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SHORT REPORT

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Tumour-like lesions in a Late Bronze Age skeleton from Gonur Depe, Southern Turkmenistan

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Abstract

The article describes tumour-like lesions in a Bronze Age skeleton from Southern Turkmenistan. The combination of pathological manifestations observed in the skeleton does not permit making exact conclusions. Based on the skeletal lesions, malignant bone tumour (chondrosarcoma or parosteal osteosarcoma) seems to be the most feasible diagnosis. If this diagnosis is correct, the skeleton represents one of the earliest cases of primary malignant tumours known to date.

KEYWORDS

Bronze Age, paleopathology, tumour-like lesion, Turkmenistan

1 | INTRODUCTION

Primary malignant tumours have been reported in numerous paleopathological publications (e.g., Arnay-de-la-Rosa et al., 2015; Arrieta, Mendonça, & Bordach, In press; Aufderheide, Ragsdale, Buikstra, Ekberg, & Vinh, 1997; Czarnetzki & Pusch, 2000; Ferrante di Ruffano & Waldron, in press; Gładykowska-Rzeczycka, 1997; Kelln, McMichael, & Zimmermann, 1967; Ortner, Ponce, Ogden, & Buckberry, 2012; Ruffer & Willmore, 1914; Smith-Guzmán, Toretsky, Tsai, & Cooke, in press; Strouhal, Vyhnánek, Horáčková, Benešová, & Němečková, 1997; Suzuki, 1987). This paper describes a case of possible parosteal osteosarcoma or chondrosarcoma which is probably one of the earliest known cases in the Late Bronze Age archaeological population from Gonur Depe (Southern Turkmenistan). It should be noted that paleopathological cases of malignant neoplasms are extremely rare in Turkmenistan in general. Two medieval skulls from Chakan-depe and Serakhs-Baba with possible metastatic carcinoma were studied by O. Babakov (2008).

Gonur Depe is a unique and one of the largest settlements of the Bactria-Margiana archaeological complex (also referred to as the Oxus civilisation) and is probably the capital city of the ancient state of Margush where more than 200 sites have been found (Gubaev, Koshelenko, & Tosi, 1998; Sarianidi, 2005, 2007). The site is located 85 km north from Bayramaly city in the South-eastern part of the Karakum desert. The C14 data from different parts of this site reveal that Gonur Depe was inhabited between 2300 and 1500 cal BCE (Sarianidi, 2005, 2007; Zaytseva et al., 2008). The skeletal sample from Gonur Depe includes human remains from nearly 5,000 tombs. A part of this sample was studied and published previously (cf. Babakov et al., 2001; Dubova & Rykushina, 2007; Kufterin & Dubova, 2008, 2013; Sperduti, Bondioli, & Macchiarelli, 2002), but only about 530 individuals from relatively late burials in Gonur Depe have been studied paleopathologically (mostly based on macroscopic methods). These materials are being prepared for publication.

2 | MATERIAL AND METHODS

The skeletal individual described in this study was excavated from Tomb 4449 which was situated at the Area 12 of the so-called "ruins" (a group of relatively late burials) of Gonur-depe, excavated in 2015. The skeletal remains from the Gonur Depe "ruins" are mainly dated to the middle of the second millennium BCE. Tomb 4449 was not apparently different from other burials at the Area 12 for which north oriented shaft graves and a right side position of the buried are typical. Grave goods are typical for the ordinary burials and included three ceramic vessels, one ceramic plate, and a fragment of a terracotta figurine. There was a skeleton of a goatling in the legs of the buried. The skeleton from Tomb 4449 is poorly preserved: The main part of the neurocranium and some long bones are fragmented (Figure 1).

