Short Report: Paleopathology

Could the study of ancient human remains help the modern clinic? Interpreting multiple osteomas, a difficult challenge

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Abstract. Some pathological features may be underestimate in clinical literature, especially the asymptomatic ones. This is the case of multiple osteomas, benign and primary bone tumors. As a matter of fact, nowadays their incidence is 2-3% of bone tumour cases. Conversely, their prevalence in the archaeological sample seems to be greater. We describe three medieval subjects from Caravate (Varese), showing cases of multiple osteomas. From these cases, our interest arose towards the relationship between prevalence and incidence of multiple osteomas. Sex determination and age estimation were performed with the standard anthropological methods, pathological features with both, clinical and paleopathological literature. We diagnosed the condition of multiple osteoma, proposing all possible pathologies related to the development of multiple osteomas. This work, in which we briefly present the state of the art of our knowledge, is a starting point for a broader reflection on this issue.

Key words: Anthropology, bioarchaeology, neoplasms, paleopathology, paleoncology

Introduction

How many pathological manifestations, especially asymptomatic ones, evading from clinical evaluations, escape to contemporary epidemiological estimates? Moreover, how many pathological stigmata still do not find in clinic, with the available data, an etiological explanation? The answer to these questions, even today, is far from simple. Recently, however, some medical disciplines have realized, also thanks to radiological, histological and molecular analyses, how the study of pathological evidence on ancient human remains, the paleopathology, can help in highlighting some characteristics of different diseases, how they occurred in the past and what has been their evolution over the course of centuries. Among the pathologies that have always posed great questions about their origin, tumors certainly have the primacy of attention and paleoncology today is detecting the presence or absence of certain tumors in antiquity and it is obvious that this will find out in the future whether some factors can really determine their onset or not. In addition to malignant tumors, some benign conditions, such as the presence of multiple osteomas, are also included in those pathological manifestations that must be explained yet. Osteomas are the most common benign and primary bone tumors of the craniofacial skeleton (1). Most are asymptomatic, with an account for 0.43% of the present population (2) and an incidence of 2-3% among all bone primary tumors (3). Osteomas can develop throughout the skeleton, such as in paranasal and mastoid sinuses, maxilla, external auditory canal, mandible, and cranial vault (4). This benign tumor's etiology is unclear and still discussed in clinical and paleopathological literature. Indeed, their presence is a real interpretative challenge. Authors have suggested various causes contributing to

their formation, for instance embryological, traumatic, inflammatory, metaplastic, hereditary and metabolic etiologies have been proposed (5). Thoma and Goldman suggested a traumatic but non-inflammatory origin (6) and Richards and colleagues considered that the stimulation of these embryonal periosteal areas may be caused by infection, trauma or overgrowth of normal bony tubercles (7,8). Moreover, for many authors, the origin of osteomas can be multi-factorial (9,10). Osteomas can be classified depending on the development tissue as central from the endosteum, peripheral from the periosteum and extra skeletal when develops within the muscle (11,12). Generally, regardless of their etiology, these small circumscribed bony lumps on the skull vault are traditionally called "button osteoma" from anthropologists and paleopathologists (13). In particular, button osteomas are smooth-surfaced and circular protrusions with demarcated margins, which are macroscopically visible and recognizable (15). According to Eshed and colleagues (16) the typical button osteoma has a dense, sclerotic, dome shaped ivory appearance and is characterized by mushroom-like shape in cross section. The dome is comprised predominantly of well-organized lamellar bone. The parallel lamellar bony bands are homogeneous in thickness and shape and poorly vascularized. The ectocranial plate shows diploeization that extends over the original ectocranial table. Although single cranial osteomas are commonly observed in osteoarchaeological remains, their etiology has been little investigated in palaeopathology. Eshed and colleagues (16) examined this tumor's frequency both in modern and archaeological samples from the Hamann-Todd Collection at the Cleveland Museum of Natural History reporting a prevalence of 37.6% (n = 585) in the modern sample (1912-1938), and 41% (n = 233) in the archaeological sample (from sites dated to the Roman-Byzantine period and to the early and late Arab period). These data present single osteomas as fairly frequent condition. However, we must highlight an underestimate incidence because at the clinic today we only recognize the most serious cases of osteoma, while in archaeology, analysing only the dry bone, is also possible to detect the most minute osteoma. Finally, the presence of multiple osteomas is a rare condition both in modern and in archaeological record. In this paper, we present three cases of multiple osteomas, tomb 1, 2 and 9 from an archaeological cemetery context of Caravate (northern Italy). Our intentional aim, in this field, is trying to find whether there is or not a correlation between the presence of multiple osteomas with other possible pathological conditions. Finally, we would like to stimulate the increase of the study of multiple osteomas conditions in paleopathology to probably add data useful in contemporary clinical reasoning.

