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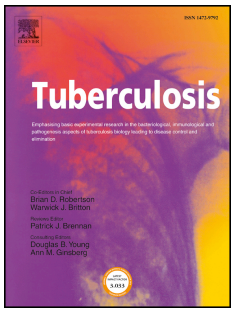

Archives and Skeletons: An interdisciplinary approach to the study of paleopathology of tuberculosis

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Archives and Skeletons: an interdisciplinary approach to the study of paleopathology of tuberculosis

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SUMMARY Tuberculosis (TB) may be an acute or chronic infection of bone and/or soft tissues. Nevertheless, human skeletons only registered a small percentage of those cases. This work aims to explore data from morbidity and mortality of individuals who contracted or died of TB after Koch bacillus discovery and before the development of antibiotics, using this information to interpret the scarcity of evidences detectable by paleopathological studies. To fulfil these goals, the Coimbra University Hospital and Coimbra Municipality Cemetery records from 1919-1928 were analyzed. As expected, pulmonary TB was the most common form of the diseases, both at hospital admission (43.7%, n=904) and as cause of death of the individuals inhumed, especially after the age of 10 years. In children under 10 years, meningeal TB was the more common form. Pott's diseases represented only 4.7% (n=98) of the hospital admission due to TB and 0.7% (n=8) of the TB deaths at the cemetery. However, in paleopathology the macroscopic evidence of TB comes mainly from Pott's disease. Documented skeletons shows that new bone on visceral surfaces of ribs can occurs in other diseases besides pulmonary TB but its presence can be also use as an indicative of possible TB infection.

Keywords: Cause of death, Paleopathology of tuberculosis, Skeleton, TB rib lesions, Morbidity, Hospital, Cemetery.

1. Introduction

Tuberculosis may affect any organ or tissue of the human body as an acute episode or as a chronic infection[1-2]. Therefore, in many cases evidence of diseases remains invisible on macroscopic examination of human skeletons, particularly when the individual died shortly after contracting the disease and/or developed other form than bone tuberculosis. Accordingly, since the first descriptions of TB in past populations made by 19th century paleopathologists, the majority of the evidence reported worldwide are cases of TB affecting bone, especially Pott diseases[2-4]. These findings were expected considering that the oldest cases of TB dates from the European Neolithic and after sedentarism and cattle domestication humans were more likely to contract this disease by *Mycobacterium bovis* ingestion of cattle meat and milk or by airborne transmission from infected animals[5]. This hypothesis is supported by the presence of tuberculous lesions in the vertebral column. Thus, before sanitary control of cattle, Pott disease was supposed to be the major form of TB. The clarification of this supposition may benefit from the analyses of data from individuals who contracted and/or died from TB after the discovery of the tubercle bacillus by Robert Koch and before the development of antibiotics. The first premise gives some confidence to the medical diagnosis while the second eventually shows how the disease affected individuals prior to chemotherapy.

In order to perform this study, data from nosological statistics from a hospital, cemetery records and documented skeletons will be analyzed.

2. Materials and Methods

The last decades of the 19th century and the 20th century were of enormous medical progress. During the evolution of the knowledge, some terms became ambiguous and unspecific by today's standards[6]. Moreover, the different nosological classifications don't have direct application to what is seen by paleopathologists. Only in 1891, at the International Statistical Institute (ISI) meeting in Vienna, which according to Rosenberg and Hoyert (2011:11)[7] 'marked the beginning of true international acceptance of statistical lists of causes of death and sickness', Jacques Bertillon, Chief of Statistics for the City of Paris, "explained that he felt it was better to group all tuberculosis together and subdivide it according to site' (Rosenberg and Hoyert, 2011:12)[7]. This conceptual change was followed

internationally, including by the Coimbra University Hospital (CUH), making the statistical data more useful to researchers.

The CUH published maps of patient's movement according to the nosological nomenclature signed in 1909 at the international convention that took place in Paris. The first map published reports data from 1919[8] and a period of 10 years was analysed. These records provide information such as the number of patients admitted by age and sex, and the form of tuberculosis diagnosed.

