTIONS IN THE 17TH CENTURY ANTHROPOLOGICAL SERIES FROM BÁCSALMÁS (HUNGARY)

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Abstract

A paleopathological study was carried out on human skeletal remains from a 17th century cemetery at Bácsalmás, and revealed three probable cases of skeletal infections.

The first one involves a male skeleton (grave No. 39), which presents signs of a severe infectious disease. The destructive lesions and some new-bone formation on the cervical, thoracic and lumbar vertebrae point to multifocal spondylodiscitis. The second case (grave No. 61) involves a young male skeleton, with a mild form of spondylodiscitis on 9 thoracic vertebral bodies, and serious osteolytic lesions and periosteal new-bone formation on 9 right side ribs. In the third case, two fragments of soft tissue calcifications were found, among the well-preserved remains of a male skeleton (grave No. 85). The morphology and the locations of the formations indicate pathological pleural calcifications.

The ankylosis of 3 right side ribs of the same skeleton should be mentioned.

The above-mentioned alterations indicate different types (hematogenous and direct spread) of skeletal infections. Skeletal tuberculosis is discussed as a possible common infection.

The differential diagnosis, which is based primarily on macroscopic methods, will be complemented by further histological and molecular biological methods.

Key words: paleopathology, 17th century, skeletal infections, tuberculosis.

Introduction

Infection of the skeletal tissues results from microbial organisms that are either bloodborne (hematogenous infection) or implanted directly into the bone. Even though bone is a very dynamic and sensitive tissue, relatively few infectious diseases produce recognizable lesions (KELLEY, 1989). Some infectious conditions, however, do affect the skeleton and careful analysis can reveal much about human adaptation in response to disease. Unfortunately, many of the infectious diseases produce morphologically overlapping responses in skeletal tissues. These responses make specific diagnosis difficult, especially in ancient bones (ORTNER and PUTSCHAR, 1985).

In spite of these difficulties, paleopathologists have made significant contributions to osteopathological diagnosis by studying dry bone remains from modern and ancient collections (e.g. MOLLER-CHRISTENSEN, 1961; HACKETT, 1976; STEINBOCK, 1976; KELLEY and EL-NAJJAR, 1980; MANCHESTER, 1984; ORTNER and PUTSCHAR, 1985; KELLEY, 1989; BUIKSTRA and WILLIAMS, 1991). The

paleopathological detection of radiologically invisible subtle bone lesions (such as the subtle periostitis of internal rib surfaces associated with pulmonary tuberculosis presented by KELLEY and MICOZZI (1984)) can promote a clinical diagnosis by providing new data.

The aim of the study of skeletal infections in paleopathology is not only the differential diagnosis of the detected lesions, but also research into the origin, evolution and spread of the infectious diseases. The present paleopathological analysis forms part of an international research program, focused on studies of the paleoepidemiological conditions of infectious diseases, based essentially on the historical anthropological collection of the Department of Anthropology at József Attila University.

Materials and Methods

The 91 graves in the Bácsalmás-Homokbánya cemetery were excavated in 1993, under the direction of ERIKA WICKER, archeologist and director of the Thorma János Museum at Kiskunhalas. The coins found in some graves revealed that the cemetery was in use during the 17th century (WICKER, manuscript). Historical data helped with the identification of the excavated cemetery (IVÁNYI, 1909; BOROVSZKY, 1910). It was used by a Serbian community living at Bácsalmás during the Turkish occupation of Hungary (WICKER, personal communication).

The subject of the anthropological and paleopathological analysis consisted of 83 skeletons, which are to be found in the collection of the Department of Anthropology at the József Attila University. The majority of the skeletal material is in a good or medium state of preservation.

The sex and age at death were determined with traditional methods used in historical anthropology (FEREMBACH et al., 1979; KNUSSMANN, 1988). The differential diagnosis was based on macromorphological methods, using both clinical and paleopathological special literature (e.g. ORTNER and PUTSCHAR, 1985; SILVERMAN, 1985; RESNICK and NIWAYAMA, 1988).

Results and Discussion

During the paleopathological study of the 83 human skeletal remains, besides other pathological conditions (traumas, degenerative joint diseases, spondylarthropathies, etc.), skeletal lesions due to probable infectious diseases could be detected in three cases. The three descriptions and discussions are presented separately.

Case No.1: Grave No.39. Male skeleton. Mature adult; relatively good state of preservation.

Description:

The most important pathological alterations of the skeleton are the erosive lesions of the vertebral bodies. The character of the lesions shows a considerable similarity: multifocal, circular, oval coalesced or irregular lytic areas in the vertebral bodies. Smooth bone resorption and small sinuses prevail; neural arch segments are uninvolved. The lesions have a maximum diameter ranging between 3 and 25 mm.