Material and Methods

In 2002-2003, the Lombardy Archaeological Superintendence excavated the medieval cemetery of Saint Agostine in Caravate for the first time. During this campaign, 13 burials were discovered, and the archaeological stratigraphy allowed us to date the site between the 9-10th century (17-18). Inside the graves, skeletal remains of the ancient inhabitants of Caravate, some of which were perfectly preserved, were discovered. In 2018 and 2019, two new archaeological campaigns performed with our research group (19-20) brought to light another cemetery area in which five primary burials and four secondary depositions were discovered. Sex determination was carried out only for adults by using macroscopic methods. They were based on the assessment of morphological characteristics of the skull (21) and on the morphology (22-23) and measures of the pelvis (24-26). For adults, age at death was estimated through the analysis of cranial sutures (27), pubic symphysis degeneration changes and auricular surface senescence (28-29). The age of subadults was estimated from the observation of epiphyseal bone fusion (28), the measurement of the length of long bones (30-31) and the evaluation of the development of teeth (32, 33). Osteomas were identified mainly through a macroscopic examination of the remains.

Results

The remains of seven adult and six sub-adult individuals, found in primary deposition, and a minimum number of twenty-four adult and five sub-adult individuals, reburied in secondary deposition, or in a different burial place than the original one, were analysed.

Paleopathological investigations of multiple osteomas conditions

Tomb 1/2002

The skeleton of tomb 1 belongs to a woman of 30-40 years of age. The frontal bone exhibits a partially healed quadrangular lesion on the right (fig. 1aI), probably the result of a trauma caused by a pointed weapon with a quadrangular section (34).

This subject shows twelve osteoblastic lesions at the level of the neurocranium (fig. 1aII). These (fig. 1bI-VII) are located mainly in the sagittal suture and are characterized by well-defined margins, oval shape, with not fully smooth margins and small dimensions (table 1).

Tomb 2/2002

The skeleton from tomb 2 belongs to a man of 35-45 years of age (fig. 2a). The skull presents a com-

