Ovarian teratoma: A case from 15^{th}-18^{th} century Lisbon, Portugal

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Abstract

This paper discusses the differential diagnosis of an unusual calcified mass found in the pelvic cavity of 45+-year-old female excavated from 15th-18th century Lisbon (Portugal). The mass is relatively large, irregularly shaped, and exhibits a concave base with malformed teeth embedded within its inner surface. Considering its macroscopic and radiological characteristics, several conditions were considered in the differential diagnosis, namely eccyesis, *fetus in fetu*, lithopaedion, and ovarian teratoma. However, the morphological features of the specimen, such as its structure, morphology, and dimensions, are diagnostic of a teratoma. Its location and the sex of the individual are more specifically compatible with a calcified ovarian teratoma. With regional and temporal variations in the frequency of tumours, the report of new cases becomes imperative, especially from geographic regions where few cases have been identified. In fact, this appears to be the first case of ovarian teratoma detected in the Portuguese archaeological record and adds to the few palaeopathological cases described in the osteoarchaeological literature worldwide.

Key words: Pelvic calcification, Tumour, Palaeopathology, Largo do Carmo.

1. Introduction

During the second season of archaeological interventions (2010/2011) carried out in the cemetery located in Largo do Carmo, outside the Church and Convent of Carmo (Figure 1), Lisbon, Portugal, an incomplete skeleton with a relatively large pelvic calcified mass caught the attention of the excavators. At that time, the recovered bones were mainly those from the lower limbs but, in the campaign of 2013/2015, the remainder of the skeleton was exhumed, enabling its analysis and reporting.

Figure 1. (a) Location of Convent of Carmo in Lisbon; (b) Location of Lisbon in Portugal (Photo credits: Google Earth).

1.1 Archaeological background

The Church and Convent of Carmo were built by Nuno Álvares Pereira as a religious vow for the Portuguese victory over the Kingdom of Castile (Spain) at the Battle of Aljubarrota in 1385 (Santa Ana, 1745; Pereira, 1989). However, the construction of this gothic monument was difficult due to the instability of the soils, being completed only after its structure collapsed twice (Sequeira, 1939). In addition, it had been damaged by the earthquake of 1531, after which it was repaired. In the 17th century the urban environment of Convent of Carmo was transformed, with the destruction of part of its early cemetery (Marques and Bastos, 2013). In the 18th century, it was once again severely damaged by the 1755 earthquake. After that, just some minor incomplete repairs were performed once it was decided to leave the monument in ruins, in remembrance the catastrophic event. Hence, it is believed that the cemetery was used between the beginning of the 15th century and 1755 AD.

Despite the location of the graveyard in an urban area, it was not a public cemetery, receiving only either members of the religious brotherhoods related to the Church of Carmo or patrons. Therefore, it can be hypothesised that most of the individuals buried outside the church would belong mainly to the middle class. Additionally, along the southern façade of the church there are inscriptions referring to several middle-class professions, such as shoemaker and tailor.

In 2010/2011, an archaeological excavation of the surroundings of the Church and Convent of Carmo led by a team from the Centro de Arqueologia de Lisboa (‘Lisbon Archaeological Centre’ - Câmara Municipal de Lisboa) was undertaken due to the implementation of an urban renewal project. The excavations recovered 42 individual burials in varying states of preservation. Most of the individuals were in an east to west orientation with head to the west (in accordance to the Christian belief in the resurrection of the soul), and were buried in simple pits, in the field surrounding the south and west fronts of the church, which began to be urbanized after the 17th century. Individual 22, described here, was lying in a supine position, with the upper limbs crossed over the waist and the lower limbs extended (Figure 2), in compliance with the standard Catholic rite of the time. The presence of strict anatomical connections is demonstrative of a primary burial (following Duday, 2009). The skeleton was surrounded by a thick layer of lime (information reported by the excavation team), presumably deposited over the corpse at the time of death (Figures 2 and 3). Lime (both CaO and Ca(OH)2) was used as a biocide, particularly in cases of mass graves due to infectious disease, in order to prevent the growth of micro-organisms and retard the rate of decomposition in the burial environment. For a more comprehensive contextualization of this collection, see Alves et al. (2017).

