Title

A male adult skeleton from the Han Dynasty in Shaanxi, China (202 BC-220 AD) with bone changes that possibly represent spinal tuberculosis

题目

中国汉代陕西地区一例成年男性骨骼个体的脊柱结核病例报告

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Keywords

Vertebral destruction

Paravertebral (psoas) abscess

Population density

Urbanism

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关键词

脊柱破骨病变

脊旁脓肿

人口密度

城邑

中国汉代

Abstract

Bioarchaeological data for tuberculosis (TB) have been published very sporadically in China or the rest of East Asia. To explore the history of TB in this area, 85 skeletons excavated from the Liuwei Cemetery in Shaanxi, China (202 BC-220 AD) were macroscopically examined to record TB related bone changes. These skeletons represented inhabitants of *Maolingyi,* an urban area that had a high population density during the Han Dynasty (202 BC-220 AD). Seventeen of the 85 skeletons had spines that were well enough preserved to observe evidence of spinal disease. Among them, a male skeleton aged around 30 years (M34-E) manifested multiple lytic lesions in the eleventh thoracic to second lumbar vertebral bodies (T11 to L2). TB was considered a possible diagnosis for the spinal lesions observed, with differential diagnoses of brucellosis and typhoid. The dense population and overcrowding in urban *Maolingyi* were considered the potential social risk factors for TB found at this site. The findings of this study contribute to limited knowledge about the history of TB in East Asia and suggest a relationship between population density and the spread of TB in *Maolingyi* at that time. However, the lack of published bioarchaeological data of TB in East Asia hinders understanding the transmission of TB within Asia and its link to the rest of the world. Further intensive review of archaeological skeletons in Asia is urgently needed.

中文摘要

中国乃至东亚地区的生物考古学研究中鲜有关于结核病的报道。本文通过鉴定中国陕西留位汉墓出土人类骨骼的相关病变情况，为中国古代结核病的研究提供新的资料。85 例人类骨骼个体中，共有 17 例个体的脊柱保存较好，可以观察结核病的脊柱病变。这其中，一例 30 岁左右男性个体的第十一胸椎、第二十胸椎、第一腰椎和第二腰椎的椎体均存在多处溶骨性病变。通过鉴别诊断，可知造成上述骨骼病变的病因最有可能是结核病。除此之外，布鲁氏菌病和伤寒病也有可能导致类似的脊柱病变。根据留位墓地的地理位置、年代以及相关历史背景，可知墓地人群极有可能是汉代茂陵邑的居民，而茂陵邑拥挤的城镇生活环境很有可能是造成结核病传播的重要社会因素。本文不仅为东亚古代结核病的研究提供了新的资料，同时也阐释了中国古代结核病的传播与人口密度之间的关系。由于亚洲地区结核病的生物考古学研究仍然存在诸多不足，因此亟需对亚洲古代人类骨骼进行系统的研究。

1. Introduction

Tuberculosis (TB) is one of the top 10 causes of death worldwide today (WHO, 2018: 1). It can be caused by any bacterium from the *Mycobacterium tuberculosis* complex (MTBC) (Stone and Ozga, 2019: 192). Among these, *M. tuberculosis* is currently responsible for most human TB (WHO, 2018: 6; Stone and Ozga, 2019: 192). Skeletal involvement in TB mainly results from hematogenous dissemination of the infection from the lung (Resnick and Niwayama, 1995: 2462). As the metaphyseal segments of bones contain hematopoietic marrow, these locations are most frequently affected (Resnick and Niwayama, 1995: 2462; Roberts and Buikstra, 2019: 326). Multiple risk factors (e.g., HIV infection, malnutrition, smoking, diabetes, alcohol misuse, indoor and outdoor air pollution, silicosis, immunosuppressive treatments, and mental illnesses) and social determinants (e.g., poverty, and compromised living and working conditions) can all increase the frequency of TB (Lönnroth et al., 2009, 2010; WHO, 2018: 6; Resnick and Niwayama, 1995: 2462).

Of particular interest in China is that new evidence of TB reported in 2017 accounted for 9% of global TB morbidity, while drug-resistant TB made up 13% of the global evidence (WHO, 2018: 178). Nevertheless, in China, Shaanxi does not currently harbor a major TB burden (Li et al., 2014; Cao et al., 2016; Zhao et al., 2011a). Furthermore, a DNA study based on 1,793 TB strains collected from across China suggested that three major strains (Bj-MG1, Bj-MG2, Bj-MG3) from the *M. tuberculosis* Beijing family are widely distributed, with Bj-MG3 being dominant (Luo et al., 2015). According to this study, these three Beijing strains originated 30,000 years ago in southern China or Southeast Asia, based on the MTBC-70 model and the available geographic information of the patients. Analyzed by Bayesian skylines, Bj-MG3 strain experienced an approximate 300-fold population expansion 7,000-6,000 years ago, marking the beginning of its dominance in China (ibid.). This population expansion most likely occurred in northern China, due to the significant higher frequency of Bj-MG3 strain among Northern Han Population of China (ibid.). This research has implications for exploring the origin, evolution, and history of TB in China.

