BMC Pulmonary Medicine

CASE REPORT

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Imaging analysis of pneumonic plague infection in Xizang, China: a case report and literature review

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Abstract

Background Plague is an acute infectious disease caused by the Yersinia pestis. Historically, it has been a major pandemic with high mortality rates, known as the "Black Death" in the 14th century, which resulted in millions of deaths in Europe. With increasing economic prosperity, more and more people are traveling to Xizang. However, this trend also hides significant safety hazards. Currently, there are few recent reports on plague, especially those with imaging manifestations available. In this study, we report the detailed clinical and radiological data of the patient with pneumonic plague in Xizang, China, in 2023.

Case presentation We report a case of pneumonic plague in Xizang, which occurred in a herdsman living in an area where dead marmots were found. The patient presented with symptoms such as fever, hemoptysis, dyspnea and coma. Chest computed tomography (CT) scans showed multiple nodules distributed in the central regions of lung lobes, consolidation distributed in secondary pulmonary lobules, and had a gravity-dependent distribution pattern. These imaging findings were consistent with pulmonary hemorrhage and diffuse alveolar damage. Despite emergency treatment, the patient died within 48 h of admission. Through retrospective medical history investigation, laboratory examination and autopsy, the final diagnosis was confirmed as pneumonic plague.

Conclusion Pneumonic plague is the most deadly infectious disease, and its pathological features mainly include damage to the alveoli, pulmonary hemorrhage, and pulmonary edema. Corresponding to CT, it manifests as acute and rapidly progressing pneumonia, alveolar damage, and pulmonary hemorrhage. The value of this article lies in the completeness and typicality of the imaging data, vivid hand-drawn illustrations of transmission pathways, and comprehensive literature review, all of which serve to enhance public understanding of plague and play an important warning role.

Keywords Plague, Lung, Computed tomography

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Background

Plague is an acute, highly contagious and highly fatal infectious disease caused by Yersinia pestis, it is a vector-borne disease prevalent among wild rodents [1]. Under certain conditions, it can be transmitted to humans through flea bites and other routes, leading to the occurrence of plague [2]. Once it occurs and spreads, it can easily become a major public health emergency. The most recent plague pandemic was the "Surat storm" in India in 1994 [3]. In China, it is classified as the first Class A communicable disease under the "Law on the Prevention and Control of Infectious Diseases". According to the World Health Organization(WHO), there were 3,248 cases of plague worldwide from 2010 to 2015, resulting in 584 deaths. According to data from the Chinese Center for Disease Control and Prevention(CDC), there has been no widespread plague in China in the past four years, with only a few sporadic cases, mainly in Inner Mongolia and Ningxia. In 2019, there were 5 reported cases of plague with 1 death. In 2020, there were 4 reported cases with 3 deaths. In 2021 and 2022, there was 1 reported case of plague each year. This article reports a case of pneumonic plague in Xizang, China, in 2023, which is a rare occurrence.

Case presentation

A 37-year-old male herdsman was admitted to the People's Hospital of Cuona County on September 19, 2023, due to cough, phlegm and lisp for 3 days accompanied by fever for 2 days. On examination, his body temperature was 38.5 °C, and respiratory rate was 46 breaths per minute. He experienced difficulty breathing and generalized fatigue. Chest computed tomography (CT) revealed diffuse nodules and patchy consolidations in both lungs, as shown in Fig. 1A-C. CT findings suggested both lung infection, and oral ibuprofen suspension was administered at that time. The next day (September 20, 2023), he was observed for further treatment. The patient had a body temperature of 40.5 °C, rapid breathing, significant cough with bloody sputum, cyanotic lips, and cold extremities.Coarse breath sounds and moist rales were audible on both sides. Blood routine examination showed that white blood cell count (WBC) and platelet decreased, electrolyte disturbance (Table 1). A follow-up chest CT showed significant progression of diffuse nodules and patchy consolidations compared to the previous day's images, as shown in Fig. 1D-F. Specific details can be seen in Fig. 2, where diffuse central nodules in the pulmonary lobes, secondary lobular consolidation with a gravity-dependent distribution, and air bronchogram were observed, consistent with pulmonary hemorrhage changes. The patient was clinically diagnosed with severe pneumonia. Continuous oxygen inhalation, electrocardiogram monitoring, antibiotics (piperacillin sulbactam sodium 3 g was administered intravenously every 8 h) and cooling treatment were given. At 1 a.m. on September 21, the patient developed unconscious, unresponsive, and had no palpable carotid artery pulse.

