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ARTICLE

A Possible Case of *Coccidioides* Infection in a Thirteenth-Century Bolivian Mummy

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Coccidioidomycosis is an infectious fungal disease endemic in Bolivia's Gran Chaco region that is caused by inspiration of the spores of *Coccidiodes* species. It is a respiratory pathology that can spread to the skeleton and produce diffuse lytic lesions in different parts of the body. This disease has rarely been described in historic populations, and we present here a new case of coccidioidomycosis in a mummified human individual. It corresponds to a female individual with an age at death of 25–35 years, dated to the Tiwanaku epoch of the thirteenth century AD. It was found inside a sepulchral cave near the city of Ulloma in western Bolivia. Radiographic examination shows numerous osseous lytic lesions with central cavitation concentrated on the cranial table and vertebral bodies. The observed condition could correspond to the secondary phase of coccidioidomycosis. This diagnosis is noteworthy because coccidioidomycosis was mainly described as a male work-related disease and has never been found in ancient western Bolivia.

La coccidioidomicosis es una enfermedad infecciosa micótica endémica de la región del Gran Chaco (Bolivia) causada por la inspiración de esporas de *Coccidiodes* spp. Puede producir lesiones líticas difusas en diferentes partes del cuerpo. Esta enfermedad rara vez ha sido descrita en poblaciones históricas, y nosotros presentamos un nuevo caso de coccidioidomicosis en un sujeto momificado, que corresponde a un individuo femenino con una edad estimada entre 25 y 35 años, datada en época Tiwanaku correspondiente al siglo trece. Se encontró dentro de una cueva sepulcral cerca de la ciudad de Ulloma, en el oeste de Bolivia. El análisis radiográfico muestra que el cuerpo momificado tiene numerosas lesiones óseas líticas con cavitación que se concentran en la tabla craneal y cuerpos vertebrales. Estas podrían corresponder a la fase secundaria de la coccidioidomicosis. El diagnóstico es históricamente importante porque ésta es una enfermedad laboral relacionada a sujetos masculinos y no había sido descrita para el oeste de Bolivia.

Keywords: fungal infection; Tiwanaku culture; paleopathology; Bolivia

Palabras clave: infección micótica; cultura Tiwanaku; paleopatología; Bolivia

Coccidioidomycosis is a nontransmissible infectious fungal disease that is endemic to arid and semi arid regions of the southwestern United States, Mexico, and South America (Aufderheide and Rodriguez-Martin 1998; Blair 2007; Patel and Cardile 2013; Temple 2006). It is caused by inhalation of the arthrospores of *Coccidioides* species (Fisher et al. 2002). *Coccidioides* is a human respiratory pathogen that typically causes respiratory infection but can be disseminated throughout the body in fewer than 5% of cases. Bones are affected in approximately 20%–50% of the disseminated cases (Aufderheide and Rodriguez-Martin 1998; Blair 2007; Patel and Cardile 2013). Although any bone can be involved, the axial structures are more commonly affected (Bisla and Taber 1976).

Coccidioidomycosis was first believed to be caused by the species *Coccidioides immitis*. Only later was it recognized that *Coccidioides* include two nearly identical species, known as *Coccidioides immitis*

and *Coccidioides posadasii* (Fisher et al. 2002; Temple 2006). *C. immitis* is indigenous to California (the "Californian" species), whereas *C. posadasii* is present in other endemic areas (the "non-Californian" species; Hector and Laniado-Laborin 2005; Saubolle 2007). Inhalation of *Coccidioides* arthrospores causes a self-limited, acute, community-acquired pneumonia-like disease as a primary form (Crum et al. 2004; Galgiani et al. 2005). In 1%–5% of all coccidioidomycosis cases, the disease can develop into a progressive, chronic, and often fatal disseminated form (Aufderheide and Rodriguez-Martin 1998; Blair 2007; Crum et al. 2004).