Figure 2. (a) The incomplete skeleton recovered in the campaign of 2010/2011 from Largo do Carmo; (b) Close-up of the calcified mass found between the *ossa coxae* (Archive photo: *Centro de Arqueologia de Lisboa*).

Figure 3. The remainder of the skeleton exhumed in the campaign of 2013/2015 from Largo do Carmo (Archive photo: *Centro de Arqueologia de Lisboa*; *Neoépica, Arqueologia e Património*).

2. Materials and Methods

Sex determination was made based on the morphology of the *os coxae* (Bruzek, 2002) and the morphometric analysis of the long bones, the calcaneus and talus (Cardoso, 2000; Wasterlain, 2000; Garcia, 2012). As the pubic symphysis was not preserved, the age-at-death estimate was taken from morphological changes of the auricular surface of the ilium (Lovejoy et al., 1985) and the sternal rib ends (Işcan et al., 1984). As the long bones were fragmented and it was not possible to measure their lengths, stature was estimated on the basis of the maximum length of the first metatarsal, following Cordeiro et al. (2009). The preservation of the skeletal remains was determined by calculating the Anatomical Conservation Index developed by Garcia (2005/2006). This index corresponds to a modification of the method developed by Dutour (1989), which divides each skeleton into 44 parts, grouped into four anatomical regions: cranium, axial skeleton, appendicular skeleton, and extremities. Each anatomical part is classified with a value between 0 (absent bone) and 1 (complete or almost complete bones). For the anatomical parts constituted by several elements (e.g., teeth, vertebrae, ribs, hands and feet), Garcia (2005/2006) suggests the calculation of the Bone Representativeness Index (BRI = Σ skeletal elements observed /number of expected skeletal elements). In short, the objective of the BRI calculation is to assist in the determination of a more accurate ACI. For further details, see Dutour (1989) and Garcia (2005/2006).

All the bones of Individual 22 were analysed by careful visual inspection under good lighting conditions. The pelvic calcified mass was carefully cleaned in the laboratory with the aid of a soft toothbrush, macroscopically observed as well as radiographed (Phillips Practix 300; voltage: 47 kV; exposure 8.00 mAs). The differential diagnosis of the mass was performed following Steinbock (1989), and taking into consideration its shape, structure, size and location, as well as the age and sex of the individual. Also, in order to make the degree of confidence an overt part of the diagnostic process and remove any potential ambiguity, the modified Istanbul Terminological Framework (Appleby et al., 2015) was adopted in the process of reaching and reporting the differential diagnosis.

3. Results

The skeletal remains represent a woman over 45 years old at the time of death. The stature was estimated as 155.95 ± 4.69 cm. Given that several bones were present in the field, but did not survive the excavation (e.g., most vertebrae, the *corpus sterni* and manubrium), the Anatomical Conservation Index score was only 52%.

Within the pelvic girdle, a calcified mass of the same colour and texture as the bones was found. The specimen, measuring 37.9 mm in length and 43.4 mm at its maximum diameter, displayed a concave base with malformed teeth embedded within its inner surface (Figure 4). After careful cleaning, it was possible to verify that both the outer and inner surfaces of the mass are irregular, exhibiting disorganized and asymmetrical bone formation.

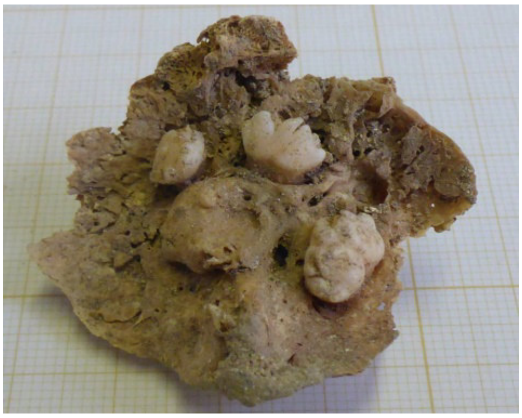

Figure 4. The calcified mass found between the *ossa coxae* of Individual 22. In its concave bony base it is possible to identify embedded malformed teeth (Photo by RVA).

Of the five observable teeth, four have morphology similar to that of human molars, with one appearing caniniform (Figure 5). Four dental elements (three molariform and one caniniform teeth) show clear cemento-enamel junctions. The other molariform tooth is extremely malformed and does not have its root.