Table 1 The patient's laboratory indicators details

	Data	Reference value
Total white cells ($\times10^9$ cells/L)	3.9	4.0–10.0
Lymphocytes ($\times10^9$ cells/L)	0.9	0.8-4.0
Neutrophils ($\times10^9$ cells/L)	2.7	2.0–7.0
Lymphocyte percentage (%)	22.0	20.0–40.0
Neutrophil percentage (%)	69.3	50.0–70.0
Erythrometry ($\times10^{12}$ cells/L)	7.12	3.50–5.50
Haemoglobin (g/L)	234	110–160
Hematocrit value (g/L)	67.7	37.0–54.0
Platelets ($\times10^9$ cells/L)	71	100–300
Platelet count value (%)	0.073	0.108–0.282
Urea (mmol/L)	9.01	1.7–8.3
Creatinine (μmol/L)	113.6	53–115
Uric acid (μmol/L)	435.2	140–480
Glucose (mmol/L)	8.80	3.89–6.10
Ka (mmol/L)	5.73	3.5–5.5
Na (mmol/L)	134.06	135–145
Cl (mmol/L)	109.45	98–106

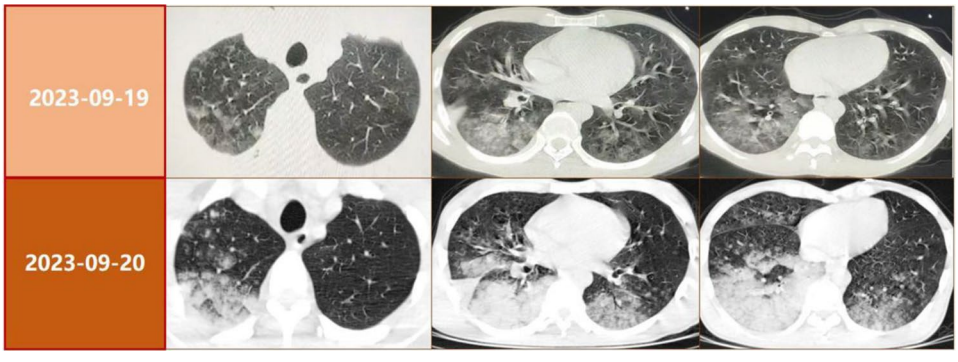

Fig. 1 Comparison of two CT scans. The patient is male, 37 years old, herdsman. On September 19, 2023, CT in Fig. 1**A**-**C** showed diffuse nodules, ground glass and solid shadow in both lungs. On September 20, 2023, CT in Fig. 1**D**-**F** corresponding to the CT level of Fig. 1**A**-**C** showed a significant increase in the number of lesions and an enlarged scope, suggesting acute exacerbation of the lesions in the short term

