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CT-SCANS OF PATHOLOGICAL CRANIAL FRAGMENTS FROM BARMAZ II, NEOLITHIC SWITZERLAND: A DIFFERENTIAL DIAGNOSIS

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ABSTRACT

Whilst undertaking a paleoepidemiological study of the neolithic and Bell Beaker culture populations of western Switzerland, a strange case was uncovered in the necropolis of Barmaz II. Individual R16 is only represented by three cranial fragments, two of them appearing grossly misshapen. Under different circumstances, the pathologies might have gone unreported, however since the project within which the analysis took place aimed to record all pathological lesions observed in the populations of neolithic western Switzerland, it seemed amiss not to pursue the case further. With the purpose of bringing a plausible explanation to the lesions observed, CT-scans were carried out, and compared to a healthy anatomical specimen. The results of this investigation are detailed below, as well as the differential diagnosis proposed.

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INTRODUCTION

A project is currently underway to establish a paleoepidemiological profile of the Neolithic population of Western Switzerland (13 sites, around 500 individuals), from the middle Neolithic to the Bell Beaker culture. The aim is to observe all bones present for pathological lesions, propose a diagnosis for these lesions whenever possible, and establish disease frequencies for this region for the chronological interval studied.

The necropolis of Barmaz is situated in the High Rhone valley, in Switzerland, and dates from the middle Neolithic (4500 – 3800 BC). It contains 59 tombs, some dug directly in the ground and some of the cistes Chamblandes type. Some of these graves contained more than one individual, bringing the total population for the necropolis to 77.

Tomb T16 (middle Neolithic I, 4300 – 4100 BC) contained a single individual, R16, represented by three cranial fragments. These present obvious pathological signs: unusual thickness, bone organization that differ from the norm, porosities. As a result, a CT-scan investigation was conducted in order to narrow down possible diagnoses.

From the CT-scan and comparison with the literature, three possible diagnoses are submitted for consideration: Paget's disease, metastatic disease, and thalassemia/severe anaemia. The diagnosis remains open. These results are significant; indeed, no matter which of the diagnosis is the right one, it would be the first case identified in the Neolithic population of Western Switzerland.

REGIONAL SETTINGS

The necropolises of Barmaz I and Barmaz II are situated in the high Rhone valley of Switzerland, in the canton of Valais, between 445 and 480 meters above sea level. Barmaz I have yielded 39 tombs of the ciste Chamblandes type, whilst in Barmaz II, 20 tombs were excavated (Honegger and Desideri 2003). The cemeteries are only 170 m apart and are contemporaneous according to 14C dates, spanning the middle and later neolithic of the region (4500-2500 BC) (Sauter 1985; Honegger and Desideri 2003). Very little funerary goods have been found in association with the individuals buried, and no particular internal organization can be discerned within either necropolis (Sauter 1949, 1950).

MATERIALS AND METHODS

This article focuses on individual R16 from Barmaz II. This was the only individual within this necropolis to be buried directly in the ground and not within a Chamblandes cist. Unfortunately, only three cranial fragments were recovered. These were first inspected macroscopically, then photographed, and finally CT scans were realized by Rubis Control SA, using a Zeiss Metronom 800-225kV, with a voxel size of 90 microns.

RESULTS

As previously mentioned, individual R16 is represented by only a few elements (figure 1), and could be an adult, judging from the appearance of the bones.

Despite only a few fragments being present, it was obvious upon macroscopic observation that they were not within the normal range of thickness and appearance for human bone.

Fig. 1: Photos of the bones present, the scale is 5 cm. A: fragment of the left parietal, outer table (left) and inner table (right). B: fragment of frontal bone, above right orbit. C: fragment of zygomatic bone.

Macroscopic appearance

Upon macroscopic examination of the bone fragments, they appeared thickened and fragile. The cross section revealed an enlarged inner and outer table, with irregular trabecular bone in between (figure 2). The outer table was irregular as well, with some porotic activity. There were some irregular traces on the outer table, but these appeared due to taphonomical conditions. The largest bone fragment was the piece of left parietal. Its maximum thickness was measured at 13.1 mm, compared to an anatomical specimen where the maximum thickness on the corresponding bone area was 5.5 mm.

Due to the sparse number of fragments available for diagnosis, the authors took the opportunity of a recent partnership with an imaging firm to have the biggest bone fragment put through a CT scanner, along with an anatomical specimen. The results of this investigation are presented in the following section.