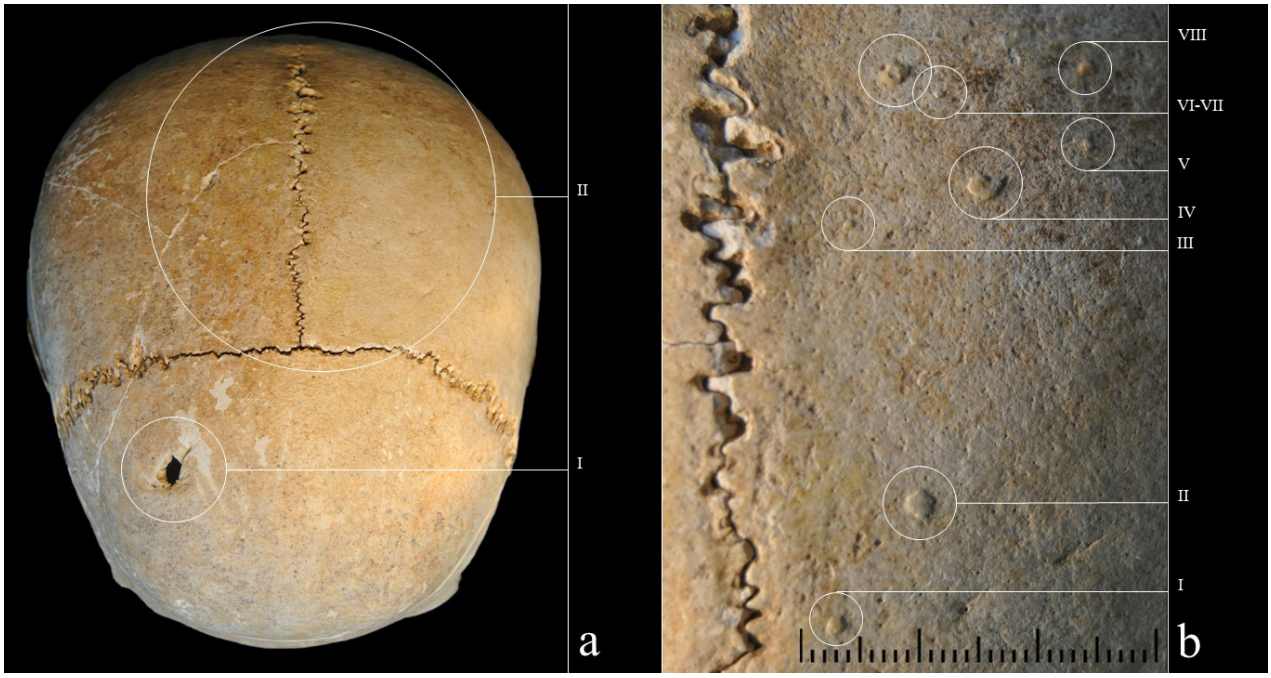

Figure 1. Tomb 1/2002. Skull of the subject, superior view (1a-b). The frontal bone shows a healed quadrangular trauma (fig. 1aI); many osteoma are located in left parietal bone, near the posterior part of the sagittal suture (fig. 1bI-VIII).

Table 1. Osteoma locations and dimension on the skeletal remains.

	Osteoma location				
	Occipital	**R parietal**	**L parietal**	**Frontal**	**Post cranial districts**
Tomb 1/2002	1.93 x 2. 32 mm	3.5 x 2.3 mm; 2.32 x 2.03 mm; 1.76 x 1.40 mm; 1.40 x 2.21 mm; 1.65 x 2.66 mm; 2.40 x 1.76 mm	2.07 x 1.76 mm; 2.74 x 3.07 mm; 3.27 x 2.35 mm; 2.82 x 1.96 mm; 1.81 x 1.80 mm	/	/
Tomb 2/2002	/	3.87mm x 3.39mm; 3.98x3.18 mm	4.24 x 3.67 mm; 2,52x3,06 mm, 3,73x3,24 mm	3.4mm x 3.25 mm	3rd proximal phalanx of the left hand 6.4 x 4.6 mm
Tomb 9/009	/	4.37 x 3.52 mm	3.39 x 2.40 mm; 3.70 x 2.99 mm; 2.63 x 2.65 mm; 2.73 x 2.47 mm; 7.06 x 2.0 mm; 7.54 x 4.63 mm	2.58 x 2.25 mm; 1.42 x 1.40 mm	/

