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Thoracic aortic aneurysm in a pre-Columbian (210 BC) inhabitant of Northern Chile: Implications for the origins of syphilis

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ABSTRACT

The aim of this work is to report a probable first case of a thoracic aortic aneurysm in the remains of a pre-Columbian individual from South America and to explore the relationship of this case to the only other paleopathological case previously described. We also consider the implications of both cases for the origins of syphilis. This study is based on the macroscopical analysis of human remains recovered during excavation of the Chiu Chiu 273 prehistoric cemetery, in the Antofagasta Region of Northern Chile. Ceramic sherds from the grave have a thermoluminescence date of 2160 ± 100 A.P. or 210 B.C. The skeletal remains of an adult individual display resorptive lesions in both the sternum and the first two thoracic vertebrae, which are suggestive of a thoracic aortic aneurysm. The lesions observed in the case described are clearly compatible with the development of an aneurysm of the thoracic aorta (ascending portion and arch). We suggest that this aneurysm has a syphilitic etiology, considering the vascular segments compromised, the type of lesions observed, and the prevalent etiology of this kind of cardiovascular pathology in pre-penicillin times. Since the only two cases of thoracic aortic aneurysms reported to date have been found in the Americas and are clearly pre-Columbian, it can be suggested that venereal syphilis was present in the Americas in times before European contact.

1. Introduction

Acute and chronic aortic diseases have been known for several centuries, with the earliest descriptions of these afflictions dating back to the time of Galen of Pergamon (Hartnett and Beatty, 1947; Ramanath et al., 2009). However, tangible evidence of their existence in bone and mummified remains of ancient populations has been elusive (Aufderheide and Rodríguez Martín 1998; Ortner, 2003), with only one possible case of a thoracic aortic aneurysm having been reported for a skeleton from Saskatchewan, Canada, radiocarbon dated at 2465 + 85 B.P. or 515 B.C. (Walker, 1983), and four additional cases of thoracic aortic aneurysms associated with bone erosion identified in individuals of the Hamann-Todd osteological collection (Kelley, 1979).

A thoracic aortic aneurysm is defined as a restricted dilation of the thoracic aorta (Agarwal et al., 2009). Anatomically, the thoracic aorta consists of three parts: (1) the ascending aorta, which commences at the left ventricle and ends near the sternal angle; (2) the aortic arch, which includes the segment between the sternal angle and the intervertebral disc located between T4 and T5; and (3) the descending aorta, which is the continuation of the arch (Woodbourne and Burkel 1994). The ascending aorta is 5 cm long, the arch 4.5 cm and the descending aorta 20 cm; its diameter is greater at its origin and diminishes gradually towards the distal end (Dotter and Steinberg, 1949; Posniak, 1990). From an epidemiological perspective, aneurysms that compromise the abdominal aorta are more common than those that affect the thoracic aorta (Lilienfeld et al., 1987; Perko et al., 1995).

Before the discovery of penicillin, venereal syphilis was probably the most frequent cause of thoracic aortic aneurysms, especially

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of the ascending aorta (Brindley and Stembridge, 1956; Heggtveit, 1964; Isselbacher, 2005, 2007; Roberts et al., 2009). The second most common cause was atherosclerosis and cystic medial degeneration (Brindley and Stembridge, 1956; Heggtveit 1964; Lilienfeld et al., 1987; Isselbacher, 2005). Other causes include Marfan's Syndrome, familial thoracic aortic aneurysm Syndrome, bicuspid aortic valve, Turner's syndrome, aortic arteritis, aortic dissection, and trauma (Hiratzka et al., 2010).

The aims of this work include presenting the probable first case of a thoracic aortic aneurysm in the remains of a pre-Columbian individual from South America and comparing this example to the case described for Saskatchewan, Canada, dated at 2465 + 85 B.P. or 515 B.C. (Walker, 1983). The differential diagnosis is discussed, as well as the implications of these two cases for the origins of Treponematosis, particularly venereal syphilis.

