

Breast cancer in the 17th century: the cases of the wives of Luis Guillermo de Moncada (1614-1672)

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Abstract. The human remains of nobles housed in the Neapolitan Basilica of Saint Domenico Maggiore (15-17th centuries) are an important series with regard to paleo-oncology, since three out of five cases of soft tissue tumours known in paleopathology worldwide are documented in this Italian series. Among the bodies of Saint Domenico Maggiore there are the first and the second wife of the Prince Luis Guillermo de Moncada (1614-1672): Maria Afán de Ribera (ca1615-1639) and Catalina Moncada de Castro (1611-1659). Both women died of breast cancer, as shown by the archival sources. The bodies of the two women are skeletonized and the radiological analysis allowed us to identify some focal osteolytic lesions of neoplastic origin. These cases constitute the first examples of breast cancer diagnoses in ancient human remains supported by the integration of archival sources and paleopathological investigations. These two new cases must be added to the three previously known malignant tumours from San Domenico Maggiore. In this Neapolitan series, out of a total of eighteen adult individuals aged 25-71 years, five (28%) were affected by cancer. Despite the small sample size, this prevalence is surprisingly comparable to that of the contemporary Western world.

Key words: Paleo-oncology, breast cancer, paleopathology, 17th century medicine, Moncada

Introduction

Breast cancer is the most frequent malignant neoplasm among women worldwide; in 2018, the GCO (Global Cancer Observatory) reported about 2.1 million diagnoses of breast cancer in women, corresponding to 11.6% of all malignant tumors, and over half a million new cases of breast cancer, equal to 26.3% of total female cancers, were diagnosed in Europe (1).

However, cancer is not a modern disease and has affected humankind since the most ancient times, as demonstrated by relevant, albeit sparse, paleopathological evidence (2, 3). The striking not high number of cancer cases in archeological populations seems correlated with a combination of several elements, among which the most relevant are a short life span and the absence of many risk factors, such as cigarette smoke, pollution, and chemical substances, in the pre-modern era (4, 5). In ancient skeletonized human remains, neoplastic conditions can be diagnosed as primary

benign or malignant bone tumors, as bone metastases secondary to tumors originating in the soft tissues, or as calcifications of tumoral masses (6).

Breast cancer has been known since antiquity. The Latin word “*cancer*” (crab) derives from the description of this specific kind of tumor provided by Galen, who compared the shape of breast cancers to the appearance of crabs (7). However, breast cancer, as other malignant soft tissue tumors, is extremely difficult to identify with certainty in ancient skeletal remains; indeed, the metastatic lesions it produces in bones are not pathognomonic and, in the majority of cases, it is not possible to determine the site of origin of the cancer whose development led to bone metastases (8, 9).

The mummified and skeletonized remains of individuals belonging to the Aragonese and Spanish vice-royal court of Naples, buried in the Neapolitan Basilica of San Domenico Maggiore (15th-17th century), constitute an important series with regard to paleo-oncology, since three of the five cases of soft

developed by hand on site, with Agfa developing for automatic processors, at a temperature of 20°C, and with Agfa fixing; for washing, in running water, drinking water from the Naples aqueduct was used.

Sex was estimated by the morphological features of the pelvis (13-16) and skull (17-20) and by the cotylo-sciatic index (21). Age at death was assessed on the basis of the morphology of os pubis (22-25), the Acsádi and Nemeskéri Complex Method (26) and the Radiographic Method of Walker and Lovejoy (27).

The nosography of Maria Afán de Ribera y Moura (ca. 1615-1639) is based on a Spanish-language anonymous manuscript stored in the National Library of Spain titled "*Discurso elocuente sobre la muerte de la Illustrissima y Excelentissima Señora Doña Maria Afán Enriquez de Ribera, Princesa de Patternò, duquesa de Bivona y de Alcalá*" and dating back to 1644-49 (28). The illness of Catalina Moncada de Castro (1611-1659) was described by Gavino Farina, the court physician of the Moncada family who attempted to cure the noblewoman, in a Latin written essay printed in 1658 and titled "*Apologia in curatione excellentissimae Catherinae Moncatae, ducissae Montisalti*" (29). For this study the edition of Farina essay stored in the University Library of Sassari has been consulted.

