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RESEARCH ARTICLE

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An osseous lesion in the maxillary sinus—Tumour or tumour-like?

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Abstract
In the bioarchaeological analysis of burials from a medieval graveyard at Hettstedt, Central Germany, a male skeleton of about 40 to 50 years at death with an unusual bony structure in the left maxillary sinus was discovered. Macroscopic examination exhibited a balloon-shaped osseous lesion with solid cortical surface 2.5 × 1.5 cm in size. Micro-CT scans revealed trabecular structures around a central cavity. The margins of the osseous lesion were well defined without infiltration of normal maxillary bone tissue. The histopathological analysis showed the presence of lamellar and woven bone. The structure and localisation of the tumour-like lesion suggest that the formation was the result of chronic inflammation and that chronic dental sinusitis seems to have triggered a large reactive ossification.

KEYWORDS
fibro-osseous lesion, middle ages, paranasal osteoma, reactive osteosclerosis

1 | INTRODUCTION

The occurrence of diseases that leave behind evidence on bones and teeth can be traced far back into the history of both humans and mammals (Aufderheide & Rodriguez-Martin, 1997; Brothwell & Sandison, 1967; Capasso, 2005; Kirkpatrick, Campbell, & Hunt, 2018; Ortner, 2003; Pales & Rivet, 1930; Steinbock, 1976). The earliest diagnosed findings of neoplasms date back 1.9-1.7 million years to hominins from Malapa and Swartkrans, South Africa. (Odes et al., 2016; Randolph-Quinney et al., 2016). Furthermore, early findings are documented in a Homo naledi individual from the Dinaledi Cave site in South Africa (Odes et al., 2016) and a Homo neanderthalensis individual from the Guattari Cave site in Italy (Colella, Cappabianca, Gerardi, & Mallegni, 2012). Numerous studies on tumours or tumour-like lesions exist from later phases of human history, and the results largely confirm the assumption that benign and malignant tumours are not just a modern phenomenon (e.g., Alt, Adler, Buitrago-Téllez, & Lohrke, 2002; Binder, Roberts, Spencer, Antoine, & Cartwright, 2014; Faguet, 2015; Grupe, 1988; Molto & Sheldrick, 2018; Nerlich, Rohrbach, Bachmeier, & Zink, 2006; Strouhal, Vhynánek, Horáčková, Benešová, & Němečková, 1996; Suzuki, 1987). With regard to incidences of benign and malignant bone tumours in the past, it can be stated in principle from the point of view of palaeopathology that bone tumours at the time exhibited the same range as today and that those neoplasm that are most frequently diagnosed today were also predominant in the past. Due to a lower average life expectancy up to the 20th century, however, there was also a lower frequency of bone tumours in the population overall. Moreover, not all neoplastic diseases leave traces on or in the bone (Marques, Matos, Costa, Zink, & Cunha, 2018). Palaeopathological assessments of ossifications in archaeological skeletal remains that go beyond a mere tentative diagnosis, however, are not easily achieved and require both specialist knowledge and the use of imaging and histological procedures (Kirkpatrick et al., 2018; Ragsdale, Campbell, & Kirkpatrick, 2018).

This case study presents an historical burial with an unusual bony structure from medieval Hettstedt, Central Germany. The osseous lesion occupied the entire left maxillary sinus. The study aimed to carry out macroscopic computed tomographic and histological examinations as well as differential diagnosis in order to establish as precise an identification as possible and expand our knowledge on the diagnostic scope with regard to osseous tissue formations. In addition to any medical implications, this also provides an insight into the general health or lack thereof in former times.