2. Materials

The human remains described in this work were recovered by archeologists Benavente and Thomas in 1995 during excavation of the Chiu Chiu 273 prehistoric cemetery (Thomas et al., 2002). The site is located 2.525 m above sea level, in the middle reaches of the Loa River in the Antofagasta Region of Northern Chile (Fig. 1). The cemetery is located within a large area where the bodies and grave goods are buried in circular or oval depressions. The recovered human remains are incomplete or represented by topographical segments (skull, thorax, pelvis or limbs), save a few complete and articulated skeletons (15% of individuals) and 1 mummy bundle. The minimum number of individuals was estimated at 48, of which 53% are subadults, with at least 8 individuals showing pathological conditions of diverse etiology. Based on the associated archeological context, this cemetery can be attributed to the Formative Period of the Andean Region, which is consistent with the thermoluminescence date of 2160 ± 100 A.P. or 210 B.C., based upon ceramic fragments associated with the grave (Thomas et al., 2002).

The skeleton is nearly complete, with only a few carpal and tarsal bones missing, along with five mandibular teeth. Among the missing teeth, the absent left third molar may represent agenesis, however this fact was not corroborated radiographically. The right and left central incisors, right third molar and distal root of the left first molar were lost postmortem based upon alveolar integrity. The left second molar was lost premortem based upon alveolar remodeling of the buccal cortical plate. Sex and age were estimated using standard forensic anthropological methods, which established the individual as an adult male (Buikstra and Ubelaker, 1994), 154–156 cm tall (Genovés, 1967) and approximately 45–50 years of age (Lovejoy et al., 1985; Meindl et al., 1985). The cranium displays artificial fronto-occipital modification caused by winding a fabric around the head (Buikstra and Ubelaker, 1994).

Pathological lesions were observed macroscopically and with magnification (10×). They were recorded photographically.

3. Case description

3.1. Sternal and vertebral lesions

The sternum displays resorptive lesions on both the manubrium and body (Fig. 2). The manubrium has a large lesion on the posterior surface associated with a perforation on the anterior aspect that partially compromises the right sternoclavicular joint, while the sternal body displays a circular cortical resorptive lesion (20 mm in diameter) on the left side of the upper third of the posterior surface. Additionally, the bodies of the first and second thoracic vertebrae display resorption, especially on the left side, most pronounced on T1 (Fig. 3); however, neither the clavicles nor the upper ribs (First and second) display any lesions. Other unrelated pathological conditions correspond to degenerative lesions of the vertebral bodies in the lumbar region, periodontal disease in both dental arches and dental caries in two teeth (18 and 28).

4. Discussion

4.1. Differential diagnosis

Given the magnitude and location of the sternal lesions; it is likely that a large mass in the anterior mediastinum compressed the posterior surface of the manubrium and the sternal body on the left side. This chronic compression would also have affected the bodies of the first two thoracic vertebrae. The location and depth of the lesions along with the age and sex of the individual suggests that the most likely cause was an aneurysm of the thoracic aorta affecting both the ascending portion and the aortic arch (Kelley, 1979; Ortner, 2003). The continual pulsations produced by the dilated arterial wall over a prolonged period of time caused resorption of the manubrium and body of the sternum (Devarajan and Subramaniam, 2011; Klokocovnik et al., 2011), as well as of the thoracic vertebrae T1 and T2. It should be noted that the list of options for a differential diagnosis is limited, and includes neoplasias—both primary and of the anterior mediastinum—and infectious processes (Shaham et al., 2004; Restrepo et al., 2009).

Most neoplasias that affect the sternum are metastases, especially of breast, lung, thyroid, kidney or colon cancers, or hematological ones such as lymphomas (Myre and Kirklin, 1956; Restrepo et al., 2009). Primary and secondary sternal tumors are uncommon (0.5% of all bone tumors) and are generally malignant (chondrosarcomas, plasmacytomas, lymphomas, osteosarcomas, fibrosarcomas) (King et al., 1986; Hoeffel et al., 1994; Martini et al., 1996; Restrepo et al., 2009; Nosotti et al., 2012). Among malignant neoplasms, chondrosarcomas are the most frequent and account for 33% of primary malignancies of the chest wall, being 80% from the ribs and 20% of the sternum (Myre and Kirklin,1956; David and Marshall, 2011). Benign primary neoplasms of the sternum are even rarer than malignant primary tumors and very few cases have been reported (Ahmad et al., 2015). Other neoplasias that could ultimately affect the sternum are tumors of the anterior mediastinum such as thymomas, particularly invasive or malignant ones (Tecce et al., 1994; Guermazi et al., 2001; Schaefer-Prokop, 2003). A primary or secondary tumor of the sternum was ruled out by the absence of blastic and destructive osteolytic lesions, a feature of skeletal malignant neoplasms of the anterior chest wall, since lesions observed in our case are resorptive with bone erosion limited to thinning of the sternum to varying depths.

