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Case Report

Secondary hypertrophic osteoarthropathy in a male from the Early Medieval settlement of Lauchheim, Germany

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ABSTRACT

Hypertrophic osteoarthropathy (HOA) is rarely diagnosed in archaeological human skeletons. Here, we report on the well-preserved skeleton of a middle-adult man from the early Medieval settlement site of Lauchheim (Germany) that exhibits pronounced multi-layered shell-like periosteal new bone formation in a bilaterally symmetric fashion on the long bones, the skeletal elements of the pelvis and those of the pectoral girdle. In addition, the two distal phalanges recovered show signs of osteoclastic resorption on their distal tuberosities. The distribution and morphology of the observed lesions are consistent with a diagnosis of HOA. The adult age at death of the individual and the co-occurrence of "healed" and "active" lesions suggest a secondary form of HOA. Given that only skeletal remains were available for study, the underlying (pulmonary or non-pulmonary) primary disease cannot be definitively ascertained in the present case. No osseous changes were found on the ribs, but signs of osteoclastic resorption were observed on the dorsal surface of the sternal body, which might indicate a retrosternal or mediastinal location of the primary disease. Thus far, only a few archaeological case studies of secondary HOA reported signs of the presumed underlying primary disease, which was of a pulmonary nature in each of the individuals.

1. Introduction

Hypertrophic osteoarthropathy (HOA) is a pathological condition that is characterized by abnormal proliferation of skin, digital clubbing ("Hippocratic fingers" or "drumstick fingers"), periostosis of the tubular bones, and synovial effusions (Yap et al., 2017). The condition has previously been known under several names, some of them connecting it to certain underlying diseases (e.g. hypertrophic pulmonary osteoarthropathy). Based on a terminological consensus in 1992 (Martinez-Lavin et al., 1993), the term hypertrophic osteoarthropathy is currently preferred in the medical literature. Besides humans, the condition has, under various names, also been reported in several other mammalian species (for a recent review see Lawler et al., 2015).

HOA can occur as a primary or a secondary entity (Martinez-Lavin et al., 1993; Yap et al., 2017). Primary HOA is a rare hereditary disease with an early onset (during childhood or adolescence) that affects males more frequently than females, with a male-to-female ratio of about 7:1 (Yap et al., 2017; Zhang et al., 2013). Primary HOA (also known as idiopathic HOA or pachydermoperiostosis) is self-limiting after adolescence and characterized by disseminated skin hypertrophy (Zhang et al., 2013). Secondary HOA is much more frequent than primary HOA, accounting for 95%–97% of all cases (Yap et al., 2017). It usually affects adults, although a few cases of secondary HOA in children have been reported, e.g. in association with mediastinal Hodgkin lymphoma (Ansari et al., 2010; Drakonaki et al., 2012). Secondary HOA is associated with a wide spectrum of primary diseases. Although most of these affect the lungs, cardiovascular, pleural, and mediastinal origins of secondary HOA have also been described, and even extrathoracic (e.g. gastrointestinal) diseases can lead to secondary HOA (Silva, 2006; Yap et al., 2017). Today, secondary HOA is frequently associated with a malignant condition, predominantly non-small cell lung cancer, and in that case can be considered a paraneoplastic syndrome (Yap et al., 2017).

The pathogenesis of HOA is a matter of debate. It is generally

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believed that increased blood flow to the affected regions causes abnormal proliferation of connective tissue in the skin and periosteal new bone formation (PNBF). The neurogenic pathway hypothesis posits that a stimulation of the vagus nerve initiates reflex vasodilation and increased blood flow to the extremities. In contrast, the humoral pathway model stresses the role of growth factors and cytokines, such as platelet-derived growth factor (PDGF), prostaglandin E_2 and vascular endothelial growth factor (VEGF) in promoting vascularity and fibroblast activity, resulting in excess soft tissue and bone formation (Yap et al., 2017). VEGF and PDGF are overexpressed in chronic hypoxic conditions that accompany different pulmonary and heart diseases (Yao et al., 2009; Yap et al., 2017).

A number of palaeopathological studies reported changes in human skeletal remains consistent with a diagnosis of HOA, pointing to the antiquity of the condition (Aufderheide et al., 1998). Identifying HOA in ancient skeletal remains is, however, a challenging task since the soft tissue characteristics that contribute to the diagnosis in clinical cases, such as abnormal skin formation, digital clubbing, and joint effusions (Resnick and Niwayama 1995a), are not available. The principal characteristic on which the diagnosis can be based is the presence of periosteal new bone. However, this is not a pathognomonic feature since a number of other diseases and pathological conditions can also cause PNBF (Weston, 2008). In addition to PNBF, other skeletal manifestations sometimes encountered in HOA include osteolysis on phalangeal tufts (tuberosities of the distal phalanges), periarticular osteoporosis, and periarticular osteophytosis (Resnick and Niwayama, 1995a). A careful differential diagnosis is therefore mandatory to distinguish HOA from other conditions, and the palaeopathological diagnosis must be based on clearly defined diagnostic criteria.