2 | MATERIAL AND METHODS

The study material presented here was recovered between 2007 and 2010 during archaeological excavations by the State Office for Heritage Management and Archaeology of Saxony-Anhalt in Halle, Germany. The burials were located in two disused graveyards at Hettstedt, Germany, which were about to be impacted by construction work in the area (Figure 1). The medieval cemetery at Hettstedt-Kirchplatz, adjacent to St. Jacob's church in the centre of Hettstedt, comprised 606 burials (253 juveniles, 353 adults, 142 females, and 160 males) and had been in use up to 1540 before a new cemetery was established outside the town walls. Due to inheritance disputes, the city was repeatedly besieged and looted (1341 and 1439) and shaken several times (1539–1683) by the plague (Spieler, 1996). The individuals uncovered have been the subject of an unpublished anthropological master's and a doctoral thesis (Rossbach, 2016). The main topics covered were demographics, mortality, pathology, histopathology, and dietary reconstruction using stable carbon and nitrogen isotope analyses. The town of Hettstedt and the entire Mansfelder Land region located in have been shaped since the 12th century by local mining operations (copper shale ore and silver; Hofmann, 1957). Mining and metallurgy were important aspects of the economic development of the region. In addition, a large part of the population were successful farmers, turning Hettstedt into an important hub for grain trading. A further privilege bestowed on the town was the holding of markets. The high proportion and severity of arthropathies (88.6%) detected in the adult skeletons from Hettstedt-Kirchplatz attest to an everyday life of high physical stress, which fits in with a more rural and agriculturally oriented society (Rossbach, 2016).

The focus of this study is on a large bony structure detected in the left maxillary sinus of a skeleton (inv. no. 270) from Hettstedt-Kirchplatz. The age and sex of the individual concerned were morphologically and metrically determined using international standard procedures (Buikstra & Ubelaker, 1994; White & Folkens, 2000). First, the fragmented maxilla was macroscopically examined and photographed (Figure 2a–d) and then analysed by means of computed tomography using a Phoenix nanotom®m (GE Sensing & Inspection Technologies GmbH, Wunstorf, Germany; 140 kV/60 μA) with a resolution of 50 μm (Department of Biomedical Engineering, University of Basel). After completion of the macroscopic assessment and imaging analysis, a sample was taken from the rear section of the osseous lesion using a Dremel tool (Figure 2d). The tissue sample was embedded in epoxy resin (Biodur® E1, E12) and cut into 60–70 μm thin sections using a saw microtome (RMS 16G3; REHA-TECH Engineering). For diagnostic purposes, the thin sections were mounted on slides and covered in Eukitt®. Microscopic analysis of the thin sections was carried out by means of transmitted light microscopy (Leica/Leitz DMRP) under polarised light (Integrative Prehistory and Archaeological Science, University of Basel). Microscopic images were recorded (Leica DMC 4500 digital camera) and analysed using "Leica Application Suite V4" software.

3 | RESULTS

3.1 | Basic information on the skeletal remains

The archaeological analyses indicate that the burial dates are most likely from the 15th or from the first half of the 16th century (Rück, 2008, unpublished). This assumption is based on the fact that

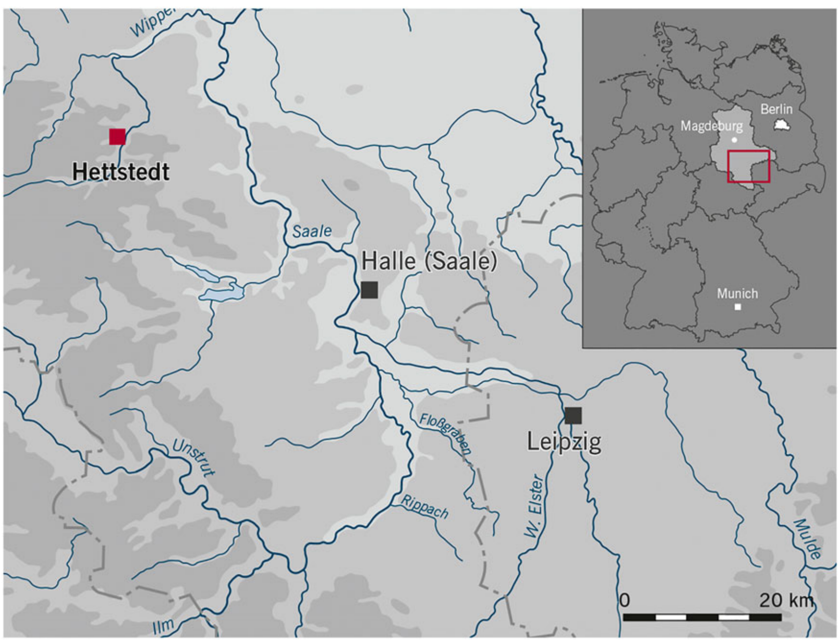

FIGURE 1 Location of the Hettstedt site, Saxony-Anhalt, Germany (LDA Halle) [Colour figure can be viewed at wileyonlinelibrary.com]