Table 1

Convincing Chinese historical records related to TB (Chen and Zhang, 2002; Chen, 2011).

Date	Document	Record
8th century BC	*Huang Di Nei Jing* (黄帝内经)	Consumption, chest obstructions, shortness of breath, visceral pain, fever
2nd-3rd century AD	*Jin Gui Yao Lue* (金匮要略)	TB of cervical lymph nodes (侠瘿), TB of axillary lymph nodes (虚劳, 马刀)
4th century AD	*Zhou Hou Bei Ji Fang* (肘后备急方)	The contagious nature of TB
7th century AD	*Cui Shi Bie Lu* (崔氏别录)	Signs and symptoms of TB
7th century AD	*Qian Jin Yao Fang* (千金要方)	Worms in the lung, TB as a pulmonary disease
8th century AD	*Wai Tai Mi Yao* (外台秘要)	Diagnosis of TB
11th century AD	*San Yin Fang* (三因方)	The contagious nature of TB (痨瘵), worms in the lung
13th-14th century AD	*Dan Xi Xin Fa* (丹溪心法)	Treatment of TB

14th-17th century AD	*Yi Xue Zheng Zhuan* (医学正传), *Li Xu Zhi Jian* (理虚之鉴), *Yi Xue Ru Men* (医学入门)	Treatment of TB
1630 AD	*Hong Lu Dian Xue* (红炉点雪)	A treatise of TB

Site	Date	Bioarchaeological evidence	Reference
Guangfulin, Shanghai	3900-3200 BC	Vertebral destruction and kyphosis, T11-L2	Okazaki et al., 2019
Meishan, Henan	2500-2000 BC	Vertebral destruction and kyphosis, T8-T9	Pechenkina et al., 2007: 267
Shengjindian, Xinjiang	300-200 BC	Ankylosis of the left knee joint and periosteal rib lesions	Li et al., 2013
?, Xinjiang	202 BC-200 AD	aDNA of *M. tuberculosis* found in 3/15 (20%) skeletons without bone changes	Fusegawa et al., 2003
Mawangdui, Changsha	168 BC	Three calcified tuberculous foci in the left lung of a mummy	Hunan Medical College, 1980: 269

The history of TB in China can be traced in a number of reliable historical records (Table 1). The earliest convincing description has been found in *Huang Di Nei Jing* (黄帝内经), a medical text dated to the eighth century BC (Chen and Zhang, 2002). Of note is the so-called 3000 BC Chinese medical text (*Shen Nong Ben Cao Jing*, 神农本草经) cited in Morse (1967: 259) and Roberts and Buikstra (2003: 179), which actually dates to 202 BC-8 AD (Chen, 2011: 31).

Table 2

The published bioarchaeological evidence for TB in China.

? = The name of the site was not given.

To date, however, there is very little bioarchaeological evidence of TB in China (Table 2) (c.f., Fusegawa et al., 2003; Hunan Medical College, 1980: 269; Li et al., 2013; Okazaki et al., 2019; Pechenkina et al., 2007: 267) or the rest of East Asia (c.f., Suzuki et al., 2008; Suzuki and Inoue, 2007; Taylor et al., 2007; Tayles and Buckley, 2004). This is in comparison to the extensive evidence found in Europe and the Americas (Roberts and Buikstra, 2003: 87-213). The lack of data in East Asia may be attributed to different training opportunities compared to elsewhere, less development of paleopathology, language barriers making access to relevant literature difficult and thus not being reported in the English language literature, and lack of funding for paleopathological project (Pechenkina, 2012: 354; Giannakopoulou and Suzuki, 2012: 446; Bazarsad, 2012: 480; Tayles et al., 2012: 534). Accordingly, the temporal and geographical history of TB in East Asia is unclear. This not only prevents understanding the links between East Asia and the wider world in relation to TB's transmission but also impedes exploring the co-evolution of *M. tuberculosis* complex organisms and their human hosts in East Asia.

Given the significance of TB in China to both East Asia and the wider world, this study reports on a skeleton with bone changes possibly representing spinal TB found among 85 skeletons excavated from the Liuwei Cemetery (202 BC-220 AD) in China. The cultural context of the people buried at this site was considered in order to assess what risk factors and social determinants for TB existed in the living environment of this population. The findings contribute to the limited extant knowledge of TB in ancient East Asia and reveal the relevance of cultural context to the occurrence of TB in past human populations.