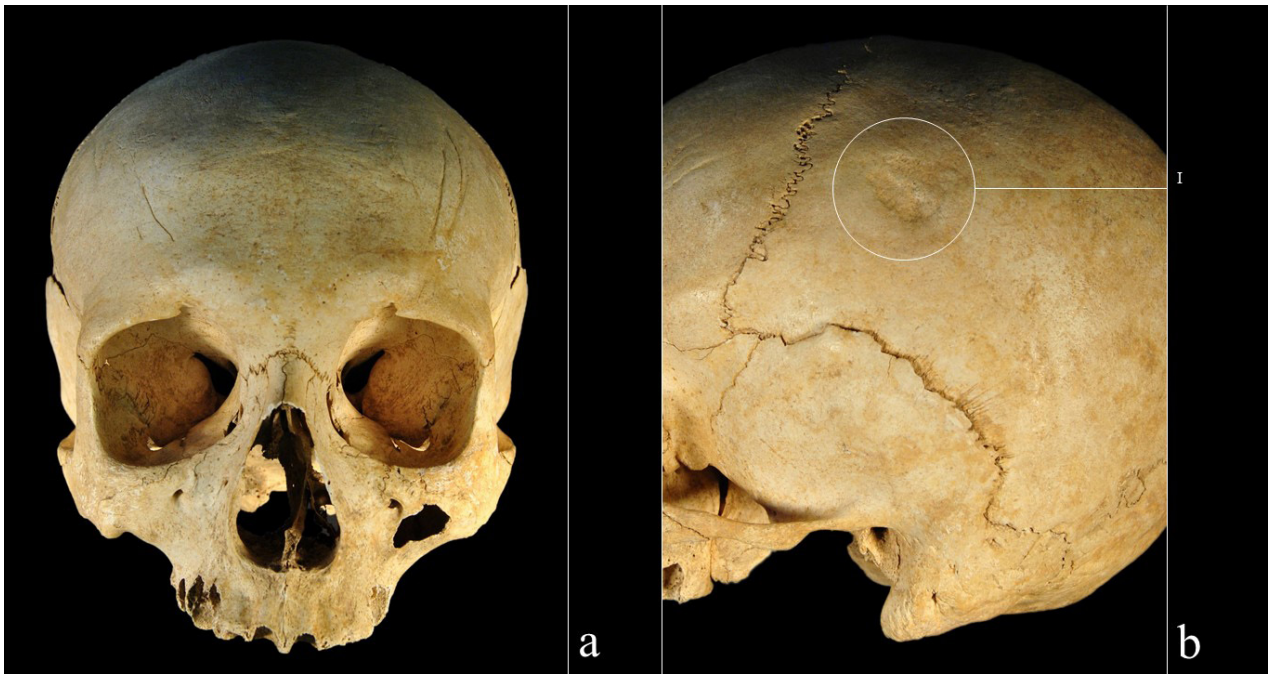

Figure 2. Tomb2/2002. Skull of the subject, frontal (2a) and left lateral view (2b). A trauma is present on the left parietal (fig. 2bI).

pletely healed depressed trauma on the left parietal bone (fig. 2bI).

The skull of the subject of tomb 2 is characterized by the presence of six osteoblastic lesions located on the frontal, on the right (one of which is near the obelion) and left parietals. They have well-defined margins and circular shape.

The individual has a well-visible oval-shaped bone formation on the dorsal surface of the 3rd proximal phalanx of the left hand (table 1).

Tomb 9/2002

The skeleton from Tomb 9 belongs to a male individual of 40-45 years of age (fig. 3a). The subject presents a small completely healed depressed trauma on the frontal bone, near the bregma (fig. 3bII).

The individual has nine osteoblastic lesions at the level of the neurocranium, located mainly on the frontal (fig. 3bI) and parietal bones, near the sagittal suture and above the lambda. They are poorly detected and are characterized by a circular or ovoid shape with irregular margins (Table 1).

Discussion

Except for the osteoma found at the level of 3rd proximal phalanx of the left hand, in all cases, the osteoblastic lesions were observed on the cranial vault. The rounded lesions of different size present a smooth surface and defined margins.

Osteoma is a benign neoplasm characterized by slow growth that affects the long and cranial bones. From a histological point of view, they result as a proliferation of either compact or cancellous bones, following endosteal or periosteal surfaces, with substantial size variations. Osteoma advances mainly in the skull, in particular facial bones and mandible are the most affected. Instead, the location in the occipital region is extremely rare. Osteoma represents the most common benign tumor of the nasal tract.

