A POSSIBLE CASE OF HYPERTROPHIC PULMONARY OSTEOARTHRopathY IN AN IDENTIFIED SKELETON FROM CEMETERY OF ÉvORA, PORTUGAL: DIFFERENTIAL DIAGNOSIS

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RESUMEN. En este trabajo estudiamos un posible caso de Osteoartropatía Hipertónica Pulmonar y su diagnostico diferencial en un hombre Portugués de 73 años que murió en Évora (Portugal). La causa de muerte es desconocida pero se sabe que estaba hospitalizado. Lo esqueleto pertenece a la colección de esqueletos identificados de Évora (CEIE), Portugal, viene de un cementerio municipal (Cemitério dos Remédios) y tiene como número de catalogo CEIE 109. Esta patología es un disturbo circulatorio asociado a tumores, más concretamente a cáncer del pulmón; pero también pude existir en casos de neoplasias de lo páncreas, estomaga o nasofaringe. Por más que en esto caso no es observable evidencias macroscópicas de neoplasias en lo esqueleto, los órganos podrían estar afectados. Bibliografía apunta lo diagnostico de

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Osteoartropatía Hipertrófica Pulmonar como desafiante en restos arqueológicas esqueléticos. Las alteraciones óseas son más severas en la tibia y peroné izquierdos pero también están evidentes en lo pie y fémur.

PALABRAS CLAVE: Osteartropatía hipertrófica pulmonar, Convento dos Remédios, periostosis, Évora

ABSTRACT. In this work we will study a possible case of Hypertrophic Pulmonary Osteoarthropathy and its differential diagnosis in a 73 years old Portuguese male died at 1970 at Évora (Portugal). Although he died at the local hospital the cause of death is unknown. The skeleton belongs to identified skeletal collection from Évora, come from a city cemetery (Cemitério dos Remédios) and has as catalogue number CEIE 109. This pathology is a circulatory disturbance disease which is associated to tumors in particular with the lung cancer; however it can exist in cases of neoplasias of pancreas, stomach and nasopharynx. In this case there are no macroscopic evidences of neoplastic conditions but it doesn’t mean it wasn’t present in the organs. Bibliography generally point to “Differential diagnosis of hyperthrophic pulmonary osteoarthropathy in archeological human remains is likely to be challenging”. These bony alterations are more severe at the left tibia and fibula but lesions are also present in the foot and femur.

KEYWORDS: Hypertrophic pulmonary osteoarthropathy, Convento dos Remédios, periostosis, Évora

INTRODUCTION

Hypertrophic Osteoarthropathy (HOA) is a clinical syndrome of unknown etiology, first described by Friedenreich (1868, in Kuhn et al., 2007). Clinically there are two forms of Hypertrophic Osteoarthropathy (HOA), the Primary form or Idiopathic and the Secondary or Pulmonary (HPO). The Primary form or Pachydermoperiostosis, usually severe, affects primarily males (Aufderheide and Rodríguez-Martín, 1998) and has been found that
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appears around puberty and it’s limited to this growth period (Christensen et al., 2011). The secondary, also called Hypertrophic Pulmonary Osteoarthropathy (HPO) is a syndrome related to several pathologies being intrathoracic cancer the most probable (Aufderheide and Rodríguez-Martín, 1998; Resnick and Krandsdorf, 2005). HPO, like the noun suggests his highly associated to pulmonary diseases. Several human paleopathology researchers connect HPO mainly with Tuberculosis (TB) (Assis et al., 2011) or Yaws (Rothschild and Rothschild, 1998), but in medical reports is highly correlated to intrathoracic tumors, in which the bronchial carcinoma accounts with 80% of the cases, (Kim et al., 2004; Utine et al., 2008) or grafts infections (Martínez et al., 1996; Golder and Wolf, 2001). Other nonpulmonary conditions may be associated with HPO including gastrointestinal, cardiovascular, hepatobiliary and endocrine disorders (Bazar et al., 2004; Shih, 2004; Vandemergel et al., 2004; Yao et al., 2009).

Both forms of Hypertrophic Osteoarthropathy are characterized by new bone deposition at periostal level of tubular bones not affecting subchondral bone, digital clubbing and painful swelling appendicular joints (Aufderheide and Rodríguez-Martín, 1998). Deposits of new bone may show macroscopically an “applique” aspect with periosteal reactions of the bone looking as had been physically pasted on the original surface, or a “surface” form appearing to be part of the surface where new bone and normal cortex merge imperceptibly. Proliferative periostitis leads to diffuse periosteal ossification with a resultant increase in the circumference of the affected bones. Typical alterations are more common at mid-diaphysis tapering toward the edges. Radiological images also allow distinguishing the nature of bone deposits by a distinct radiolucent line, in the first case. Both forms could be present in the same skeleton nevertheless usually not on the same bone (Rothschild and Rothschild, 1998). The majority of HPO cases are bilateral and symmetrically distributed and lesions are more frequent on tibiae, fibulae, radii and ulnae but not uncommon on hand and feet (eg. Ortner, 2003).

