

## Paradoxical Infarct in Tuberculous Meningitis: A Case Report

Hiroshi Morioka<sup>1</sup>, Shuuichi Matsumoto<sup>2</sup>, Eiji Kojima<sup>2</sup>, Kazuto Takada<sup>2</sup>,  
Susumu Iwata<sup>2</sup> and Shoutaro Okachi<sup>3</sup>

---

### Abstract

---

We describe a case of 78-year-old woman with a 1-week history of fever and left hemiparesis. Head magnetic resonance imaging showed a small infarct. After admission, she showed altered consciousness and another small infarct. She finally had diagnoses of miliary tuberculosis (miliary-TB) and tuberculous meningitis (TBM). She recovered after receiving anti-tuberculous therapy (ATT) with prednisolone. However, 5 weeks later, we found another infarct. This is a rare case of TBM with recurrent infarcts in atypical lesions in spite of ATT. We suggest the possibility that the new infarct after ATT was due to a paradoxical reaction.

**Key words:** tuberculous meningitis, paradoxical reaction, miliary tuberculosis, infarct, central nervous system tuberculosis

(Intern Med 51: 949-951, 2012)

(DOI: 10.2169/internalmedicine.51.6830)

---

### Introduction

---

Tuberculous meningitis (TBM) is one of the most severe manifestations of extrapulmonary tuberculosis. The mortality and neurological sequelae rates associated with TBM are around 18% to 42% and 46% respectively (1, 2). It is difficult to diagnose TBM because a large variation exists between the presentation and clinical course of TBM.

We present a case of a 78-year-old woman with a small, atypical infarct who was finally diagnosed with miliary-TB and TBM.

---

### Case Report

---

A 78-year-old woman presented at the emergency department with a 1-week history of fever and left hemiparesis. On examination, she was found to have a temperature of 38.1°C, heart rate of 64 beats/min, blood pressure 144/80 mmHg, and oxygen saturation on room air 98%. Her neurological test revealed Glasgow coma scale (GCS) score of 15, absence of stiff neck and jolt accentuation. Her manual muscle testing (MMT) was 5/5 for muscles in the right side of

the body and 4/5 for muscles in the left upper and lower proximal muscles. Data of the laboratory test, chest radiography and urinalysis showed no abnormalities. Cranial magnetic resonance imaging (MRI) showed low-intense on T1 and high-intense on T2, FLARE and diffusion-weighted imaging (DWI) in the right temporal lobe (Fig. 1a). She was diagnosed with cerebral infarct and was treated with aspirin and argatroban. Two sets of blood cultures were obtained to exclude infectious endocarditis.

