Tuberculous Valvular Endocarditis With Brain Abscesses
A Case Report and Literature Review

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Abstract: Tuberculous endocarditis (TBE) is a rare clinical entity, usually encountered during the course of miliary tuberculosis. Brain abscess is a very rare complication of TBE. Here, we report a case of valvular TBE presenting with meningoencephalitis due to septic embolization. The literature on well-documented cases of valvular TBE was also reviewed. Early diagnosis, an appropriate treatment strategy, surgical intervention, and close follow-up may lead to favorable outcomes in TBE. Surgical intervention (valve replacement and repair) may be required in 70% of TBE cases.

Key Words: tuberculosis, endocarditis, septic emboli

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Mycobacterium tuberculosis is rarely a causative agent of infective endocarditis. Endocardial involvement has been reported in the literature in the form of mass lesions or as valvular endocarditis.[1–4] A thorough search of citation indexes back to 1966 revealed no confirmed tuberculous endocarditis (TBE) cases complicated by septic brain embolization. Here, we report a case of valvular tuberculosis endocarditis presenting with meningoencephalitis due to septic embolization. A brief review of the literature on well-documented valvular TBE cases is also presented after the case report.

CASE REPORT

A 39-year-old female patient was brought to the emergency department with a high fever and altered mental status. She had a history of unexplained fever over the previous 45 days, since undergoing an in vitro fertilization procedure. On physical examination, the patient had a tendency to sleep and was uncooperative. Her body temperature was 39°C, and nuchal rigidity was evident. Laboratory tests revealed the following results: hemoglobin, 12 g/dL; leukocyte count, 5.6×10^9/L; platelet count, 145×10^9/L; C-reactive protein, 16 mg/L; and erythrocyte sedimentation rate 50 mm/h. Fundoscopic examination result was normal. Lumbar puncture showed clear cerebrospinal fluid (CSF) with a leukocyte count of 90/μL (90% lymphocytes), a glucose concentration of 25 mg/dL (blood glucose was 105 mg/dL), and a protein concentration of 145 mg/dL. Gram staining, Venereal Disease Research Laboratory (VDRL) and Wright tests as well as aerobic culture of CSF, were all negative. Magnetic resonance imaging of the brain revealed multiple ring-enhancing lesions located in the cerebellum (Fig. 1A). Transesophageal echocardiography (TEE) revealed a 10 mm × 15 mm oscillating mass located on the tip of the mitral valve anterior leaflet, consistent with fresh vegetation (Fig. 1B). Computed tomography of the thorax revealed an atypical miliary pattern in the upper and middle lobes of both lungs, with small cavitations (Fig. 2). An empirical antituberculosis regimen consisting of isoniazid, rifampicin, ethambutol, and pyrazinamide was initiated immediately, and intravenous dexamethasone (8 mg) was added to the therapy with a tapered dosage over 8 weeks. Meanwhile, polymerase chain reaction analysis of CSF for *M. tuberculosis* (Seeplex MTB Nested ACE Detection; Seegene, Seoul, South Korea) yielded a positive result. Symptomatic relief was achieved on the fifth day of treatment, and the patient was discharged after a fever-free episode of 10 days. Follow-up TEE examinations at 3 and 6 months after diagnosis established that the vegetation was diminished to 7 mm × 5 mm and had healed with calcification. Cerebral abscesses regressed within 1 month. The patient followed an uneventful course of anti-TB maintenance therapy for 6 months.

DISCUSSION

Valvular tuberculosis endocarditis is an infrequent but important cause of left-sided blood culture–negative endocarditis. Its true prevalence may be underestimated because of the relative difficulty in making a precise microbiologic diagnosis.

Demographic, clinical, laboratory, and treatment data from well-documented cases in the literature are summarized in Table 1. Ten patients with proven infective endocarditis caused by *M. tuberculosis* were identified between 1990 and 2015. The mean age was 40.2 ± 17.9 years (range, 17–78 years). Only 2 patients were immunocompromised.

Clinical presentations comprised long-lasting fever in 9 cases, heart failure syndrome in 4, neurological disorders (altered mental status, stroke, hemiparesis, and meningoencephalitis) in 3, gangrene of the foot in one, and atrioventricular block in one.

Including the present case, TEE findings have been reported for 11 cases. In 7 of these, there were identifiable vegetations located on mitral (n = 5), tricuspid (n = 1), or aortic valves (n = 1), and all 3 valves were characterized as thickened. One patient had a paradoxical involvement of the mitral valve. Three patients had vegetations greater than 1 cm in size (1-3.2 cm).

A culture for *M. tuberculosis* was positive in specimens from 6 patients (2 blood cultures, 2 excised mitral cusps, one right atrial tuberculoma, one sample of CSF, and one of bone marrow). Ehrlich-Ziehl-Neelsen staining was positive in samples from 2 patients' vegetations, although their cultures for *M. tuberculosis* remained negative. Both culture and polymerase chain reaction of CSF from one patient and bone marrow from another were positive for *M. tuberculosis*.

Seven patients underwent surgical interventions. Aortic valve replacement was performed in 4 patients, mitral valve replacement and repair in 5, and both aortic and mitral valve replacement in 2.

