

## A case of intracranial aneurysm and subarachnoid hemorrhage with tuberculous meningitis

Jee-Hoon Roh MD PhD, Do Young Kwon MD PhD, Moon Ho Park MD PhD

Department of neurology, Korea University Medical College, Ansan, Republic of Korea

### Abstract

A global increase in the incidence of tuberculosis has prompted the need for earlier diagnosis, treatment, and isolation of the disease. In tuberculosis, concomitant tuberculous meningitis and vascular complications such as intracranial aneurysms and subarachnoid hemorrhage are very rare. Because of the poor prognosis of tuberculous meningitis as well as intracranial aneurysm and subarachnoid hemorrhage, early diagnosis and management are crucial. We present the case of a 76-year-old woman who had two intracranial aneurysms complicated by subarachnoid hemorrhage, who had concomitant tuberculous meningitis. She remained well with medical management.

### INTRODUCTION

Globally, there were an estimated 9.27 million incident cases of tuberculosis in 2007, with most of these cases from Asia.<sup>1</sup> Once infected, active disease develops in about 10% of cases, usually within 1 to 2 years after exposure.<sup>2</sup> The remaining individuals enter a state of latency, which could reactivate at a later stage.<sup>3-7</sup> Tuberculous meningitis (TBM), which is the most severe form of tuberculosis, has a high mortality and morbidity.<sup>3-6</sup> Hydrocephalus and cerebral ischemia are commonly associated with TBM, while infectious intracranial aneurysms and subsequent subarachnoid hemorrhage (SAH) are rarely encountered.<sup>8-16</sup> Infectious intracranial aneurysms, or mycotic aneurysms, are rare. The cerebrovascular lesions represent 0.7-5.4% of all intracranial aneurysms, and an aneurysm complicated by SAH could be a major factor contributing to a poor prognosis.<sup>17</sup>

Although a relationship between TBM and these vascular complications has been addressed in previous reports<sup>3,5,8-16</sup>, there has been limited discussion regarding the possible relationship. We present a patient who had two intracranial aneurysms complicated by SAH that was presumed to be caused by TBM.

### CASE REPORT

A 76-year-old woman was referred to our hospital for confusion and diplopia after a severe headache that developed insidiously and persisted for 10 days. She also complained of anorexia, weight

loss, and low-grade fever that accompanied the headache. She did not have a history of hypertension. Neurological examination revealed drowsiness and confusion, nuchal rigidity, and left-side third nerve palsy. Initial CT showed mild hydrocephalus and dilatation of the right side proximal middle cerebral artery (MCA). The initial CSF study showed elevated opening pressure (26 cm H<sub>2</sub>O), turbid yellow color, elevated white blood cell count (WBC) (320/ $\mu$ l, 80% neutrophil and 20% lymphocyte), elevated red blood cell count (RBC) (6,100/ $\mu$ l, 80% old form and 20% fresh form), elevated protein (354 mg/dL), and decreased CSF/serum glucose ratio (0.2). The adenosine deaminase (ADA) value of the CSF was elevated to 21 U/L (normal range, 5-10 U/L). The CSF examination for PCR of tuberculosis and other viruses, as well as investigations for fungus and bacteria were all negative. The brain MRI showed an enhancement around the basal cistern and hydrocephalus involving the bilateral lateral and third ventricles (Figure 1). The day after admission, a follow-up CSF study revealed elevated WBC (1,700/ $\mu$ l, 90% lymphocyte), RBC (4,200/ml, 80% old form and 20% fresh form), elevated protein (525 mg/dL), and a decreased CSF/serum glucose ratio (0.2). Prior to receiving the results of nested-PCR for tuberculosis, anti-TBM therapy and dexamethasone were initiated under the tentative diagnosis of TBM (probable TBM<sup>17</sup>). Cerebral angiography on fifth day showed right-side distal internal carotid artery aneurysm (7.7 mm) and proximal MCA aneurysm (2.0 mm). The aneurysms were thought to be the cause of