Figure 5. Malformed teeth recovered from the inner surface of the calcified mass found associated with Individual 22. The dental element on the left can be classified as caniniform, while that of the right is molariform. (Photo by RVA).

A radiographic view (Figure 6) of the calcified mass did not show any other bone structure inside the mass. The root of the *in situ* tooth was completely formed.

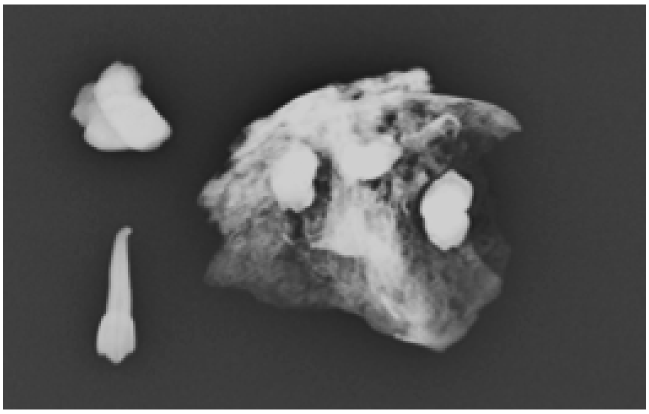

Figure 6. An x-ray image of the calcified mass and malformed teeth found associated with Individual 22.

The skeleton did not exhibit any bone changes directly related to the calcified mass. Only a remodelled fracture of the fourth proximal phalanx of the left hand is noteworthy. The skeleton did not show any signs of infection, but did demonstrate new bone formation around the margins of the left proximal tibia. Some thoracic vertebral bodies also displayed slight marginal osteophytes.

4. Discussion

The differential diagnosis of the calcified pelvic mass gives rise to several possible aetiologies, namely, eccyesis, *fetus in fetu*, lithopaedion, and ovarian teratoma.

Eccyesis, or ectopic pregnancy, is a potentially life-threatening condition involving the development of a fertilized ovum outside the uterus, most frequently (80% of cases) within a fallopian tube (Lobo, 2012; Klaus and Ericksen, 2013; Panelli et al., 2015). Without treatment (the first successful operative treatment was performed in 1883 in England by Lawson Tait), this situation leads to ever-increasing haemorrhaging that may culminate in the mother’s death (Lobo, 2012). About 75% of the women with fatal ectopic pregnancies die in the first 12 weeks of gestation, while 25% perish after the first trimester. However, certain ectopic pregnancies may resolve without treatment. In such cases, the foetus is sequestered, being progressively resorbed until the end of the first trimester (Lobo, 2012), or even remaining and calcifying within the mother’s body. In fact, one of the possible terminations of extra-uterine pregnancies is lithopaedion (Lachman et al., 2001; Ramos-Andrade et al., 2014; Medhi et al., 2014).

Lithopaedion (from the Greek *lithos*, meaning stone and *paidion* meaning child) is an obstetric phenomenon where a dead foetus becomes calcified within the abdominal or retroperitoneal space of the mother (Burger et al., 2007). It is an extremely rare phenomenon, occurring in 0.0054% of all gestations (less than 300 have been reported in the clinical literature). Lithopaedion was first described in the 10th century by a surgeon of the then Arabic-dominated era of medicine, Albucasis. Since then, lithopaedion has been identified in women aged between 20 to 100 years old at the time of diagnosis, most of them being over 40 years old, varying in the period of the retention, with estimates ranging from less than 18 months to 60 years (Lachman et al., 2001; Medhi et al., 2014; Ramos-Andrade et al., 2014). Lithopaedion physically resembles a foetus, with identifiable skeleton and teeth in different stages of development depending on the age-at-death of the foetus (Lachman et al., 2001; Klaus and Ericksen, 2013).