Adult males are more often infected (almost 70% of cases; Crum et al. 2004), probably because of occupational dust exposure. However, hormonal or genetic components could be involved (Ampel et al. 1989). This study describes a probable case of coccidioidomycosis in a mummified individual found in western Bolivia, in an area where no ancient case of coccidioidomycosis has been diagnosed, according to a bibliographic search in international journals.

Materials and Methods

The Anthropology Museum of Federico II University of Naples in Italy possesses four human mummies from South America that its founder Giustiniano Nicolucci acquired in the late nineteenth century (Borrelli and Capasso 2019). The first scientific news of these mummies can be found in an article published by De Blasio (1900).

These are artificially mummified individuals in accordance with Andean funerary practices. They show the classic cutting lesion in the lower abdomen area, which was used as an opening for extraction of the bowels and preservation of the body by the straw method. In addition, rows of small holes at the level of the cuts are evident; they represent the remains of the sutures used by the embalmers to close the abdominal wall. The abdominal cavities were filled with coca leaves and straw, which were mixed with some natural balms. The skulls were artificially deformed, assuming a strongly dolichocephalic shape (Borrelli and Capasso 2019). Cranial deformation was a marker of ethnic/group identity and had spiritual and aesthetic significance for Andean cultures (Allison et al. 1981; Bloom 2005), as did the use of coca leaves (Borrelli and Capasso 2019). According to De Blasio (1900), this practice follows the belief that children born with deformed skulls were superior beings; therefore, there was a tendency to deform the skulls of healthy born children to emphasize the superiority of a certain class compared to the others.

The mummy of this study (catalog no. MA2971) was purchased by Emilio di Tommasi, royal consul of Italy in Bolivia in 1897. It was found in the burial grounds of Ulloma, a province of La Paz (Bolivia), on August 27 of that same year (Figure 1; see De Blasio 1900:Figure 5). The place of discovery and the type of funerary bundle—also found on the body of another mummy at the Anthropology Museum that came from the same archaeological site of Ulloma (Borrelli and Capasso 2019)—suggest the attribution of the mummy we studied to the Pacaxas (Pakasa) population of Aymara origin. This population's culture was influenced by that of Tiwanaku, albeit with regional characteristics (Kesseli and Pärssinen 2005). Therefore, the mummy has been attributed to the Tiwanaku culture. The sex was determined from the bones' grossly visible morphology, according to the methodology of Ferembach and others (1980), and the age at death was calculated through the study of dental wear (Brothwell 1981).

Radiocarbon analyses were performed by the CIRCE laboratory of the Luigi Vanvitelli University of Campania, in Caserta, Italy. The radiographs were done by the IRCCS SDN Centre of Naples.

Results

The mummy is a female individual with an age at death of between 25 and 35 years. The individual was embalmed in a curled-up sitting position, with her legs folded into her chest and her hands on her shoulders. Radiocarbon analysis dated this individual to 765 ± 43 BP (DSH-8697_FV; rope; $\delta^{13} = -13‰$). For this date the calibrated age range is 1182–1294 cal AD (2σ, IntCal2013).

The mummy shows paleopathological alterations in the skeleton. The radiographs highlight bone lesions that affected some vertebrae of the dorsal and lumbar tracts and the neurocranium bones: they show multiple unmerged osteolytic lesions with sclerotic margins in the cranial vault and thoracic

Figure 1. Map of Bolivia with the location of Gran Chaco Region where *Coccidioides* spp. are endemic.

and lumbar vertebrae. The lesions involve the inner table, and they are lytic and well demarcated, showing central cavitation because of the massive destruction of the cancellous bone. They vary widely in size and are circular in shape. We observed at least four circular lesions of the frontal bone, especially near the coronal suture, and a great concentration of small (about 0.5 cm) lesions widely spread on the parietal bones (Figure 2). The lesions are also visible on vertebral bodies, especially in the lumbar tract (Figure 3). The last lumbar vertebrae show clear signs of arthrosis with the formation of osteophytes and deformations of the vertebral bodies (Figure 4). The posterior elements of the vertebrae show pathological alterations (Figure 5). The analyses did not show any other osteolytic lesions in other regions of the skeleton.