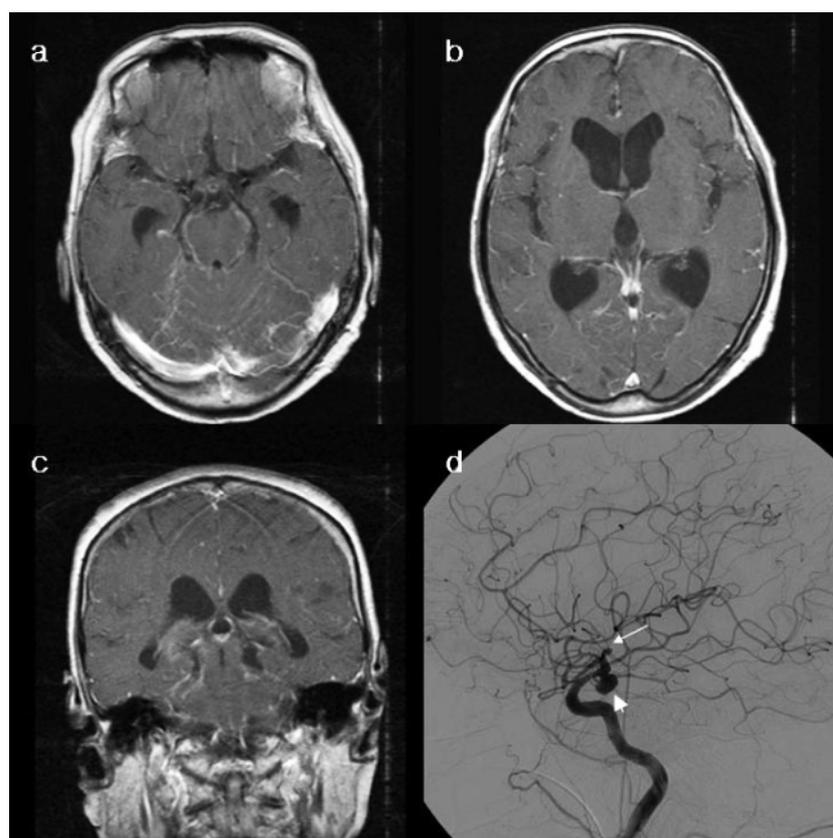


Figure 1. Exudative tuberculous meningitis in a 76-year old woman. Axial (a, b) and coronal (c) T1-weighted MRI shows diffuse enhancement of basal meninges and complicated hydrocephalus involving the third and both lateral ventricles. Cerebral angiogram (d) reveals saccular aneurysms arising from the right side distal internal carotid artery (arrowhead) and proximal middle cerebral artery (arrow).

the SAH. The third nerve palsy was thought to be from inflammation of the basal cistern. The repeat CSF study on 5<sup>th</sup> day revealed markedly decreased WBC (100/ $\mu$ l, 90% lymphocyte), RBC (1,080/ $\mu$ l, 80% old form), and protein (78 mg/dl), with a decreased CSF/serum glucose ratio (0.2). Because the patient showed clinical improvement and the CSF RBC and WBC counts were decreased after administration of the anti-TBM medications, we treated the aneurysm conservatively. After one month, the patient's confusion improved, though the headache and third nerve palsy persisted. She was given anti-TBM medications for 12 months. Her condition was last reported to be stable.

## DISCUSSION

TBM is a devastating disease of the central nervous system that usually presents with signs and symptoms of chronic basilar meningitis.<sup>16</sup> The inflammation often initially involves blood

vessels, producing secondary vasculitis and subsequent stroke. Early diagnosis is important for the success of the treatment.<sup>3,18</sup> Our patient's diagnosis was compatible with probable TBM.<sup>19</sup> She had altered mentation, focal neurologic signs, lymphocyte-dominant CSF leukocytosis, subacute onset of illness, and a low CSF glucose. She also had elevated ADA level, which was compatible with TBM.<sup>20</sup> The weighted diagnostic index scores for TBM, which sum the index scores of age (older than 36), mild blood leukocytosis (less than 15,000/ml), duration of illness (longer than 6 days), CSF WBC counts (less than 900/ml), and CSF neutrophil percentage (less than 75), had a score of 3. This is consistent with TBM with high sensitivity (97%) and specificity (91%).<sup>6</sup> The brain MRI findings of enhanced basal cistern, hydrocephalus, and the clinical improvement with anti-TBM treatment, are also supportive of TBM.<sup>12</sup>

