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A probable case of metastatic carcinoma in the medieval Netherlands

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ABSTRACT

Despite recent considerable gains, our knowledge of cancer in antiquity is still limited. This paper discusses an adult individual from a Dutch medieval hospital site who demonstrates osteoblastic and osteolytic lesions on the ribs, scapula, clavicle, and vertebrae. The morphology, radiographic appearance, and distribution of the skeletal lesions suggest that this individual was affected by metastatic carcinoma. This case increases the number of publications that present an osteoblastic and osteolytic response to cancer and contributes to the body of evidence for archaeological neoplastic disease. For the Netherlands, this individual presents the first published case of probable metastatic carcinoma with mixed skeletal lesions.

1. Introduction

In modern times, cancer is the second leading cause of death worldwide (World Health Organisation (WHO, 2018). In 2015, the disease was responsible for 8.8 million deaths, meaning that one in six deaths was due to cancer (Bray, 2014; World Health Organisation (WHO, 2018). As a result of the second epidemiological transition, many countries witnessed a decrease in infectious disease and a concomitant increase in mortality associated with chronic, non-communicable diseases, such as cancer (Bray, 2014; Harper and Armelagos, 2010). In the last decades, cancer prevalence has also increased in low-income countries as a result of population growth and increasing ages-at-death as well as the adoption of certain behavioural and lifestyle habits common in industrialised countries such as the consumption of calorie-dense foods, smoking, and physical inactivity (Bray, 2014). This has drastically increased the global cancer burden (Bray, 2014; Jemal et al., 2010).

Even though more knowledge on neoplastic diseases is gained every day, still little is known about cancer in antiquity (Binder et al., 2014; Capasso, 2005; Marques et al., 2017). Its infrequent observation in archaeological human remains from past populations has resulted in the misconception that neoplastic diseases are only associated with modern living conditions and longer life spans (Binder et al., 2014; Lieverse et al., 2014; Marques et al., 2017). Although indeed an uncommon encounter in past populations, cancer is not a solely modern disease. Bony lesions associated with cancer in hominins appear to date back to 1.7 million years ago (Odes et al., 2016) and in the last 20 years there has been an increase in reported cases from archaeological remains dating to various time periods (Assis and Codinha, 2009; Binder et al., 2014; Caruso et al., 2017; Lieverse et al., 2014; Marques et al., 2017; Melikian, 2006; Schultz et al., 2007; Smith, 2002; Wasterlain et al., 2011). However, publications on neoplastic diseases in archaeological skeletons remain scarce. To contribute to the growing body of evidence for cancer in past populations, this paper presents a case of probable metastatic carcinoma from the medieval Netherlands.

2. Materials and methods

The individual (S4051V1051) with lesions suggestive of metastatic carcinoma was found in a cemetery belonging to a medieval hospital in Kampen, the Netherlands (Fig. 1). The infirmary, dedicated to St. Gertrude, was established in CE 1382 and was in use until 1598. Historical records indicate that the hospital initially functioned as a place where travellers and the sick were cared for temporarily. Later however, the infirmary also offered permanent housing to the chronically ill and elderly (Klomp, 2016). In preparation for construction on the site, the area of the infirmary and associated cemetery were excavated in 2014 by archaeologists from the municipality of Zwolle and a team from the Laboratory for Human Osteoarchaeology, Leiden University. Although a large part of the cemetery was already disturbed by previous construction, a total of 89 primary inhumations and many unassociated human skeletal elements were recovered (Klomp, 2016; Schats, 2016). All primary inhumations have been analysed osteologically (see Table 1). The individual who is the subject of this paper was poorly preserved and incomplete; only fragments of the left scapula, left clavicle, ribs, and one thoracic neural arch remain (Table 2). Therefore,

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Fig. 1. Map of the Netherlands. Kampen is indicated in light grey.

Table 1
Sex and age-at-death distribution Kampen osteological collection (n = 89).

Age-at-death in years	Males		Females		Indeterminate		Total	
	n	%	n	%	n	%	n	%
< 0							0	–
0–3							0	–
4–12					5	–	5	5.6
13–18					6	–	6	6.7
19–25	5	33.3	7	46.7	3	20.0	15	16.9
26–35	12	75.0	3	18.8	1	6.3	16	18.0
36–45	10	52.6	7	36.8	2	10.5	19	21.3
46+	8	72.7	3	27.3	0	–	11	12.4
Indet.	7	41.2	4	23.5	6	54.5	17	19.1
Total	42	47.2	24	27.0	23	25.8	89	100

reliable estimations of age-at-death and sex were not possible. However, the morphology of one unidentified sternal rib end (phase 5–6, (Işcan et al., 1984)) indicates that the individual was probably a middle to old adult (35+ years of age-at-death).