Fetus in fetu (FIF), first described by Johann Friedrich Meckel during the late 18th century, is defined as the inclusion of a monozygotic, diamniotic, monochorionic, malformed foetus, inside the body of another normally developing foetus. This extremely rare phenomenon (overall clinical prevalence is 1:500,000 live births, with fewer than 100 cases reported worldwide) is believed to be connected with unequal division of parasitic blastocyst totipotent cells (Gangopadhyay et al., 2010; Klaus and Ericksen, 2013). It is usually a benign condition, more frequently found in infants and children (about 90% of cases are identified before 18 months of age) (Karaman et al., 2008; Gupta et al., 2010; Mohta and Khurana, 2011), although there have been reports of cases in adults (Massad et al., 2001). Symptoms occur due to the parasitic twin compressing the surrounding organs of its host (Reddy et al., 2012). The most common location is in the retroperitoneum (80%), but they can also occur in other parts of the body, namely the cranium (8%), and sacrococcygeal region (8%) (Maryńczak et al., 2014). The FIF is usually anencephalic and acardiac, but in almost all cases presents a defined vertebral column (91%) with recognizable limbs or limb buds (82.5%) (Gangopadhyay et al., 2010). The lower limbs are frequently more developed than the upper limbs (Reddy et al., 2012; Klaus and Ericksen, 2013). FIF may contain multiple foetuses (Gangopadhyay et al., 2010). The presence of a vertebral column is considered an important but not indispensable feature to distinguish FIF from a teratoma (Gangopadhyay et al., 2010; Mohta and Khurana, 2011; Maryńczak et al., 2014).

Teratoma (from the Greek *teras*, meaning monster and *onkoma* meaning swelling) is a tumour characterized by multiple tissue types derived from all three primitive germ layers (endomeso- and ectoderm), such as hair, teeth, bone, rudiments of thyroid gland, etc. (Kitamura and Inokuchi, 1988; Comerci et al., 1994; Charlier et al., 2009; Armentano et al., 2012; Khan et al., 2014). They may exhibit varying levels of maturation, ranging from very slight differentiation (an immature teratoma) to perfectly differentiated tissues (a mature teratoma) (Charlier et al., 2009). Even if teratomata can form in males, mature tooth and bone-forming teratomata are usually of ovarian origin (Klaus and Ericksen, 2013). In fact, mature teratomata are the most common ovarian tumours, accounting for 10-20% of all ovarian tumours (Kim et al., 2011; Khan et al., 2014). Although the majority of these tumours arise in the gonads, other possible locations are the mediastinum, retroperitoneum, intracranium, and sacrococcyx (Main, 1970). Teratomata are known to occur at any age, but most develop during the reproductive years (Main, 1970; Kitamura and Inokuchi, 1988; Kim et al., 2011). The majority of them are monolocular, displaying a rounded, white shiny mass, the Rokitansky protuberance, or the umbo, projecting from the wall of the ovary towards the centre. When teeth or bone are present, they are typically situated in this area (Comerci et al., 1994). According to Main (1970), the frequency of dental constituents in ovarian teratomata is *circa* 26-39%. The number of teeth in any one specimen is usually two or three, although this number may be greater. Teratomatous teeth are morphologically similar to normal teeth, and tend to exhibit a permanent dental morphology. They usually resemble canines, premolars and molars but are smaller in size, assuming a bulbous, deciduous form (Main, 1970). Despite possessing distinct components such as tooth crowns, roots, and dentin, the roots are often semi-complete (Klaus and Ericksen, 2013).

The most frequent size of a teratoma ranges between 5 and 15 cm in diameter, but some reach 45 cm. In 60% of cases, patients are asymptomatic, although sometimes the development of the tumour results in displacement and subsequent functional disturbances of adjacent organs (Comerci et al., 1994; Armentano et al., 2012). It should be noted, however, that teratomata present a distinct malignant potential, particularly at the Rokitansky protuberance (Comerci et al., 1994; Massad et al., 2001). Teratomata can co-exist with FIF (Mohta and Khurana, 2011).

The morphological and radiological characteristics of the pelvic mass of Individual 22 from Largo do Carmo were not consistent with the first two conditions (eccyesis and lithopaedion). Eccyesis could be excluded because the bony remains are not consistent with those of a foetal skeleton; the teeth are too highly developed and thus anatomically inconsistent with a foetal dentition, even if this had been an advanced ectopic pregnancy that persisted into a second or third trimester. On the other hand, lithopaedion was eliminated due to the degree of anatomical disorganization exhibited by the analysed mass.