Results

The bodies of the two individuals, completely skeletonized, were preserved in wooden coffins in the Sacristy of San Domenico Maggiore in Naples. The two skeletons, almost complete, have not undergone taphonomic alterations, since they have been preserved in coffins suspended over the gateway of the Sacristy, several meters above the ground, in an airy and dry environment.

The epigraphs placed on the coffins and bearing the names and titles of the two noblewomen have facilitated the identification (30), confirmed by the anthropological study: the individual NASD 32, marked by the epigraph with the name MARIA HENRIQUEZ A RIBERA, is an adult female of about 25-30 years of age; the individual NASD 31, marked by the epigraph of CATERINA DE MONCADA, is a female of 45-55 years of age.

Recently, a new, accurate study of the radiological documentation allowed to detect some focal osteolytic lesions, which had previously, at the time of the first investigation, gone unobserved.

The skeletal remains of NASD 32 (Maria Afán de Ribera y Moura) exhibit osteolytic lesions ranging from 8 mm to 35 mm in size and lacking reparative sclerotic borders on the head of the right humerus (Figure 2A) and of the right femur (Figure 2B).

In the case of NASD 31 (Catalina Moncada de Castro), irregular and roughly circular osteolytic lesions ranging from 10 to 20 mm in size and displaying no signs of reparative bone reaction are visible on the head and neck of the right humerus (Figure 2C), on the neck and at the base of the greater trochanter of the right femur (Figure 2D), on the lateral epicondyle of the left femur (Figure 3E), on the fibular notch of the right tibia (Figure 2F), and on the medial malleolus and fibular notch of the left tibia (Figure 2G). Finally, a small irregular osteolytic area is present on the squamous part of the frontal bone.

In breast cancer, bone metastases typically involve the ribs, pelvic girdle, vertebrae, skull, scapulae and proximal ends of the femora and humeri, favoring highly vascularized sites (31). Lesions are generally osteolytic, although osteoblastic and mixed metastases can also occur (32).

The course of the disease affecting Maria Afán de Ribera y Moura (ca. 1615-1639), the first wife of Prince Luis Guillermo, is described in an anonymous manuscript stored in the National Library of Spain and dating back to 1644-49 (28). According to that available written source, she developed breast cancer at a very early age and was tormented by the disease in the last three years of her life, from 1636 to 1639. She was submitted to a brutal procedure in use at the time, consisting in the surgical removal of the tumoral mass through cauterization. Unfortunately, this procedure was unsuccessful in treating the cancer and Maria died in 1639, at just about 25 years of age (28).

As for the second wife of Prince Guillermo, Catalina Moncada de Castro (1611-1659), a description of her illness was compiled directly by Gavino Farina, the court physician of the Moncada family who attempted to cure her (29). According to his account, the first symptoms of mammary cancer appeared five

years before her death, when she was aged 44. The tumoral mass grew progressively, but the princess was never submitted to surgical intervention. The physician Farina administered slightly invasive Galenic therapies, including bloodletting, purges, and herbal tablets containing solanum, purslane, and burnet.