2. Materials and methods

2.1. Liuwei Cemetery, Shaanxi, China

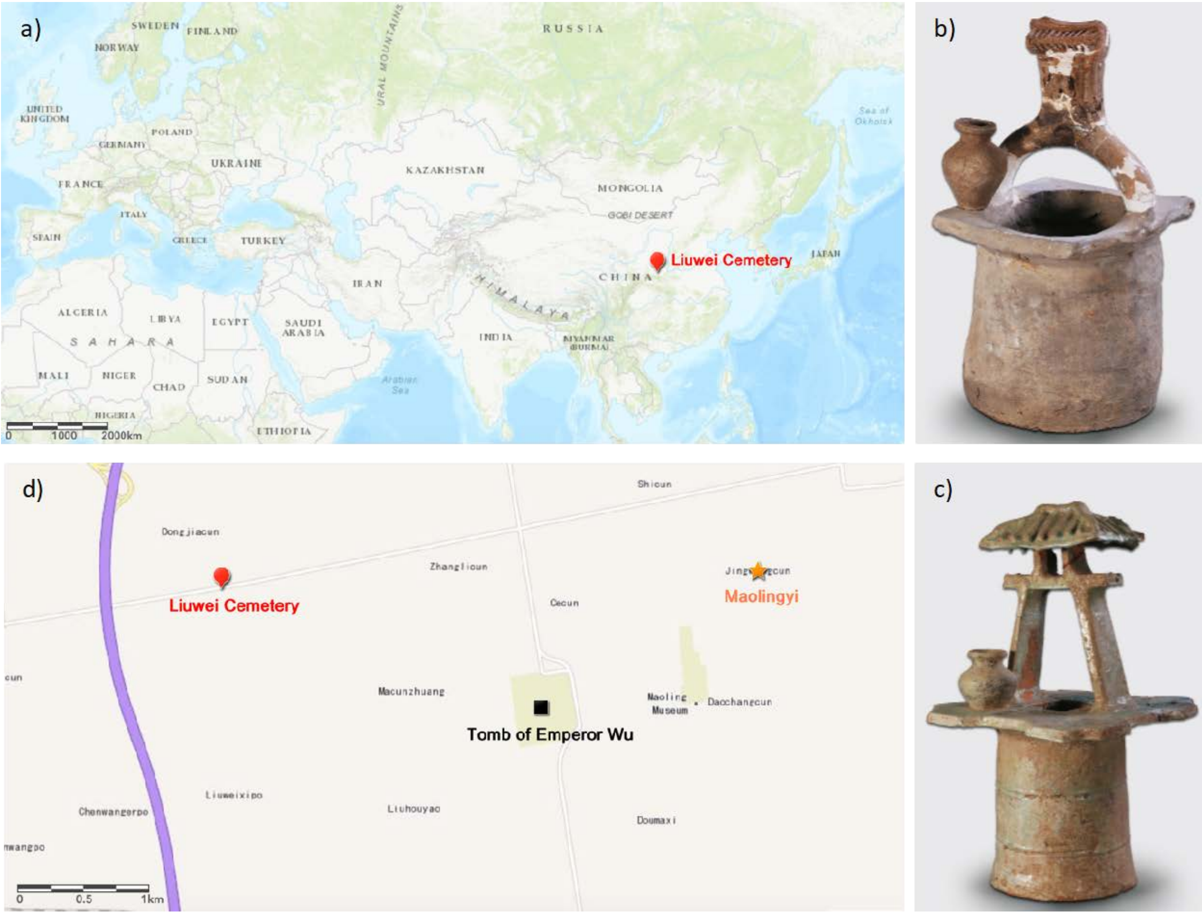

Fig. 1. The Liuwei Cemetery. a) location of the cemetery in China. b) and c) pottery miniatures of wells. d) locations of the cemetery, *Maolingyi*, and the tomb of Emperor Wu (images: ArcGIS Online and Shaanxi Provincial Institute of Archaeology, 2015).

The skeleton of interest (M34-E) was excavated from the Liuwei Cemetery in Shaanxi Province, China (Fig. 1a). In 2014, 14 brick-chamber tombs dated to the Han Dynasty (202 BC-220 AD) were excavated due to modern construction taking place; grave goods consisting of pottery vessels and pottery miniatures of wells, ovens, and animals were found (Fig. 1b, c) (Shaanxi Provincial Institute of Archaeology, 2015). Eighty-five skeletons were excavated. Detailed archaeological data, such as the grave goods found in each tomb and the characteristics of the associated residential area, are unavailable owing to the limited time and labor invested in this rescue excavation.

As Liuwei was located in the western part of *Maoling* (茂陵), which is the cemetery associated with Emperor Wu of the Western Han Dynasty (202 BC-8 AD) (Fig. 1d) (Shaanxi Provincial Institute of Archaeology, 2015), the general living environment in this region can be reconstructed from Chinese historical records and other archaeological studies related to *Maoling*. For example, *Han Shu* (汉书), written by *Ban Gu* (班固, 32-92 AD), a historian of the Eastern Han Dynasty (25-220 AD), thoroughly summarized the history of the Western Han Dynasty (202 BC-8 AD). According to this document, Emperor Wu built a town called *Maolingyi* (茂陵邑) near his cemetery in 139 BC, and financial and land compensation was offered in 138 BC to attract migrants to *Maolingyi* (Ban Gu: 158). In 127 BC and 96 BC, Emperor Wu commanded two large-scale migrations of rich people in the eastern region of the country to relocate to *Maolingyi* (Ban Gu: 170, 205). At the end of the Western Han Dynasty, 277,277 people were recorded as taxpayers in *Maolingyi* (Ban Gu: 1547). After the collapse of the Western Han Dynasty, *Maolingyi* became *Maoling* County (茂陵县) during the Eastern Han Dynasty (25-220 AD) (Liu, 2008).