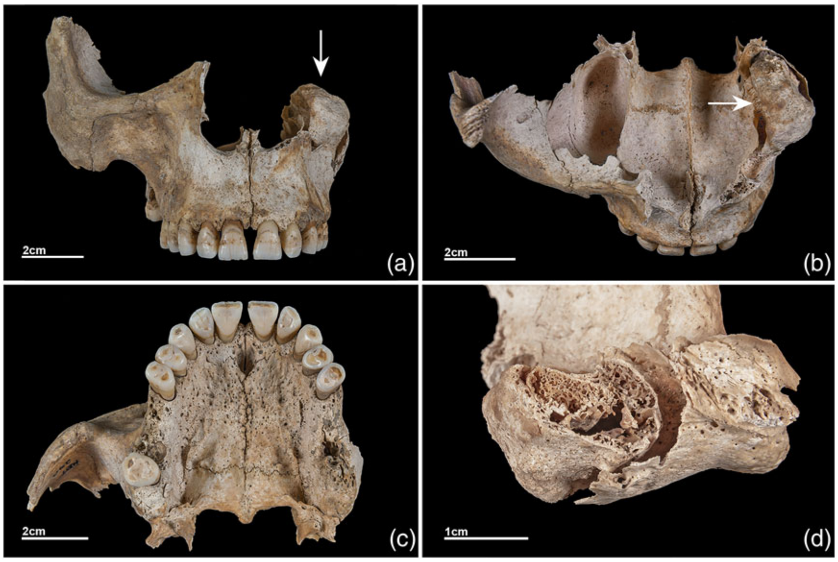

FIGURE 2 Maxilla of a medieval burial (Ind. 270, male, 40–50 years) from Hettstedt, Germany, with an unusual bony structure in the left maxillary sinus in (a) frontal view and (b) superior view. (c) Occlusal view of the maxilla with ante-mortem tooth loss and reactive changes to the alveolar bone. (d) Cross-sectional view of the sampled lesion (coronal plain) shows trabecular bone around a central cavity [Colour figure can be viewed at wileyonlinelibrary.com]

most burials were aligned with the nave built from 1445 onwards, and because a new cemetery outside the city walls was used after 1540. The osteological examination revealed that the skeletal remains were those of a male with an age at death of approximately 40 to 50 years. With regard to general dental health, the individual exhibited well-preserved anterior maxillary teeth (Figure 2a,c). However, all molars except for the right wisdom tooth were missing (Figure 2c). The premolars of the left maxilla had slightly more occlusal wear than those of the right side. Residual roots in the molar region (second molar) of the right maxilla, reactive changes on the alveolar processes of the right and left maxillae, and general periodontal insufficiency with distinct atrophy of the alveolar ridge in the area of the molars were the most marked pathologies. Moreover, porosity of the hard palate indicated chronic stomatitis. Apart from the dental pathological changes and the osseous lesion in the left maxillary sinus, the skeletal remains of the individual showed arthropathies that indicate high physical stress during his lifetime.

3.2 | Macroscopic examination

The macroscopic examination revealed a 2.5 cm long (mediolateral) and 1.5 cm wide (anteroposterior) unusual bony structure with a maximum height of approximately 3.2 cm in the left maxillary sinus. It took up that the entire left maxillary sinus was easily distinguished from the left sinus wall and had left the autochthonous structures largely unaffected (Figure 2a,b). The cortical surface appeared completely intact and showed a rough and solid appearance. In the area of the two rearmost molars (second and third molars of the left maxilla, lost ante-mortem), the elongated oval lesion was attached to the left maxillary bone, without affecting the surrounding bone structures. The site of the biopsy (coronal section) offered a view into the internal structure of the lesion, which exhibited a trabecular texture surrounding a central cavity (Figure 2d). In contrast, the right maxillary sinus was free of any pathological changes.