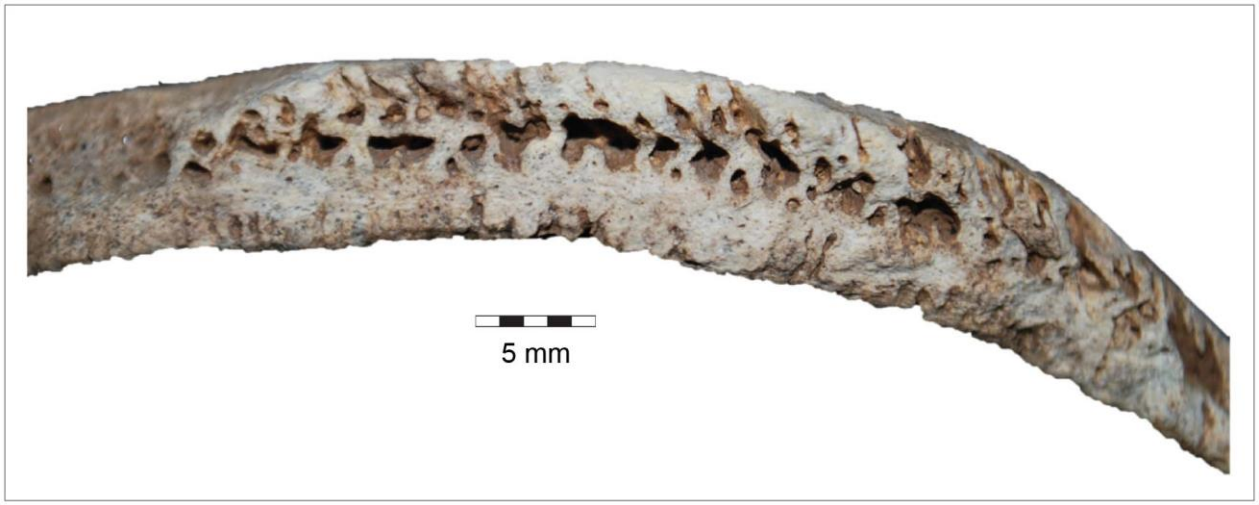

Fig. 2: Fragment A, parietal bone. Notice the thickened inner and outer tables. The scale is 5 mm

CT scan investigation

The CT-scanner used for the data acquisition is a Zeiss Metrotom 800-225kV, with a voxel size of 90 microns. A 10-minute scan was carried out on the largest bone fragment from Barmaz II R16, as well as on an anatomical specimen, for comparison purposes. Figure 3 below shows the differences in thickness and inner bone distribution between the pathological specimen (A) and the healthy one (B). The inner and outer tables of R16 appear thickened, and the trabecular area within seems expanded, with some lytic defects (white arrows), demonstrating obvious osteoclastic activity.