Osteoma of the facial bones is a fairly asymptomatic condition but in severe cases it can alter the sinus drainage and sinusitis or even deform the bones of the orbits and expand under the oral mucus.

Contrary to the single osteoma which may have no pathological significance, the presence of multiple osteomas may indicate a disease condition. The presence of multiple osteomas is a less common condition.

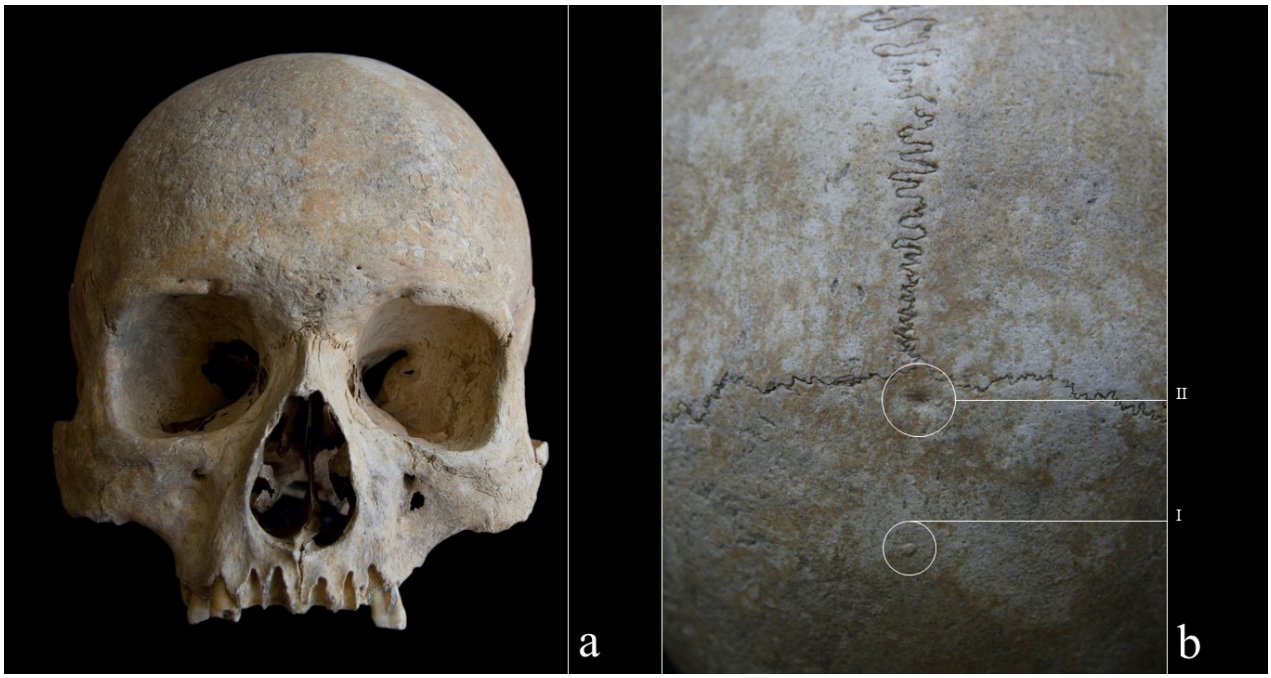

Figure 3. Tomb 9/2002. Skull of the subject, frontal (3a) and superior view (3b). A trauma is present on the frontal, near the bregma (3bII). Moreover, in this photograph is visible one osteoma on the frontal bone (3bI).

The literature examines different hypotheses regarding their formation, comprising the idea that the lesions may be produced by congenital anomalies or that chronic inflammation may originate within neoplastic proliferation. The growth of osteomas may also be a consequence of trauma or embryogenetic changes.

Osteomas as a consequence of congenital skin abnormalities are poorly documented. For these cases their development has been suggested from embryonic cell remains as heterotopic formations. As chronic inflammation osteomas can lead from a chronic mucosal inflammation (35).