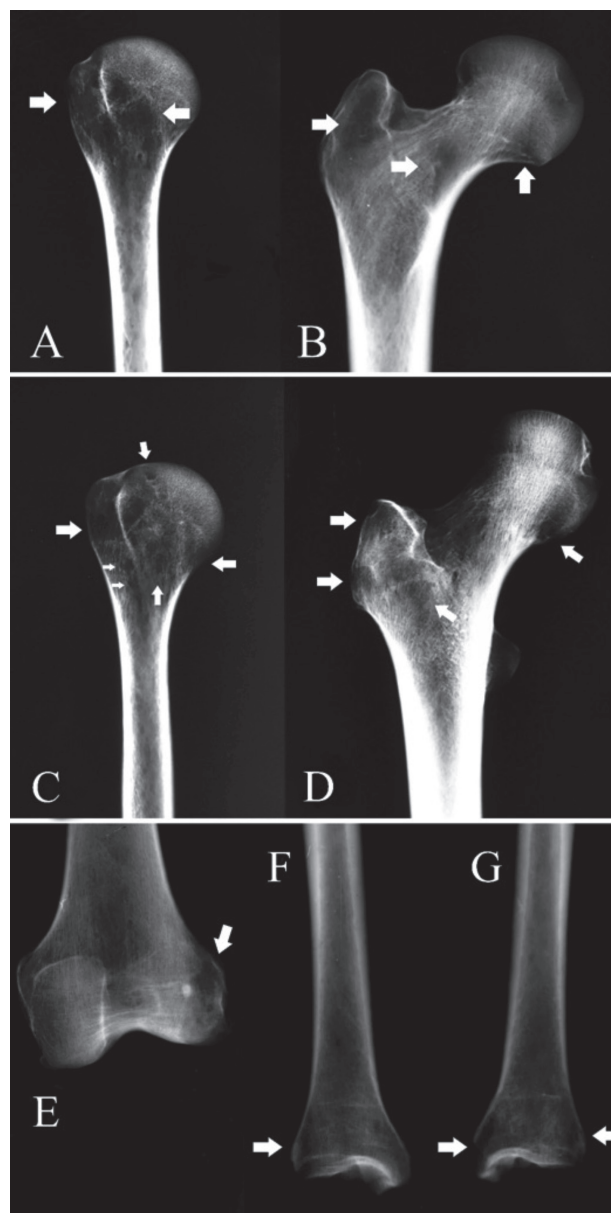


Figure 2. X-ray of the right proximal humerus (A) and right proximal femur (B) of Maria Afán de Ribera y Moura, duchess of Montalto (ca. 1615-1639). X-ray of the right proximal humerus (C), right proximal femur (D), left distal femur (E) and distal tibiae (F-G) of Catalina Moncada de Castro (1611-1659). The arrows indicate osteolytic lesions and areas of rarefaction without any reparative sclerotic borders.

Nevertheless, treatment was unsuccessful in this case as well, and Catalina died in 1659, at the age of 49.

The anamnestic-nosographic data and the morphology of the osteolytic lesions detected thanks to the radiological images allowed us to conclude that the two wives of Louis Guillermo de Moncada both died of breast cancer.

Discussion

The Sicilian Luis Guillermo de Moncada (1614-1672), Prince of Paternò and Duke of Montalto, was one of the most important political figures of the Spanish Empire in the 17th century. Under the reign of King Philip IV (1621-1665), he was first President of the Kingdom of Sicily (1635-1639), and later Viceroy of Sardinia (1644-1649) and Valencia (1652-1658) (33). The two wives of Luis Guillermo both died of breast cancer, as confirmed by the analysis of historical documents reporting details about their disease in combination with the paleopathological assessment of their skeletal remains.

Maria Afán de Ribera y Moura (ca. 1615-1639), whose precise date of birth is unknown, has an estimated skeletal age at death of about 25 years. Considering the young age of onset of the disease, it can be hypothesized that Maria suffered from hereditary breast cancer (probably breast cancer 1 or breast cancer 2) (34).

The great Italian surgeon Girolamo Fabrici d'Acquapendente left a detailed description of the typical breast cancer operation in the early 17th century: after grasping and holding the mass firmly with pincers, the surgeon used a sharp, hot knife to remove the tumor and, at the same time, stop the bleeding (35) (Figure 3). This surgical treatment was clearly destined to fail in the case of metastatic spread, i.e. at an advanced stage of tumor development, as already observed by Galen, who wrote: "We have often cured this disease in the early stages, but after it has grown to a noticeable size no one has cured it with surgery." (36). Thus, it can be supposed that Maria was diagnosed with breast cancer when the disease was already at a late stage and that treatment was therefore ineffective.

Most 17th century physicians still accepted the traditional Galenic etiology of tumors as localized

manifestations of a humoral excess of black bile, but there were very different schools of thought regarding methods for the treatment of cancer (37).

