International Journal of Paleopathology 12 (2016) 11–16

Contents lists available at ScienceDirect

International Journal of Paleopathology

journal homepage: www.elsevier.com/locate/ijpp

Case report

Characterization of hypertrophic osteoarthropathy in an identified skeleton from Évora, Portugal, using combined and comparative morphology and microscopy

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ARTICLE INFO

Article history:
Received 24 July 2015
Received in revised form 28 October 2015
Accepted 4 November 2015

Keywords:
Hypertrophic osteoarthropathy
Morphology
Light microscopy
Scanning electron microscopy

ABSTRACT

Hypertrophic osteoarthropathy (HOA) is a bone pathology that can be associated with a number of focal or systemic diseases, particularly those affecting the respiratory system. HOA is characterized by proliferative periostosis of the long bones, especially in their distal and periarticular regions. This report presents a probable case of HOA in the skeleton of an elderly Portuguese male from Évora, Portugal, who died in 1970.

The skeleton was evaluated by morphological, radiological, and histological methods. We found bilateral periosteal proliferation of the tubular bones, remodeling of the phalanges of the feet, and new bone formation on rib visceral surfaces. Bone alterations are more severe on the left tibia and fibula, where lesions display a 'tree bark' appearance, leading to severe thickening of the diaphysis.

Microscopically, we observed deposition of porous woven bone. Our evaluation also considers a differential diagnosis of the lesions, which includes melorheostosis, hypervitaminosis A, fluorosis, thyroid acropachy, tuberculosis, and treponematosis.

1. Introduction

Hypertrophic osteoarthropathy (HOA) is a bone pathology that can be associated with a number of disease conditions. HOA is found mainly in dogs (Headley et al., 2005; Cetinkaya et al., 2011; Lawler et al., 2015) and humans (Golder and Wolf, 2001; Utine et al., 2008), but has been observed occasionally in various other species (Lenehan and Fetter, 1985; Golder and Wolf, 2001; Mair and Tucker, 2004; Ferguson et al., 2008; Guyot et al., 2011). Although HOA was described in 1868 by Friedenreich (as cited in Kuhn et al., 2007), the exact aetiology remains unknown.

Clinically, there are two forms of HOA, the primary, or idiopathic form, and the secondary, formerly called hyperthrophic pulmonary osteoarthropathy. Only the secondary form is described in dogs. The primary form, also called pachyodermoperiostosis or Touraine-Solente-Golé syndrome, is a rare genetic disease that is inherited in an autosomal fashion (Latos-Bielenska et al., 2007), recently mapped to human chromosome 4q33–q34 and to gene mutations encoding 15-hydroxyprostangladin degradation (Uppal et al., 2008; Yao et al., 2009). This form, usually severe, affects primarily males (Aufderheide and Rodriguez-Martín, 1998), appears around the time of puberty, and its progression is limited to the puberal growth period (Christensen et al., 2013).

Secondary HOA is also called Marie-Bamberger syndrome or hyperthrophic pulmonary osteoarthropathy, emphasizing the pulmonary diseases that represent the major human associates of HOA. Among pulmonary diseases carcinomas are the major cause of HOA. In fact, bronchial carcinoma accounts for 80% of human HOA, pleural tumors for 10%, other intrathoracic tumors for 5%, and, rarely, Hodgkin's lymphoma is observed (Atkinson et al., 1976; Aufderheide and Rodriguez-Martín, 1998; Resnick and Kransdorf, 2005). Several studies suggest an association between HOA and tuberculosis (Mays and Taylor, 2002; Assis et al., 2011). Other extra-pulmonary conditions that may be associated with HOA include various gastrointestinal, cardiovascular, hepatobiliary, and endocrine disorders (Bazar et al., 2004; Shih, 2004; Vandemergel et al., 2004; Yao et al., 2009).

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http://dx.doi.org/10.1016/j.ijpp.2015.11.001
1879-9817/

HOA is characterized by deposition of periosteal new bone, especially on the tibia, fibula, ulna, and radius. Subchondral bone is unaffected. Clinically, HOA is characterized by digital clubbing and painful swelling of distal limbs (Jajic et al., 2001; Armstrong et al., 2007; Yao et al., 2009). Proliferative periostosis leads to diffuse periosteal ossification and increased circumference of affected bones. Lesions occur more frequently at mid-diaphysis, tapering toward the proximal and distal bone ends. Radiographically, affected bone may suggest having been "pasted" onto the cortex (identified by a distinct radiolucent line between the original and new bone), or may appear to be a dense part of the original cortex where new bone and normal cortex merge imperceptibly (Rothschild and Rothschild, 1998). Primary and secondary forms of HOA can be present in the same skeleton, but usually not on the same bone (Rothschild and Rothschild, 1998).