For the same time period (1919-1928), the burials books from Coimbra Municipality Cemetery were analyzed and age and sex of the individuals who had tuberculosis as cause of death were transcribed, too.

The third source of data comes from skeletons and associated documentation to the Coimbra identified collection from early 20th century.

3. Results and Discussion

The pathogenic agents are in permanent change[9], including acquiring resistance to antibiotics. In different periods, geographies, living conditions, among others factors, the host immune response can be different and the *Mycobacterium* itself may have changed[10]. Despite that, patients who lived and/or died previous to chemotherapy, probably had a response not very different from the skeletonised individuals studied by paleopathologists, and data from them can be useful to trace the history of TB. Another advantage of hospital/sanatorial archives is that they record not only the cases that resulted in death, but also the survivals for each type of TB considered. Nonetheless, there are pitfalls in retrospective studies and diagnoses[11].

The statistic maps of the Coimbra University Hospital revealed that 2067 patients with a diagnosis of tuberculosis were admitted between 1919 and 1928 (Figure 1) and 352 (17%) died (Table 1) during hospitalization.

Pulmonary TB was the most common form at hospital admission (43.7%, n=904). Looking by year, the percentage of pulmonary TB cases varied from 34.5%, in 1923, and 52.3%, in 1919, while Pott's diseases various from 7.4%, in 1919, to 13.3%, 1927. Tuberculosis affecting soft tissues were also frequent, for example 8.8% of the patients were diagnosed with abdominal TB and 1.8% (n=38) with meningeal TB. All the others forms were responsible for 54.4% (n = 1125) of the internments. Pott's diseases represented 1.1% (n=4) of death from TB. Generalized TB caused the death of 37

(10.5%) patients. The zero deaths from miliary acute TB are expected, because dissemination of infection may occur. Thus, some of these cases, if not all, were reported under generalized TB.

These data are from patients hospitalized and not from the general population. Thus, a similar research was conducted in the records from the Coimbra Municipality Cemetery. From 1919 to 1928 the burial books recorded 6383 inhumations, 1101 (17.3%) of which due to TB. From these, 6 don't have the age at death recorded and were excluded for further analyses.

For the 42 children under 1 year of age (19 females and 23 males), 31 (73.8%) died with meningeal TB, 8 (19.0%) with TB involving the lungs, 2 (4.8%) with TB and 1 (2.4%) due intestinal TB. For the next age groups considered, the forms of TB were more diverse and a selection of the results was made. For the 170 individuals (81 females and 89 males) who died from 1 to 10 years old, meningeal TB was also the main cause with 86 (50.6%) deaths, while 39 (22.9%) involved lungs, Pott disease affected 5 (2.9%) children, 4 (2.4%) had bone or joint involvement, and the remaining 36 (21.2%) deaths happen due to enteritis, peritoneal and intestinal TB, among other locations. The third age class considered grouped 175 individuals from 11 to 20 years, 135 (77.1%) had pulmonary involvement, 18 (10.3%) meningeal TB, 4 (2.3 %) had bone TB, Pott disease was the cause of death of one (0.6%) individual, and 12 (6.9%) died with other forms of TB. In the adults group, with 714 inhumations, 622 (87.1%) died from pulmonary TB, 14 (2%) with meningeal TB, Pott disease was recorded as cause of death of 2 (0.3%) individuals, 7 (1%) with bone or joint TB, and for 63 (8.8%) were recorded other types of TB affecting mainly soft tissues.