Discussion

The primary focus of coccidioidomycosis is the lungs, but infection can disseminate to other tissue and organs, and bone and joint involvement occurs in approximately 20%–50% of disseminated cases. The disease most frequently affects the axial skeleton—the spine, skull, sternum, and ribs (Crum et al. 2004)—and favors bony prominences, such as the acromion, the coracoid, the styloid process of the radius and ulna, and epiphyses of the humeri, tibiae, and clavicles (Ortner and Putschar 1981). The osseous disease is chronic and progressive.

Figure 2. X-ray of the skull (lateral view): arrows indicate osteolytic areas without signs of peripheral sclerosis.

Radiographs are an important tool for the diagnosis of *Coccidioides* infections. A long-standing infection shows single or multifocal lytic, "punched-out" destructive lesions, with a loss of bone tissue and irregular borders (Blair 2007). However, X-rays with these features might also suggest other kinds of infectious and non-infectious processes. The vertebral involvement could be attributable primarily to tuberculosis (Wesselius et al. 1977), myeloma (Micarelli et al. 2019), or other fungal infections (Aufderheide and Rodriguez-Martin 1998; Bried and Galgiani 1986; Dalinka et al. 1971). Therefore, it can be difficult to distinguish among early stages of spinal mycotic infections.

We relied on the morphology and distribution of the lytic lesions found on the mummy, as well as geographic, ecological, biological, and clinical information, for the differential diagnosis. Multiple

Figure 3. X-ray of the spine (frontal view): arrows indicate osteolytic lesions on the vertebral bodies of the lumbar tract.

Figure 4. X-ray of the spine (lateral view): arrows indicate osteophytes and deformation of vertebral bodies caused by arthrosis.

Figure 5. Lumbar tract: a lesion with a confluent circular profile and a thickened antero-inferior margin is visible on one of the posterior laminae of L3 as a hyper-diaphanous area (black circle).

myeloma is characterized by small uniform lesions that are spherical and that have irregular margins and no signs of osteoblastic activity. Usually, a diagnostic tool for identifying multiple myeloma is the presence of small lytic lesions on the skull. The destruction of the vertebral bodies often leads to the collapse of multiple vertebrae, resulting in kyphosis or scoliosis. However, these defects are spread throughout the skeleton and usually affect males older than 40 years old (Aufderheide and Rodriguez-Martin 1998). Given the age of the mummy, the distribution of lesions, and the absence of vertebral collapse, kyphosis, or scoliosis, multiple myeloma can be reasonably excluded as the lesions' causal agent.

Nearly 200 species of fungi are known to be responsible for human diseases (Pinto et al. 2008). Among fungal diseases that can affect bone are aspergillosis, cryptococcosis, blastomycosis, and coccidioidomycosis, all of which can affect the same bone regions and produce well-defined lytic lesions (Temple 2006). Determination of which fungus caused the condition of our mummy was therefore problematic. The lesion morphology and positions, together with the geographic and ecological information, were key factors in the diagnosis.

Spinal involvement with *Aspergillus* is not very common and is usually limited to the lumbar region (Tack et al. 1982). In *Cryptococcus* infection, bone lesions can usually be found on the spine in the

lumbar and the cervical regions (Jain et al. 1999). *Cryptococcus* lytic lesions can be similar to those in coccidioidomycosis; however, abscess formation by this fungus is rare (Kim et al. 2006).

The most common extrapulmonary site for blastomycosis is the skin, in the form of dermal skin and hypodermic lesions (Teodori 1981): these lesions were absent in this mummy. There were also no collapsed vertebrae nor gibbous deformities of the vertebral column, as are often caused by *Blastomyces* infections (Kim et al. 2006).

Lesions for the present sample match the clinical description of coccidioidomycosis, although with some differences, particularly the absence of lesions in the extremities of the long bones, hands, and ribs. When considering only bone lesions, the diagnosis of coccidioidomycosis is difficult. Epidemiological data (e.g., the area of diffusion of these fungi), however, can support the diagnosis of coccidioidomycosis.