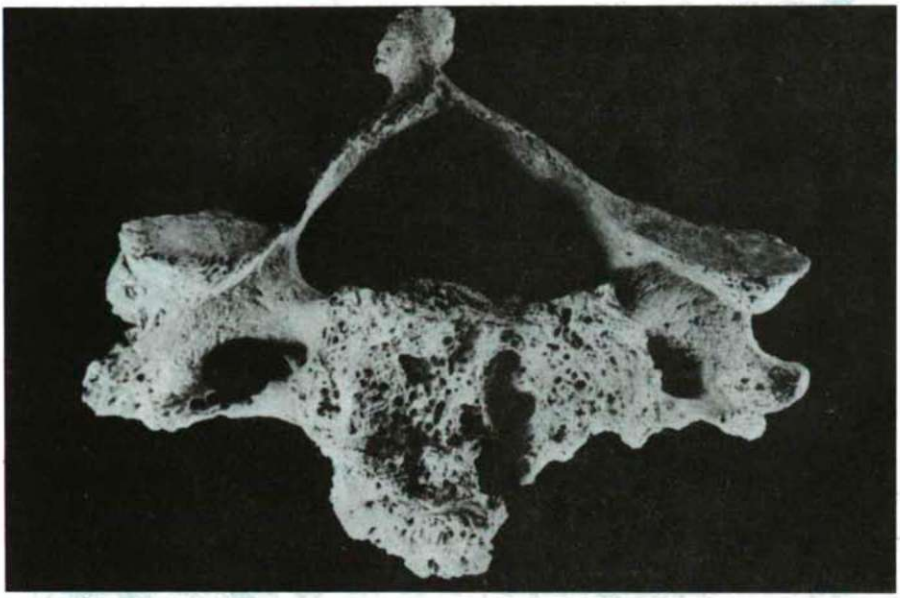

Fig. 1. Osteolytic destruction of the 4th cervical vertebral body. (Case No. 1: Grave No. 39)

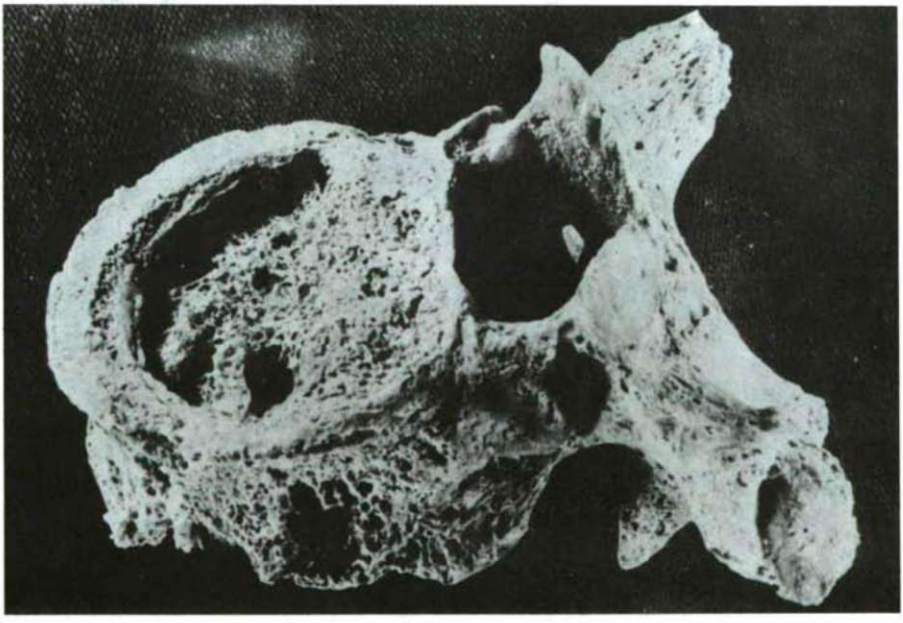

Fig. 2. Osteolytic foci in the 9th thoracic vertebral body. (Case No. 1: Grave No. 39)

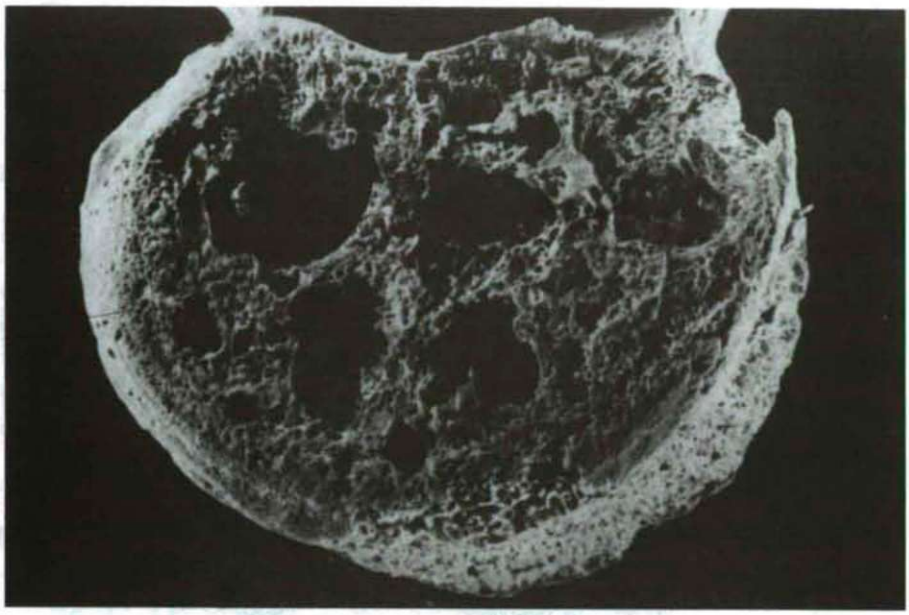

Fig. 3. Multifocal osteolytic destruction in the 2nd lumbar vertebra. (Case No. 1: Grave No. 39)