It is impossible to known how many of these individuals developed skeletal changes. But, according to Aufderheide and Rodríguez-Martín (1998)[1] compilation of data published by several clinical authors for lesion distribution and frequency in TB, the spine was the region of the skeleton more frequently affected (43%). This is not in accordance with the data collected from the Coimbra University Hospital and Municipality Cemetery. In the current study, the numbers concerning Pott diseases are quite unexpected, especially because in publications from the 1930s, physicians from Coimbra were still concerned with presence of Koch bacillus in the cows and with the poor sanitary conditions of animals and stall[12]. In this period, pulmonary TB was definitely more common in hospitalized patients and as cause of death. Nonetheless, the paleopathological evidence of TB came mainly from Pott's disease[2-4].

For many decades was accepted that only cases of TB involving bone could be identified in the skeletons, in particularly, if the individuals lived long enough to produce pathological changes

detectable macroscopically by paleopathologists. This puzzling situation has been discussed by many researchers, including at the light of "osteological paradox", alerting researchers to the danger of making direct inferences on the health of past populations. Surprisingly, studies on documented collections from Hamann-Todd[13] and Terry[14], both from USA and the Coimbra[15-16] and Lisbon[17], Portugal, revealed that ribs can contribute to history of diseases. Previous works suggested that the type of bone formed and the location of lesions may allow for the differential diagnosis of pulmonary TB, bronchitis, peritonitis, or neoplastic, among other conditions[15-17]. These small, thin and often fragmented bones, are prone to present new bone formation in the visceral surface in individuals who had pulmonary tuberculosis recorded as cause of death. Thus, "[a]lthough nonspecific, bone addition to the internal aspects of the ribs may be associated with TB[18].

The lesions existent in the ribs are not all similar in the type of new bone, in the distribution on the rib cage and in the cause of death recorded for the individuals. Skeletons from individuals who died from other pulmonary diseases and from extrapulmonary non-TB causes of death, also presented lesions in their ribs[15-17]. This is the case of individual 407 from the Coimbra University Collection, a male, aged 31, who died in 1931 with pulmonary aspergillosis. The skeleton is well preserved and had new bone formation in the vertebral end and shaft from the 3rd to the 10th ribs, but with slight difference in the appearance when compare with individuals with pulmonary TB as cause of death. New bone formation in also visible in both scapulae, humerus, radius, ulnae, hands, femurs, tibiae, fibulae and feet bones, which in compatible with a diagnostic of hypertrophic osteoarthropathy. A hypothesis of a misdiagnosis with pulmonary TB or the co-existence of both diseases was also considered. However, by chance a paper written by Trincão in 1932[19], the physician who assisted this man at the Coimbra University Hospital was found and his dramatic history in now known. In short, his clinical history revealed that at the age of 20, he got gonorrhea and developed a wound in the glans that took months to heal. Later, sores in his mouth and on the skin appeared. He was treated with anti-syphilitic treatment with mercury. He married in 1923, his wife became infected with syphilis, and had two sons and one abortion. He was admitted at CUH in January 1931 due to evening fever, cough, asthenia, with 41 kg (90.2 lbs), flat thorax and fetid sputum. The physician considered the possibility of TB and during the 5 months of hospitalization 12 sputum analyses, including with hemoptysis, were done, all negative for Koch bacillus. Wasserman reaction was also negative. Other exams were preformed to the digestive, nervous, and circulatory systems. Auscultation and radiography led to diagnoses of bronchitis and peribronchitis on the right lung, or possible pulmonary syphilis.

Radiographies repeated in March shown the right lung was healed and the left was opaque with pleural lesions, among other signs. Finally, the presence of *Penicilium glaucum* or *P.cristaceum* was identified in his sputum and he started a new treatment with potassium iodide to treat the pulmonary aspergillosis. His clinical condition improved, gained 5kg (11 lbs), sputum became less fetid and blood exams had better results. Sadly, in June he had a massive haemoptysis and died.

This case reinforces the importance of a carefully record of the lesions, including the new bone appearance and distribution. It is also important to note that besides pathologies frequently described in paleopathological books, many other conditions potentially can leave skeletal lesions[20] but the unspecificity of the signs left in bones and the lack of diagnosis criteria led to miss them from the paleopathological record.

