· Case Report ·

A case of systemic disseminated tuberculosis with cerebral infarction as the initial symptom

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Abstract

This article reports the diagnosis and treatment process of a middle-aged woman with systemic disseminated tuberculosis infection. Her initial symptoms were speech impairment and left limb weakness, and the preliminary diagnosis was cerebral infarction. After admission, she began to complain of headache and developed a fever. Lumbar puncture was then performed, which revealed tuberculous meningitis. During treatment, pulmonary lesions and intestinal obstruction occurred. Acid-fast staining of alveolar lavage fluid and stool were positive. The final diagnosis was systemic disseminated tuberculosis.

Keywords: cerebral infarction, tuberculous meningitis, systemic disseminated tuberculosis

Clinical Data

A 47-year-old Han Chinese woman, who worked as a farmer, was admitted to the Neurology Department of our hospital because of a 20-day history of speech impairment and 6 days of progressive left limb weakness. She had been originally treated in a rural clinic with intravenous fluids and unspecified medications; although she experienced improvement initially, her symptoms recurred, and she presented to our hospital's emergency department. The patient denied nausea, vomiting, difficulty swallowing, breathing difficulties, diarrhea, limb convulsions, and incontinence. Computed tomography (CT) of the head showed lacunar cerebral infarction in the right basal ganglia (Figure 1). Since the onset of illness, the patient reported reduced food intake, poor sleep, and normal bowel and bladder movements. Her medical history was notable for hypertension treated with nifedipine. She had no other chronic diseases or infectious disease history, and no contact with livestock.

Physical Examination

Vital signs were as follows: temperature, 38°C; pulse, 102/minute; respiratory rate, 22/minute; and blood pressure, 132/79 mm Hg. The patient was normally devel-

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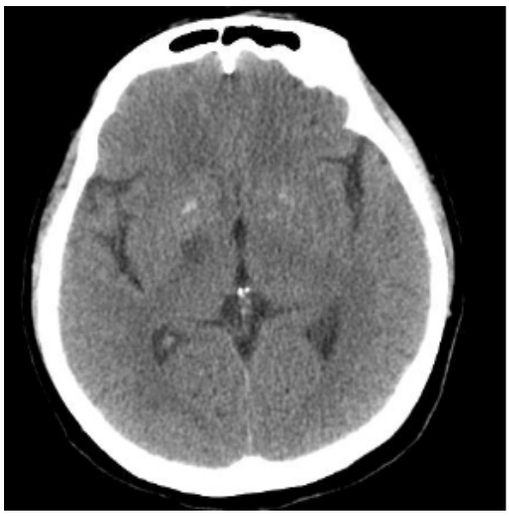


Figure 1. Lacunar cerebral infarction in the right basal ganglia.

oped but had a slightly impaired mental state. Memory and calculation abilities were normal, but speech was not fluent. Gaze was conjugate without nystagmus. Her pupils were round, 3 mm in diameter, and reactive to light. Facial muscle movement was symmetric. Tongue protruded in the midline. Left limb muscle strength was graded 3+ on manual muscle testing; right limb muscle strength was normal. Muscle tone in all four limbs was normal, as were deep and superficial sensations. Finger-to-nose and heel-to-shin tests were normal, as were deep tendon reflexes in all four limbs. Babinski testing was negative. The neck was supple without rigidity. Breath sounds were clear in both lungs without rales or pleural friction sounds. The precordial area was not raised, and no thrills were felt. The heart rhythm was regular. The abdomen was flat with no visible peristalsis or venous engorgement. The abdomen was tympanic to percussion without shifting dullness. Bowel sounds were normal. The lower limbs were without pitting edema.