Multiple osteomas may also refer to hereditary adenomatous colic polyposis (APC) associated with Gardner syndrome (GS) (36). This pathology is a consequence of the mutation of the locus of adenomatous polyposis coli (APC gene) located on chromosome 5q21-q22 and is characterized by the development of hundreds or thousands of intestinal adenomas (familial adenomatous polyposis FAP) that lead to the development of colon or intestinal cancer (37)

Clinical studies report that 50% of patients with GS presents three or more osteomata in the maxilla or in other locations (36). For some authors, the diagnosis can be considered in the presence of more than three osteomata on the maxillo-facial complex (38-39). Moreover, GS diagnosis can be advanced in presence of dental anomalies (40-41), such as osteomatous lesions, ectopic teeth, supernumerary teeth, and compound odontoma (43-44). From osteoarchaeological point of view, GS could be indicated by the presence of numerous skeletal osteomas, above all in the cranial level.

Only a few cases of multiple osteomas are reported in the palaeopathological literature. The skull belonging to a female individual of 20-25 years old, discovered in an ossuary of the eighteenth century in Czech Republic, showed two osteoblastic overgrowths (45). Another case, recovered in a Switzerland Iron Age site, is represented by a skeleton of a woman of 30–50 years old with multiple osteosclerotic lesions to the skull (46). Finally, the remains belonging to a female individual of 40–50 years old, from the Medieval site of Pieve di Pava (Siena, Central Italy), show six osteoblastic lesions on the cranial vault and three similar lesions on post-cranial bones (47). For the last two cases, a possible diagnosis of Gardner syndrome was proposed but not confirmed in the absence of DNA analysis.

In our case, no osteoblastic lesions were detected on the bones of the splanchnocranium. Moreover, no bone alterations of the maxilla and mandible or dental anomalies were observed. Therefore, without viscera or organs, the diagnosis of Gardner's Syndrome cannot be advanced. Indeed, in our sample the lesions are very little, and this fact complicates the diagnosis.

For multiple osteomas, a traumatic etiology is also debated. According to Kim et al. (2017) a combination of trauma and muscle traction may be a possible cause, where subperiosteal bleeding from trauma combined with an elevated muscle traction force can cause an osteogenic reaction. In this case, the development of osteomas has been associated with, rather than a neoplastic process. This etiology may cause smaller numerous lesions, rather than a single larger one (10).

Eshed et al. (2002) (16) highlights that the irregular bony overgrowth of the cranial vault due to reactive post-traumatic events is histologically characterized by rich vascular channels, a lack of laminated structure and by the presence of numerous osteocytes and Haversian system. Furthermore, the distinction between the lesion and the ectocranial table is not clear. Therefore, these characteristics distinguish this type of lesions from those that are commonly called "button osteoma".

In our sample, all skulls present a healed trauma condition, therefore it is possible to admit this pathological significance, as the association of multiple osteoma conditions with traumatic injuries has been advanced in literature. Since in our skulls osteomas are mainly located on the parietal districts, the hypothesis that this condition is linked to muscle stress cannot be excluded.

Conclusion

In our study, we elaborated a possible pathological explanation of multiple osteomas condition. As we can find in literature, both in pathological and clinical field, different causes have been associated with the onset of multiple osteomas up to severe conditions such as Gardner's syndrome.

The issues connected to the study of osteomas are mainly related to the difficulty of diagnose them. In paleopathology, this can be due to the scarce preservation of ancient human remains, with the result of underestimating the condition. On the other hand, in modern clinics, the under-representation may be associated to the asymptomatic nature of the condition that characterizes the majority of cases.

May we therefore today, as in the past, link different meanings to the presence of multiple osteomas?

Unfortunately, we still know little about the causes that lead to the onset of multiple osteomas.

The shortage of paleopathological cases of multiple osteomas reveals the need for more extensive researches on paleoncology and paleotraumathology, especially through systematic examination on human osteological collections.

Paleopathological cases prove again to be useful to the contemporary clinic for better understanding the condition of multiple osteomas.

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