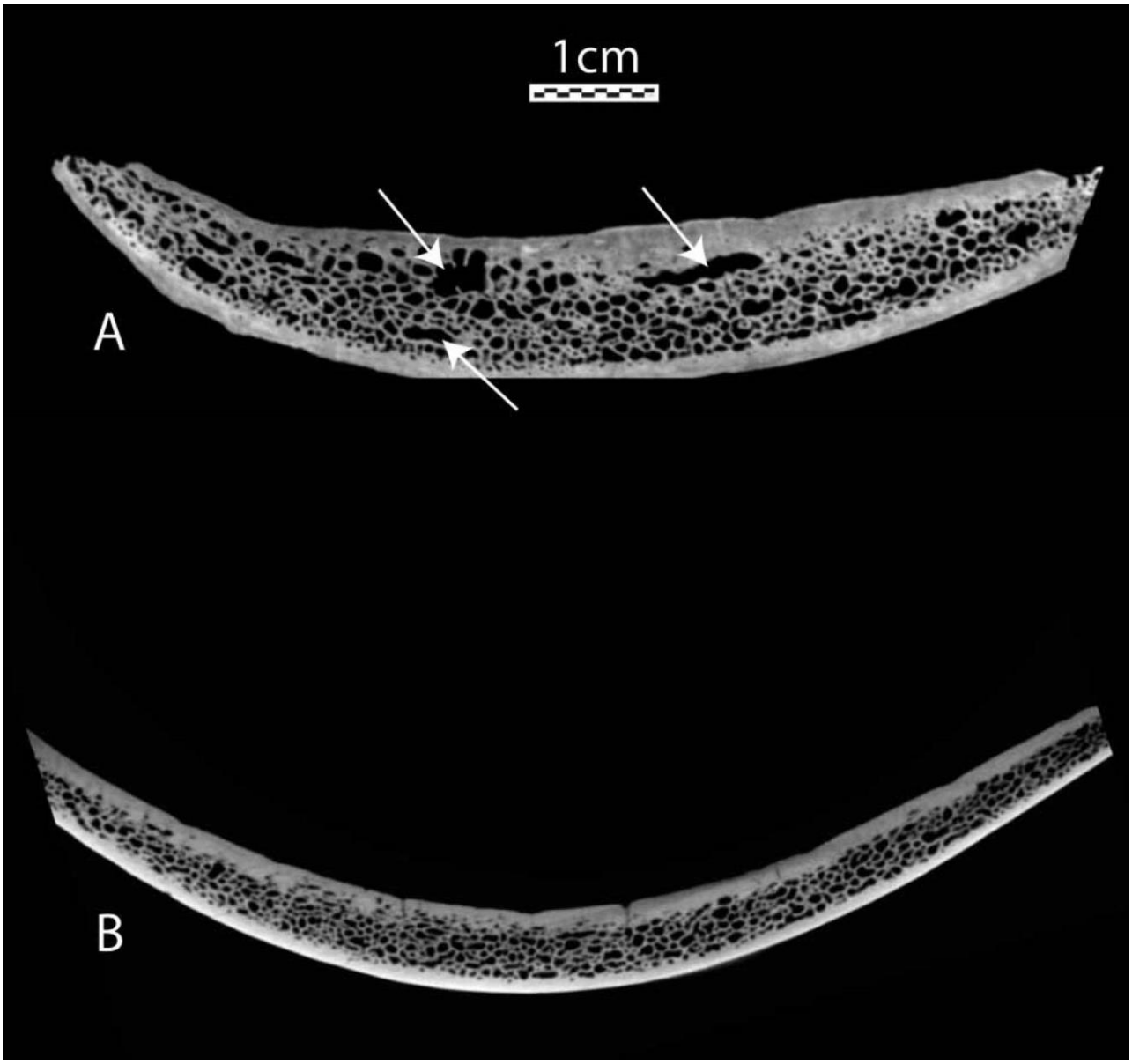

Fig. 3: CT scan of fragment A (left parietal), comparison between R16 (A) and a healthy anatomical specimen (B). Notice the enlarged diploic space and lytic defects (white arrows)

DISCUSSION

Considering the pathological characteristics described above, five conditions known to cause serious hyperostosis of the skull were isolated: Paget's disease, diffuse metastatic disease, thalassemia/severe anaemia, hyperostosis interna, and fibrous dysplasia. Fibrous dysplasia

('the expansion and replacement of normal cancellous bone with proliferative cellular stroma' (Ramsay and Barker 2014) seems an unlikely possibility due to the lack of concordance between the lesions described in the literature and that observed on R16 (Ortner and Putschar 1981; Aufderheide, Rodriguez-Martin, and Langsjoen 1998). The same can be said of hyperostosis interna, which mostly affects the frontal bone, creating 'raindrop-like' growths on the inner table (Hershkovitz et al. 1999; Hajdu et al. 2009; Wilczak and Mulhern 2012). The three other conditions (Paget's disease, diffuse metastatic disease, and thalassemia/severe anaemia) are all possible diagnosis. Arguments for and against each diagnosis are provided in turn.

Paget's Disease

Paget's disease of bone has been described at length in the medical literature, slightly less in the archaeological literature. Paget's disease of bone, or osteitis deformans as it was first called, is the result of an increase in bone turnover in localised area(s) of the skeleton, leading to pain and a variety of side effects (Selby 2013), including (but not limited to) fractures, nerve compression, cranial neuropathies, seizures, and general deformity in the area affected (Gruener and Camacho 2014). In terms of the bones affected, there is a prevalence in bones of the axial skeleton, with the pelvis, femurs, tibias, skull, and spine being frequent sites of onset (White and Rushbrook 2013).

The diagnostic features of Paget's are the following. First the bone undergoes loss of mass, resulting in lytic lesions, followed by a phase of accelerated and disorganised bone formation (Menéndez-Bueyes and Fernández 2017). The result is, to the naked eye, an enlarged, deformed, and fragile bone (Aufderheide, Rodriguez-Martin, and Langsjoen 1998). This pathology is often detected through X-rays, where its expression depends in which phase the bone is. In the osteolytic stage, areas of bone loss would be noted. In the osteoclastic phase, the researcher observes a thickening of the trabeculae, accompanied by a classic 'mosaic pattern' caused by the superposition of woven and lamellar bone (Cortis, Micallef, and Mizzi 2011).

In terms of aetiology, some researchers have hypothesised a Neolithic origin of the disease, resulting from genetic changes and a closeness to domesticated animals (Falchetti, Masi, and Brandi 2010; Bolland and Cundy 2013). It is interesting to note that the industrialisation process and therefore the lack of contact between humans and domesticated animals could be the cause of the decrease in cases observed in recent years (Falchetti, Masi, and Brandi 2010).