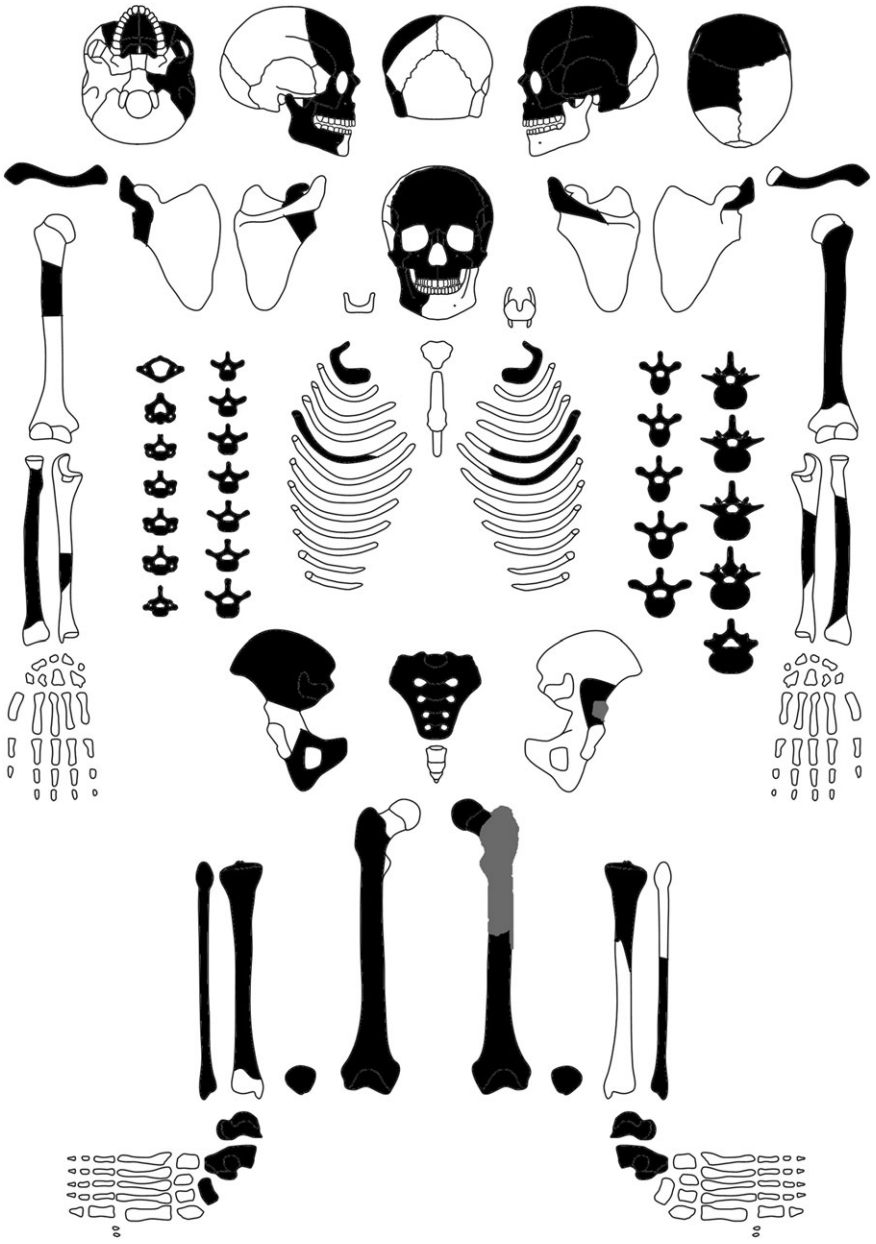

FIGURE 1 Skeletal inventory diagram showing the elements recorded as present for Tomb 4449 (black) and those with evidence of tumour-like lesions (grey)

Therefore, some parts of the skeleton were restored using polyvinyl acetate emulsion and wax-colophony mastic.

Sex and age of the individual were determined using standard methods (Buikstra & Ubelaker, 1994). Gross visual paleopathological examination was carried out following Aufderheide and Rodriguez-Martin (1998), Ortner (2003) and Waldron (2009). Additionally, X-ray and computed tomography (CT) images were obtained at the Scientific and Clinical Centre of Oncology (Ashgabat, Turkmenistan).

3 | RESULTS

The gross osteological examination suggests that the skeletal remains from Tomb 4449 belonged to a 35- to 50-year-old male (based on pubic symphyseal and auricular surface morphology). His stature, estimated from the length of the right fibula using the Trotter & Gleser formula for Whites (Trotter & Gleser, 1958) was approximately 165 cm (average male stature at Gonur Depe was 168.3 ± 5.6 cm [Dubova & Rykushina, 2007: 314]). Muscle and ligament attachment sites on all available long bones are developed moderately or weakly. Cranial morphology of the individual is typical for southern Caucasoid (so-called "Mediterranean") type and fit well into the wide range of morphological variation observed in the Gonur Depe sample (Babakov et al., 2001).