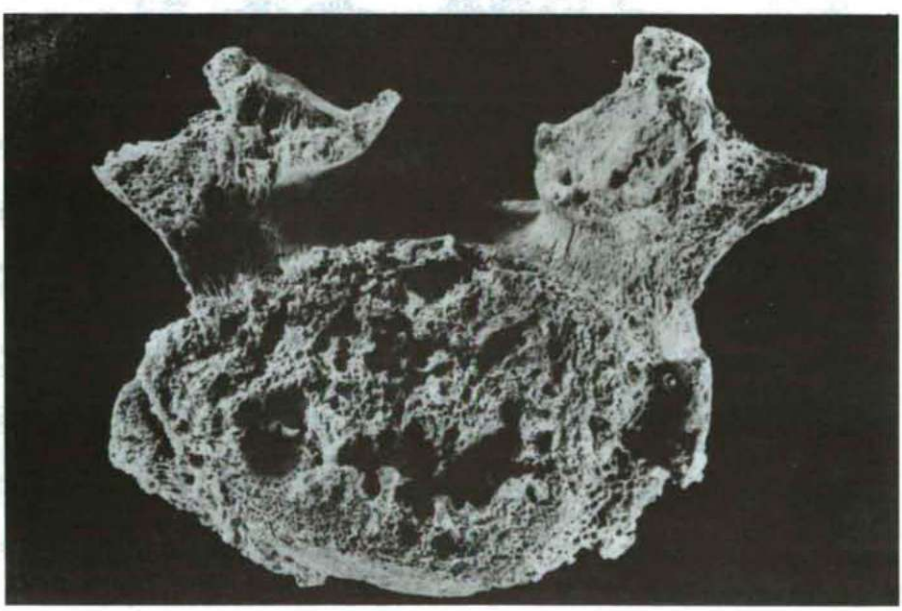

Fig. 4. Erosive and proliferative lesions on the 5th lumbar vertebra. (Case No. 1: Grave No. 39)

The lesions affect the vertebral column in several locations:

Cervical spine: two involved segments (C3-C4 and C4-C5) can be identified. The most important damage affects the 4th cervical vertebra: the bulk of the vertebral body is destroyed by the lytic process (Fig. 1). There is a little bony regeneration and remodeling of the trabecular system.

Thoracic spine: osteolytic involvement of the vertebral bodies between T5 and T11. Resorptive areas are to be found in the central portion of the body, sometimes extending to the antero-superior or antero-inferior margins. In some cases, small sinuses perforate the vertebral bodies and open in the lateral or anterior surfaces (Fig. 2). The most advanced stage of the alteration is to be seen in segments T8-T9.

Lumbar spine and lumbo-sacral border: two important foci can be differentiated. The first affects segments L2-L3 in the form of multifocal osteolytic destruction of the adjacent vertebral bodies (Fig. 3). There is a little bony regeneration around some lytic foci and slight periosteal and osteophytic development on the bodies. The second focus of advanced stage involvement is the lumbo-sacral border. There is massive osteolytic destruction of the adjacent bodies in segments L5-S1 and slight marginal osteophytic formation (Fig. 4).

For the purpose of diagnosis, it is important that slight periosteal new-bone formation can be observed on the distal part of the two tibiae, fibulae and calcaneums. The right side tibia shows signs of thickening and pathological axial deformation. With the exception of the above-mentioned alterations, there is no evidence of other infection or trauma and the bones do not exhibit any signs of demineralization. Other pathologies in case 1 are caries of the left maxillar first molar and spondylolysis of L5 (Fig. 4).

Discussion:

Although the *in vivo* process is evident in the bone-forming reactions (periosteal or osteophytic new-bone formation), in the case of osteolytic reactions it is difficult to exclude taphonomic effects. In the present case, the limited form of the lesions, the slight sclerotic margin of the lytic areas and the reactive new-bone formation suggest an evident *in vivo* process (ORTNER and PUTSCHAR, 1985).

The localized alterations (dental caries and spondylolysis) reveal independent pathological conditions. As far as the alterations of the lower limb bones are concerned, it is known that several pathological conditions may be associated with periosteal bone reactions. In this case, the morphology of the lesions suggest that a post-traumatic pyogenic infection is most likely (BULLOUGH and VIGORITA, 1984).

The above-mentioned spinal lesions are easily distinguishible from degenerative, traumatic or inflammatory (spondylarthropathies) processes (BUIKSTRA, 1976; KELLEY and EL-NAJJAR, 1980; ORTNER and PUTSCHAR, 1985). Metastatic carcinomas can produce resorptive foci in vertebral bodies, but they are frequently associated with neural arch and rib lesions and the intervertebral discs are not affected (LAPIS, 1989); consequently, they can be excluded in our case.