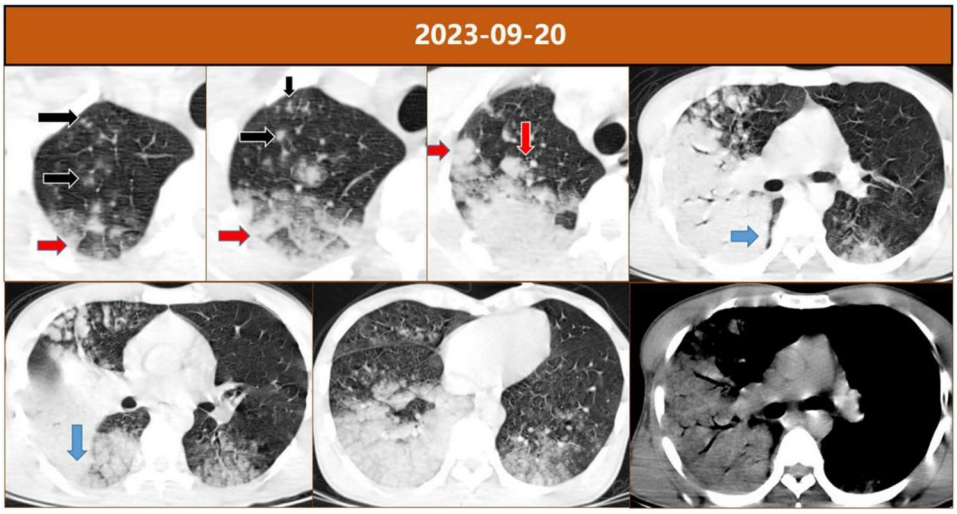

Fig. 2 Detailed analysis of CT scan on September 20, 2023. CT in Fig. 2**A**-**G** showed multiple lobular core nodules in both lungs (as shown by black arrows in Fig. 2**A**-**B**), and secondary lobular distribution lesions were shown by red arrows in Fig. 2**A**-**C**. The air bronchial sign, as shown in Fig. 2**D**, showed smooth and natural bronchial shape, and no necrosis or cavity was found in the consolidation. In Fig. 2**D**-**E**, the blue arrow showed the falling interlobar fissure, indicating the trend of gravity distribution of the lesion and indicating obvious exudation of the lesion. Figure 2**F** showed obvious lesions in the low-hanging position of the both lungs, further indicating the trend of gravity distribution of the lesions. The mediastinal window in Fig. 2**G** showed a typical air bronchial sign. In summary, the imaging diagnosis is consistent with the changes in alveolar hemorrhage

Despite resuscitation efforts, the patient could not be revived and was pronounced clinically dead. Epidemiological tracing found that there were dead marmots in the patient's residence. The patient was clinically highly suspected of plague infection and immediately sent to the Xizang Autonomous Region CDC. The results of autopsy showed that the lung tissue was swollen and congested with a dark purple color, and there was no adhesion between the lung tissue and the chest wall. There were multiple hemorrhagic spots of varying sizes on the surface of one lung lobe, dark red exudate on the lung section, and bloody effusion in the pleural cavity. Yersinia pestis was isolated and cultured from the autopsy specimens. Based on the clinical presentation and autopsy results, the F1 antigen test was positive, so the patient was finally diagnosed with pneumonic plague.

Discussion and conclusions

Plague, also known as the "Black Death", is a severe infectious disease caused by the gram-negative bacterium Yersinia pestis [2]. It has erupted many times in history and is typically classified into three types: bubonic plague, pneumonic plague, and septicemic plague [4]. By consulting pubmed and web of science databases, the literature from 2020 to 2023 were reviewed worldwide (Table 2) [1, 4–8], we learned that bubonic plague is the most common type, which is mainly characterized by lymph node swelling and paining. Pneumonic plague is the most deadly type and primarily spreads through the respiratory tract. Within 24–36 h of onset, patient may experience difficulty breathing, coughing, coughing up large amounts of frothy pink or bright red blood, chest pain. The paucity of pulmonary signs are often disproportionate to the severity of systemic symptoms. Septicemic plague is the rarest but most severe type and can lead to septic shock and multiple organ failure [5, 9, 10]. The patient in this article had acute onset, mainly manifested as cough, hemoptysis and dyspnea, accompanied by varying degrees of high fever, without palpable lymph node enlargement, which are the typical presentations of pneumonic plague. The main route of transmission for plague is through intermediary hosts such as rodents or fleas [11], and it can also spread through human-to-human contact, especially in cases of pneumonic plague (Fig. 3). Our patient in this article was herdsman who had not left the local area since June 2023. Dead marmots were found in the patient's residence, but the family denied peeling them. It is inferred that the patient may have been infected through flea bites, but the possibility of being infected by contact with dead marmot cannot be ruled out.

After the invasion of Yersinia pestis into the human body, it primarily affects the lymphoid tissue, causing acute swelling, bleeding, and necrosis of the lymph nodes, forming visible gray-white necrotic foci [12]. A large number of neutrophils and monocytes can be seen infiltrating the lymph nodes. If Yersinia pestis further invades the entire lymphatic system, it can lead to severe systemic infection [13]. In pneumonic plague, extensive necrosis and hemorrhage occur in the lung tissue, with the alveoli filled with a large amount of exudate and red blood cells [14]. The interstitial tissue and peribronchial

Table 2 Cases of plague described in the literature worldwide(2020–2023)