A number of pathological changes and stress markers were observed on the skeleton. First, the individual suffered from virtually all dental diseases, including dental caries, linear enamel hypoplasia, dental abscesses, antemortem tooth loss, and dental calculus. However, patterns of dental attrition are corresponding to the skeletal age of this individual. In fact, a high frequency of dental diseases is one of the most characteristic features of health status of the Gonur Depe archaeological population (Babakov et al., 2001; Kufterin & Dubova, 2013). A number of traumatic injuries were identified as well, including healed fractures of the ribs and nasal bones which might evidence an interpersonal violence. The last thoracic vertebra display signs of a compression fracture. The vertebra is fused with the

adjacent superior and inferior vertebrae by ossification of the anterior longitudinal ligament that bridges the vertebral bodies. Finally, marked osteoarthritis of the knee joints and periostitis of the tibia and fibula were observed. There were no other non-specific lesions or stress markers on the available skeletal elements.

3.1 | Tumour-like lesion description

The pathological changes on the left femur (Figure 2) are discussed below in detail. An expansive proliferative lesion, approximately 164 × 98 × 97 mm in size, can be seen on the proximal third of femoral diaphysis. The lesion encompasses the bone uniformly (Figure 3). The upper edge of the newly built bone is located in the area of the *trochanter major*, the lower edge—at a distance of about 287 mm proximal from the articular surface of the *epicondylus lateralis*. Macrostructure of the lesion can be described as an irregular heterogeneous dense nodular mass partially covered with cancellous bone. On the posterior surface, about six large (up to 12 mm) lytic foci that penetrate the outer cortex are observed. The margins of the lytic lesions show some remodelling. Deposits of spiculated reactive new bone radiate continuously from these foci of cortical destruction, mainly in the distal part of the lesion. These deposits created a highly irregular topography of the lesion ("c" on the Figure 3). Length of the bone is not apparently changed. A similar bone proliferation is probably present on the fragment of the left ilium (dimensions are not determined, owing to poor preservation due to the taphonomic factors; Figure 4). There is no specific bone proliferation on the sacrum and vertebrae.

3.2 | CT image

A massive lobular bone proliferation can be seen in the CT image in anteroposterior projection of the proximal third of the left femoral diaphysis. The lesion is better observable along the posterior bone contour, where the proximal third of the diaphysis is encased by an irregularly shaped osseous mass (Figure 5). The mass is predominantly detached from the diaphysis, attaching at a single point on the proximal part of the lesion, as indicated by the thin radiolucent line separating the mass. The CT image also shows that the newly built bone is associated with destructive processes within the bone cortex. Thus, there probably was an invasion into the medullar cavity. The pattern of margins can be described as invisible; the bone is encased by necrotic mass with increased density (Ragsdale, Campbell, & Kirkpatrick, In press). The type of periosteal reaction can be characterised as continuous with a destruction of underlying cortex (lobulated or ridge shell type; Ragsdale et al., in press). The bone masses consist of separate "spherical" formations with well-defined uneven margins, in some cases divided by strips of abnormal bone tissue in different directions and with massive bone plates. Thus, the CT image demonstrates an irregular distribution of osteolysis and

FIGURE 2 Left femur with probable parosteal osteosarcoma or chondrosarcoma. General view. Photo by V.V. Kufterin

FIGURE 3 Proximal left femur with probable parosteal osteosarcoma or chondrosarcoma: a = fibroblastic, irregular component, b = chondroblastic, nodular component, c = osteoblastic, spicula-forming component. Photo by V.V. Kufterin

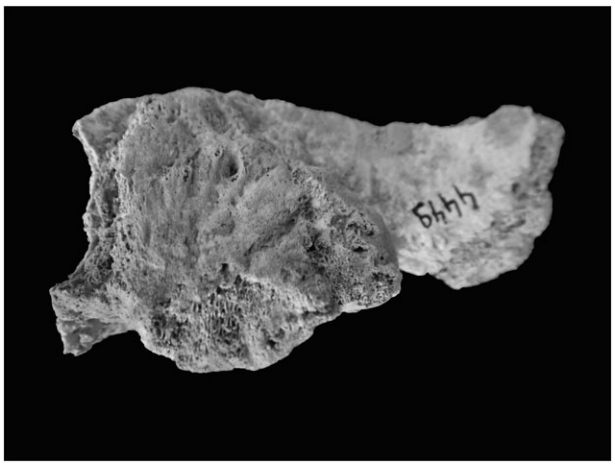

FIGURE 4 Tumour-like bone lesion on the fragment of the left ilium. Photo by V.V. Kufterin