The destructive lesions and some new-bone formations on the cervical, thoracic and lumbar vertebrae reveal multifocal spondylitis with a probable hematogenous

spread (HORVÁTH and FORGÁCS, 1984; BAHK, 1994). Within the group of spinal infections, a large series of microorganisms can produce similar pathological alterations. Resorptive foci on the vertebrae are not infrequent in the skeletal involvement of actinomycosis, tuberculosis, pyogenic osteomyelitis, coccidioidomycosis or blastomycosis (DE SEZE and RYCKEWAERT, 1983; RESNICK and NIWAYAMA, 1988; KELLEY, 1989). In the rare cases of osseous involvement due to actinomycosis, the mandible is the most commonly affected element; neural arch lesions occur as frequently as those of the body, and the disk space is maintained (BUIKSTRA, 1976; ORTNER and PUTSCHAR, 1985).

In skeletal tuberculosis, which is the most probable diagnosis in this case, the most common lesion is tuberculosis of the vertebral bodies and intervertebral discs, or tuberculous spondylodiscitis (MARTINI, 1988). Although the classical and relatively easily recognizable form in advanced Pott's disease is angular kyphosis with ankylosis of the vertebral bodies involved, in active tuberculous spondylitis, erosive lesions, smooth bone resorption and osteolytic changes of the subchondral region of the vertebral body are most frequently seen (MARTINI and OUAHES, 1984; KELLEY 1989). The study by KELLEY and EL-NAJJAR on documented cases of skeletal tuberculosis revealed a considerable variability of the vertebral lesions (KELLEY and EL-NAJJAR, 1980).

The anatomo-pathological changes of hematogenous pyogenic spondylitis are very similar to those of skeletal tuberculosis. Unlike pyogenic bone infection, tuberculosis affects the spine more frequently than the long bones. Tuberculous spondylitis commonly involves multiple vertebrae, whereas pyogenic osteomyelitis always involves two neighboring vertebrae only (BAHK, 1994).

In addition to the above-mentioned diseases, fungal infections can also be implicated in the differential diagnosis of tuberculosis. Of the fungal infections, blastomycosis and coccidioidomycosis are perhaps the most difficult to distinguish from tuberculosis in human skeletal remains. Bone involvement, in the form of multiple resorptive foci, is frequent in the disseminated form of both diseases (RESNICK and NIWAYAMA, 1988).

Case No. 2: Grave No. 61. Male skeleton. Young adult; relatively good state of preservation.

Description:

The relatively robust skeleton of a 20 to 25-year-old male is in a good general state, without any signs of demineralization. Pathological alterations are seen exclusively on the bone remains of the thorax.

Ribs (right side): The most characteristic lesions are the diffuse periosteal new-bone formation on 9 (4th to 12th) of the right side ribs. The lesions affect predominantly the visceral surface of the ribs. Morphologically, these lesions consist of plaques of new bone with discrete pits indicating the inflammatory reaction of the periosteum. Focal lytic lesions, ranging from 5 to 35 mm, are found on the pleural aspects of the 5th to the 10th ribs (Fig. 5a-d). In some cases, the osteolytic lesions are