3.3 | Micro-CT analysis

Images from the micro-CT analysis showed a clearly defined unilocular bony mass in the left maxillary sinus (Figure 3a–c, sagittal sections). The tumour-like lesion had extended far into the maxillary sinus without affecting the adjacent maxillofacial structures. Its cortical surface was clearly distinguishable from the trabecular bone whose structure appeared radiolucent with diffuse radiopacity. The lesion's trabecular structure exhibited a heterogeneous texture with areas of both greater and lesser density surrounding a central cavern, which opened inferiorly and was connected with the alveolus of the second molar lost ante-mortem. Since the alveolus was not completely resorbed, the loss of this molar had occurred not long before death. The sagittal section showed a seamless trabecular transition between the lesion and the alveolar bone (Figure 3b). Another more lateral sagittal section clearly showed sparse cancellous bone around a central cavity (Figure 3c), which was probably filled with soft tissue during the individual's lifetime. Further information was given by a coronal section (Figure 4a,b), which clarified the transition from the alveolar process to the lesion. The lesion was attached to the alveolar bone without disturbing the maxillary structures. In comparison to the contralateral side, the left alveolar process was clearly altered by diminution of trabecular bone (Figure 4b). The right maxillary sinus showed no irregularities.

3.4 | Histology

It is important for the histopathological examination to bear in mind that in general archaeological skeletal remains no longer contain any soft tissue. Therefore, only the mineralised components can be assessed. Deposits of crystals that were visible between the trabeculae are artefacts: Over the centuries, soil minerals had penetrated the bones (Figure 5a,b asterisk). Histological images of the osseous lesion showed well-defined solid edges with a sparse trabecular structure towards the centre (Figure 5a). Around the central cavity, cell-rich trabeculae (many osteocyte lacunae), some with a lamellar structure, were found beside cell-poor and untextured bone formations that could be identified as woven bone (Figure 5b–d).

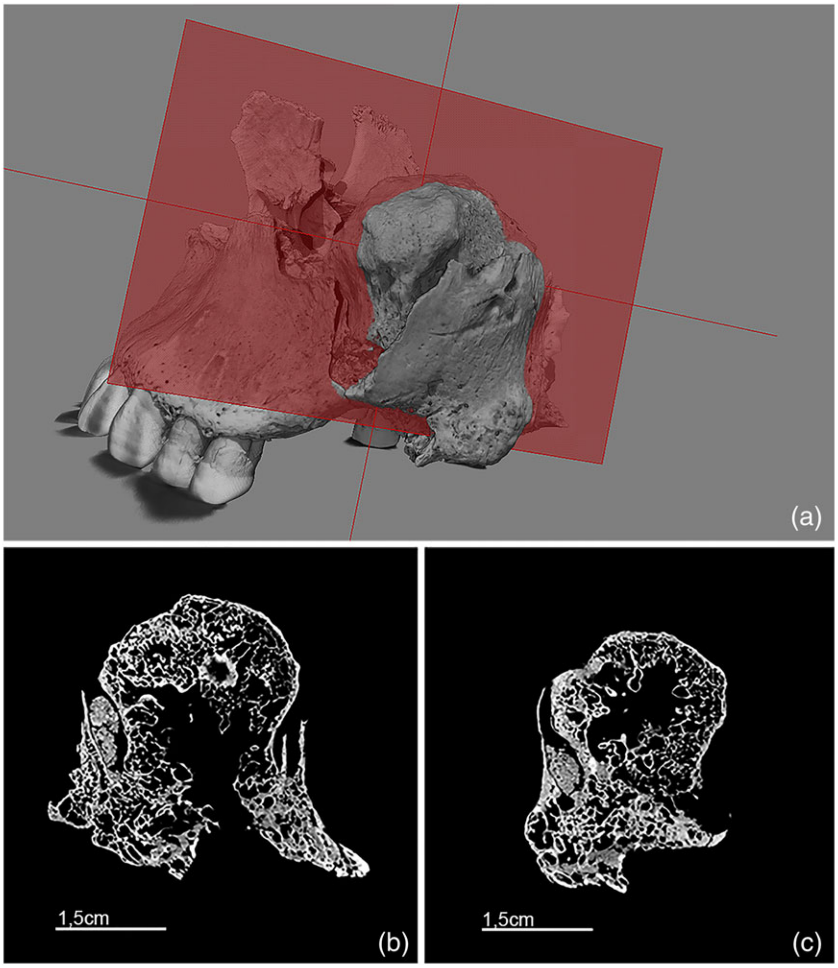

FIGURE 3 Micro-CT images. (a) Localisation of the sagittal sections. (b) The sagittal micro-CT scan of the centre of the lesion shows well-defined margins with trabecular formations of varying density and an open central cavern. (c) Further sagittal section of the rear area of the lesion with a loose trabecular structure towards the central cavern [Colour figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