The location of *Maolingyi* (Fig. 1d), about three kilometers from the Liuwei Cemetery (measured via ArcGIS online), has been revealed by an archaeological survey carried out between 2006 to 2008. A rectangular area (about 1845 x 1543 meters) surrounded by a ditch (about two to five meters in width) was identified; within this ditch, seven roads, some walls, and construction materials were excavated (Zhang et al., 2011). However, whether the residents of *Maolingyi* only lived within the ditched enclosure or also inhabited the surrounding regions has not been discussed in relevant studies. Nevertheless, if the recorded 277,277 taxpayers all lived within the ditched enclosure, then the population density of the ditched area (about 2.85 km^2) would be 97,398 per person / per km^2. In contrast, in 2017 the average population density in urban areas of China was 2,477 per person / per km^2, while the population density in Beijing was only 1,144 per person / per km^2 (National Bureau of Statistics of China, 2017). It seems almost impossible for *Maolingyi*, an urban area dated to the Han Dynasty (202 BC-220 AD), to have a much higher population density than a modern metropolis such as Beijing. For this reason, the residents of *Maolingyi* would have inhabited the surrounding regions, including Liuwei. Thus, Liuwei was associated with urban *Maolingyi*, which clearly had a high population density during the Han Dynasty (202 BC-220 AD).

2.2. Methods

All 85 skeletons excavated from the Liuwei Cemetery were analyzed by the first author in August 2018 in the Human Osteology Laboratory at Northwest University, China, where the skeletons are curated. Sex and age at death were estimated using population-specific standards (Zhang, 2007; Shao, 1985; Zhang, 1986; Zhang and Li, 1988; Wu and Bai, 1965; Zhu, 2004) (Supplementary information 1). In total, there were 26 males, 31 females, 19 subadults, four unsexed adults, and five individuals attributed an unknown sex and age category due to poor preservation.

All bones were macroscopically observed for pathological changes, according to guidelines in Roberts and Connell (2004: 35). Bone formation and bone destruction were recorded along with their distribution patterns. TB related bone changes were examined based on standard criteria (Resnick and Niwayama, 1995; Roberts and Buikstra, 2019: 321-351; Assis et al., 2011; Hershkovitz et al., 2002; Roberts et al., 1994) (Supplementary information 1). All potential diagnoses for the abnormalities observed were then considered.

3. Results

3.1. Individual M34-E

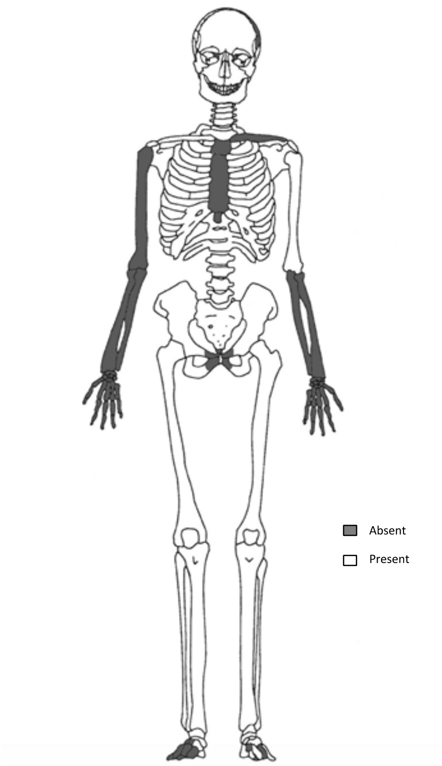

Fig. 2. Preservation of individual M34-E (skeleton line drawing from Buikstra and Ubelaker, 1994: Attachment 3a).

The skeleton of individual M34-E was well-preserved (Fig. 2). The skull was almost intact, with only the left parietal and temporal bones being damaged post-mortem; both lacrimal bones and the hyoid bone were absent. The left clavicle, sternum, both pubic bones, coccyx, right humerus, both radii, both ulnae, all the bones of hands, and some bones of the feet were missing. All vertebrae were well-preserved, although post-mortem breakage was noted in several vertebral bodies and all the vertebral arches.

The features of the greater sciatic notch, preauricular sulcus, and composite arc were consistent with a male, while the morphology of the sacrum and the skull indicated a probable male (Shao, 1985; Zhu, 2004; Zhang, 2007). The estimated age at death was around 30 years, based on degenerative changes of the auricular surface (Zhang and Li, 1988; Stage II: 23-29) and dental wear (Wu and Bai, 1965; Stage III: 30-38).