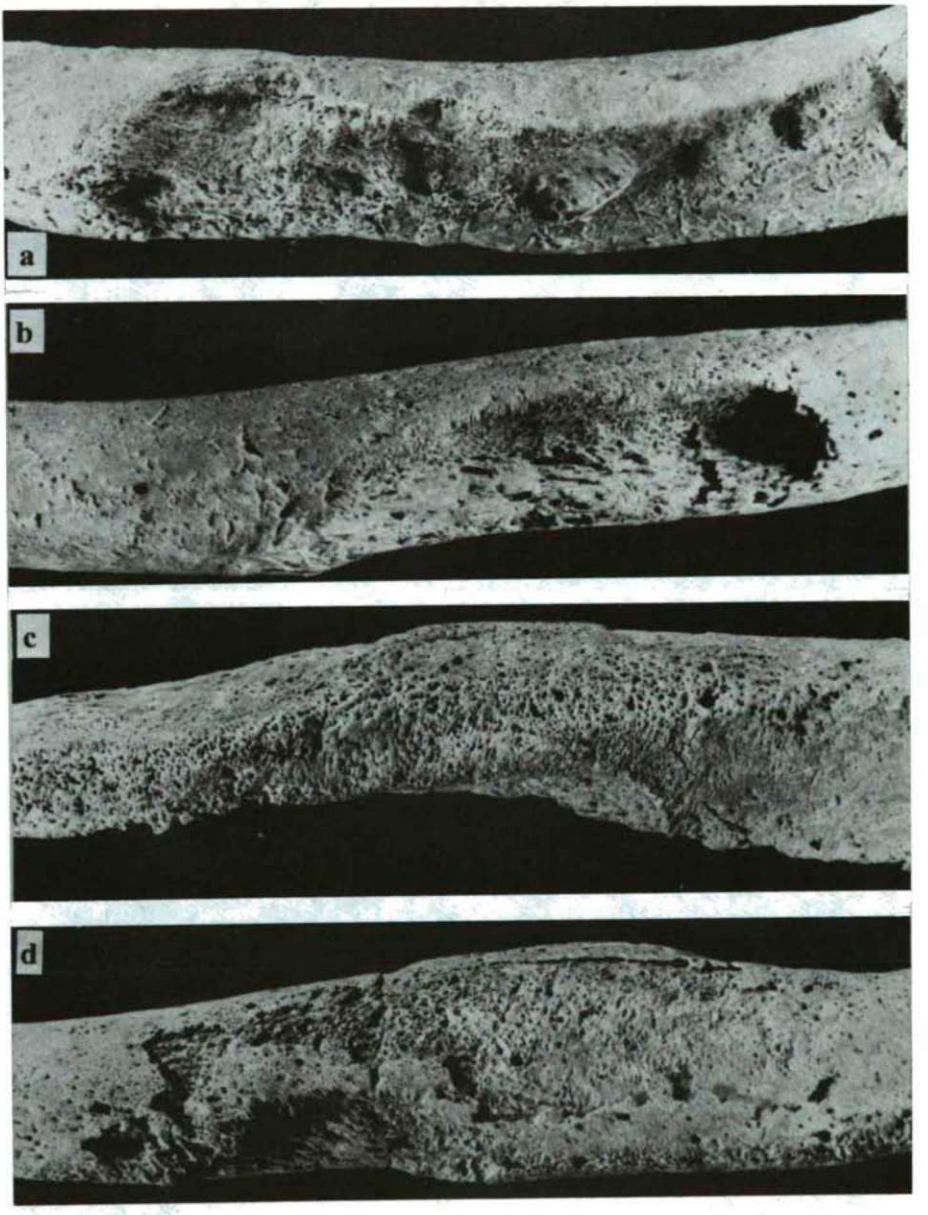

Fig. 5a-d. Periostitis and osteolytic lesions on the visceral surface of the 6th (a), 7th (b), 9th (c), and 10th (d) right ribs. (Case No. 2: Grave No. 61)

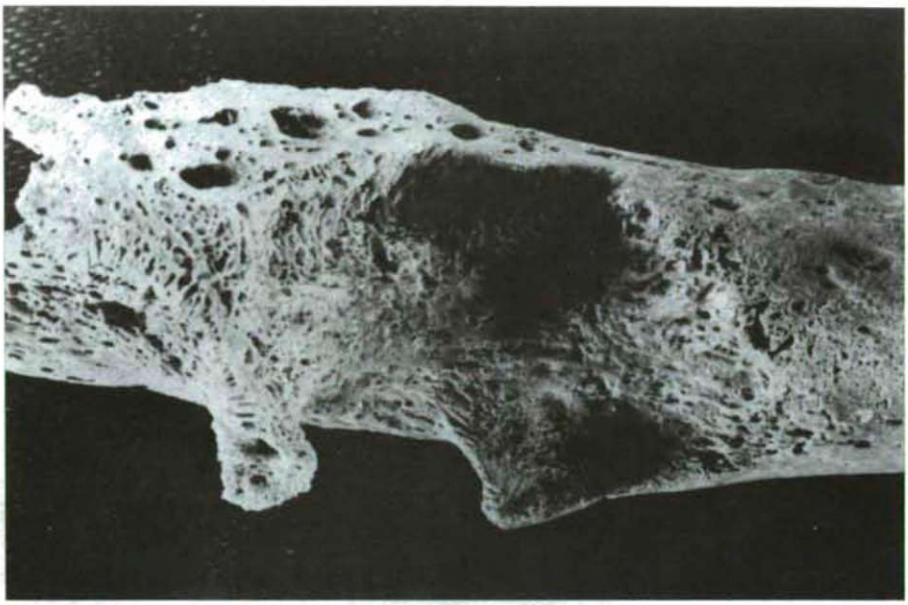

Fig. 6. Reactive new-bone formation around an osteolytic focus of the 5th right rib. (Case No. 2: Grave No. 61)

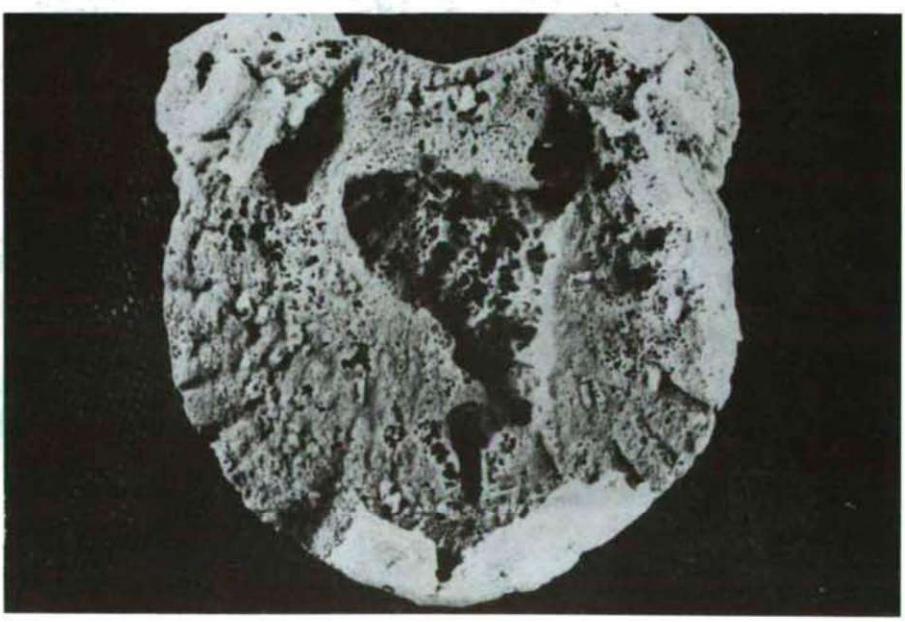

Fig. 7. Irregular lytic lesion on the 6th thoracic vertebral body. (Case No. 2: Grave No. 61)