The vascular complications of TBM are

**Table 1: The infectious intracranial aneurysm and/or intracranial hemorrhage in the tuberculous meningitis**

Year/Author	Case age/sex	Aneurysm site	Hemorrhage	Probable pathogenesis
1951 / Brown <sup>8</sup>	??	??	-	adjacent to the tuberculoma
1972 / Suwanwela <i>et al.</i> <sup>9</sup>	22/F	Both ACA, Rt MCA, Lt PCA	-	calcification in arterial wall; bathed in thick inflammatory basal exudate
1981 / Whelan <i>et al.</i> <sup>10</sup>	??	Lt MCA trifurcation	-	adjacent to the tuberculoma of parietal lobe
1988 / Leiguarda <i>et al.</i> <sup>11</sup>	<14/?	MCA horizontal portion	-	bathed in thick inflammatory basal exudate
1994 / Gupta <i>et al.</i> <sup>12</sup>	24/M	MCA	-	bathed in thick inflammatory basal exudate
2000 / Griffiths <i>et al.</i> <sup>13</sup>	9/M	PICA	SAH, IVH	bathed in basal tuberculous arachnoiditis
2002 / Tsuboi <i>et al.</i> <sup>14</sup>	55/F	MCA	SDH	pseudoaneurysm
2003 / Yeh <i>et al.</i> <sup>15</sup>	50/F 34/M	- -	SAH SAH	the bleeding of the inflammatory vessels the bleeding of the inflammatory vessels
2011/ Present report	76/F	ICA, MCA	SAH	bathed in thick inflammatory basal exudate

F, female; M, male; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; ICA, internal carotid artery; SAH, subarachnoidal hemorrhage; IVH, intraventricular hemorrhage; SDH, subdural hematoma;

common and serious.<sup>21</sup> Cerebral infarct and hydrocephalus are also commonly associated with TBM.<sup>3-5,22</sup> SAH is thought to be due to vasculitis or rupture of a mycotic aneurysm, which are other complications of TBM.<sup>13,15,22</sup> These are the likely causes of SAH in our patient.

There have been several mechanisms suggested for the pathogenesis of infectious intracranial aneurysms.<sup>23</sup> It could result from the degradation of the arterial wall secondary to microbial infection.<sup>24</sup> The infectious process leads to an acute infiltration of both the media and adventitia of the vessel wall by polymorphonuclear cells<sup>25</sup>, as well as marked proliferation of the intima and destruction of the internal elastic lamina. Hydrostatic pulsation and thrust against the infected arterial wall then promotes aneurysmal development and subsequent enlargement. The putative source of infectious intracranial aneurysmal formation may be due to the following. Firstly, an endovascular spread or intravascular source.<sup>11</sup> This hematogenous spread begins with the septic embolization from an infection source and hematogenous dissemination of tubercle bacilli into the arterial wall via the vasa vasorum.<sup>26</sup> The bacteria seed into the intima of the vessel

wall, leading to arteritis and local perforation with pseudoaneurysm. This mechanism applies in bacterial endocarditis with bacterial mycotic aneurysm.<sup>23</sup> The septic emboli preferentially lodge at the distal branch points of the middle cerebral artery, accounting for the anatomic preference and multiplicity of the aneurysms. However, tuberculous embolic vasculopathy remote from primary tuberculous lesions appears to be rare, although cutaneous leukocytoclastic vasculitis associated with intrathoracic tuberculosis has been reported.<sup>26,27</sup> Secondly, there could be hematogenous spread with autoimmune response to tuberculosis. Although potentially immune-mediated, TBM vasculitis appears to be restricted largely to infected or inflamed tissue, and not a typical multi-system immune vasculopathy.<sup>26</sup> A third mechanism involves direct extravascular infection, in mycotic aneurysms which originate from the base of the cranium through extravascular origin. The portion of the artery around the basal cistern is bathed in thick inflammatory exudates. This include the circle of Willis and its perforating branches.<sup>26</sup> Meningeal inflammatory exudate is known to encroach on the adventitia, progressively weakening the vessel wall, and