Among fungi that could result in spinal infection, only *Coccidioides* spp. are associated with dry soils (Temple 2006). Little is known about the areas of coccidioidomycosis in Bolivia, but the endemic area seems to be the Gran Chaco region in southern Bolivia (Ajello 1967). We therefore considered coccidioidomycosis to be the most likely diagnosis for the mummy's bone lesions.

Tuberculosis is the most common diagnostic error for *Coccidioides* lesions; indeed, the skeletal lesions of Ulloma's mummy could also be attributed to this infectious disease. Tuberculosis is a bacterial infection that typically involves the lower thoracic and upper lumbar vertebrae, as does mycotic infection (Kim et al. 2006); the skull is rarely involved in skeletal tuberculosis, and it affects young individuals. Moreover, cranial tuberculous lesions are purely destructive from the outside to the inside of the skull (Aufderheide and Rodriguez-Martin 1998). The skull of the mummy of Ulloma shows no external cranial lesions but only those involving the internal cranial table. Multifocal, noncontiguous vertebral involvement is common both in tuberculosis and mycotic diseases (Dalinka et al. 1971). A tuberculosis vertebral infection usually spares the posterior elements of the vertebrae, which is an important aspect in the differential diagnosis with mycosis (Aufderheide and Rodriguez-Martin 1998). Unlike tuberculosis, mycotic infection affects the posterior elements of the vertebrae, as in the present case, and could cause large abscesses (Kim et al. 2006). The hip joint, with lesions of the femoral head and acetabulum, is frequently involved in cases of bone tuberculosis. Likewise, the sacroiliac joint is commonly the site of tuberculous infection, with evident destruction of the sacral wing; along with the involvement of the hip joint, the infection could cause a pelvic deformity (Kremer and Wiese 1930; Ortner and Putschar 1981). The thoracic cage, knee, ankle, tarsal, and tubular bones of the hands and feet may also be involved in skeletal tuberculosis (Ortner and Putschar 1981). However, these tuberculous lesions were not found in our case.

Indeed, it was difficult to determine whether the lesions observed were attributable to tuberculosis or coccidioidomycosis, given that tuberculosis was present in the past in the Andean areas of Peru and Chile (Wilbur et al. 2008), although it was not described in the Ulloma region. Even though the skull and spinal lesions could be related to tuberculosis, the vertebral collapse with gibbus formation and the perforation of the cranial vault from the outside to the inside usually caused by tuberculosis were absent. At the same time, no lesions were observed in other regions of the postcranial skeleton that are typically involved with tuberculosis.

The differential diagnosis between tuberculosis and coccidioidomycosis remains difficult. However, the geographic origin of the mummy—the semiarid environment of South America—and some pathological signs, such as the morphology of the cranial lesions and the involvement of the posterior vertebral elements, support the diagnosis of coccidioidomycosis. Thus, tuberculosis does not appear to be the correct diagnosis for this mummy.

The diagnosis of coccidioidomycosis is particularly interesting because of the mummy's sex. This infection is work-related and usually affects males with a hormonal or genetic predisposition (Ampel et al. 1989; Crum et al. 2004). This mummy is female, which suggests that in the Tiwanaku Andean culture of twelfth-century Bolivia, both sexes could carry out the same everyday work activities; in addition, those belonging to the higher social classes engaged in open-air recreational activities. Moreover, the presence of the disease on an individual from western Bolivia might be an indication of the mummy's provenance from the Gran Chaco region.

Conclusion

Coccidioidomycosis is caused by inhalation of *Coccidioides* spp. spores. Although it is a respiratory disease, it can also affect the skeleton. Because its bone lesions are similar to other mycotic and non-mycotic diseases, their morphology and distribution are important but not always sufficient elements for making a diagnosis on ancient human remains.

Epidemiological data can contribute to the diagnosis. In our case, the geographic location was a key factor for the identification of coccidioidomycosis, which was found in an adult woman, even though women generally did not suffer from mycosis.

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