Bone tumours or tumour-like lesions in the areas of the face and jaws have often been identified in archaeological skeletal remains (Bartelink & Wright, 2011; Colard, Gabart, & Blondiaux, 2008; Gresky, Kalmykov, & Berezina, 2018; Silva & Wasterlain, 2010). Establishing a diagnosis, however, is a complex task; macroscopic assessment is therefore not sufficient, and radiological or histopathological analyses are required even in archaeological specimens. Because soft tissues are not present, an important component in differential diagnosis is unavailable. However, statements can nevertheless be made with the aid of the calcified components, and in many cases, tumours or tumour-like pathologies can be identified and distinguished (Marks & Hamilton, 2007; Ragsdale et al., 2018).

The margins of the osseous lesion in the case presented here were well defined. Neither osteolytic nor osteoblastic remodelling could be identified on the normal bone components. Infiltration of healthy bone tissue had not occurred, and the possibility of an aggressive and potentially malignant bone tumour can thus be excluded (Fowler, 1999). Most odontogenic tumours can be eliminated because they generally originate and expand within the tooth-bearing jawbones, usually in highly characteristic locations (e.g., multifocal involvement and lesions around the dental roots), which does not fit with the case presented here (Baumhoer, 2017). Moreover, except for cemento-ossifying fibroma (COF) and odontoma, most of these neoplasms only scarcely produce solid matrix, which makes a differential diagnosis from this group of lesions even more unlikely (Baumhoer, 2017; Baumhoer, 2018; Jundt, Bertoni, Unni, Saito, & Dehner, 2005; van der Waal, 2005).

A highly probable diagnosis is that therefore the bony structure in the left maxillary sinus was the result of a benign fibro-osseous lesion, such as fibrous dysplasia (FD), cemento-osseous dysplasia (COD), COF, and reactive osteosclerosis, usually caused by chronic inflammation (Baumhoer, 2017; Eversole, Su, & El-Mofty, 2008; Hall, 2012; MacDonald, 2015; Slootweg & El Mofty, 2005; Su, Weathers, & Waldron, 1997). This group of lesions is characterised by monomorphic fibroblastic stroma in combination with bone and cementum-like material (Baumhoer, 2017), which fits very well with the micromorphological structure of the case presented. Furthermore, some of these lesions tend to expand into the maxillary sinus. However, other nonodontogenic neoplastic formations such as paranasal osteoma must also be included in the differential diagnosis (Baumhoer, 2017; Eversole et al., 2008). We will discuss possible pathologies in detail in the following section.

4.1 | Differential diagnostic considerations

4.1.1 | Fibrous dysplasia

FD may involve single (monostotic) or multiple (polyostotic) bones (Baumhoer, 2017; Hall, 2012; MacDonald-Jankowski, 2009). The polyostotic form can be excluded in this case because none of the