surrounded by osteoblastic formation. On the inner surface of the lytic cavities, fine reactive new-bone formation and remodeling of the ancient trabecular bone can be seen (Fig. 6). Pathological changes can be detected not only in the subperiosteal and cortical region: the subcortical trabecular bone is completely remodeled in several localizations.

Right clavicle: the bone is thickened and quasi-completely covered by periosteal new-bone formation.

Thoracic spine: Irregular lytic areas are present on the adjacent vertebral bodies of segments T4 to T12. Their extent varies between 4 and 25 mm; the maximal depth reaches 7 mm (Fig. 7). Very discrete new-bone formation can be detected in some of the lytic foci.

Discussion:

In spite of the difficulties in the explanation of periostitis in paleopathology, the observed periosteal new-bone formation on the right side clavicle and ribs suggests infectious conditions (BULLOUGH and VIGORITA, 1984; ORTNER and PUTSCHAR, 1985; RESNICK and NIWAYAMA, 1988). The osteolytic alterations of the ribs (evidently due to an in vivo process, which is justified by the detected sclerotic new-bone formation) also indicate an osteitis of infectious origin (BRAUNER et al., 1982). Osteolytic alterations of the ribs are frequently seen in some tumorous and tumor-like conditions, e.g. in multiple myeloma or osteolytic metastatic carcinoma (ORTNER and PUTSCHAR, 1985). In this case, howewer, the morphology, the skeletal pattern of the lesions and the lack of typical locations of myeloma or carcinoma metastases (skull, pelvis, vertebral bodies, proximal femoral epiphyses, etc.) do not favor such a diagnosis. Subchondral erosions of the vertebral bodies could suggest the presence of SCHMORL'S nodes, but their irregular aspects, their considerable dimensions and the presence of reactive new-bone formation point to a more likely early-stage spondylodiscitis (MARTINI, 1988).

As for the location of the lesions of the thoracic cage, the asymmetric (unilateral) character of the rib lesions suggests that a direct infectious process is more probable than a hematogenous infection. In the case of the detected vertebral lesions, a hematogenous spread seems more possible.

There are relatively few references about periosteal rib lesions in radiological or pathological diagnostic reports on infectious diseases (KELLEY and MICOZZI, 1984). This fact results from the often very subtle character of these alterations (ROBERTS et al., 1994). Osteomyelitis of the ribs, in the form of geode-like cavities, solitary or multiple lytic lesions, is reported in cases of actinomycosis, blastomycosis, coccidioidomycosis, typhoid or paratyphoid osteomyelitis, pyogenic osteomyelitis, syphilis and skeletal tuberculosis (BRAUNER et al., 1983; DE SEZE and RYCKEWAERT, 1983; MARTINI, 1988; RESNICK and NIWAYAMA, 1988). The lack of specific diagnostic criteria (e.g. typical cranial or tibial lesions in treponematosis and lumbar affection in typhoid or paratyphoid osteomyelitis) and the pattern of the observed lesions help to exclude some of the mentioned diseases.

The unilateral infections of the ribs in this case suggest the possibility of direct

extension from right side pleural and/or lung foci. Thus, the major diagnostic problem is to distinguish between the infectious processes which can provoke pulmonary diseases and may disseminate through the pleura to the ribs. The possibility of direct extension in rib lesions is described in cases of pulmonary tuberculosis, actinomycosis, nocardiosis, blastomycosis and coccidioidomycosis (RESNICK and NIWAYAMA, 1988). In all of these infections the osseous involvement of the ribs by direct spread is characterized by a combination of lysis and sclerosis. As the specificity of microbial methods used in modern clinical practice is much higher than that of radiological methods, insufficient data are available to differentiate these lesions on this basis. As far as the most widespread (and, from an epidemiological point of view, the most important) of these infectious diseases, human tuberculosis, is concerned, the differential diagnostic questions of periosteal rib lesions are neglected in the medical literature, because of the more frequent and more typical osteologic lesions due to the hematogenous infection (ROBERTS et al., 1994).