eventually resulting in an infectious aneurysm.<sup>11</sup> Fourthly, the direct extension from a contiguous focus such as tuberculoma.<sup>10</sup> However, there was no tuberculoma in this case. Fifthly, there could be pre-existing congenital or degenerative intracranial aneurysms detected coincidentally with tuberculous meningitis.

In a previous report of infectious intracranial aneurysms arising from a variety of primary infection foci, such as infective endocarditis, bacterial meningitis or cavernous sinus thrombophlebitis<sup>23</sup>, approximately 52% of patients were male and the median age was 35.1 years. We performed a comprehensive literature search on infectious intracranial aneurysms and/or intracranial hemorrhage in TBM (Table 1).<sup>8-15</sup> Our review showed that infectious intracranial aneurysms and/or subarachnoid hemorrhage caused by TBM are extremely rare. Approximately 40% of patients with concomitant intracranial aneurysm or intracranial hemorrhage were male. The mean age was 35.5 years.

TBM has a high mortality and morbidity.<sup>3-5</sup> The outcome of infectious intracranial aneurysms in TBM is uncertain because of its rarity.<sup>13</sup> Due to the rarity of these lesions, variability in their evolution and clinical presentations, and the lack of population-based epidemiological data, there is no widely accepted management. The management decision of an individual patient should probably include the location of aneurysms, surgical accessibility, number of lesions, and whether a bleed has occurred, with the latter carrying significant mortality.<sup>13,28</sup> In TBM patients with or without intracranial aneurysm, antituberculous therapy should be initiated as quickly as possible. The antituberculous therapy should be continued after successful treatment of aneurysms.<sup>13,29-31</sup>

In summary, aneurysm and SAH are complications of TBM.

## DISCLOSURE

Source of support in the form of grants, equipments or drugs: None

Conflict of interest to declare: None

## REFERENCES

- World Health Organization. WHO report 2009- Global tuberculosis control. [online]. Available at: [http://www.who.int/tb/publications/global\\_report/2009/key\\_points/en/index.html#](http://www.who.int/tb/publications/global_report/2009/key_points/en/index.html#).
- Canaud L, Marzelle J, Bassinet L, Carrie AS, Desgranges P, Becquemin JP. Tuberculous aneurysms of the abdominal aorta. *J Vasc Surg* 2008; 48:1012-6.
- Garg RK. Tuberculous meningitis. *Acta Neurol Scand* 2010; 122:75-90.
- Berger JR. Tuberculous meningitis. *Curr Opin Neurol* 1994; 7:191-200.
- Marais S, Thwaites G, Schoeman JF, et al. Tuberculous meningitis: a uniform case definition for use in clinical research. *Lancet Infect Dis* 2010; 10:803-12.
- Thwaites GE, Chau TT, Stepniewska K, et al. Diagnosis of adult tuberculous meningitis by use of clinical and laboratory features. *Lancet* 2002; 360:1287-92.
- Hong YJ, Jung S, Kim JY, et al. Complete Binocular Blindness as the First Manifestation of HIV-Related Cryptococcal Meningitis. *J Clin Neurol* 2007; 3:212-4.
- Brown RA. Polycystic disease of the kidneys and intracranial aneurysms. The etiology and interrelationship of these conditions: review of recent literature and report of seven cases in which both conditions coexisted. *Glasgow Medical Journal* 1951; 32:333-48.
- Suwanwela C, Suwanwela N, Charuchinda S, Hongsaprabhas C. Intracranial mycotic aneurysms of extravascular origin. *J Neurosurgery* 1972; 36:552-9.
- Whelan MA, Stern J. Intracranial tuberculoma. *Radiology* 1981; 138:75-81.
- Leiguarda R, Berthier M, Starkstein S, Nogues M, Lylyk P. Ischemic infarction in 25 children with tuberculous meningitis. *Stroke* 1988; 19:200-4.
- Gupta RK, Gupta S, Singh D, Sharma B, Kohli A, Gujral RB. MR imaging and angiography in tuberculous meningitis. *Neuroradiology* 1994; 36:87-92.
- Griffiths SJ, Sgouros S, James G, John P. Intraventricular haemorrhage due to ruptured posterior inferior cerebellar artery aneurysm in tuberculous meningitis. *Childs Nerv Syst* 2000; 16:872-4.
- Tsuboi M, Adachi H. [A ruptured distal aneurysm, thought to be a mycotic aneurysm, associated with acute subdural hematoma: case report and review of the literature]. *No shinkei geka* 2002; 30:177-81.
- Yeh ST, Lee WJ, Lin HJ, Chen CY, Te AL, Lin HJ. Nonaneurysmal subarachnoid hemorrhage secondary to tuberculous meningitis: report of two cases. *J Emergency Med* 2003; 25:265-70.
- Koh SB, Kim BJ, Park MH, Yu SW, Park KW, Lee DH. Clinical and laboratory characteristics of cerebral infarction in tuberculous meningitis: a comparative study. *J Clin Neurosci* 2007; 14:1073-7.
- Nakahara I, Taha MM, Higashi T, et al. Different modalities of treatment of intracranial mycotic aneurysms: Report of 4 cases. *Surg Neurol* 2006; 66:405-9; discussion 409-10.
- Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J. British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *J Infect* 2009; 59:167-87.
- Thwaites GE, Nguyen DB, Nguyen HD, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. *N Engl J Med* 2004; 351:1741-51.