First Author	Publication year	Gender	Age	Symptom	Imaging manifestations	Diagnostic method	Outcome
Kehrmann J [5]	2020	M	38	Fever, abdominal pain, hematemesis	/	Laboratory examination	Died
		F	37	Fever, diarrhea, abdominal pain, vomiting and headache, swollen lymph nodes in the neck	/	Laboratory examination	Died
Zhou H [8]	2020	M	43	Cough and vomiting with fever, chest pain and difficulty breathing	HRCT scan of the lungs shows multiple patchy consolidation and ground glass shadows	Laboratory examination	Recovered
		F	46	Cough and vomiting with fever, chest pain and difficulty breathing	HRCT scan of the lungs showed multiple patchy solid shadow and air bronchogram	Laboratory examination	Died
Dale A P [6]	2021	M	67	Tachycardia, shortness of breath, fever, cough and sputum, soft tissue swelling	Normal	Laboratory examination	Recovered
Li J [4]	2021	M	55	Left axillary lymph node enlargement with high fever	/	Laboratory examination	Recovered
		F	48	Left inguinal lymphonitis	/	Laboratory examination	Recovered
Xi J [1]	2022	M	45	High fever, mild cyanosis, axillary lymph node enlargement, confusion	/	Laboratory examination	Died
Erly B [7]	2023	M	16	Fever, discomfort and back pain, cough and difficulty breathing	/	Laboratory examination	Died
		F	52	Fever, vomiting, diarrhea and difficulty breathing	X-rays reveal wide borderless shadows on both sides	Laboratory examination	Died
		M	31	Fever, vomiting, diarrhea and difficulty breathing	/	Laboratory examination	Recovered
		M	38	Fatigue, fever, armpit tenderness, nausea, hemoptysis and shortness of breath, spotty rash, local blackening of the skin	/	Laboratory examination	Died
		M	28	Chills, headache, abdominal pain, diarrhea and bloody vomiting, shortness of breath and swollen axillary lymph nodes	/	Laboratory examination	Died
		M	15	Fever, headache and swollen inguinal lymph nodes	/	Laboratory examination	Died
		M	9	Vomiting and abdominal pain, fever, tachycardia and supraclavicular pain	/	Laboratory examination	Died
		F	16	Pain in the left armpit, neck, fever, chills and vomiting	Normal	Laboratory examination	Died
		M	60	Fever, body aches and cough, shortness of breath	/	Laboratory examination	Died

tissue may also be affected, leading to varying degrees of inflammation. Increased cell permeability can result in secondary exudative pulmonary edema [12]. Therefore, the pathological changes of pneumonic plague were characterized by alveolar hemorrhage, pulmonary edema, and inflammatory exudative changes. The gold standard for laboratory diagnosis of plague is the isolation and identification of the Yersinia pestis pathogen from clinical specimens [15]. At present, F1 antigen is the typical target antigen for immunological detection of plague [12, 15]. In our case, histological examination showed consolidation of the lung tissue, and Yersinia pestis was isolated. The alveolar wall was hyperemic, edematous and fractured, and there was a large amount of exudate in the alveolar cavity. The pulmonary interstitium were filled with edema, and scattered inflammatory cell infiltration were found. These findings were consistent with previous literature.

The imaging manifestations of plague are rarely reported and are not specific. By reading a large number of literature, we summarized the following: (1) Pulmonary consolidation: patchy, localized, or diffuse

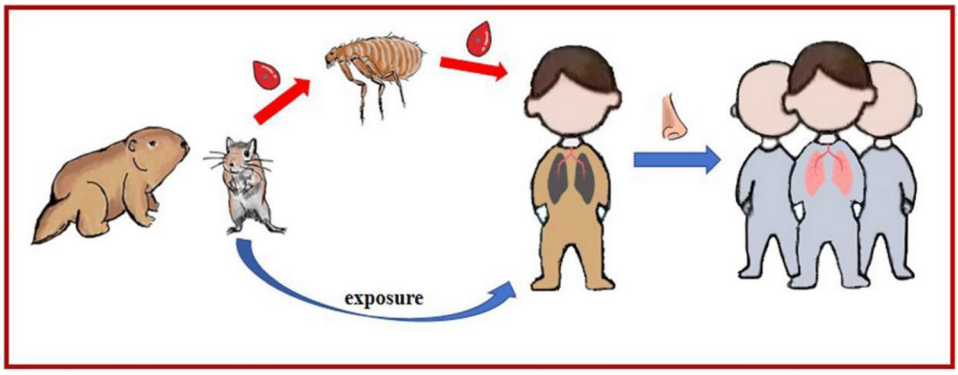

Fig. 3 Hand-drawn picture of the plague transmission route. **A**: rodents carrying Yersinia pestis infect humans through direct contact; **B** and **C**: fleas infect humans through bites after absorbing the blood of infected animals; **D**: humans carrying Yersinia pestis infect other people through respiratory transmission