The skeletal remains were examined using gross inspection following the standard palaeopathological guidelines (Ortner, 2003; Waldron, 2009). The pathological changes were described, photographed, and measured whenever possible. Additionally, radiographs were taken of the skeletal remains using a handheld Nomad Pro x-ray (75 kV, 2.0 μA, exposure: 0.1–0.2 s.).

3. Results

3.1. Gross examination

All surviving bones of this individual display osteolytic lesions and new bone formation located both subperiosteally and intramedullary. An overview of all skeletal lesions is presented in Table 2. The left scapula (Fig. 2) shows diffuse and small osteolytic lesions with sharp margins, ranging from 0.5 to 1 mm in size, with surrounding reactive bone on the anterior and posterior lateral border and on the inferior angle resulting in an irregular surface appearance. The supraspinous, infraspinous, and subscapular fossae also display new subperiosteal bone formation which has a spiculated appearance, but with fewer osteolytic lesions (Fig. 2). The patches of new bone formation range from 15 to 23 mm in size. The glenoid fossa, besides showing early indications of osteoarthritis, does not appear to be affected by this pathological process.

In total, 21 rib fragments were recovered, all of which appear to be from the left side of the body, although not every piece can be sided due to the substantial fragmentation. The rib fragments demonstrate subperiosteal and intramedullary new bone formation and show destructive lesions on both visceral and exterior surfaces. The appearance of the exterior surface is less irregular and mainly displays a diffuse osteolytic process with ill-defined margins (Fig. 3a–b). The small osteolytic lesions on the exterior surface perforate the cortex and are sharp and rounded, ranging in size from 1 to 6 mm. The visceral surface shows more reactive bone deposition extending across the complete fragment, as well as larger osteolytic lesions (8–10 mm) with round margins, which are mainly concentrated in the costal groove (Fig. 3c–e). Additionally, four of the rib fragments show transverse fractures of the body (Fig. 3f), most of which are healed, with possible non-union in one instance but this difficult to determine due to taphonomic damage. Although impossible to judge definitively, the many rib fractures may be related to the pathological process responsible for the other skeletal lesions.

An unidentified neural arch fragment, most likely thoracic, shows major destruction of the cortical bone surface as well as marked new bone formation (Fig. 4a). The posterior surface is mainly affected but the anterior surface also shows a small area of destruction. The lateral end of the left clavicle (Fig. 4b) also appears affected by the pathological process. The superior aspect shows only a few small osteolytic lesions (0.5–1 mm), while the inferior aspect is irregular with multiple, slightly larger osteolytic lesions with rounded margins (1–2 mm).

3.2. X-ray examination

The x-ray images confirm that the skeletal lesions have a mixed character: the radiographs show areas of bone loss and clear regions with increased radiodensity. There is an overall loss of definition in the internal bone architecture. Osteolytic lesions (with moth-eaten margins) are especially apparent on the images from the rib fragments, however, there are also clear areas with sclerosis (Fig. 5a–b). Radiographs show destruction of most of the original cortex of the rib fragments and the mottled appearance of the ribs points to disorganised bone formation in the medullary cavity. In comparison to a non-pathological rib from another individual from the same site, there appears to be an increase in radiodensity (Fig. 5c). The scapula also shows strong evidence for both osteolytic and osteoblastic lesions. On the inferior portion of the lateral border, osteolytic lesions are particularly apparent, but the entire bone shows evidence for the deposition of disorganised new bone on the internal aspect (Fig. 5d). The clavicle fragment shows retention of normal cortical structure in most parts, however, the internal bone architecture appears disorganised and demonstrates increased radiodensity and osteolytic foci (Fig. 5e). The neural arch fragment (Fig. 5f) also has a mixed character on x-ray with clear areas of increased radiodensity.

4. Discussion

4.1. Differential diagnosis

The disease process in this individual is characterised by osteolytic activity as well as marked irregular periosteal and endosteal new bone formation. On x-ray, it is clear that there is an increase in radiodensity