3.2. Pathological profile of individual M34-E

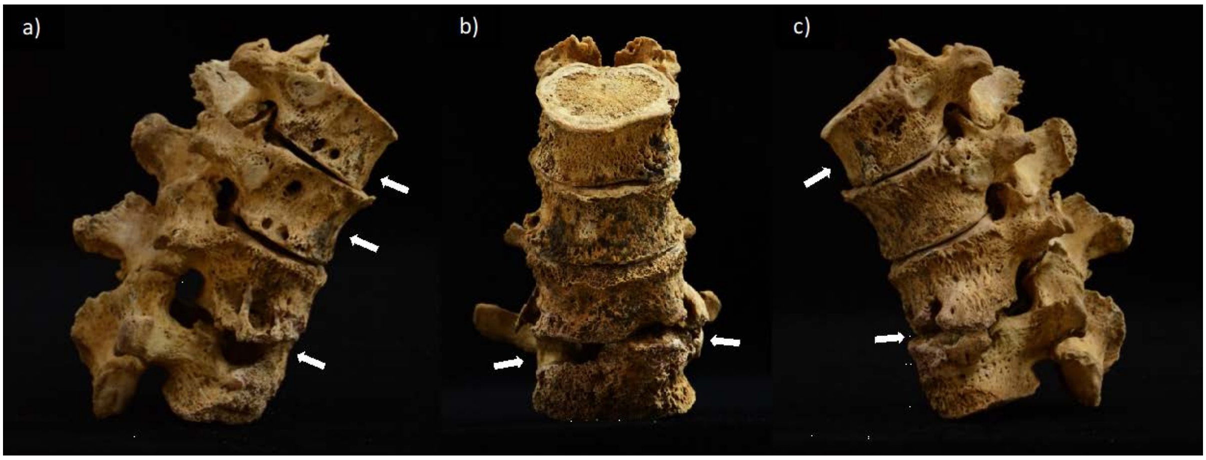

Fig. 3. Eleventh thoracic to second lumbar vertebral bodies of individual M34-E showing multifocal lytic lesions. T11 is shown at the top of the figure and L2 at the bottom in each of the views. a) right lateral view and b) anterior view showing lytic lesions of vertebral bodies. c) left lateral view showing a lytic focus on the eleventh thoracic vertebral body and bony extensions on the first and second lumbar vertebral bodies.

Seventeen spines of the 85 skeletons excavated were well enough preserved to observe for evidence of spinal disease. Individual M34-E manifested multiple lytic lesions on the eleventh thoracic to second lumbar vertebral bodies (T11 to L2) (Fig. 3). The predominant abnormalities were partial destruction of the inferior vertebral body of L1 and the superior vertebral body of L2 (Fig. 4b, 5b). Lamellar bone was present, characterized by shell-like bony extensions on the left side of the vertebral bodies of L1 and L2, suggesting a possible healed paravertebral (psoas) abscess (Fig. 3c). Nevertheless, the left proximal femur where the psoas muscle attaches and the os coxae appeared normal. All vertebral arches were normal. Overall, as indicated by lesions in vertebral bodies showing margins without remodeling of lytic foci, in addition to lesions that were remolded, the spinal lesions observed were chronic in nature but some were active at the time of death. The vertebral destruction present did not lead to spinal collapse. The rest of the skeleton, such as the joints, flat bones, and ribs, did not show any TB related bone changes. Detailed descriptions of each affected vertebra are summarized in Supplementary information2.

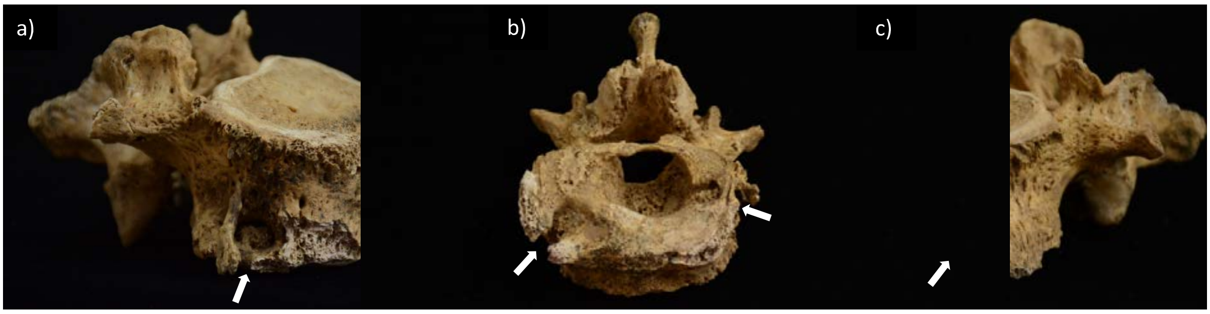

Fig. 4. First lumbar vertebral body of individual M34-E. a) right lateral view showing a bony spicule and a cloaca containing a central sequestrum. b) inferior view showing extensive destruction of the vertebral body. c) left lateral view showing new bone formation as bony extensions.

