A Rarely Encountered Case: A Patient with Primary Pituitary Tuberculosis and Stroke

Min Chen¹ · Chengru Song² · Hongbo Liu¹

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Dear Editor,

Infections are a common cause of stroke, and tuberculosis is one of the most dangerous causes of central nervous system (CNS) diseases [1]. For example, cerebral infarction is a relatively common and serious CNS disease associated with tuberculosis [2]. Patients with intrasellar tuberculosis are extremely rare [3], and stroke caused by primary pituitary tuberculosis has not yet been reported.

The present case report describes a 52-year-old Chinese man who was referred to the Neurology Clinic with a 3-month history of fluctuating bitemporal headache, fatigue, nausea, anorexia, and several instances of fever. The patient had no history of cough and exhibited no weight loss, visual field defects, diminution of vision, or contact history of tuberculosis. Two months before the patient presented at our department, he was admitted to a local hospital due to bitemporal headache. His brain magnetic resonance imaging (MRI) scan was normal apart from a slightly enlarged pituitary. His cerebrospinal fluid (CSF) pressure was 220 mmH₂O, the white blood cell (WBC) count was $176 \times 10^6/L$, and the protein, glucose, and chloride levels were 836.3 mg/L, 8.27 mmol/L, and 119.9 mmol/L, respectively. The patient was diagnosed with viral encephalitis, and an antiviral drug was administered *via* intravenous drip. During the patient's hospital stay, his CSF pressure increased to 180–310 mmH₂O. His headache disappeared by July 22, 2016, ~40 days after

admission, but he still felt fatigue and the lesion in his pituitary was growing. Because his diagnosis had yet to be established, he presented at our department.

Upon admission, the patient was languid with a positive Lasague sign, and laboratory investigations revealed microcytic anemia (Hb level: 115 g/L) and anterior pituitary hormone deficiency (Table 1). A review of all past CSF profiles revealed a light-to-moderate elevation in WBCs ($54\text{--}400 \times 10^6/L$), moderate-to-severe elevation in protein (700 mg/L–1200 mg/L), and a CSF pressure of 120–310 mmH₂O (Table 2). The patient's erythrocyte sedimentation rate and procalcitonin and C-reactive protein levels were normal. In addition, a workup for disseminated tuberculosis, which included computed tomography scans of the chest and abdomen, was unremarkable, and an HIV test was negative.

Immunohistochemical analyses for *Mycobacterium tuberculosis* antigens in the blood and CSF were both positive. Immunofluorescence was used to test ESAT-6 (6-kDa early secreted antigen target) secreted by *M. tuberculosis*. MRI scans revealed an enlarged pituitary gland, which measured $\sim 14 \times 13 \times 10 \text{ mm}^3$, with thickening of the pituitary stalk and bilateral inter-cavernous extension (Fig. 1A). Subsequently, the patient was advised to undergo a brain biopsy but neither he nor his family consented to this procedure; as a result, the diagnosis was considered to be probable rather than definite, based on the MRI data, CSF profile, and positive blood and CSF tests for *M. tuberculosis* antigens. The patient was given anti-tuberculous medications (isoniazid, 0.6 g/day through intravenous drip; rifamycin, 0.75 g/day through intravenous drip; pyrazinamide 1.5 g/day per os; and ethambutol 1.0 g/day per os, as well as corticosteroid therapy).

During the course of the disease, the patient experienced central diabetes insipidus and lost his appetite. On August

✉ Hongbo Liu
liuhongbo369@126.com

¹ Department of Neurology, First Affiliated Hospital, Zhengzhou University, Zhengzhou 450051, China

² Department of MRI, First Affiliated Hospital, Zhengzhou University, Zhengzhou 450051, China

Table 1 Endocrine profile of the patient.