20. Kashyap RS, Kainthla RP, Mudaliar AV, Purohit HJ, Taori GM, Dagainawala HF. Cerebrospinal fluid adenosine deaminase activity: a complimentary tool in the early diagnosis of tuberculous meningitis. *Cerebrospinal Fluid Res* 2006; 3:5.
21. Loureiro R, Bezerra HG, Sarwar A, Pale R, Houser S, Cury RC. Tuberculous pseudoaneurysms of the thoracic aorta: comprehensive evaluation by cardiovascular magnetic resonance. *Circulation* 2009; 120:e285-7.
22. Leonard JM, Des Prez RM. Tuberculous meningitis. *Infectious Disease Clinics of North America* 1990; 4:769-87.
23. Ducruet AF, Hickman ZL, Zacharia BE, et al. Intracranial infectious aneurysms: a comprehensive review. *Neurosurg Rev* 2010; 33:37-46.
24. Yoon JO. Not just an aneurysm, but an infected one: a case report and literature. *J Vasc Nurs* 2006; 24:2-8; quiz 9-10.
25. Kanno S, Thomas SV. Intracranial microbial aneurysm (infectious aneurysm): current options for diagnosis and management. *Neurocrit Care* 2009; 11:120-9.
26. Lammie GA, Hewlett RH, Schoeman JF, Donald PR. Tuberculous cerebrovascular disease: a review. *J Infect* 2009; 59:156-66.
27. Minguez P, Pintor E, Burón R, Díaz-Pollán B, Puche JJ, Pontes JC. Pulmonary tuberculosis presenting with cutaneous leukocytoclastic vasculitis. *Infection* 2000; 28:55-7.
28. Morawetz RB, Karp RB. Evolution and resolution of intracranial bacterial (mycotic) aneurysms. *Neurosurgery* 1984; 15:43-9.
29. Gropper MR, Schulder M, Sharan AD, Cho ES. Central nervous system tuberculosis: medical management and surgical indications. *Surg Neurol* 1995; 44:378-84; discussion 384-75.
30. World Health Organization. Treatment of tuberculosis: guideline for national programmes, 3rd ed. Geneva, Switzerland: World Health Organization, 2002.
31. Blumberg HM, Burman WJ, Chaisson RE, et al. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: treatment of tuberculosis. *Am J Respir Crit Care Med* 2003; 167:603-62.