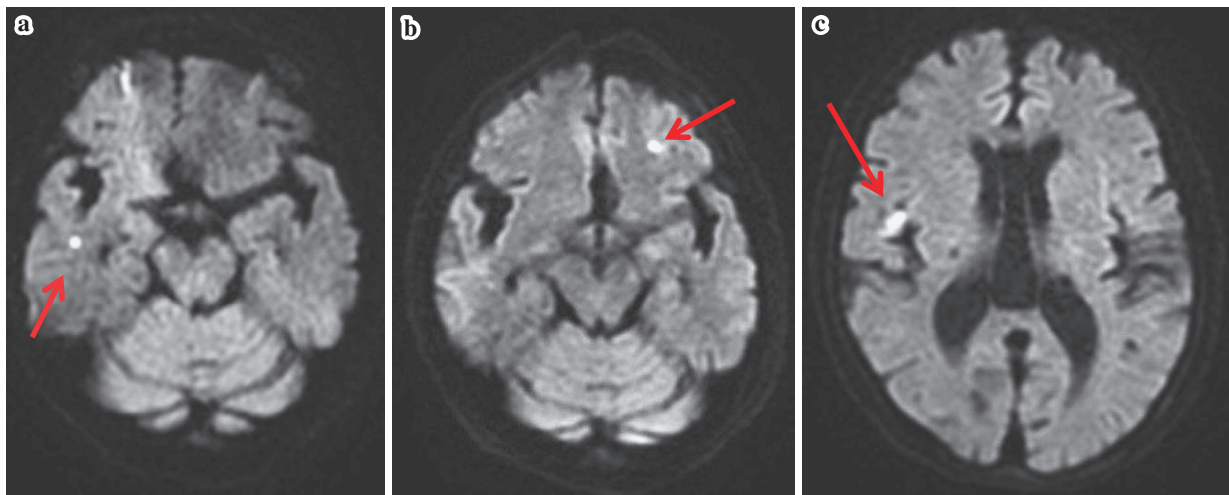
On the 5th day after admission, she still had a fever of over 39°C. Her level of consciousness deteriorated; her GCS and left MMT scores were 13 (E3V4M6) and 3/5, respectively. However, she did not have stiff neck. Blood cultures on admission showed negative results. Her erythrocyte sedimentation rate was 53 mm/h, but her white blood cell count (WBC), C-reactive protein level and blood glucose level were 4,400/ $\mu$ L, 0.16 mg/dL and 129 mg/dL respectively. Cranial MRI showed another small high intensity area (HIA) on DWI in her left anterior lobe (Fig. 1b). Her chest CT showed disseminated small nodules throughout the lungs (Fig. 2). Lumbar puncture was performed and the result of cerebrospinal fluid (CSF) examination were as follows: WBC count 18/ $\mu$ L (lymphocyte 83%), protein level 92.1

---

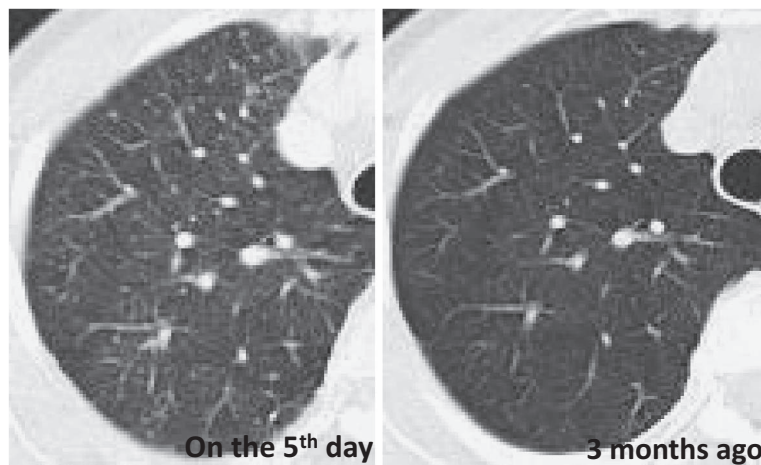
<sup>1</sup>Division of Infectious Disease, Tokyo Metropolitan Komagome Hospital, Japan, <sup>2</sup>Division of Respiratory and Allergy Medicine, Komaki Municipal Hospital, Japan and <sup>3</sup>Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Japan

Received for publication November 5, 2011; Accepted for publication January 5, 2012

Correspondence to Dr. Hiroshi Morioka, h-morioka@cick.jp



**Figure 1.** Serial diffusion weighted magnetic resonance imagings show small infarcts in the right temporal lobe (on admission: a), in the left frontal lobe (on the 5th day: b) and in the left temporal lobe (on the 40th day: c).



**Figure 2.** Chest CT shows new disseminated small nodules compared to 3 months ago.

mg/dL, chloride level 112 mEq/L, and glucose level 53 mg/dL. The results of Gram stain and acid-fast stain of the CSF sample were negative. We strongly suspected miliary-TB and TBM because of the clinical course, chest CT and CSF findings. Therefore we started anti-tuberculous therapy (ATT) with isoniazid (200 mg), rifampicin (450 mg), pyrazinamide (1,000 mg), ethambutol (500 mg) and prednisolone (40 mg) after performing bronchoscopy and bone marrow aspiration. Bronchoscopy revealed no specific finding. We performed bronchial washing in the right middle lobe. Prednisolone treatment was given for 2 months, with tapering of the dose.