The prehistoric archaeological record for Paget's disease is virtually non-existent. The only case dating from the Neolithic is cited as one described by Pales in 1929, on a femur from a site in Lozère (France), and whilst some say that the given description is a match for Paget's features, others have argued that it must be discounted due to the absence of histological or microscopic images, and lack of re-investigation (Wells and Woodhouse 1975). There are however well-established cases of Paget's disease in historical times, and Mays (2010) has provided a detailed investigation of the literature from 1889 to the present, with the following results: 109 archaeological cases, the earliest dating from the Roman Empire (1st to 4th century AD), 94% of them from England. Roches et al. (2002) have described two cases originating from Medieval France, describing 'irregular bony fragments with a thickened and disorganised trabecular pattern'. Upon microscopic investigation, the authors described 'a mosaic [pattern] trabecular thickening of bone, excessive bone resorption and formation' (Roches et al. 2002).

In the case of R16, some diagnosis features of Paget's disease appeared present (enlarged bone, mix of bone proliferation and lytic lesion, 'pumice stone' aspect), but the few fragments available for observation forbids any definitive interpretation, and the next two differential diagnoses could be equally valid.

Diffuse metastatic disease

Diffuse metastatic disease is a general term used in medicine to describe the consequences of the diffusion of a neoplastic condition from its original location to a distant other one (Chambers, Groom, and MacDonald 2002; Nguyen 2011). Common origin sites include the breasts, lung, and prostate (Mundy 2002). The treatment depends on the stage of the cancer and on its progression, but it is worth noting that the spread of the disease from one organ to a distant other is the main culprit in most cancer deaths, and as such a lot of the current medical research is focused on understanding the pathways through which this process takes place (Riihimäki et al. 2014).

Since the expression of the disease on the bone depends on the type of cancer under consideration, the results can take various forms. One might observe lytic or blastic lesions, or a mix of both, including on the skull (Aufderheide, Rodriguez-Martin, and Langsjoen 1998). In terms of skull imaging, the most common observations are general deformity (which in the living patient can lead to neurological compromise) and lytic, blastic, or mixed lesions (Ramsay and Barker 2014). Cases of metastatic cancer in the archaeological record are well documented (Assis and Codinha 2009; Wasterlain, Ascenso, and Silva 2011; Abegg and Desideri 2018), exhibiting a variety of the specifics described above.

Thalassemia/severe anaemia

Conditions that cause severe metabolic disruptions, and most prominent amongst them thalassemia, can result in the kind of features observed in R16's case. Thalassemia is a hereditary disorder that is often accompanied by severe anaemia (Hilliard and Berkow 1996) and can cause marrow proliferation resulting in expansion of the medulla, thinning of the cortical bone, resorption of the cancellous bone, and widening of the diploic space in the skull (Bouguila, Besbes, and Khochtali 2015). In addition, under X-rays a 'hair on end' phenomenon might be observed. The consequences for the living subject can be severe: facial deformities, pain, fractures, spinal deformities (Haidar, Musallam, and Taher 2011).

In terms of archaeological cases, there have been several published cases of thalassemia (Aufderheide, Rodriguez-Martin, and Langsjoen 1998; Thomas 2016), all of which tend to underline the diagnostical value of the 'hair on end' aspect of the thickened skull. It is worth noting, however, that other metabolic conditions such as scurvy and various anaemias can also cause a thickening of the cranial vault (Zuckerman et al. 2014).

In R16's case, we did observe an expansion of the diploic space, possibly combined with marrow expansion, but the characteristic 'hair on end' aspect under X-rays was absent.

CONCLUSION

In conclusion, this short study of three pathological cranial fragments proved informative. In the other individuals observed, both within the necropolis and the larger 400+ strong corpus, no comparable pathology was observed. The aspect of the bone fragments left no doubt as to their pathological nature, and three possible diagnoses are proposed: Paget's disease, a metastatic condition, or a severe metabolic problem (thalassemia/anaemias). Whatever the case, this gives us precious information to include in our wider study of the paleoepidemiology

of western Switzerland. A case of Paget's during the Neolithic of this region would be significant in terms of the paleohistory of the disease; the presence of a metastatic condition is similarly important; and the presence of a metabolic problem that would cause such an impact on the bones raises questions as to the metabolic health of the rest of the population. Whilst it is here impossible to give a definite diagnosis, it proves that few fragments and/or lesser preservation does not mean that nothing can be said about the individual represented and his/her health.

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