4. Conclusion and future scope of work

The conjugation of data from archives and documented skeletons seem useful to the study of paleopathology of tuberculosis. In this study, pulmonary TB was by far the most common type of tuberculosis found both in hospital and cemetery records as well as in the documented skeletal collections. However, the majority of paleopathological evidences comes from bone TB, in particularly located in the vertebral column. Thus, this study shows the need of more research in order to interpret the slight differences in the lesions visible in the ribs. It is necessary to go back to Hamann-Todd, Terry, Coimbra and Lisbon collections to re-evaluate carefully these parameters, and to conduct similar analyses in other documented collections. Additionally, archaeological derived samples should be re-observed because ribs examination may have been neglected in the past. Taking advantage of the new imagiological techniques and histology the role of bone deposition in diverse diseases process should be investigated in clinical exams. Together, these clues may bring new support to the history of diseases and our knowledge about paleopathology of tuberculosis will give one more step forward.

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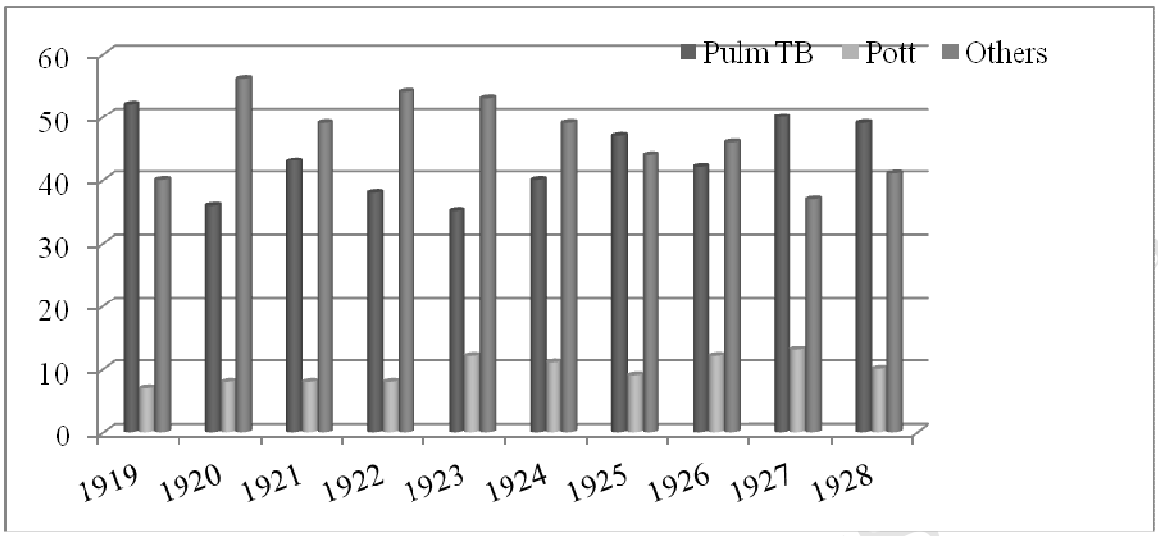

Figure 1. Percentage of individuals admitted at the Coimbra University Hospital by years with pulmonary TB, Pott disease, and all the other forms.

Table 1

Distribution of individuals who died from different forms of tuberculosis during their hospitalization at the Coimbra University Hospital.

Types of TB	**Total**		**Male**		**Female**	
	N	**%**	N	**%**	N	**%**
Pulmonary	**228**	**64,8**	137	60.1	91	39.9
Miliary acute	0	0,0	0	0	0	0
Meningeal	27	7,7	12	44.4	15	55.6
Abdominal	**31**	**8,8**	16	51.6	15	48.4
Pott' disease	4	1,1	3	75	1	25
White tumor	6	1,7	4	66.7	2	33.3
Other organs	19	5,4	13	68.4	6	31.6
Generalized	**37**	**10,5**	21	56.8	16	43.2
Total	**352**	**100**	**206**		**146**	