consolidation shadows appear in the lungs, with blurred edges that can merge into large areas, and may even show "white lung" changes [16]. The pathological basis of this change is diverse and may be pulmonary hemorrhage, pulmonary edema, or inflammatory exudation. (2) Pleural effusion: pneumonic plague can cause pleural effusion [14]. (3) Lymphadenopathy with necrosis: formation of multiple irregular enlarged lymph nodes with low-density areas inside [6]. (4) Cellulitis: cellulitis is a severe complication of plague, characterized by subcutaneous soft tissue swelling in the affected area, forming multiple high-density honeycomb-like shadows [7]. In our case, CT revealed multiple acinar nodules distributed along the core of the pulmonary lobules in both lungs, with indistinct margins and partial fusion, as well as patchy high-density shadows distributed along the secondary pulmonary lobules, demonstrating air bronchogram sign. The density of the dependent lung zones was higher, and the density near the interlobar fissure in the upper lungs was also relatively high, and the interlobar fissure was sagging, which was a typical gravity distribution, indicating fluid accumulation. All the above manifestations supported the changes consistent with alveolar hemorrhage, which was in line with the pathological features of plague.

In addition to pneumonic plague, which can cause diffuse alveolar hemorrhage, the following diseases need to be distinguished: (1) ANCA-associated vasculitis: this is a connective tissue disease that typically has a chronic course and is positive for ANCA antibodies [17]. Multiple systems are often involved, such as rash and renal impairment. Granulomatosis with polyangiitis can lead to the formation of granulomatous lesions with cavity formation in the lungs. (2) Leptospirosis: the patients usually have a history of contact with infested water, and have an acute onset. The main clinical manifestations are fever, myalgia, fatigue, and conjunctival hyperemia [18]. Imaging findings show diffuse ground-glass opacities in both lungs, with indistinct borders and a predominant peripheral distribution [19]. Thickening of interlobular septa is also observed, indicating diffuse hemorrhagic changes in the lungs. (3) Hantavirus pulmonary syndrome: This is a disease caused by infection with the Hantavirus [20]. Clinical manifestations mainly include fever, shock, and acute renal failure. Imaging manifestations included pulmonary edema, pulmonary hemorrhage, and pleural effusion. The imaging features in our case are consistent with diffuse alveolar hemorrhage and damage. Although these findings lack specificity, they can help clinical exclude other common pathogens such as pyogenic bacterial and mycobacterium tuberculosis.

At present, the primary treatment of plague is the use of antibiotics, and the commonly used drugs are doxycycline and streptomycin [21]. Supportive cares, including rehydration and nutritional support, are also necessary to maintain stable vital signs. In addition, patients should be isolated immediately to prevent transmission to others. Medical staff should strictly follow protective measures when handling patients, dead bodies, or objects that may contain Yersinia pestis.

Plague is one of the most severe infectious disease, which can be divided into many types. The pathological characteristics of pulmonary plague primarily include alveolar damage, alveolar hemorrhage, and pulmonary edema. CT findings may show diffuse nodules, consolidation of secondary pulmonary lobules, gravity-dependent distribution, air bronchogram sign, and pleural effusion. The combination of clinical and imaging can help us to diagnose and treat as soon as possible to save lives. This article aims to raise awareness among tourists visiting regions such as Xizang, Qinghai, Gansu, etc., urging them to stay away from rodents and marmots as a precautionary measure.

Abbreviations

CT	Computed tomography
WHO	World health organization
CDC	Center for disease control and prevention

WBC White blood cell

Acknowledgements
Not applicable.

Author contributions
Wei Wang and Xiaoran Li have contributed equally to this work.Conception and design: XL, JW, XF. Acquisition, analysis, and interpretation of the data: WW, BL. Drafting of the manuscript: XL, XF. All authors reviewed and approved the final version of the manuscript. All authors had read and approved the manuscript.

Data availability
All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
The present study was approved by the local ethics of Shannan People's Hospital. Written informed consent was obtained from the patients prior to inclusion in the study.

Consent for publication/Consent to publish
Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the informed consent form is available for review by the Editor of this journal.

Competing interests
The authors declare no competing interests.

Received: 16 February 2024 / Accepted: 26 July 2024
Published online: 01 August 2024

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