Taking the controversies regarding the differentiation between FIF and ovarian teratoma into account, more attention was given to the characteristics that would distinguish between these two possible diagnoses. While in the past the presence of the axial skeleton has been considered mandatory for a positive diagnosis of FIF (Reddy et al., 2012; Klaus and Ericksen, 2013), over the years several cases of FIF lacking a vertebral column have been reported (Mohta and Khurana, 2011). Instead, the major difference between these two conditions is that whereas a teratoma is composed of one or more of the three primary embryonic germ layers in a discordant mode and shows less organization, a true *fetus in fetu* exhibits a higher degree of structural organization (Massad et al., 2001; Mohta and Khurana, 2011). Therefore, and according to the modified Istanbul Protocol criteria, the appearance of the described specimen, namely its structure, morphology, and dimension, could be described as 'diagnostic of' a mature teratoma. Its location and the sex of the individual are more specifically compatible with a calcified ovarian teratoma.

Although the absence of soft tissues precludes determination of the mass as being benign or malignant, it should be noted that the skeleton does not present any bone changes related to the presence of the teratoma, namely identifiable metastatic lesions. The only lesion worth noting is a remodelled fracture in the fourth proximal phalanx of the left hand which bears no relation to the phenomenon described herein whatsoever. Regarding the implications that this condition could have had on the life of this woman, it is important to note that, although teratomata are, in most cases, benign and asymptomatic (Comerci et al., 1994), they sometimes lead to displacement of the adjacent organs and consequent disturbances, infection and anaemia (Armentano et al., 2012). However, based only on the available observations, it is impossible to know if this ovarian teratoma had any effect on the life or contributed to the death of this woman. The fact that this woman's corpse had been covered with lime (a very uncommon practice at that time) suggests that an infectious/contagious disease could have been the cause of her death, not the teratoma, although it is not possible to be more positive than this.

With regional and temporal variation in the frequency of tumours, the report of new cases becomes imperative, especially from geographic regions where few cases have been identified previously (Ortner, 2003; Brothwell, 2012). As already mentioned by several authors (Strouhal, 1991; Marks and Hamilton, 2007), documentation of tumours in antiquity represents a significant contribution to palaeopathology in light of the increasing epidemiological, demographic, and clinical importance of cancer today. Some types of tumours that are thought to be characteristic of the present times and commonly attributed to the western civilization are also found in past populations (Schultz et al., 2007). This case appears to be the first case of ovarian teratoma detected in a Portuguese archaeological assemblage and adds to the few palaeopathological cases described in the osteoarchaeological literature worldwide (Charlier et al., 2009; Armentano et al., 2012; Klaus and Ericksen, 2013). In 2003, Komar and Buikstra made the differential diagnosis of a biological object recovered from the pelvic region of an adult female excavated from the Koster

(Illinois) site. While a diagnosis of lithopaedion could not be ruled out, calcified lymph node or amputated ovary were considered as most probable.

5. Conclusions

Differential diagnosis in osteoarchaeological specimens is always difficult, being limited due to the absence of clinical attributes. A more confident diagnosis can be achieved by performing histological analysis of the lesions, which was not allowed in this case since it is a destructive procedure. Even so, based on the macroscopic and radiological characteristics of the mass found at the Largo do Carmo, Lisbon, Portugal, the first case of mature ovarian teratoma in the Portuguese osteoarchaeological record is reported, joining only three other known cases described in the palaeopathological literature (Charlier et al., 2009; Armentano et al., 2012; Klaus and Ericksen, 2013). Although it is not possible to determine if the mass was benign or malignant, the skeleton does not present any bone changes related with the presence of the teratoma. Moreover, based only on the available observations, it is impossible to know if this ovarian teratoma had any effect on the life of this woman. The fact that this woman's corpse had been covered with lime suggests that an infectious/contagious disease could have been the cause of her death, not the teratoma, although it is not possible to be sure of that. With regional and temporal variances in the frequency of tumours, the report of new cases becomes imperative, especially from geographic regions where few cases have been identified previously (Ortner, 2003; Brothwell, 2012). Documentation of tumours in antiquity represents a significant contribution to palaeopathology in light of the increasing epidemiological, demographic, and clinical importance of cancer today (Strouhal, 1991; Marks and Hamilton, 2007). Some types of tumours that are thought to be characteristic of modern societies and commonly attributed to Western civilization are also found in past populations (Schultz et al., 2007). This case also draws attention to the importance of conducting meticulous archaeological excavation in order to preserve rare, but significant findings. During excavation of human remains, materials from body cavities, which may provide clues not directly accessible from the skeleton, should always be sought and recovered with care.

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