After initiation of ATT, her level of consciousness and neurological status improved. Granulomas were detected in the bone marrow aspirate smear on the day 13th. In addition, her Quanti-FERON-TB Gold In-Tube Test (QFT-3G) revealed a positive result (TB Response 0.92 IU/mL, Mitogen 2.37 IU/mL, Nil 0.21 IU/mL) and her adenosine deaminase (ADA) level was elevated to 9.8 IU/L. The acid-

fast staining and cultures of sputum, bronchoalveolar lavage fluid, urine and bone marrow fluid showed negative results respectively.

She was discharged on the 21st day without any neurological sequelae. On the 40th day, she complained of dizziness. A small HIA on DWI in the right temporal lobe was found again (Fig. 1c). Lumbar puncture was performed, however the result of CSF examination showed improvement tendencies (Table 1). Few days later, her dizziness improved. She has a good clinical course since then.

## Discussion

Both TBM and miliary-TB in immunocompetent adults are rare in developed country. TBM and miliary-TB constitute 0.7-1.3% and 2.3% of all new cases annually (3, 4). In Japan, 171 cases of TBM had been reported in 2008 (4). Central nervous system tuberculosis is clinically recognized in 10-30% of the patients with miliary-TB (5). Kalita re-

**Table 1.** The Result of Serial Cerebrospinal Fluid Analysis

	5 <sup>th</sup> day	12 <sup>th</sup> day	16 <sup>th</sup> day	40 <sup>th</sup> day
Cells ( $\mu$ L)	18	75	44	19
monocyte ( $\mu$ L)	15	66	38	17
protein (mg/dL)	92	63	56	39
ADA (IU/L)	9.8	9.3		4.7
TB-PCR		negative	negative	

ported that 12% of the patients with TBM had miliary-TB of the lung (6).

As for the microbiological test, direct microscopy of CSF for acid-fast bacilli was positive in only 1% to 8% of TBM cases. The culture of CSF was positive in 38.9-62% of the TBM cases (1, 2). It is impossible to diagnose all TBM cases on the basis of bacterial gold standards; some other definitions to diagnose TBM were required (7).

According to the criteria for TBM, this was a probable TBM case (7). The clinical parameters (symptom duration, focal neurological deficit and altered consciousness), the CSF parameters (appearance, cell counts, lymphocytic predominance, CSF to plasma glucose ratio), the cerebral imaging criteria (infarct) corresponded with TBM. Her chest CT findings, positive finding in the QFT-3G, high ADA level ( $>8$  IU/L) in CSF and the presence of granulomas in the bone marrow specimen strongly supported miliary-TB and TBM. According to Tuon et al., ADA level higher than 8 IU/L is indicative of TBM. ADA level higher than 8 IU/L show a 59% sensitivity and a 96% specificity (8).

Patients with TBM show varied imaging patterns, hydrocephalus, basal meningeal enhancement, tuberculomas, and infarcts. MRI has shown infarcts in up to 57% of the patients with TBM (9). Despite this incidence of infarct, 25% to 58% of the cases of TBM infarcts were reported to be asymptomatic (9, 10). In up to 75% of the patients, the infarcts are located in the "tubercular zone" which comprises of the head caudate nucleus, the anteriomedial thalami, the anterior limb and genu of the internal capsule. It is believed that cerebral infarcts in TBM patients are mainly caused by arteritis (11). To the best of our knowledge, development of small infarcts in the temporal lobes and recurrent infarcts after therapy are rare presentation. The location of these infarcts, i.e., the temporal lobe was different from that of typical ischemic infarcts; therefore, these infarcts were related to TBM.