Several important pathological and paleopathological studies have been carried out during the past fifteen years. As a result, several of these questions have been clarified. KELLEY and EL-NAJJAR (1980) presented rib lesions which show a considerable degree of diversity, resemble our cases and come from a documented series of skeletal tuberculosis. Research by KELLEY and MICOZZI (1984) on the Haman-Todd osteological collection recorded that 39 (8.8%) of a total of 445 skeletons of people dying of tuberculosis exhibited periosteitis or evidence of localized abscess adjacent to the visceral surface of one or more ribs. The authors suggested that the rib lesions were a result of pulmonary tuberculosis. Other studies have also noted inflammatory lesions of the ribs from ancient and modern contexts (MOLTO, 1990; BUIKSTRA and WILLIAMS, 1991; PFEIFFER, 1991; ROSE and HARTNADY, 1991; WAKELY et al., 1991; ROBERTS et al., 1994). Tuberculosis was proposed in the differential diagnosis of these bone changes. In the most recent (and the most representative) of these studies, the authors investigated the frequency of periosteal new-bone formation on the visceral surfaces of the ribs of 1718 individuals from the Terry collection (ROBERTS et al., 1994). Their results demonstrate that rib lesions were much more common in individuals dying from tuberculosis (61.6%, or 157/255) than in individuals dying from other causes (15.2%, or 165/1086).

Taking into consideration the diagnostic criteria, the case histories and epidemiological data found in the medical and paleopathological literature, it can be concluded that in case 2 the rib lesions suggest pulmonary infection. Although the pathological changes of the visceral surfaces are consequences of a possible direct spread through the pleura, the hematogenous spread from a pulmonary focus cannot be excluded because of the spondylodiscitis of the thoracic vertebrae. Direct infection and/or hematogenous spread can result in inflammatory lesions of the right clavicle.

Fig. 8. Ankylosis of the 7th to 9th right ribs in the area of the costotransverse articulations. (Case No. 3: Grave No. 85)

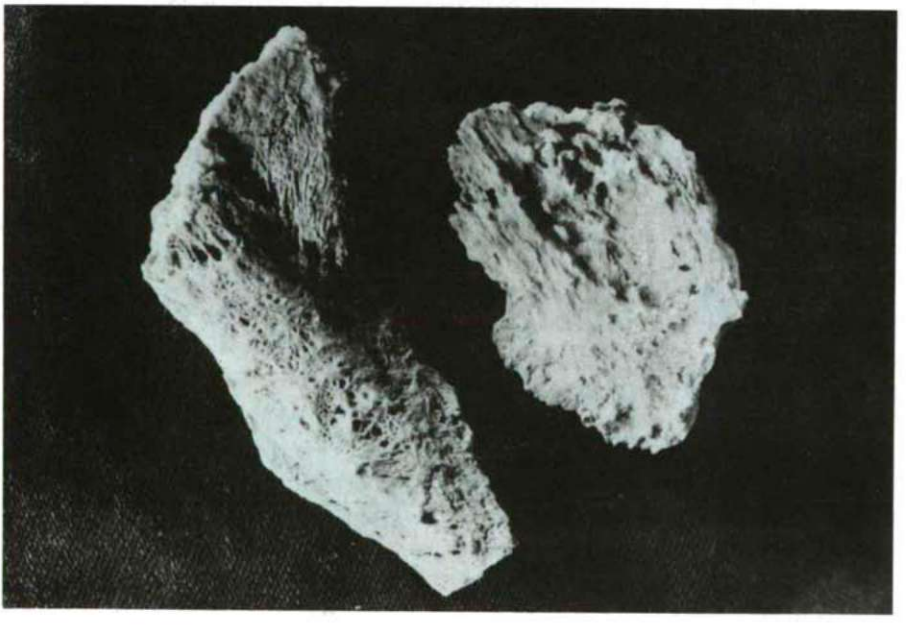

Fig. 9. Soft tissue calcifications suggesting pleural plaques. (Case No. 3: Grave No. 85)

Case No. 3: Grave No. 85. Male skeleton. Mature adult; very good state of preservation.

Description:

This case involves the well-preserved skeleton of a 50-60-year-old man.

The quasi-complete and very robust skeleton displays a good state of mineralization. There is dental caries in the left lower third molar. In spite of enthesopathic signs in the areas of some muscular insertions (calcaneums, pelvis and some vertebral bodies), which are not sufficiently developed to allow a diagnosis of diffuse idiopathic skeletal hyperostosis, there is no sign of a generalized pathological condition.

However, two surprising phenomena must be mentioned. The first is the ankylosis of 3 right side ribs (Fig. 8). The bony fusion affects the 7th to 9th right ribs, in the area of the costotransverse articulations. The superficial new-bone formation on the visceral surface should be mentioned. The process is unilateral and exclusively localized in this area. The other bones of the complete and well-preserved thoracic cage do not present any pathological lesions.

The second interesting phenomenon is the presence of soft tissue calcifications. Among the osseous remains of the rib cage of the skeleton, two pathological formations were found (Fig. 9). (We have no more valuable locations of this calcified material from an archeological context.) The dimensions are as follows: 62 mm x 30 mm x 3-4 mm; and 62 mm x 25 mm x 4-6 mm. Macroscopically, they are hard and flat, with a slight curvature of the longer fragment. Their surface is irregular, and some lamellar character can be recognized.

Discussion:

Pathological changes of costotransverse and costovertebral joints can occur (relatively rarely) in certain rheumatologic or metabolic diseases. There are several literature references to inflammatory changes and ankylosis in these locations in seronegative spondylarthropathies. In cases of advanced stage diffuse idiopathic skeletal hyperostosis, the costotransverse ligaments may be ossified, but the articular surfaces are not affected (RESNICK and NIWAYAMA, 1988). In these conditions, however, the diseases affect predominantly other parts of the skeleton, and the processes affect the ribs bilaterally.