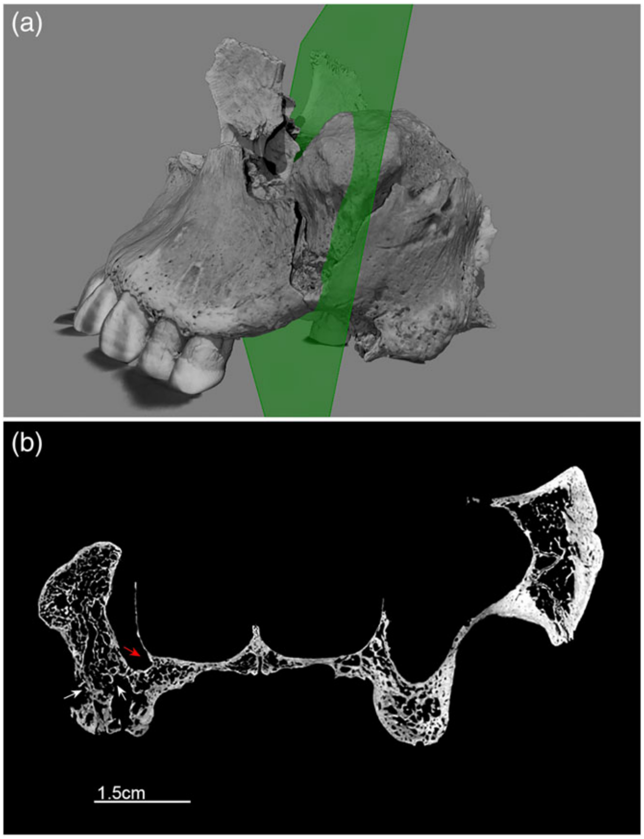

FIGURE 4 Micro-CT images. (a) Localisation of the coronal section. (b) In the coronal micro-CT scan, the transition from the left maxillary bone to the lesion is almost seamless (white arrows). Compared with the right maxilla the left alveolar bone is altered by a loss of trabecular bone, particularly near the floor of the maxillary sinus and the palatine process (red arrow), due to resorption processes as a result of ante-mortem tooth loss [Colour figure can be viewed at wileyonlinelibrary.com]

other skeletal remains exhibited any distinct changes. In contrast, monostotic FD can appear in all skull bones and occur in many different forms. This type of FD often extends to several adjacent bones; margins are not well defined and can lead to expansion and bone deformity that can sometimes cause disfigurement. Radiologically, it typically shows attenuation of homogeneous signal intensity, termed ground glass. The process is usually self-limiting and is followed by maturation of the fibrous tissue into bone. Particularly, the lack of host bone expansion and also the dense sclerosis and sharp delineation argue against FD (Baumhoer, 2017; MacDonald, 2015).

4.1.2 | Cemento-osseous dysplasia

COD can be divided into three groups: periapical, focal, and florid COD (Baumhoer, 2017; de Noronha Santos Netto, Machado Cerri, Menezes Aguiar Miranda, & Ramôa Pires, 2013; Eversole et al., 2008; Hall, 2012). Periapical COD is the most common form of fibro-osseous lesion (Hall, 2012; Slootweg, 2009; Su et al., 1997). Depending on the subtype, COD can occur focally or multifocally and always involves the roots of the teeth (de Noronha Santos Netto et al., 2013; Hall, 2012). Apart from the florid form, which often involves all four quadrants and can therefore definitely be excluded, the other COD forms do not lead to expansion of the jaw and, in most cases, the lesions gradually ossify without causing any symptoms (Eversole et al., 2008; Su et al., 1997). A case of COD in a Bronze Age burial recently published by Gresky, Kalmykov, and Berezina (2018) clearly differs from the findings of the histopathological analysis and micro-CT images in the Hettstedt burial. Moreover, COD can be excluded as a possible diagnosis due to the location of the lesion.

4.1.3 | Cemento-ossifying fibroma

Two bioarchaeological case studies with osseous lesions in the maxillary sinus from Portugal (3710–3620 BC, Silva & Wasterlain, 2010) and Spain (sixth–seventh centuries AD; Colard et al., 2008), both of which have been identified as COF, bear clear macroscopic similarities with the case presented here. As a rule, COFs (ICD-O code: 9262/0) are monostotic unilocular tumours (Baumhoer, 2017; MacDonald, 2015; Slootweg & El Mofty, 2005) that can reach considerable