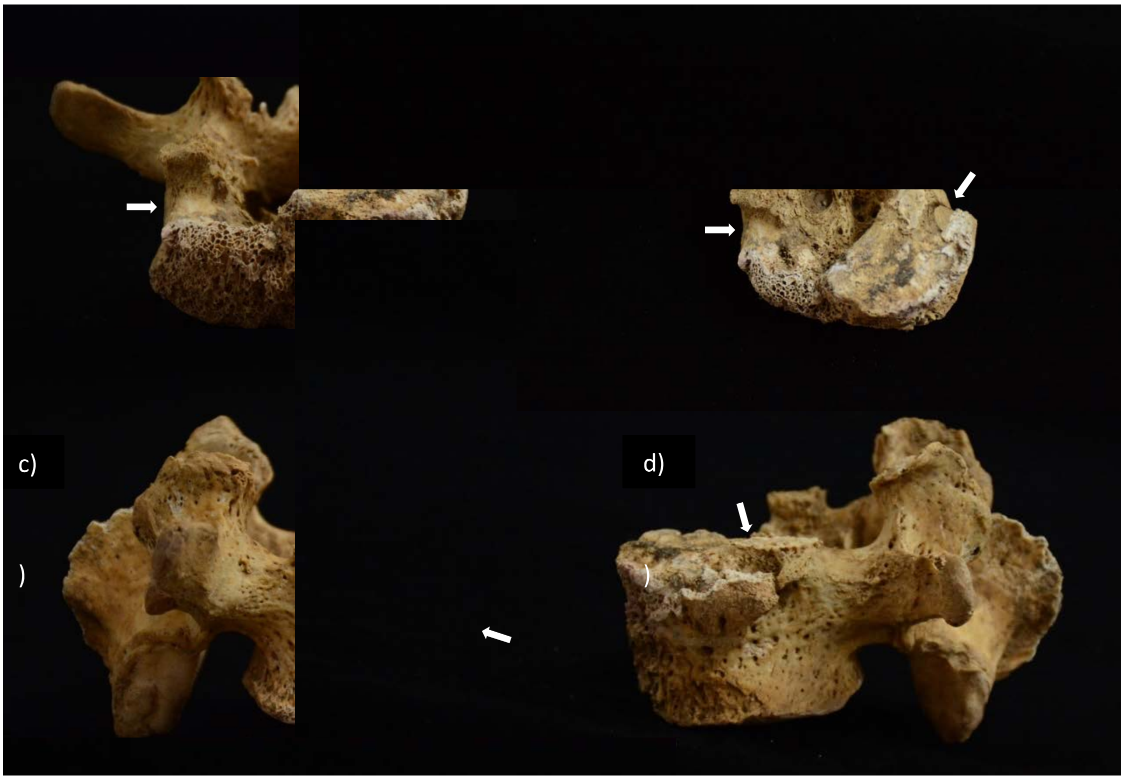

Fig. 5. Second lumbar vertebral body of individual M34-E. a) anterior view, b) superior view, and c) right lateral view showing marked destruction of the vertebral body. d) left lateral view showing new bone formation as bony extensions.

4. Discussion

4.1. Differential diagnosis of individual M34-E

The pathological changes of interest in individual M34-E are the multifocal lytic lesions on the vertebral bodies of T11 to L2. For this reason, spinal diseases that do not cause osteolysis in the manner of TB were excluded, including Scheuermann's disease, Paget's disease, compression fracture, and rheumatoid spondylitis (Resnick and Niwayama, 1995; Buikstra et al., 2017; Roberts and Buikstra, 2003: 96). Among the diseases causing lytic lesions on vertebrae, blastomycosis (*Blastomyces dermatitidis* and *B. brasiliensis*; endemic in America and Africa), coccidioidomycosis (*Coccidioides immitis*; endemic in America), and histoplasmosis (*Histoplasma capsulatum* and *H*. *duboisii*; endemic in the US and Africa) are rarely found in China today, with the first person being reported in 1958 (Liang et al., 2018; Pan, 2013; Zhao et al., 2011b). Hence, it was unlikely for individual M34-E who lived during 202 BC-220 AD to be affected by these diseases. Actinomycosis, echinococcosis, pyogenic osteomyelitis, sarcoidosis, and tumors affect the vertebral arches of the spine as often as the vertebral body (Resnick and Niwayama, 1995), whereas all vertebral arches in individual M34-E appeared normal. Furthermore, Langerhans cell histiocytosis primarily affects the skull and pelvis (Resnick and Niwayama, 1995: 2214; Grauer, 2019: 507), which were not seen for individual M34-E. Typhoid fever is more likely to cause a solitary focus rather than multiple foci (Resnick and Niwayama, 1995: 2455; Laloum et al., 2005), which is not consistent with the lesions found in individual M34-E. In addition, parrot-beak like osteophytes, the characteristic feature of brucellosis (Resnick and Niwayama, 1995: 2457; Jones, 2019), were not observed in individual M34-E, although this disease could have been the cause of death of individual M34-E before the formation of osteophytes. The detailed differential diagnoses are summarized in Table 3.

Table 3

Differential diagnostic options for the spinal lesions observed in individual M34-E.