Localized ankylosis of bones or joints is more likely following traumas or localized infection (ORTNER and PUTSCHAR, 1985). In the present case, the latter possibility seems more probable because of the location of the alterations. There is no evidence, however, of fracture or other localized traumas in the affected area. The superficial, reactive new-bone formation on the visceral face of the ankylosed ribs in the affected area suggests an inflammatory reaction due to a probable infection. The localized character reveals an infection from some neighboring focus.

The morphology and the location of the calcified formations indicate pathological pleural calcifications. These cases are very similar to the well-documented cases of pleural plaques presented in the paleopathological literature

(KRAMAR, 1984; BAUD and KRAMAR, 1991). In those cases, the authors dicuss the possibility of the infectious or traumatic origin of the calcifications. In our cases, the lack of traumatic processes makes the former version more acceptable.

The pathological and radiological literature indicate that calcifications of the pleura appear following chronic pleurisy, especially in cases associated with pulmonary tuberculosis (LAPIS, 1989). In primary tuberculosis, the necrotic foci in any component (lung or pleura) heal by progressive fibrosis, hyalinization and calcification. Pleurisy is very common in primary tuberculosis and large free pleural effusions may develop during the infection. The localized thickenings and the secondary calcifications may persist until late in the disease (SILVERMAN, 1985). From paleopathological material, ZIAS (1991) presents cases of calcified pleura, which are interpreted as evidence of tuberculosis.

In case 3, we can suggest a correlation between the two observed alterations, due to a presumed pulmonary infection.

Conclusions

During the paleopathological study of human skeletal remains from the 17th century cemetery at Bácsalmás, three probable cases of skeletal infections have been identified.

In case 1, the morphology, location and pattern of the vertebral lesions suggest (similarly as for other cases reported in the paleopathological literature (BUIKSTRA, 1976; STEINBOCK, 1976; KELLEY and EL-NAJJAR, 1980; KELLEY, 1989; BÉRATO et al., 1991; POWELL, 1991)) a diagnosis of an active multifocal tuberculous involvement. On the basis of morphological investigations, however, the possibility of an atypical disseminated pyogenic infection (possibly correlated with the observed lower limb alterations) or a disseminated fungal disease, cannot be ruled out.

The periosteal and erosive rib lesions discussed in case 2 suggest a pulmonary infection. In addition to the assumed direct spread through the pleura to the ribs, hematogenous infection can also be presumed. The literature data indicate that the most probable cause of such lesions is pulmonary tuberculosis (KELLEY and EL-NAJJAR, 1980; KELLEY and MICOZZI, 1984; PFEIFFER, 1991; ROBERTS et al., 1994). Actinomycosis or some fungal infection, such as blastomycosis or coccidioidomycosis, also have to be taken into consideration (RESNICK and NIWAYAMA, 1988; MOLTO, 1990).

The rib lesions and especially the pleural calcifications seen in case 3 are probable consequences of a pulmonary infection. Special literature data mention the possibility of these alterations in different cases of tuberculosis (SILVERMAN, 1985; LAPIS, 1989; BAUD and KRAMAR, 1991). We know of no references describing similar lesions as a result of other infections mentioned above. As the examined reactions are secondary signs of a primary pulmonary infection, we cannot exclude, at least theoretically, the possibility of a primary fungal infection.

The results of the present paleopathological diagnostic study therefore suggest that tuberculosis is the most probable common cause of the infectious conditions described.

Finally, it proved possible to understand the limits of morphological studies in the paleopathological diagnosis of infectious diseases. It seems probable that further macroscopic investigations of the presented lesions will not clarify the etiological questions of these lesions further. The use of biomolecular analysis of bone for mycobacterial DNA in appropriate skeletal material, as to be seen in some recent publications (SPIGELMAN and LEMMA, 1993; DIXON et al., 1994), may promote further discussion.

The aim of this work was to attract attention to the possibility of the identification of "atypical" forms of skeletal tuberculosis. The prevalence of tuberculosis in archaic human skeletal remains is traditionally based on the paleopathological diagnosis of Pott's disease of the spine, or pathological changes in major weight-bearing joints of the body (e.g. FORMICOLA, 1987; DUTOUR et al., 1991; STIRLAND and WALDRON, 1989; STROUHAL, 1991), although any bone of the body can be affected by a considerable range of tuberculous lesions. This phenomenon characterizes the results of our research in Hungary: during the previous diagnostic studies, only the "classical" cases were taken into consideration (MARCSIK, 1972; FARKAS et al., 1976; PÁLFI, 1991; PÁLFI et al., 1992; MARCSIK and PÁLFI, 1993; MARCSIK et al., 1994). It seems necessary to reexamine the previously detected inflammatory rib lesions, for example in the case published by ÉRY (1982).

In order to be able to carry out a better paleoepidemiological analysis, we must examine further historical populations, and develop the morphological diagnosis via the histological and molecular biological methods mentioned above.

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