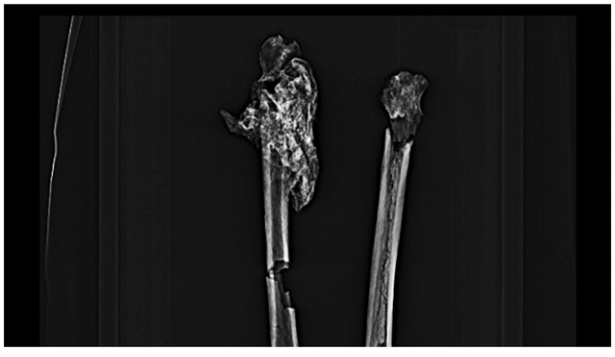

FIGURE 5 Computed tomography image of the left (with tumour-like lesion) and right (normal) femora of the individual from Tomb 4449

osteosclerosis, which is manifested in focal lucencies clearly visible against a background of increased radiodensity (Ragsdale et al., in press).

3.3 | Differential diagnosis

Morphological features of the lesion suggest the following possible diagnosis: myositis ossificans traumatica or bone tumour. Therefore, the main aim of our differential diagnostic procedure of this case was to differentiate between a traumatic lesion (myositis ossificans or heterotopic ossification traumatica) and neoplasms (metastatic prostate cancer, osteosarcoma, and chondrosarcoma). Such differentiation is not straightforward, because some neoplasms "… needed to be differentiated from heterotopic ossification traumatica (HOT) and this may sometimes prove problematic, especially as they will lack the cartilaginous cap in the dry bone" (Waldron, 2009: 175).

At the first stage of differential diagnosis, our aim was to exclude myositis ossificans traumatica, because tumours (particularly parosteal osteosarcoma) and myositis are usually confused. In this case, the absence of a thin band of lucency clearly separating the formation from adjacent bone along its entire length is evidence against a post-traumatic myositis. Additional evidence against myositis ossificans is the unevenly distributed X-ray density of the ossification, medullar involvement and destruction of the original cortex (Table 1; cf. Burgener, Kormano, & Pudas, 2008).

TABLE 1 Differential diagnosis of the paleopathological case from Tomb 4449 (Gonur Depe) based on X-ray and CT examination[1]

Symptom	Parosteal osteosarcoma	Myositis ossificans	Tomb 4449
A thin band of lucency along the entire length of the lesion	no	yes	no
Uniform X-ray density of ossification	no	yes	no
Clear delimitation of peripheral areas of ossified lesion	no	yes	yes

[1]Adapted from Burgener et al. (2008).

Based on the age at death and sex of the individual, morphology and localisation of pathological changes, we hypothesise the three most probable paleopathological "diagnoses": metastatic prostate cancer, osteosarcoma (most likely parosteal or juxtacortical variant), and chondrosarcoma (cf. Siek, 2014). The following traits are evidence of malignant nature of the pathological process: irregular shape and structural pattern of the neoplasm, abnormal degree of calcification, "erosion" and unevenness of the tumour contours (Burgener et al., 2008). Differential diagnosis is outlined in Table 2, from which it is evident that the least probable diagnosis is metastatic prostate cancer.

The carcinomic metastases are least probable "diagnosis," because there are no widespread periosteal reactions on the skeleton and, in general, the defect is localised abnormally. However, prostate cancer cannot be reliably excluded because tumour-like lesion is observed on the fragment of the left ilium as well. Compressed fracture of the last thoracic vertebrae may also be secondary to lytic metastases (Ortner, 2003: 535). Another possible reason for abnormal growth on the pelvis is osteosarcoma, which "… can develop in multiple sites and can metastasize to other bones, producing multicentric osteosarcoma" (Ortner et al., 2012: 246). Differentiating between osteosarcoma and chondrosarcoma is more difficult in this case. The difficulty is not only due to the overall complexity of differential diagnosis on skeletal materials, in particular when it comes to neoplasms (Brothwell, 1967, 2012; Ortner, 2003; Ragsdale et al., in press), but also because of the wide variety of X-ray and morphological features of osteogenic sarcomas (Burgener et al., 2008). However, taking into account skeletal age of the individual, chondrosarcoma seems to be a more likely diagnosis. It might emerge as a result of a malignant transformation of a previously benign tumour (Ortner, 2003: 526), because in mature and senile individuals osteosarcoma is more often observed as secondary to Paget's disease (deforming ostosis; Aufderheide & Rodriguez-Martin, 1998: 377; Ortner, 2003: 524). No traits of Paget's disease were identified on the studied skeleton. In addition, it is necessary to emphasise that periosteal osteosarcoma is an extremely rare condition as it only occurs in approximately 1% of