Diagnosis	Etiology	Spinal lesion	Individual M34-E	Reference
Actinomycosis	Bacteria: *Actinomyces israelii*, *A. bovis*, *A. naeslundii*, *A. viscosus*, and *A. odontolyticus*	Lytic lesions with marginal sclerosis; intervertebral discs are spared; vertebral arches are affected; paravertebral abscesses are small; spinal collapse is uncommon	No. All vertebral arches appeared normal.	Resnick and Niwayama, 1995: 2503
Blastomycosis	Fungi: *Blastomyces dermatitidis* and *B. brasiliensis*	A thoracolumbar predilection; lytic lesions with or without periosteal new bone formation; spinal collapse; intervertebral disc space destruction; paravertebral abscess	No. Although a thoracolumbar predilection, lytic lesions, and a paravertebral abscess have been observed, blastomycosis is endemic in America and Africa. It is very rare in Asia, with only a few people with it being reported in China, India, Saudi Arabia, and Israel.	Resnick and Niwayama, 1995: 2506, 2507; Saccente and Woods, 2010; Kumar et al., 2014; Zhao et al., 2011b
Brucellosis	Bacteria: *Brucella melitensis, B. suis,* and *B. canis*	A lumbar predilection; multiple lytic lesions with marginal sclerosis; paravertebral abscess; healing causes bony ankylosis; parrot-beak like osteophytes formation	Yes. Although marginal sclerosis and parrot-beak like osteophytes were not observed, the involvement of L1-L2 and the slight osteophyte formation on T12 could result from brucellosis.	Resnick and Niwayama, 1995: 2457; Jones, 2019
Coccidioidomycosis	Fungus: *Coccidioides immitis*	Solitary or multiple involvements of vertebral bodies and adjacent ribs; paravertebral abscess; uncommon spinal collapse; uncommon fistula tracts (holes)	No. Although multiple involvement of vertebral bodies and a paravertebral abscess have been observed, coccidioidomycosis is endemic in America. It was first reported in China in 1958. Only 38 people with the infection have been reported (1959 to 2017) and none lived in Shaanxi.	Resnick and Niwayama, 1995: 2509-2510; Liang et al., 2018
Echinococcosis	Parasite: *Echinococcus granulosus* and *E. multilocularis*	Rarely affects bones; lytic lesions on the spine; involvement of the vertebral arches and adjacent ribs; absence of osteoporosis; absence of sclerosis	No. The vertebral arches of the affected vertebrae appeared normal. Osteoporosis was found on the vertebral body of T11.	Resnick and Niwayama, 1995: 2539-2540

Histoplasmosis	Fungi: *Histoplasma capsulatum* and *H*. *duboisii*	Rarely affects bones; multiple round lytic lesions on the cranial vault, long and short bones of extremities, ribs and pelvis; vertebral lesions result from *H*. *duboisii* and are cystic	No. The cranial vault, long and short bones of the extremities, ribs, and pelvis were all normal. Furthermore, histoplasmosis is endemic in the US and Africa. The first clinical evidence in China was reported in a person traveling from the US to China in 1958. From 1991 to 2011, 300 people with the disease have been reported, with 75% being found in southern China.	Resnick and Niwayama, 1995: 2510, 2515; Pan, 2013; Grauer and Roberts, 2019: 443
Langerhans cell histiocytosis	Unknown	Children are more likely to be affected than adults; the cranium and pelvis are the commonly affected sites; a solitary lytic focus is more common than multiple lytic foci	No. The skull and pelvis appeared normal. Multiple lytic foci were found on T11 to L2.	Resnick and Niwayama, 1995: 2214; Grauer, 2019: 507
Pyogenic osteomyelitis	Bacterium: *Staphylococcus aureus*	There is a lumbar predilection, lytic lesions, spinal collapse, and paravertebral abscesses ascending or descending along the spine, with involvement of vertebral arches	No. The vertebral arches of the affected vertebrae were spared. The paravertebral abscess remained localized rather than extending above or below the lesions.	Resnick and Niwayama, 1995: 2424; Roberts and Buikstra, 2003: 96
Sarcoidosis	Granulomatous disease of unknown etiology	The common sites affected are the hand and foot bones, and nasal lesions are characteristic. Vertebral involvement is rare. There is a thoracolumbar predilection, and there are lytic lesions with marginal sclerosis in one or more vertebral bodies. The extension of the lesion to the pedicles is common.	No. No abnormalities were discerned in the nasal region or the preserved bones of the feet. All vertebral pedicles appeared normal.	Resnick and Niwayama, 1995: 4333; Roberts and Buikstra, 2019: 470
Tumors	Unknown	Metastasis, plasma cell myeloma, haemangioma, lymphoma, chondroblastoma, giant cell tumor, osteoblastoma, chordoma, Ewing's sarcoma, and aneurysmal bone cysts cause lytic lesions commonly in more than two	No. Four adjacent vertebral bodies were affected. The vertebral arches of the affected vertebrae were normal.	Resnick and Niwayama, 1995: 3626; Marques, 2019: 641-642; Roberts and Buikstra, 2003: 96

		noncontiguous vertebrae, as well as the vertebral arches and the associated ribs.		
Typhoid fever	Bacterium: *Salmonella typhi*	Rarely affects bones (1%); the shaft of long bones and vertebral bodies are the main sites; a solitary focus is the rule, although multiple foci can occur.	Yes. Multifocal lytic lesions on the vertebral bodies of T11-L2 could result from typhoid fever.	Resnick and Niwayama, 1995: 2455; Laloum et al., 2005