Despite appropriate treatment with ATT and prednisolone, MRI showed another infarct on the 40th day. Clinical deterioration during ATT has been known as a paradoxical reaction (PR) since the 1950s (12). PR is defined by a clinical or radiological worsening of pre-existing tuberculous lesions or the appearance of new tuberculous lesions in spite of ATT. Poor compliance, drug resistance, progression of original disease, and secondary diagnoses should be ruled out to

diagnose PR. In our patient, it is possible that a new infarct developed on the 40th day due to PR. Lee et al. reported paradoxical progression of intracranial tuberculoma and infarct during ATT (13), however in this case, the same infarct deteriorated. According to Kalita et al., of the 42 patients with infarcts on admission, 9 developed additional infarcts during their follow-up (9). Although infarct such as PR might not be a rare form of all TBM-infarcts, in a developed country the number of TBM cases itself is very less. For reasons of good clinical course, atypical new infarct and improvement of CFS findings, we need to consider the possibility of PR on worsening of clinical symptoms of TBM.

As for the management, it is not necessary to change or discontinue ATT. Monga et al. have mentioned a case report in which prednisolone was effective for treating PR in TBM (14). Our patient's dizziness improved naturally, and therefore we decided not to administer more prednisolone. More studies are necessary to decide how to treat infarcts and PR in TBM.

**The authors state that they have no Conflict of Interest (COI).**

## References

- Christensen AS, Andersen AB, Thomsen VO, et al. Tuberculous meningitis in Denmark: a review of 50 cases. *BMC Infect Dis* **22**: 47, 2011.
- Hsu PC, Yang CC, Ye JJ, et al. Prognostic factors of tuberculous meningitis in adults: a 6-year retrospective study at a tertiary hospital in northern Taiwan. *J Microbiol Infect* **43**: 111-118, 2010.
- CDC. Reported Tuberculosis in the United States, 2009. Atlanta, GA: U.S. Department of Health and Human Services, CDC, October 2010.
- Tuberculosis Surveillance Center. Tuberculosis Annual Report 2008—Series 1. Summary of TB notification statistics in 2008. *Kekkaku* **84**: 693-696, 2009 (in Japanese, Abstract in English).
- Sharma SK, Mohan A, Shara A, et al. Miliary tuberculosis: new insights into an old disease. *Lancet Infect Dis* **5**: 415-430, 2005.
- Kalita J, Misra UK, Ranjan P. Tuberculous meningitis with pulmonary miliary tuberculosis: a clinico-radiological study. *Neurol India* **52**: 194-196, 2004.
- Marais S, Thwaites G, Schoeman JF, et al. Tuberculous meningitis: a uniform case definition for use in clinical research. *Lancet Infect Dis* **10**: 803-812, 2010.
- Tuon FF, Higashino HR, Lopes MI, et al. Adenosine deaminase and tuberculous meningitis—a systematic review with meta-analysis. *Scand J Infect Dis* **42**: 198-207, 2010.
- Kalita J, Nair PP, Misra UK. Predictors of stroke and its significance in the outcome of tuberculous meningitis. *J Stroke Cerebrovasc Dis* **18**: 251-258, 2009.
- Chan KH, Cheung RTF, Lee R, Mak W, Ho SL. Cerebral infarcts complicating tuberculous meningitis. *Cerebrovasc Dis* **19**: 391-395, 2005.
- Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. *J Neurol Sci* **303**: 22-30, 2011.
- Chloremis CD, Padiatellis C, Zoumboulakis D, et al. Transitory exacerbation of fever and roentgenographic findings during treatment of tuberculosis in children. *Am Rev Tuberc* **72**: 527-536, 1955.
- Lee SI, Park JH, Kim JH. Paradoxical progression of intracranial tuberculomas and anterior cerebral artery infarction. *Neurology* **71**: 68, 2008.
- Monga PK, Dhaliwal U. Paradoxical reaction in tubercular meningitis resulting in involvement of optic radiation. *Indian J Ophthalmol* **57**: 139-141, 2009.