Auxiliary Examinations

Liver and kidney function testing were normal. Sodium and chloride levels were 133 and 97 mmol/L, respectively. Fibrinogen level was 4.1 g/L. B-type natriuretic peptide, myoglobin, and troponin levels were normal. Respiratory virus panel and COVID-19 nucleic acid tests were negative. Ultrasonography showed carotid artery atherosclerosis and a narrow left vertebral artery with increased flow resistance. On echocardiography, left ventricular systolic function was normal, but diastolic function was reduced. No significant abnormalities were found on vascular ultrasonography of the lower limbs. Magnetic resonance imaging of the brain showed acute cerebral infarction in the posterior limb of the right internal capsule and lateral thalamus, a softening lesion in the right corona radiata, a dominant right vertebral artery, developmental variation in the intracranial segment of the left vertebral artery, and a fenestrated basilar artery (Figure 2). Chest CT showed a few linear opacities in both lungs (Figure 3).

Treatment Course

After admission for a diagnosis of cerebral infarction, the patient was treated with Xuesaitong to improve circulation, aspirin and clopidogrel as antiplatelet agents, butylphthalide for neuroprotection, cefoxitin for anti-infection, and ibuprofen for fever reduction. After experiencing recurrent fevers of unknown cause in the first week after admission, the patient was transferred to the Infectious Disease Department. At this time, the patient

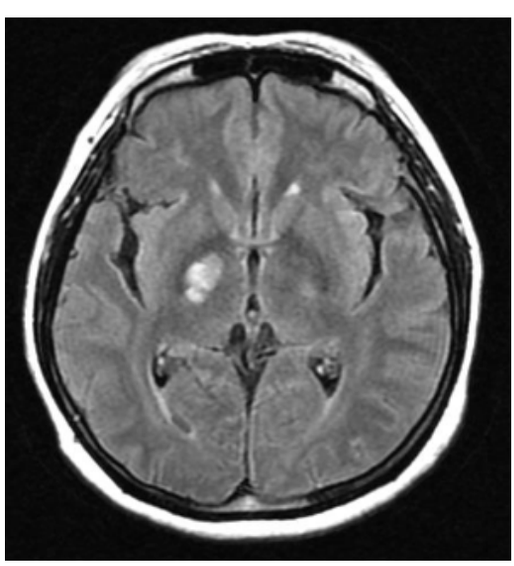


Figure 2. Acute cerebral infarction in the posterior limb of the right internal capsule and lateral thalamus.

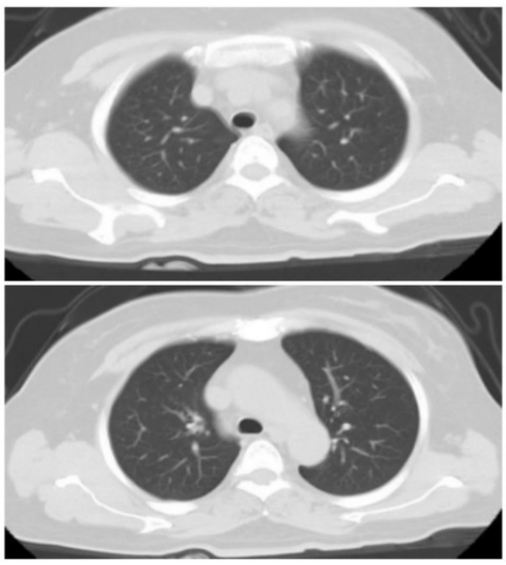


Figure 3. A few linear opacities in both lungs.



Figure 4. Bronchitis, a few linear opacities, and dependent changes in both lungs.

exhibited impaired consciousness, irritability, and conjunctival edema; she was unable to fully cooperate with the physical examination. Mannitol and glycerol fructose were administered to reduce intracranial pressure, methylprednisolone 40 mg to suppress inflammation, and ceftriaxone 2 g/day for anti-infection. Xuesaitong, antiplatelet agents, and butylphthalide were continued. A gastric tube, urinary catheter, and protective restraints were also placed. CT of the head and chest were performed 2 days later. The lacunar cerebral infarction in the right basal ganglia was unchanged, but the ventricular system was slightly widened, the cerebral sulci were shallow, and the brain tissue was swollen. Bronchitis and a few linear opacities were noted in the lungs, as well as dependent changes caused by lying supine (Figure 4).