Primary osteomyelitis of the sternum is a rarity and may occur as the result of infection, hemoglobinopathies or other immunosupressed states (Kelly and Chetty, 1985; Gill and Stevens, 1989; Upadhyaya et al., 2005; Restrepo et al., 2009; Sendi et al., 2015). Among the bone changes observed in sternal osteomyelitis are demineralization, destruction, and sequestra (Restrepo et al., 2009; Sendi et al., 2015), but none of them are present in our case.

4.2. Thoracic aortic aneurysms

Diseases of the thoracic aorta include congenital anomalies, degenerative abnormalities, atherosclerosis, and inflammation (Hiratzka et al., 2010; Stone et al., 2015) with aneurysm and dissection being the principal thoracic aortic diseases (Olsson et al., 2006). Thoracic aortic aneurysms can involve one or more aortic segments of the aorta and are classified according to which part is affected (Isselbacher, 2005, 2007; Irarrázaval et al., 2006; Hiratzka et al., 2010). In a population study conducted in 1982, Bickerstaff

Fig. 1. Map of northern Chile. The circle indicates the location of the Chiu Chiu archaeological site.

et al. found that the ascending aorta was compromised in 52% of cases, the aortic arch in 11%, and the descending aorta in 37% of cases.

The mechanisms that form thoracic aortic aneurysms are similar to those of aortic dissection and to a large extent involve medial degeneration, with focalized degeneration of the elastic and muscular tissue within the tunica media of the aortic wall (Hiratzka et al., 2010; Stone et al., 2015). As a result, the wall weakens and dilates from the intraluminal blood pressure (Isselbacher, 2005; Ramanath et al., 2009). The natural history of thoracic aortic aneurysms has not been well defined to date, and both the etiology and location of the aneurysm affects its growth rate (Isselbacher, 2005). Davies et al. (2002) established a mean growth rate for all thoracic aneurysms of 0.1 cm/year, but the rate of expansion was greater for aneurysms of the descending aorta (0.19 cm per year) than for those of the ascending aorta or aortic arch (0.07 cm per year) (Isselbacher, 2007; Hiraztka et al., 2010).

Erosion of the sternum and the vertebrae caused by aortic aneurysms are well described in the clinical literature (Brindley and Stembridge, 1953; Bromley, 1967; LeRoux et al., 1971; Leung et al., 1977; Kelley, 1979; Fulton et al., 1996; Aufderheide and Rodríguez-Martín, 1998; Lorusso et al., 2000; Carvalho et al., 2001; Bodhey et al., 2005). The anatomical proximity of the ascending aorta-aortic arch and the sternum, coupled with the fact that the anterior-posterior diameter of the thoracic cavity is minimal in this location. This could imply that a large aneurysm would eventually

Fig. 2. Erosive lesions on the posterior face of the manubrium and body of the sternum.