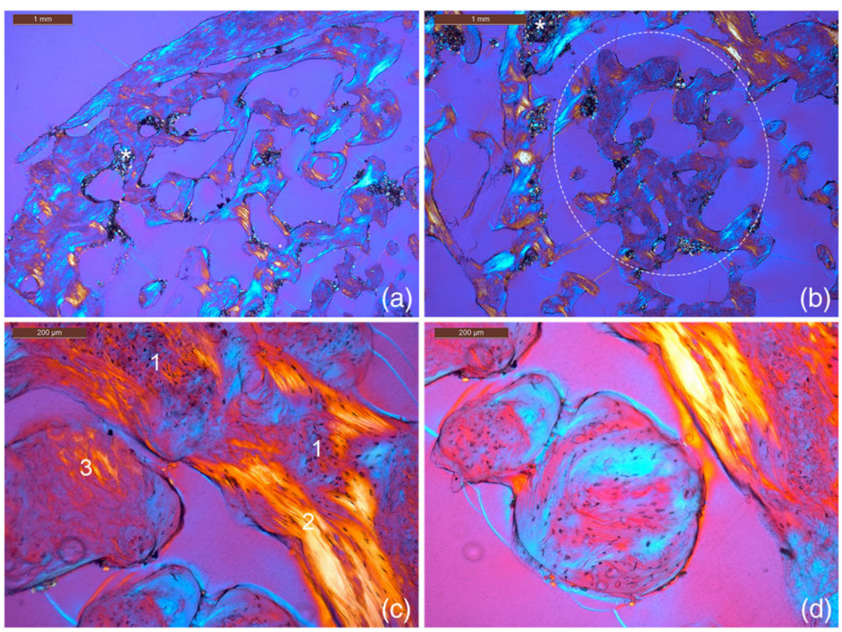

FIGURE 5 Histological images of the osseous lesion (coronal section). (a) Well-demarcated margins with very sparse trabecular structure towards the interior. (b) Cell-poor trabeculae with a diffuse structure (hardly any osteocyte lacunae) in the centre (circle). (c) Cell-rich areas (1) with a partially lamellar structure (2) next to cell-poor unstructured bone formations (3). (d) Cell-rich trabecula with a partially concentric structure. Images taken under polarised light. *Example of taphonomic crystalline deposits [Colour figure can be viewed at wileyonlinelibrary.com]

proportions and cause significant functional and cosmetic problems (Agarwal, Kumar, Singh, & Usmani, 2015; Kuta, Worley, & Kaugars, 1995; Lawson et al., 2010). Histologically, COF is composed of fibrous tissue and varying amounts of calcified components such as woven and lamellar bone (Slootweg, 2009; Slootweg & El Mofty, 2005; Zegalie, Speight, & Martin, 2015). Smoothly contoured deposits can sometimes be found amongst the mineral components, and these are interpreted as cementum-like material. This special type of matrix formation is a unique characteristic in odontogenic lesions (Baumhoer, 2017; Baumhoer, 2018). COFs are divided into three variants, which can be distinguished on the basis of localisation, patient age, and histopathological traits. The conventional form (CCOF) belongs to the group of odontogenic tumours and can be eliminated as a possible diagnosis in this case because it only occurs within tooth-bearing jawbones, the mandible in particular (Baumhoer, 2017). CCOF also occurs far more frequently in women than men (de Noronha Santos Netto et al., 2013). The two other variants, the juvenile trabecular and the juvenile psammatoid ossifying fibroma (JTOF and JPOF), are classified as bone tumours and can also occur in bones other than the mandible or maxilla (Baumhoer, 2017; El Mofty, 2002; Zegalie et al., 2015). In fact, JPOF is more often found in areas other than the jawbones, especially in the sinusoid walls, most frequently affects patients between the second and fourth decades of life, and is somewhat more prevalent in men than in women (Baumhoer, 2017; Zegalie et al., 2015). Psammatoid matrix mineralisations characteristic of JPOF were not identified in this case, and one would also expect to find expansion of the sinusoid wall, which was not the case here.

4.1.4 | Paranasal osteoma

Paranasal osteoma is usually found in the frontal sinus and more rarely in the maxillary sinus (Borumandi, Lukas, Yousefi, & Gaggl, 2013; Jundt et al., 2005; Kaplan, Nicolaou, Hatuel, & Calderon, 2008). It is a benign bone tumour that generally occurs as a small-scale structurally dense lesion but can sometimes also reach considerable size. Peripheral and central variants are known. Peripheral osteomas arise on the cortical plate, whilst central osteomas originate from the endosteal surface of the bone. Paranasal osteoma is most often diagnosed in patients aged between 20 and 50, with men being more frequently affected (Jundt et al., 2005; Kaplan et al., 2008; Sayan, Uçok, Karasu, & Günhan, 2002). Besides a neoplastic origin, traumatic and infectious causes have also been discussed (Boffano, Roccia, Campisi, & Gallesio, 2012; Kaplan et al., 2008; Sayan et al., 2002). Multiple osteomas are found in association with Gardner syndrome (Jundt et al., 2005; Kaplan et al., 2008). Histologically, two characteristic forms are distinguished. Ivory osteomas, the most common form, are characterised by a very dense bone structure lacking the Haversian system, whereas mature osteomas exhibit normal trabecular bone structure with medullary spaces (Fu & Perzin, 1974; Sayan et al., 2002). Mixed forms consisting of ivory and mature osteoma also occur. From a histological point of view, the ivory form can definitely be excluded as a possible diagnosis in the Hettstedt case. The lesion presented shows a sparse trabecular structure with a central cavity, which may originally have been filled with soft tissue. Moreover, the histological images predominantly show normal lamellar bone including a Haversian system and components of immature woven bone. Based on the macroscopic and histopathological features, the matching age and sex-specific preference and a possible infectious origin, a mature peripheral osteoma of the maxillary sinus would indeed be a possible diagnosis here.