Further history-taking revealed that the patient had experienced fever more than 20 days prior, accompanied by intermittent headaches. She had self-medicated with painkillers and antipyretics. Based on this clue, tuberculous meningitis was considered a likely diagnosis. A lumbar puncture was performed, which revealed a cerebrospinal fluid (CSF) pressure of 550 mm H_2O. Mannitol 250 mL, furosemide 20 mg, and methylprednisolone 80 mg were then administered to treat the intracranial pressure. The CSF appeared colorless and transparent. CSF testing was as follows: Pandy's test, positive; nucleated cells, 288 × 10^6/L; polymorphonuclear cells, 8.3%; mononuclear cells, 91.7%; protein, 0.98 g/L (above normal); glucose, 1.75 mmol/L (below normal); and chloride, 114.9 mmol/L (below normal). CSF metagenomic next-generation sequencing results showed a high confidence for detection of *Mycobacterium tuberculosis* complex. The T-cell test for tuberculosis infection was positive.

Anti-tuberculosis treatment was then initiated with isoniazid 0.3 g/day, rifampin 0.6 g/day, ethambutol 0.75 g/day, and pyrazinamide 1.5 g/day. Three days later, the patient's symptoms had not improved, and she continued to have high fevers. Gastric retention also had developed. Bedside chest radiography showed right lung infiltration and possible intestinal obstruction (Figure 5). CT of the head showed that the right basal ganglia infarction had increased in size (Figure 6); the other previous findings were unchanged. CT of the chest and abdomen demonstrated right lower lobe bronchial obstruction with atelectasis, right upper lobe inflammation,

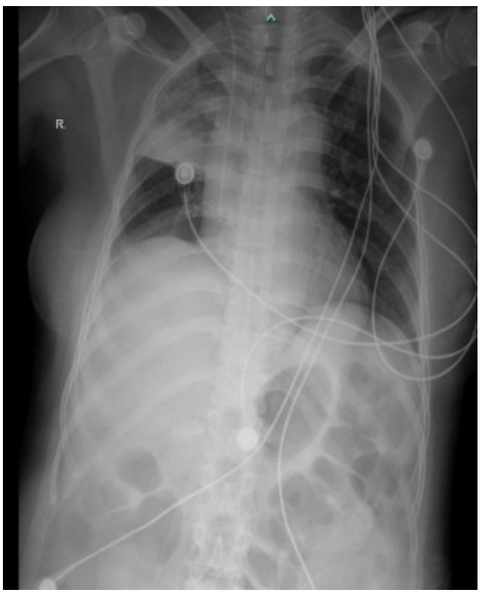


Figure 5. Right lung infiltration and possible intestinal obstruction.



Figure 6. The right basal ganglia infarction had increased in size.

and widespread intestinal dilation, suggesting intestinal obstruction (Figures 7 and 8). For the intestinal obstruction, enteral nutrition was ceased and enemas initiated. Aggressive chest physiotherapy including mechanical vibration was administered to address the lung infection. Acid-fast staining of stool samples was positive. Bedside bronchoscopy was performed to collect lavage fluid for acid-fast staining and GeneXpert MTB/RIF testing, both of which were positive. Detailed results of MTB/RIF testing were as follows: 681 sequences of *M. tuberculosis* complex were detected, JL1 MTB gene test was positive, and JL2 RIF resistance was negative. Thus, the diagnosis of disseminated tuberculosis (CSF, lung, intestine) was confirmed. Although anti-tuberculosis treatment was continued, the patient's condition did not significantly improve after 6 days. She then voluntarily



Figure 7. Right upper lobe inflammation.