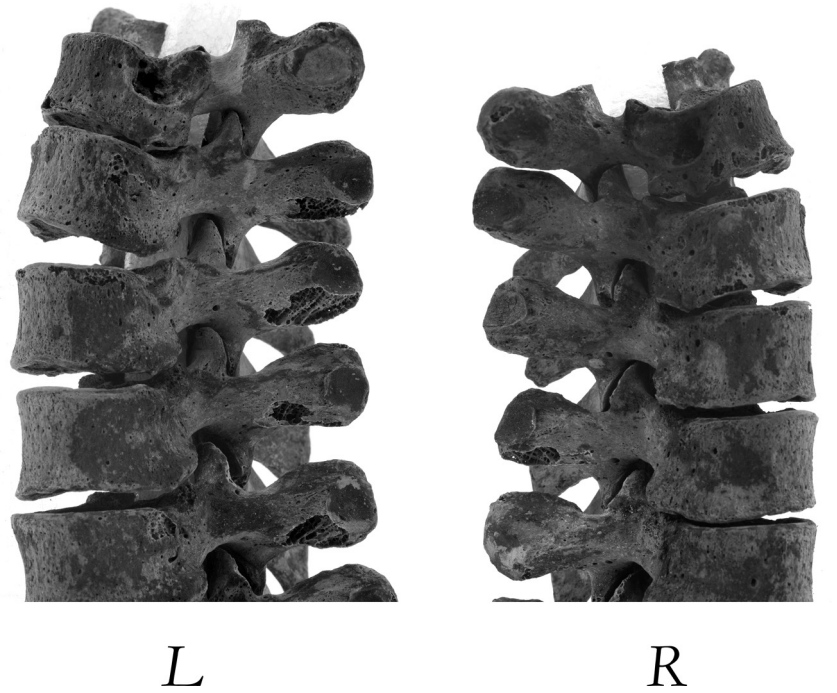

Fig. 3. Erosion on the left side of vertebral bodies of T1 and T2.

affect the sternum and/or vertebrae, especially given the rigidity of the trachea, which is situated immediately behind the aorta at this point (Fulton et al., 1996). Additionally, the irritation caused by the throbbing mass, which would act like an incessant liquid hammer, would produce an increase in osteoclastic activity, leading to bone erosion (Ortner, 2003; Bodhey et al., 2005).

4.3. Etiology of thoracic aortic aneurysms

In present-day populations, the incidence of thoracic aortic aneurysms is estimated to be around 10.4 cases per 100.000 person-years (Hiratzka et al., 2010) with atherosclerosis being the main cause. Most of them occur in the descending aorta (Joyce et al., 1964; Bickerstaff et al., 1982; Lilienfeld et al., 1987; Agarwal et al., 2009). Other causes include medial degeneration, aortic dissection, trauma, bacterial infections, aortitis and congenital aneurysms. Prior to the 1950s, the prevalent cause was venereal syphilis, followed by atherosclerosis and medial degeneration (Posniak et al., 1990). Brindley and Stembridge (1956) analyzed 9273 autopsies conducted between 1892 and 1953, finding 369 cases of aortic aneurysms; 77% of the earliest 100 cases, occurring between 1892 and 1928, had a syphilitic etiology, while just 49% of the last 100 cases, occurring between 1943 and 1953, were caused by syphilis.

The presence of cardiovascular disease in patients with untreated syphilis is one of the most thoroughly described conditions in 20th century medical literature. This condition occurs 10 to 20 years after the primary infection, and it is estimated that in the pre-penicillin era it accounted for 10 to 15% of all clinical cardiovascular illnesses. Cardiovascular disease was demonstrated in 3.9 to 83% of syphilitic patients autopsied (Rosahn, 1947; Clark and Danbolt, 1955; Singh and Romanowski, 1999; Agarwal et al., 2009). The Tuskegee study, begun by the U.S. Public Health Service in 1932, tracked African American males with untreated syphilis for a period of 40 years. The study found that 50% of patients infected for 10 years or more displayed compromised cardiovascular function (Peters et al., 1955).

The direct pathogenic effects of *Treponema pallidum* on blood vessels can include a variety of cardiovascular effects, among which are aortitis and aortic valve disease, aortic aneurysms and ostial disease of the coronary arteries (Rajendran, 2004; Klausner and Freeman, 2009; Horvath, 2011). Studies have demonstrated that pathological changes occur mainly on the ascending aorta, followed by the aortic arch, and the descending aorta (Cormia, 1935; Nicol, 1950; Heggtveit, 1964; Klausner and Freeman, 2009; Horvath, 2011; Conrad and Cambria, 2011; Stone et al., 2015). In the case of aneurysms, these are usually more likely to be saccular rather than fusiform, and in over 50% of cases they involve the ascending aorta (Heggtveit, 1964; Singh and Romanowski, 1999; Rajendran, 2004; Isselbacher, 2007). This means that the location of an aneurysm can point to its cause, and therefore, if it only compromises the ascending aorta, the cause would generally be associated with an annuloaortic ectasia, syphilis, aortic valvular disease, or infectious or non-infectious aortitis; atherosclerosis, in contrast, rarely affects this segment alone (Bromley, 1967; Fomon et al., 1967; Tadavarthy et al., 1981) and when it does, tends to be associated with diffuse aortic atherosclerosis. In addition, arch aneurysms are most often due to medial degeneration, syphilis or other infections (Isselbacher, 2007).