4.1.5 | Inflammatory/reactive processes

Based on the evidence of reactive processes in the left maxillary molar region and the loss of those molars, probably due to caries, periapical inflammation around the apex of a tooth must be considered as a possible cause in the case presented here (Alt et al., 2008). Periapical granulomas and radicular cysts generally have a clearly defined cortical rim and radiolucent interior (Alt, Türp, & Wächter, 1998). In chronic conditions, as must be assumed for historical times because no treatments were available, inflammation can result in reactive new bone formation (Eversole et al., 2008; Hall, 2012). Moreover, it is possible in tooth infections caused by low-virulence bacteria for chronic sclerosing osteomyelitis to occur, which does not lead to regular inflammatory reactions but activates osteoblast activity and thus the formation of bone tissue (Eversole et al., 2008; Hall, 2012). Typical features include dense sclerotic bone structures that show the same histological traits as fibro-osseous lesions (Hall, 2012). These lesions are usually associated with the root apex of an infected tooth. The case presented here also exhibits a connection between the alveolus of the second molar of the left maxilla which was lost ante-mortem probably due to caries, and the cavity of the bony structure in the left maxillary sinus (Figures 2c and 3b). This makes a chronic infectious origin of the observed osseous lesion highly likely, but chronic sclerosing osteomyelitis is very unlikely to protrude into the maxillary sinus without expansion within and swelling of the alveolar bone. Because the original structures of the maxillary sinus remained unaffected, the process must have arisen primarily within the sinus itself. It is known that chronic sinusitis can stimulate reactive ossification in the paranasal sinus (Barnes, Brandwein, & Som, 2001; Eversole et al., 2008; Pilch, 2001). Taking this into account, it seems plausible that periapical inflammation connected to the loss of the second molar of the left maxilla led to chronic dental sinusitis, which then triggered an ossification process in the maxillary sinus. Effects of periodontal or dental disease on the maxillary sinuses are often underestimated. Only a thin layer of bone exists between the root tips of the upper posterior teeth and the maxillary sinus, and the roots often protrude into the sinus (Abrahams & Glassberg, 1996; Bomeli, Branstetter, & Ferguson, 2009; Shanbhag, Karnik, Shirke, & Shanbhag, 2013). Inflammatory tissue can spread over the infected root apexes and lead to swelling and histopathological changes of the adjoining sinus mucosa, which can result in fibrosis and hyperplastic changes.

The maxillary sinuses are part of the respiratory system and are involved in warming and moistening of the air, the resonance enhancement of the voice, and the sense of smell. It is possible that the male individual from Hettstedt was impaired in these functions accompanied by a feeling of pressure and a tendency to experiencing headaches. Numerous dental diseases (individuals with caries 79%; caries-affected teeth 21%; and individuals with periapical lesions 53%) could be detected in the adult skeletons from Hettstedt-

Kirchplatz, indications of sinusitis were found in 19 adults (Rossbach, 2016). However, the lesion described remains an isolated case.

5 | CONCLUSION

The study presents an osseous lesion measuring 2.5 × 1.5 cm that completely filled the left maxillary sinus of a male skeleton from a medieval graveyard at Hettstedt, Central Germany. The macroscopic, computed-tomographic, and histological features point to a benign formation of additional bone with high mineral content that is clearly distinguishable from the adjacent sinus wall with a connection to the alveolus of the second molar. Although some of the characteristics are the same from a radiological and histopathological point of view, FD and COD, odontogenic tumours, and sclerosing osteomyelitis can largely be excluded. Two types of disease appear to be of particular diagnostic probability: chronic sinusitis with reactive and tumour-like ossification or a sinus osteoma. Because chronic inflammation is considerably more prevalent in the maxillary sinus than osteoma, which more often develops in the frontal and ethmoid sinus, we believe that dental sinusitis with reactive ossification appears to be the most likely cause for the unusual bony structure found in this medieval burial.

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