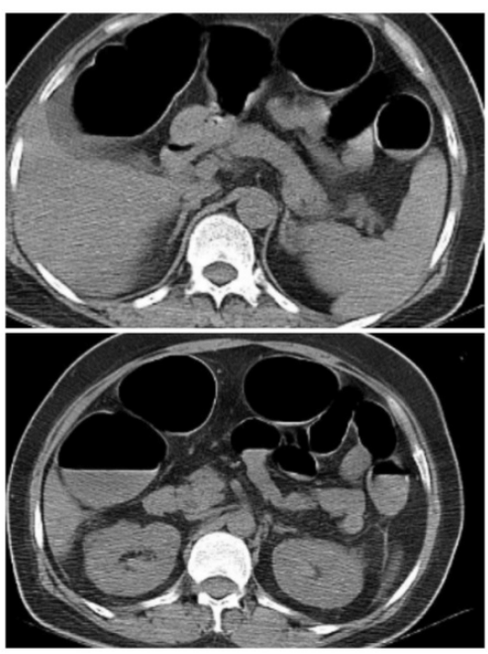


Figure 8. Widespread intestinal dilation, suggesting intestinal obstruction.

discharged herself to seek treatment at Beijing Chest Hospital. A follow-up 14 days later revealed that she was on a ventilator with no improvement in consciousness; 1 month later, she had been weaned off the ventilator, but remained unconscious.

Discussion

This case is an example of systemic disseminated tuberculosis with cerebral infarction as the initial symptom. Because typical tuberculosis lesions were absent, the patient was initially misdiagnosed with simple cerebral infarction, and the possibility of cerebral infarction secondary to tuberculous meningitis was overlooked. As a result, appropriate treatment was delayed and the patient's clinical outcome was poor.

In recent years, clinical reports of tuberculous meningitis complicated by cerebral infarction have been increasing. Studies have shown that the incidence of cerebral infarction in tuberculous meningitis in certain regions of China is 10%[1], while in less developed countries such as India and Thailand, the incidence can be as high as 37%[2]. The risk of cerebral infarction increases with factors such as advanced age, hyperlipidemia, diabetes, and hypertension, all of which are considered traditional risk factors for cerebrovascular disease[3-4]. Tuberculous meningitis complicated by cerebral infarction has high rates of mortality and disability, making early diagnosis crucial to achieve good patient outcomes.

Tuberculous meningitis is the most common type of central nervous system tuberculosis, typically presenting with subacute onset. The clinical symptoms are non-specific and include fever, headache, fatigue, nausea, and psychiatric abnormalities. Tuberculous meningitis is mainly caused by the dissemination of pulmonary tuberculosis and is the most severe form of extrapulmonary tuberculosis. The patient in this case also presented with fever and headache as the initial symptoms. Later, after speech difficulties and limb weakness had developed, she sought medical attention. Early in the process, no tuberculosis-related tests or treatments were conducted, which led to a worsening of her condition. Additionally, chest CT at the time of admission did not show pulmonary tuberculosis, which further contributed to overlooking tuberculous meningitis as a diagnosis. Delayed treatment can lead to rapid disease progression, especially when tuberculous meningitis is complicated by cerebral infarction. Failure to promptly diagnose and treat can result in high rates of disability and mortality. Wang et al.[5] reported a case of pregnancy complicated by tuberculous meningitis and cerebral infarction, where the patient presented with headache and unilateral limb weakness, rapidly progressing to impaired consciousness, coma, and ultimately death. Aryal et al.[6] reported a woman with tuberculous meningitis complicated by cerebral infarction who initially presented with fever and personality changes, followed by incontinence and limb weakness. By the time of admission, she exhibited impaired consciousness, and a lumbar puncture was promptly performed to confirm the diagnosis. After aggressive treatment, the patient's condition improved, and she was discharged. Therefore, when a patient without pulmonary or other form of tuberculosis is suspected of having tuberculous meningitis, CSF examination should be performed as early as possible. For those with a known diagnosis of some form of tuberculosis, the diagnosis of tuberculous meningitis is relatively straightforward when symptoms suggesting meningitis appear. Shao et al.[7] reported a case of tuberculous meningitis complicated by massive cerebral infarction in 2023. The patient was initially diagnosed with pulmonary tuberculosis and was receiving anti-tuberculosis treatment. She stopped taking the medication without physician approval owing to headache and nausea, and later presented with impaired consciousness. A lumbar puncture

confirmed tuberculous meningitis.