In 1632, the Neapolitan surgeon and physician Marco Aurelio Severino edited the text *“De recondita abscessum natura”*, in which he advocated intervention- al surgery for the removal, with a scalpel or cautery, of tumoral masses, as well as axillary nodes that appeared enlarged at the time of radical excision of the affected breast (38). Severino’s theoretical and practical influence extended from the Hospital for the Incurables in Naples, where he worked, to most of the Spanish domains in southern Italy (39) and Moncada’s first wife, Maria, was likely treated by a follower of this great Neapolitan surgeon.

In the case of Catalina di Moncada de Castro, second wife of Luis Guillermo de Moncada, considering the age

of onset of the disease (44 years), it can be hypothesized that the tumor could have belonged to a premenopausal type of breast cancer (40). Catalina was treated by the Sardinian court physician Gavino Farina, who belonged to a completely different school from that of Severino. In fact, he favored a limited recourse to surgery, refusing the use of scalpel and cautery on the tumoral mass. Similarly to Farina, other 16th-17th century physicians and surgeons with significant practical clinical experience, like Ambroise Paré (1510-1590), argued that the surgical removal of tumors was almost completely useless (36).

The two cases of Moncada’s wives, although reflective of a common interpretation of the etiology of breast cancer, which was correlated to the humoral theory, are representative of the two contemporary, but opposite tendencies in breast cancer treatment during the 17th century.



Figure 3. Mastectomy. Drawing attributed to a Dutch artist, 17th century. Pen and grey ink and grey wash within brown ink framing lines, 9.9 x 12.8 cm [courtesy of Wellcome Collection. Attribution 4.0 International (CC BY 4.0)].

The historical and archival sources provide documentary evidence of metastatic carcinomas in these noblewomen; hence, the paleopathological analysis of their skeletal remains appeared crucial to confirm the diagnosis.

What is worth noting is the presence of two cases of breast cancer within the same aristocratic family and, interestingly, in two individuals who were not consanguineous. Today, it is known that the failure of breastfeeding is a risk factor for the development of breast cancer (41-43). Maria and Catalina, mothers of one child and three children respectively, did not breastfeed their children, as was the custom for the nobility. Indeed, the habit of entrusting the nursing of babies to wet nurses was common among the aristocracy of the modern age and was aimed at facilitating a quick return of fertility after delivery in mothers, and, consequently, the birth of new heirs (44, 45). If Maria's breast cancer was probably favored by hereditary factors, in the case of Catalina, the lack of breastfeeding in three pregnancies may have played a role in the onset of the disease. Owing to this social behaviour, it can be suggested that, at least in some historical periods, breast cancer could have had a higher incidence than expected among the upper classes.

Conclusions

Thanks to the integration of paleopathological investigation and archival and nosographic sources, an unquestionable retrospective diagnosis of breast cancer could be formulated in two noble ladies of the 17th century. These two new cases must be added to the three malignant tumors previously known from the aristocratic series of the Basilica of San Domenico Maggiore in Naples (10). Therefore, out of a total of eighteen adult individuals, including twelve men and six women, five (28%) were affected by cancer, with cases documented in an age range between 20 and 71 years. Despite the small sample size, this prevalence is surprisingly comparable to that of the contemporary Western world (1). In this context, it can be hypothesized that cancer could have had an incidence not dissimilar to the present one in past human groups with analogous social and dietary habits, as seems to be the case for these members of the

15th-17th century nobility. Moreover, this historical perspective confirms the fundamental role of a correct lifestyle in cancer prevention.

While screening and early diagnosis, surgical treatment and adjuvant chemotherapy have significantly improved the prognosis of breast cancer, which has become one of the most treatable and curable tumors today (46), in the past, the natural course of the disease could never be changed, even with the sporadic recourse to surgery.

Ancient cases of cancer are of particular interest not only in relation to the history of medicine, but also to modern medicine; in fact, besides expanding the current knowledge about the incidence of neoplastic diseases in past populations, they can contribute to a better understanding of the evolution and contemporary patterns of carcinogenesis.

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