In contrast, in spinal TB, lytic lesions commonly develop in the anterior portion of several adjacent vertebral bodies, although the involvement of a solitary vertebral body or “skip lesions” (normal vertebrae between diseased ones) can occur (Resnick and Niwayama, 1995: 2464-2465). The first lumbar vertebra is most frequently affected (Resnick and Niwayama, 1995: 2463). Involvement of the pedicles, laminae, transverse and spinous processes is extremely rare (Resnick and Niwayama, 1995: 2465). Anterolateral extension of the infection to the adjacent soft tissues is common; in the lumbar region, this causes a paravertebral (psoas) abscess (Resnick and Niwayama, 1995: 2465). All these features were concordant with the spinal lesions observed in individual M34-E, including the multifocal lytic lesions on the vertebral bodies of T11 to L2, the spared vertebral arches, and a paravertebral (psoas) abscess that had developed on the left side of L1 and L2. Although the vertebral collapse, kyphosis, and ankylosis of destroyed vertebrae, the typical features of spinal TB (Resnick and Niwayama, 1995: 2467, 2473), were not discerned in individual M34-E, this could be attributed to the death of individual M34-E before the more chronic and later stages of spinal TB occurred. Therefore, TB was considered the most likely diagnosis of the spinal lesions observed, with brucellosis and typhoid being important entities in the differential diagnoses.

4.2. The cultural context of TB

Socioeconomic factors, including poverty, poor living and working conditions, can increase TB morbidity (Lönnroth et al., 2009, 2010; Resnick and Niwayama, 1995: 2462; Roberts and Buikstra, 2003: 44-86). Among these, urban areas are the optimal environment for TB to spread, especially in places where rapid urbanization occurs, including the impact of immigration to those areas (Lönnroth et al., 2009, 2010; Roberts and Buikstra, 2003: 64). The reason is that a dense population, crowded living spaces, and poor sanitation, which are commonly seen in an urban setting, greatly increase the likelihood of human exposure to droplet infection (Antunes and Waldman, 2001; Dhanaraj et al., 2015; Kirenga et al., 2015; Lönnroth et al., 2009, 2010). For example, the global history of TB has shown that rapid industrialization and urbanization in the 17th to 18th centuries increased TB incidence (Lönnroth et al., 2009). Today, TB morbidity is still higher in urban areas compared to rural regions (Lönnroth et al., 2006; Oren et al., 2011).

Maolingyi, in which the Liuwei Cemetery was located, was built in 139 BC and had a core area of about 1845 x 1543 meters (Ban Gu: 158; Zhang et al., 2011). At the beginning of the first century AD, its population reached 277,277 (Ban Gu: 1547). Such rapid population growth largely resulted from two large-scale migrations in 127 BC and 96 BC, respectively (Ban Gu: 170, 205). Given the size and the population of *Maolingyi*, overcrowding and poor sanitation would likely have been a favorable environment for TB to spread. Therefore, the living environment in *Maolingyi* during the Han Dynasty (202 BC-220 AD) and influxes of people via large-scale migrations probably contributed to the presence of TB found in individual M34-E.

4.3. TB in China, East Asia, and the wider world

A review of all five published bioarchaeological studies of TB in China showed that the earliest evidence for TB is dated to the Late Neolithic Period (3900-3200 BC), and all the evidence is later than the timing of the transition to agriculture and animal domestication in China (Okazaki et al., 2019; Pechenkina et al., 2007: 267; Li et al., 2013; Fusegawa et al., 2003; Hunan Medical College, 1980: 269). The earliest evidence of TB in China is also the earliest for all of East Asia (Suzuki et al., 2008; Suzuki and Inoue, 2007; Taylor et al., 2007; Tayles and Buckley, 2004). This supports the argument that TB was transmitted to East Asia from China around 400 BC (Suzuki et al., 2008; Suzuki and Inoue, 2007).

Contemporary with the presence of TB in Shaanxi, four more individuals with TB have been found, including three in Xinjiang (Fusegawa et al., 2003) and one in Changsha (Hunan Medical College, 1980: 269). Meanwhile, TB has also been reported in other East Asian regions, including Japan (454 BC-124 AD, Suzuki and Inoue, 2007), Korea (the 1st century BC, Suzuki et al., 2008), Southern Siberia (400 BC-400 AD, Taylor et al., 2007), and Thailand (300 BC-500 AD, Tayles and Buckley, 2004). This might suggest a TB epidemic in East Asia during this time period. However, this interpretation is based on very sparse published bioarchaeological data for TB in Asia. The transmission of TB in Asia and its link to the wider world remain unclear until further evidence is published.

5. Conclusion

A male aged around 30 years (M34-E) excavated from the Liuwei Cemetery in Shaanxi, China and dated to 202 BC-220 AD manifested multiple lytic lesions on the vertebral bodies of T11 to L2. TB was considered a possible diagnosis for the spinal lesions observed, with differential diagnoses of brucellosis and typhoid. A dense population and overcrowding in *Maolingyi*, an urban area during this time period, were advantageous to the transmission of the infection. Around the same time period, TB was also present more widely in East Asia, which might hint at a TB epidemic in this region. The findings of this study contribute to limited knowledge about the history of TB in East Asia and suggest a relationship between population density and the spread of TB in *Maolingyi* at that time. However, the lack of published bioarchaeological data of TB in East Asia hinders understanding the transmission of TB within Asia and its link to the rest of the world. Further intensive review of archaeological skeletons in Asia is urgently needed.

Conflict of interest

The authors declare that they have no conflict of interest.

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