TABLE 2 Differential diagnosis of the paleopathological case from Tomb 4449 (Gonur Depe), gross anatomical features[1]

Differential diagnosis	Metastatic prostate cancer	Osteosarcoma	Chondrosarcoma	Tomb 4449
Age	Increased risk over the age of 40–50 years	10–30 years	30–60 years	35–50 years
Sex	males	males, or no predilection	males, or no predilection	male
Anatomic region predilection	pelvis, sacrum, lumbar, and thoracic vertebrae	distal femur, proximal tibia, proximal humerus	pelvis, long bones (proximal and distal femur, proximal humerus), ribs, scapula	pelvis, proximal femur
Appearance of mass	nodular, dense bone or mixed with osteolytic and osteoblastic lesions	highly variable	lobulated, dense bone	lobulated, dense bone
Medullary involvement	yes	depends of the type	very rare	probably yes
Cortical destruction	yes	yes	yes	yes
Lesion type	sclerotic/osteoblastic	osteoblastic	osteoblastic	osteoblastic
Periosteal new bone	Widespread throughout the skeleton	none	none	tibia and fibula, distal metaphysis

[1]Adapted from Ortner (2003), Waldron (2009: 179), Siek (2014: 159), and Ferrante di Ruffano and Waldron (in press).

all osteosarcomas (Aufderheide & Rodriguez-Martin, 1998: 379). However, parosteal osteosarcoma "… is two to four times more common than periosteal variant, and occurs in slightly older adults" and "sometimes simulating myosistis ossificans" (Aufderheide & Rodriguez-Martin, 1998: 379). Atypical localisation of the discussed lesion also does not allow us to insist on the diagnosis of osteosarcoma (cf. Ferrante di Ruffano & Waldron, in press). Diagnosis of chondrosarcoma is also problematic, because this type of cancer is difficult to diagnose in a dry skeleton without using histological analysis (Waldron, 2009: 181). Thus, the nature of the lesions represented by the studied individual precludes an exact diagnosis. Therefore, it is preferable to use a broader diagnosis and attribute the observed condition as a "tumour-like lesion" (Brothwell, 2012; Marques, Santos, & Cunha, 2013).

4 | CONCLUSIONS

Summing up, we can conclude that the probable case of a chondrosarcoma or parosteal osteosarcoma described in this study is the second known case of a malignant tumour observed in the Gonur Depe skeletal sample. A possible case of multiple myeloma was previously diagnosed by V.V. Kufterin (2011). In addition, a case of multiple osteochondromas was described on another juvenile skeleton from Gonur Depe "ruins" (Kufterin, 2008). Unfortunately, by the present time paleopathological examination has been carried out only for a part of the Gonur Depe sample (530 skeletons from more than 5,000 excavated burials). For this reason, further studies can reveal new cases of neoplastic (and other uncommon) diseases in the Gonur Depe archaeological population. On one hand, our finding expands and complements existing views regarding the peculiarity of the pathological status of this ancient population (e.g., Dubova & Rykushina, 2007; Kufterin & Dubova, 2008, 2013). On the other hand, it provides new data about geographical and chronological dispersal of malignant tumours in antiquity (Capasso, 2005; Capasso & Di Tota, 1996; Strouhal, 1994; Strouhal & Němečková, 2009). However, in this paleopathological case, it is difficult to reliably differentiate between the two neoplasms: parosteal osteosarcoma and chondrosarcoma. It should be also noted that myositis ossificans cannot be completely excluded. This condition mimicking malignant bone tumours and can affect adjacent bones (as the left ilium in the described case), and it may grow to a very considerable size. It should be pointed out as well that histological, more detail radiographic and, probably, biomolecular analyses might be useful for specifying the diagnosis.

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