To explain HPO pathophysiology there are three main theories: the arteriovenous shunt or circulatory theory (Cudkowicz and Armstrong, 1953), the neuronal or neurogenic (Golstraw and
Walbaum, 1976), and the endocrinal or hormonal (Loredo et al., 1996). More recently a unifying theory by Bazar et al. (2004) suggests that this process may occur as part of a normal physiology process or by an abnormal mechanism involving chemoreceptor activation.

In this paper, we present a possible case of Hypertrophic Pulmonary Osteoarthropathy and its differential diagnosis in a skeleton from the identified skeletal collection of Évora, exumed at a city cemetery and housed in University of Évora (Portugal).

MATERIAL AND METHODOLOGY

The case report (CEIE109) belongs to the Identified Skeletal Collection of Évora, housed at University of Évora, Portugal. It comes from the Cemitério dos Remédios, a city cemetery and was identified as a male, 73 years old, who died at 1970. Although he was hospitalized when he died the cause of death is unknown.

The skeleton is very well preserved and complete. The only missing pieces are both clavicles, all distal phalanges from the feet and hands, apart from the first toe in the two feet. It’s also missing all carpals apart from the right hamate and capitate. Proximal phalanges are all present in the hands and feet, however the left 5th finger couldn’t be found. The right 5th metatarsal isn’t present. Almost all intermediate and distal phalanges aren’t present apart from 5th right and 2nd finger, but the right 3rd and 4th fingers haven’t only the distal phalanges. The one tarsal not recovered is the right cuboid.

The radiology (42 KV and 12mA) approach was only possible to the left tibia and fibula because of funds related to this methodology.

RESULTS

On the left lower limb (tibia, fibula, femur and foot) we found several and severe osseous proliferations which confer a thickening, a highly irregular and gummy surface (mainly like the “applique” form proposed by Rothschild and Rothschild, 1998) and, at left tibia and fibula, proliferations leads to the attachment of these bones
(Fig. 1) in the distal diaphysis, therefore the x-ray images reveal (Fig. 1) diffuse hyperostosis of the left fibula and tibia. In the tibia’s mid and distal diaphysis is clearly visible the original cortex. The left tibia show macroscopically, new bone formation especially at the mid and distal diaphysis of the tibia and fibula. The same happen with the left femur (Fig. 2), being lesions more proliferative at the muscular/ligament insertions, like the *linea aspera*. At distal diaphysis of the left femur the two types of periosteal reaction were observed, mainly the applique form, reaching an aspect similar to a melted candle, but also the surface form is present specially at the anterior-posterior face of the metaphysis, like it is continuing the muscular insertions from the diaphysis to the metaphysis although never including the articular zone. The new bone led thickening of the posterior distal diaphysis of femur.

**Figure 1.** Photograph and x-ray image of left tibia and fibula showing the connection between them due to periostosis where the mid-diaphysis is the most affected area.
Macroscopically, there are periostosis on the right femur, affecting the same regions as in the left femur, mostly on the posterior mid and distal diaphysis, but less severe resulting in an asymmetrical pattern. There is micro and macroporosity in the distal epiphysis (never affecting the joint surface). In the medial malleolus there are striated bone and a subtle layer of new bone in the mid and distal posterior diaphysis of the right tibia, but the radiographic image showed thicker bone than what was expected. In both right femur and tibia the distinguishable layers of periosteal new bone are only surface form, never showing candle wax neither applique form similitude. At the inter-osseous ligament zone of the right tibia there is also periosteal new bone formation.

Navicular and calcaneus are the most affected bones of the foot, showing irregular periostosis similar to lesions above described. Lesions at navicular cover the entire surface except facets joints. A facet trocleo-fibular can be observed in the calcaneus probably due to the fusion of the tibia and fibula. There is woven bone in the plantar face of the right calcaneus, between the facet to the talus and the tuberosity. The left superior-dorsal intermediate face close to the articulatory facet to second and third metatarsals show the same lesions as the other tarsals, and also in the medial superior face. First toe differ from the others left toes, once, distally, metatarsal shows like tiny punctuations of new bone and thickening of the diaphysis. The distal phalange of the same toe also presents new bone deposits at the posterior distal epiphysis, proximal diaphysis in the postero-medial zone and epiphysis.
### TABLE 1. Resume of the main lesions observed on the skeleton, where “-” means non observable lesion, “T” is for thoracic and “L” for lumbar vertebra and “S” is from Sacral or Sacrum