Although many studies have examined the relationship between tuberculous meningitis and cerebral infarction, the underlying mechanism remains unclear and requires further research. Tuberculous meningitis can cause vasculitis, mainly affecting large, medium, and small cerebral arteries, especially the middle cerebral artery[8]. Vasculitis leads to varying degrees of vascular degeneration, proliferation, and necrosis, causing arterial stenosis or occlusion, local arterial wall necrosis, and thrombosis, ultimately leading to cerebral ischemia, edema, or infarction. Tuberculous meningitis-related vasculitis is generally believed to be caused by mycobacteria-induced damage of the vascular wall, the resulting immune response, and pro-atherosclerotic inflammatory responses[9]. Depending on the location of the vascular occlusion, different neurological symptoms may appear. For example, involvement of the lenticulostriate artery can lead to necrosis of the basal ganglia and thalamus, clinically presenting with choreoathetosis and Cushing's ulcers.

The earlier tuberculous meningitis is treated, the better the patient outcome. Delayed treatment increases mortality and the incidence of sequelae. A retrospective study showed that advanced age and high CSF lactate level are risk factors for a poor long-term outcome in patients with severe tuberculous meningitis, while a high Glasgow Coma Scale score at admission predicts a good outcome. Therefore, clinicians should focus on these factors to improve patient outcomes[10]. A study from Tianjin Haihe Hospital indicated that cerebral venous sinus thrombosis is a factor associated with poor prognosis in these patients [11].

The reasons for the diagnostic difficulty and poor prognosis in this case are as follows: 1) The patient had fever and headache in the early stages of the disease but did not seek medical attention. Later, because of impaired speech, she could not accurately describe her symptoms, and the rural clinic's limited resources prevented further examinations, leading to the oversight of these symptoms. 2) During the patient's hospitalization in the Neurology Department, although she had a fever, her speech impairment prevented her from accurately describing headache and nausea. Additionally, the inflammatory markers in the auxiliary examinations were not significantly elevated. 3) The initial treatment focused on cerebral infarction, with large amounts of fluid replacement and circulation improvement to increase blood and CSF volume. Additionally, tuberculosis infection increases fibrin exudation, leading to basal adhesion and progressive intracranial pressure elevation, resulting in conjunctival edema and increased risk of cerebral herniation. 4) The patient developed intestinal tuberculosis and stopped enteral nutrition, leading to insufficient nutritional intake and affecting the efficacy of anti-tuberculosis drugs. 5) Intestinal tuberculosis damages the intestinal barrier, allowing mycobacteria to enter the bloodstream through the intestinal mucosa, accelerating mycobacterial dissemination and promoting disease progression. 6) The initial physician's lack of clinical experience led to delayed diagnosis.

Conclusion

In conclusion, patients presenting with headache, hemiplegia, and other cerebrovascular symptoms should be suspected to have tuberculous meningitis if any of the following are also present: 1) fever, 2) personality changes, 3) decreased serum sodium, and 4) rapid onset of impaired consciousness. Since tuberculous meningitis complicated by cerebral infarction has a high mortality rate, and the presence of other forms of tuberculosis further increases the difficulty of treatment, leading to higher disability and mortality rates, clinicians should enhance their understanding of this disease for early di-

agnosis and treatment.

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Author contributions

Liu Yang: conceived and designed the case report, supervised the work, and served as the corresponding author. Qian Wang: collected clinical data and drafted the initial manuscript. Xue Bai: contributed to the literature review and interpretation of findings. Qian Chen: assisted in manuscript revision and provided critical feedback. All authors read and approved the final version of the manuscript.

Conflicts of Interest

All authors declare no conflicts of interest.

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