Hormone	Value	Reference range
Thyroid-stimulating hormone	1.22 μ IU/mL	0.34–5.6
Free thyroxine	7.07 pmol/L	7.9–18.4
Follicle-stimulating hormone	1.05 mIU/mL	1.5–12.4
Luteinizing hormone	<0.10 mIU/mL	1.7–8.6
Prolactin	18.44 ng/mL	4.04–15.2
Morning cortisol	22.71 μ g/L	62–194

13, 2016, he exhibited motor deficits: the muscle strength of his left limbs was Grade 3, and the Babinski sign was positive on the left, while sensory and cognitive functions were normal. The MRI scan revealed a watershed stroke between the middle cerebral artery (MCA) and the posterior cerebral artery (PCA; Fig. 1B). Magnetic resonance angiography (MRA) revealed stenosis in the cavernous segment of the internal carotid artery (ICA) (Fig. 1C), showing compromised integrity of the circle of Willis. The PCAs were not open (Fig. 1D). In addition, high-resolution MRI scans with contrast enhancement showed concentric vessel wall thickening (Fig. 1E). Based on the acute onset of neurological deficits and the results of

Table 2 CSF profile of the patient.

Item Date	Pressure (mmH ₂ O)	Type of white cell (%)					White cell (10 ⁶ /L)	Protein (mg/L)	Glucose (mmol/L)	Chloride (mmol/L)
		Lymphocyte	Monocyte	Activated monocyte	Neutrophil	Eosinophil				
2017-6-10	220	79	13	0	4	4	176	836.3	8.27	119.9
2017-7-10	310	–	–	–	–	–	400	970	3.15	124
2017-7-15	180	–	–	–	–	–	300	860	3.52	126
2017-7-24	180	76	10	2	10	2	54	1277.4	4.63	120.4
2017-8-3	120	87	7	–	6	–	82	820.8	6.9	143.2

Fig. 1 **A** Homogeneous enhancement of the pituitary with bilateral intercavernous extension and a thick pituitary stalk (arrow). **B** Acute lesions within the right hemisphere (arrows). **C** Stenosis in the cavernous segment of internal carotid artery (arrow). **D** Compromised

integrity of the circle of Willis. The posterior communicating arteries were not open (arrow). **E** T1-weighted contrast-enhanced MRI revealing concentric vessel enhancement (arrow).

Fig. 2 The pituitary lesions regressed (**A**, arrow) and the stenosis of the intracranial artery disappeared (**B**) after antituberculosis therapy for 6 months.

the scans, a diagnosis of stroke was made [4]. After continued anti-tuberculosis and ICA dilatation therapies, the muscle strength in his left limbs recovered to Grade 5 within a week. Follow-up assessments over 6 months revealed that the CSF protein level decreased to 510 mg/L, the WBC count was $18 \times 10^6/L$, and the pituitary lesion was decreased in size (Fig. 2A); the anterior pituitary hormone levels had returned to normal, and the ICA stenosis had disappeared from the MRA scan (Fig. 2B).

CNS tuberculosis takes three clinical forms: meningitis, intracranial tuberculoma, and spinal arachnoiditis [5]. Intracranial tuberculoma accounts for 0.15%–4% of all intracranial masses in India [6], while the prevalence of pulmonary tuberculosis is higher. Primary pituitary tuberculosis in the absence of other forms of intracranial or systemic tuberculosis is extremely rare and difficult to diagnose [7]. The pituitary lesion in the present patient grew rapidly over 2 months, and his CSF analyses revealed an inflammatory response. Thus, the qualitative diagnosis was a type of infection. Based on the CSF characteristics and the failure of antiviral treatments, tuberculosis was suspected. MRI scans of the pituitary revealed a thickening pituitary stalk, which can be useful for differentiating pituitary tuberculoma from adenoma [8]. Ultimately, a diagnosis was established *via* immunohistochemical detection of the *M. tuberculosis* antigen. In addition, during the course of the disease, the patient suffered a watershed stroke between the MCA and PCA, possibly due to ICA stenosis, hypoperfusion, and/or insufficient compensation by the circle of Willis.

Primary pituitary tuberculoma with stroke has not been previously reported, and the precise mechanisms underlying tuberculosis-induced intracranial large-vessel

arteriopathy remain unclear. Although tuberculosis is more commonly associated with arthritis [9], it may contribute to atherosclerosis as well [10]. In this case, the features of the ICA wall lesions revealed by high-resolution MRI were consistent with cerebral vasculitis.

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