Considering that the lesions observed in this case are compatible with an aneurysm of the ascending aorta and aortic arch, and that previous to the discovery of antibiotics this pathology had an essentially syphilitic etiology (Fomon et al., 1967; Evangelista et al., 1999), we argue that this case would be one of the first to demonstrate syphilitic cardiovascular disease. The other forms of treponematosis—namely endemic syphilis (bejel) and pinta—do not lead to compromised cardiovascular function either in the early or late stage of the disease (Perine et al., 1984). Although it has been generally accepted that tertiary yaws does not result in cardiovascular or neurological disease, new clinical evidence shows the presence of cardiovascular disease, especially aortitis almost identical to that caused by syphilis in patients affected by tertiary yaws (Edington, 1954; Román and Román, 1986; Dutta, 2012; Mitja et al., 2013); however, cases of aneurysms of the aorta attributed to this disease have not been reported in the clinical literature.

4.4. Venereal syphilis and aortic aneurysms

There is general consensus that approximately 15–30% of individuals who have had syphilis develop late complications (tertiary syphilis), while the rest remain asymptomatic for the rest of their lives. Additionally, despite the lack of widely accepted epidemiological data regarding the real incidence and prevalence of gummatous, cardiovascular and neurosyphilis, an estimated 15% of those affected by late complications develop gummatous lesions (late benign syphilis), with 70% of the gummas affecting the skin, 10% the bone tissue and another 10% the mucosae (Donovan and Dayan, 2012). Another 10% also develop vascular complications (Nicol, 1950; Cates, 1998; Roberts et al., 2009, 2015; Horvath, 2011) and 10% display neurological compromise (Cates, 1998). Cardiovascular syphilis has been demonstrated in 3.9%–83% of autopsied syphilitic patients' (Cormia, 1935; Rosahn, 1947; Cates, 1998; Baker et al., 1999; Singh and Romanowski, 1999), and when associated with other lesions, these correspond mainly to neurosyphilitic lesions. If in association with gummatous lesions, most of these lesions affect the skin and only 1% are linked to bone (Cormia, 1935). This low level of association could explain the absence of bone lesions in other regions of the body in our case. Additionally, the presence of sternal and/or vertebral erosion resulting from aortic aneurysms has been proposed as one of the candidates for diagnostic criteria for venereal syphilis in paleopathological cases (Hackett, 1975).

The lesions observed in our case are similar to those described by Walker (1983) for the remains of Saskatchewan, Canada, and which were attributed to syphilis in consideration to the fact that this is the most probable etiology for aneurysms of the ascending aorta in preantibiotic times. On the other hand, the presence of *Treponematosis* in pre-Columbian Andean populations has been suggested by numerous authors (Allison et al., 1982; Standen et al., 1984; Verano and Lombardi, 1999; Standen and Arriaza, 2000), and in the case of northern Chile, Standen and Arriaza (2000) report an 18.5% incidence of bone lesions attributable to non-venereal *Treponematosis* of the yaws type in Archaic (4900–2500 B.C.) coastal populations from Arica and a 3.9% incidence in late Formative (2500 BC–500 A.D.) and Middle Intermediate (500–1000 A.D.) inland populations from the same region. In addition Castro et al. (2016) report a case from the coast of Antofagasta dated to the Middle Period (400–1000 A.D.), which has bone lesions attributable to treponemal disease (caries sicca and saber shin tibiae).

It is noteworthy that the only cases of thoracic aortic aneurysm reported to date in the paleopathological literature have been found in pre-Columbian human remains from the Americas, and both correspond to aneurysm of the ascending aorta. Thus, it can be suggested that these cases reinforce the proposal that both the venereal and non-venereal form of treponematoses were present in the New World before European contact (Harper et al., 2008; de Melo et al., 2010). Moreover, syphilis still remains as a major cause of aneurysms of the ascending aorta with or without involvement of the other aortic segments (Roberts et al., 2009, 2015).

5. Conclusions

The sternal and vertebral lesions observed in the case described are clearly compatible with the development of an aneurysm of the thoracic aorta, both in the ascending portion and in the aortic arch. We argue that this aneurysm has a syphilitic etiology, considering the vascular segments compromised (ascending aorta and aortic

arch), the type of lesions observed, and the prevalent etiology of this kind of vascular pathology in pre-penicillin times.

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