The goals of this report are to describe morphological, radiological, and histological findings of HOA, to consider the differential diagnosis of the observed lesions, and to discuss possible aetiologies.

2. Materials and methods

2.1. Subject

The case report (CEIE109) and specimen belong to the Identified Skeletal Collection of Évora, curated at the University of Évora, Portugal. The collection comes from the Cemitério dos Remédios, a city cemetery. The subject of this report was identified as a male, 73 years old, who died in 1970. The skeleton is very well preserved and complete, as shown in Fig. 1.

The Identified Skeletal Collection of Évora contains 160 skeletons of individuals who died during the 19th and 20th centuries (90 males, 70 females) and upon which research is still in progress. Data that are maintained for each skeleton of this collection come from inhumation registrations and include: age at death (mean age 60 years, range 3–91 years), sex, nationality, occupation, and, in some cases, the cause of death.

2.2. Macroscopic evaluation

All the bones were surveyed by naked eye inspection and with a magnifying glass in order to identify and describe lesions.

2.3. Radiological evaluation

The bones exhibiting the most severe lesions, the left tibia and fibula, were submitted to radiographic assessment which was performed with a digital system Mammo Diagnost UC system (Philips), at 28 kV and 25 mA, coarse focus, using Kodak Min-R screen film.

2.4. Histological evaluation

For histological evaluation, 2–3 cm samples of the 7th right rib, from the area where lesions are evident, were cut transversally to the long axis with a bone saw [Materials Science (NW) Ltd., Settle, England] and embedded in resin (Technovit® 9100, Heraeus Kulzer, Germany) according to the manufacturer's instructions.

The samples were placed in hermetically sealed containers and left to polymerise at −20 °C during 5 days. After polymerization 80 μm transverse sections were obtained using a saw microtome (Leica 1600, Germany). The undecalcified and unstained sections were observed through a transmitted light microscope Nikon Eclipse 600 (Nikon, Kanagawa, Japan), and digital pictures were collected with a Nikon DN100 camera (Nikon, Kanagawa, Japan).

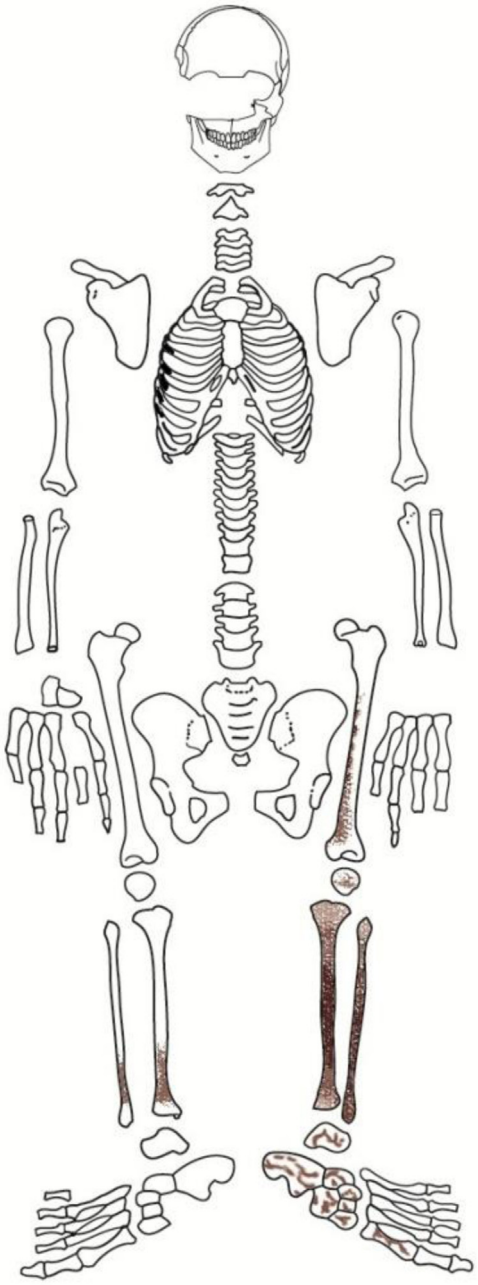

Fig. 1. Drawing indicating the preserved parts of the skeleton. Black shading represents more severe lesions and grey shading more mild lesions. All bones were surveyed visually and with a magnifying glass to identify and describe lesions.

2.5. Scanning electronic microscopy

Scanning electron microscopy (Hitachi TM 3000, and SU-70, 30 keV) was performed to study the affected bone surface morphology of the vertebral extremity of the 7th right rib. No previous preparation of the rib sample was needed.

3. Results

3.1. Macroscopic and radiological evaluations

The pathological changes were observed on the right ribs and lower limbs. The fourth through the eighth right ribs display a thin gray layer, not demarcated from the underlying cortex, of woven