The type and distribution of skeletal changes in HOA have been described in detail in a number of older studies and textbooks of pathological anatomy (e.g. Axhausen et al., 1937; Gall et al., 1951; Haubrich, 1972). On this basis, it should generally be possible to distinguish HOA from other conditions causing PNBF and, as a consequence, to diagnose HOA with a certain degree of confidence in skeletal remains. Osseous features consistent with a diagnosis of HOA are: 1) the presence of periosteal new bone on the tubular bones of the appendicular skeleton, 2) a shell-like character of the periosteally apposed bone layer(s), 3) absence of alterations of the compact bone, the endosteal surface of the bone, and the marrow spaces of the affected bones, 4) a pronounced bilateral symmetry of the osseous lesions, and 5) an overall increase in lesion severity from proximal to distal within the limbs and from the upper to the lower extremities (Axhausen et al., 1937; Gall et al., 1951; Haubrich, 1972; Resnick and Niwayama, 1995a). Evaluation of these features requires almost complete skeletons, a precondition that is not always met in archaeological specimens.

Thus far, only a few presumed cases of HOA have been published in the international palaeopathological and bioarchaeological literature. The earliest known case is the largely complete La Ferrassie 1 Neanderthal skeleton (Fennell and Trinkaus, 1997). In archaeological skeletons of anatomically modern humans, changes consistent with HOA have been described in a young male from the Neolithic of Hungary (Masson et al., 2013), an individual from the Canary Islands (dating to 1000 BP; González-Reimers et al., 2015), a young male from the Sudan dating to the 2nd-3rd century CE (Binder and Saad, 2017), two individuals from pre-Hispanic Mesoamerica (Martinez-Lavin et al., 1994), and a few individuals from the Medieval period of Europe (Arendt and Ullrich, 1970; Christensen et al., 2013; Gladykowska-Rzeczycka and Prejzner, 1993; Mays and Taylor, 2002). In addition, a putative case from ancient Peru dating to about 1000 CE has been reported (Allison et al., 1976). In some of these cases, however, the diagnosis of HOA is debatable. Reasons for this include the incompleteness of the skeletons and lacking radiographic information on the marrow spaces and/or the compact bone of the affected skeletal elements.

Although nowadays HOA is most frequently associated with lung diseases, it seems unwarranted to *a priori* assume such an association in each case of HOA diagnosed in archaeological skeletons given the existence also of non-pulmonary diseases that can cause HOA. Thus far, only three studies of archaeological human skeletons provided evidence for the underlying (primary) disease. In a Neolithic (Masson et al., 2013) and two medieval specimens (Mays and Taylor, 2002), morphological and biomolecular findings pointed to tuberculosis as the cause of HOA. In a further case, deposition of woven bone on the visceral surface of the ribs was interpreted as indicative of an underlying chronic pulmonary disease (Binder and Saad, 2017).

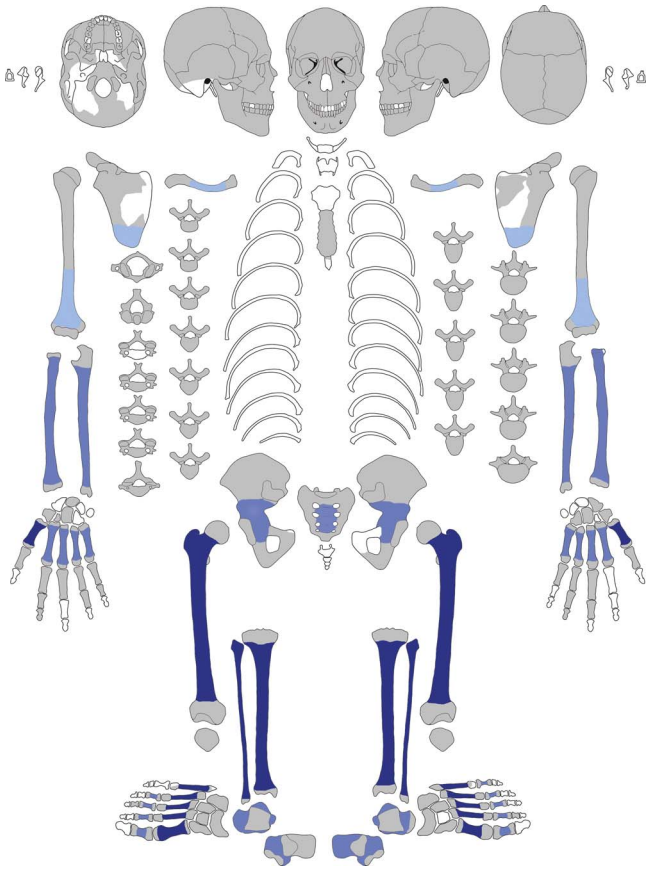

Fig. 1. Diagrammatic illustration of the Lauchheim 39 skeleton. Preserved parts are shaded except for the ribs, which were almost completely present but fragmented. Skeletal elements affected by PNBF are highlighted in blue with the color tone indicating lesion severity (light blue for mild, medium blue for moderate, and dark blue for severe changes). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The present study reports findings on the skeleton of a middle-adult man from the Early Medieval site of Lauchheim, Germany. The almost complete and well-preserved skeleton exhibits lesions consistent with a diagnosis of secondary HOA. Signs of extended osteoclastic resorption on the dorsal surface of the sternal body are discussed as a possible consequence of an underlying disease. The skeleton also exhibits changes in the lumbar region of the vertebral column that are atypical for HOA and most likely represent a further pathological condition.

2. Materials and methods

From 1986 to 2005, a large Early Medieval (Merovingian period; 6th to early 8th century CE) cemetery, comprising about 1300 burials, was excavated at Lauchheim (federal state of Baden-Württemberg, Germany; 48° 52′ N, 10° 14′ E). An associated settlement was also excavated and revealed some additional burial groups with another 78 skeletons from the Merovingian period. The skeleton described here was found in situ (burial 39) and excavated in 1999 as part of one of