<table>
<thead>
<tr>
<th>Bone/ Type of Reaction</th>
<th>Periostosis (associated to HOA)</th>
<th>Degenerative joint disease</th>
<th>Degenerative non articular disease</th>
<th>Lamellar bone reconstruction</th>
<th>Woven bone</th>
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<tr>
<td></td>
<td>Applique</td>
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<td>T3 to L5</td>
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<td>Osteophytes and sindesmophytes</td>
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<td>S1</td>
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<td>L4 and L5</td>
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<td>Lower Limbs</td>
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<td>Left Foot</td>
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<td>Coxae</td>
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<td>Right ribs</td>
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<td>Ribs fragments</td>
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There is evidence of several lesions due to degenerative joint (or non articular lesion all described on the Table 1, and also probably traumatic lesions and localization and form of periostosis. In particular, the fourth to the eighth (inclusive) right ribs show woven bone at the visceral vertebrae extremities, measuring around 2cm long with a rectangular form. The fifth and sixth right ribs also show lamellar bone remodeling of what looks like to be traumatic lesions, the same is visible in other two ribs, which were impossible to identify the laterality at least.

**DISCUSSION**

Based on the type and distribution of the lesions, the differential diagnostic lead us to Hyperthropic Osteoarthropathy, melorheostosis or tuberculosis, treponematosis, fluorosis, hypervitaminosis A. A more certain diagnosis was the ribs fractures.

There are several forms of Tuberculosis, the ones which could be included on this diagnosis are tuberculosis of the long bones or pulmonar. Neither vertebra nor joint were affected so this forms of TB were immediately discharged. Although TB of the long bones has characteristic osteolytic lesions, began under the periosteum and may spread into the epiphysis of the tibia, ulna, radius, humerus, femur and fibula and affect rarely adults (Ortner and Putschar, 1985; Roberts and Buikstra, 2003; Dabernat and Cruzébi, 2010), the periosteum may respond with new bone formations. The woven bone observed on the ribs may be due to TB or intrathoracic tumor – bronchial carcinoma due to its high prevalence in recent populations. Only ribs radiographic images could discharge one from the diagnosis, once as referred by Santos and Roberts (2006) TB has typical enlargement of the ribs, and according to Marques et al. (2011) metastatic carcinoma lead to lytic reactions on the bone. Therefore the presence of lytic lesions on the ribs can be already undistinguishable due to bone reconstruction.

*Treponematosis* has typical cranial and face lesions, for example *caries sicca*, (Christensen et al., 2011; Rissech et al., 2011) not found on this case and cortical alterations (gummatous lesions) usually tend to be “continuous” and to affect endosteam as well. The long
bones usually affected are the tibiae and the femur, being the periosteum the most reactive zone producing new bone mainly on the distal diaphysis giving the resemblance of a fusiform expansion (Aufderheide and Rodríguez-Martín, 1998). According to the data on the cemetery record the male had medical care since he died at the hospital, therefore less probably he wouldn’t be diagnosed with Syphilis, which beyond the bone lesions is highly disfigurative.

Two metabolic pathologies can almost explain the periostial reactions: Fluorosis and Hypervitaminosis A. Fluorosis and Hypervitaminosis are easily to discharged, the first always affects the vertebra and not only the periosteal bone is altered and also the endosteal is, but the both only affect the axial skeleton (Aufderheide and Rodríguez-Martín, 1998).

Melorheostosis is a skeletal dysplasia, also called Leri’s hyperostotic osteopathy, is a syndrome that cause periosteal reaction almost identical to the one presented, like candle wax, usually affects only one bone or one limb (Leri and Joanny, 1922; Freyschmidt, 2001; Abdullah et al., 2011). Though the similarity, the case presented affects more than one bone and both right and left limbs, this pathology could only explain the left side once the right the periostosis isn’t resembling candle wax.

Hypertrophic Osteoarthropathy explain some of the reaction observed in the lower left limb however the asymmetric lesions when the tibiae are compared cannot be understrood. Rothschild and Rothschild (1998) explained the applique and surface form of the periostium reactions do not appear associated to the same bone however shouldn’t result in asymmetry so much demarked. There are some examples of grafts which lead to asymmetrical HOA, due to infection. Golder and Wolf (2001) reported a case of a man, whose blood cultures analysis were positive for Proteus mirabilis, Gemella haemolysans, Escherichia coli and Streptococcus constellatus due to a graft infection resulting on a asymmetrical HOA. Only with data from the Hospital there would be sure of surgical intervention.
CONCLUSION

The differential diagnosis lead to Hypertrophic Osteoarthropathy due to bilateral type of periosteal bone reactions, mainly applique form in the lower left limbs observed and also the absence of reactive endosteum.

Hypertrophic Pulmonary Osteoarthropathy is the most probable diagnosis. To confirm this diagnostic and the presence of other paleopathologies associated with HOA, apart from the funds, histological sections as well as total skeleton radiology images would be helpful, in particular of the ribs to be sure the presence or absence of intrathoracic cancer (metastatic carcinoma) or chronic intrathoracic infection.

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BIBLIOGRAPHY


