Paleopathology is a science located in a crossroad between history, archaeology, anthropology, and medicine and can offer unique historical knowledge by using techniques of traditional pathology as well as other branches of Medicine, which is especially fruitful when applied to ancient subjects in which soft tissues are preserved: mummies.

Key words: paleopathology, mummy.
Methods used in paleopathology

The term paleopathology has traditionally been related to physical anthropologists given their experience dealing with bony remains. However, the appearance of mummified soft tissues is frequently neglected as an important source of information about human diseases that leave no trace in skeletal remains. In fact, it was a common practice to strip bones of these soft components in order to achieve better access to morphological information from them. Mummies, like any other remains, can have different degrees of preservation, in part depending on the mummification process. Thus, preservation of outer parts of the body like skin and muscles of artificial mummies from ancient Egypt is very good but the inner organs are often lacking due to the classical practice of evisceration. Also, the use of ointments for better preservation produces artefacts in these subjects that hamper histological examination. Other artificial mummies such as those of the Chinchorro culture, are possibly the oldest known and are difficult to interpret since their preservation was based on stripping soft tissues, disarticulation of bones and ulterior articulation and covering with colorful clays [14]. Some of the best preserved subjects were naturally mummified by rapid cold desiccation, such as the Tyrol man [15, 16] or the Andean child mummies [17].

When approaching a mummified subject, the first question is if the degree of preservation is good enough to allow a meaningful study, and this decision is usually based on the extent of soft tissue preservation, the experience of the “paleopathologist” and, finally, the success of the histopathological examination. Another important question is to what extent the mummy can be “harmed” by extraction of its information. For instance, can a full autopsy be performed? Can only small superficial biopsies be obtained? Must the subject be “reconstructed” after the autopsy for exposition?, etc. And, very importantly, the possibility of non-invasive techniques such as conventional radiology, computerized tomography or even magnetic resonance studies [18, 19, 20] should be considered, although the latter is not the best study technique in dried specimens. In some instances, the use of minimally invasive procedures such as endoscopy using a flexible cystoscope or a flexible fibrogastroscope can provide very useful images and samples [21, 22].

Once the soft tissue is obtained, a technical procedure similar to that used in conventional samples of fresh tissue can be followed: formalin fixation, paraffin embedding, microtome sectioning and histochemical staining. Nonetheless, all of this is only possible if we first return the tissue to a rehydrated state with the use of some simple solutions like those
of Ruffer or Sandison, which are mainly based on an alcoholic solution with sodium carbonate [8, 9, 23, 24].

Samples processed in this way can be then analyzed with light or even electron microscopy [25] (Figs. 2, 3). Moreover, if tissue preservation is relatively good, immunohistochemical staining and molecular tests are also possible (Fig. 4) [23, 26, 27, 28, 29]. Recently, advances in proteomics have succeeded in identifying several proteins related to immune response and inflammation in mummified tissue samples, thus providing evidence of active pathogenic infection related to the cause of death [30].

Pathology in mummies

Different types of pathological conditions have been reported in mummies, including both neoplastic and non-neoplastic diseases. Apart from osseous evidence of malignancies and benign tumors [31, 32], several types of neoplasms such as histiocytomas, adenocarcinomas and metastases have been described in mummified tissues [6, 33-37]. Malignant neoplasms are scarce in paleopathological studies, probably due to a variety of causes including the absence of chemical environmental contamination leading to less carcinogenic exposure, shorter life expectancy or simply the disappearance of tissue evidence given the frequent origin in and involvement of soft tissues [6, 36, 38, 39]. Contrarily to cancer, infectious diseases such as tuberculosis and treponematosis in ancient Egypt and, Helicobacter pylori, malaria, smallpox and different types of parasitic diseases [40-46] in the pre-Columbian New World are abundant in the literature. Other conditions have been described in mummies, including degenerative bone processes in South American mummies indicating the high prevalence of vertebral degenerative changes and the scarcity of metastases to bone in this area [47] as well as some endocrine pathologies including goitre [48], tissue deposits as in pneumoconiosis [49] or gout [50] and acquired, heritable, nutritional or hormonal skin disorders [51].

Seminal studies in paleopathology

There have been many important paleopathological studies since the first in the XIX century, therefore, a review of previous extensive studies in paleopathology would be of great interest [4, 5, 6]. The special relevance of some paleopathological studies may lie in the technical advances applied to this discipline, the discovery of relevant pathological conditions from a medical point of view in a historical context in “common” subjects or in the analysis of famous historical subjects irrespective of the interest of the findings.

Elliot Smith, Ruffer and Lucas performed extensive breakthrough studies in a large number of Egyptian mummies which were the starting point of the scientific development of the field of paleopathology [see 4, 5 for a review]. As mentioned previously, technical developments such as the fixation methods by Ruffer and Sandison, pioneer molecular approaches for the study of genetic material by Pääbo [26], the multidisciplinary approach to the study of the Tyrolean Iceman [15, 16, 49], and similarly, well preserved...
subjects such as the Arctic and bog mummies [2, 52] have fuelled the extraction of a massive amount of relevant information from paleopathological projects on “commoners”.

There have been important medical discoveries in subjects of historical relevance, usually from royal families. For instance, according to the microscopic and molecular results provided by Marchetti et al. [35], Ferrante I of Aragon, the King of Naples during the XV century, most likely died of colorectal cancer. Indeed, to our knowledge, this was the first bona fide molecular demonstration of a malignant neoplasm in an historical mummy. Similarly, the death of Francesco I of Medici by malaria and the severe gout of Emperor Charles V of Augsburg, most likely influenced some historical events during the XVI century [50, 53]. Indeed, it is within the context of the capacity of paleopathology to provide explanations related to the health of historical subjects who potentially influenced historical events that this discipline acquires special relevance. Nevertheless, at times it is the systematic study of anonymous populations which provides critical insights into the history of medicine, a clear example being the now demonstrated fact that tuberculosis existed in South America before the arrival of the conquistadors [54].

Thus, there have been many reports on paleopathological studies in mummies, but only a few have attracted intensive media coverage due to the importance of the subjects studied or the impact of the discoveries from a strictly scientific point of view. The exhaustive analysis of the Tyrolean man and the diseases affecting Tutankhamun and his possible cause of death [55, 56] have been widely covered by the media and have attracted special attention to paleopathology. Likewise, the scientific studies of the mummified cardiac remains of Richard the Lionheart provided renewed interest in this famous monarch [57].

In summary, paleopathology is a medical discipline that combines several approaches (historical, anthropological, archaeological and medical) for the study of ancient remains, with special interest in mummified tissues. In addition, this discipline poses technical and intellectual challenges which can produce very interesting knowledge for better understanding the evolution of disease and medicine and their impact along human history.

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References