With the exception of one patient, all were treated with 4- or 3-drug regimens. One patient (patient 8) died suddenly, owing to acute respiratory syndrome, before the initiation of antituberculosis

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Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent form is available for review by the editor-in-chief of this journal.

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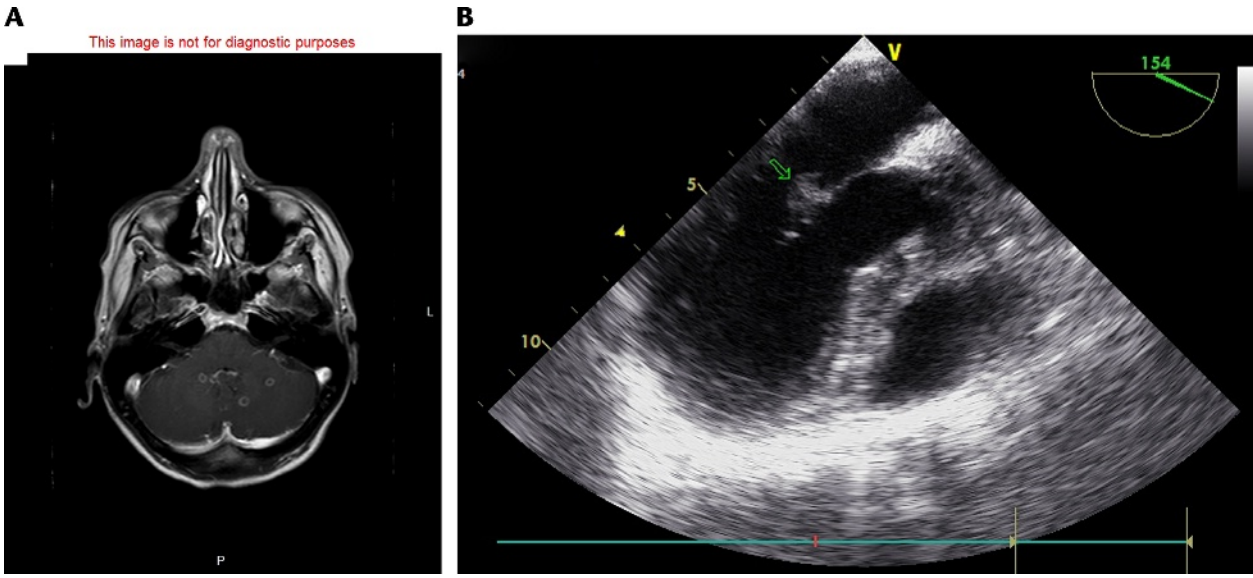

FIGURE 1. A, T1 postgadolinium axial image, showing multiple ring-enhancing lesions. Cerebrospinal fluid (CSF) was confirmed as positive for tuberculosis (TB), and the lesions thus represent numerous intracranial tuberculous granulomas. B, Image of the 10 mm × 8-mm filamentous vegetation found on the mitral valve.

therapy. The duration of antituberculosis regimens were 1 year for 2 patients, 9 months for one patient, and 6 months for our own patient. Only one patient (10%) died among the reported cases.

In this review, we noticed that all patients described weeks to months of fever and fatigue before the diagnosis was established. Clinical findings were suggestive of valvular TBE in most of the patients, and concomitant miliary disease was confirmed by autopsy findings in early reports.[1] In contrast, recently reported cases presented with symptoms similar to those of subacute bacterial endocarditis.[3–8] Many cases could have been identified only at autopsy by histopathological examination, and in only a few cases, the diagnosis could have been confirmed by acid-fast staining and tuberculosis cultures.[1,9] In recently published cases, tuberculosis culture and molecular techniques were used.[10]

Endocarditis caused by *M. tuberculosis* is uncommon. A comprehensive literature review of endocarditis revealed 26 cases specifically caused by *M. tuberculosis* between 1892 and 2010.[1] Our own review of the literature identified 6 additional cases reported in the last 5 years.

Although the precise mechanism is unknown, an uncontrolled immune reaction against tuberculosis antigens is the most accepted cause of paradoxical reaction in tuberculosis.[11] This complication usually occurs during TB treatment and presents with enlarged lymphadenopathy or with other unique presentations.[12] One patient noted in our review had a paradoxically involved mitral valve, which had not previously been reported in the literature as a manifestation of tuberculosis paradoxical reaction.[7] Similarly, the case described in the present report had the distinctive feature of septic cerebral embolization of vegetation material. Systemic embolization occurs in 22% to 50% of cases of infective endocarditis caused by common pathogens, and up to approximately 65% of embolic events involves the central nervous system.[13] In our review, 2 patients other than our case had confirmed or suspected central nervous system embolic events. One of them presented on admission with hemiparesis and a gangrenous foot, the other with hemiplegia.[14,15]

Most of the patients in our review were treated as they would have been for miliary tuberculosis, with no consensus on the duration of therapy. Before the introduction of antituberculosis drugs in the 1970s, all patients with TBE had died, and were diagnosed only at autopsy with histological confirmation.[1] The availability of novel anti-TB drugs and the standardization of treatment regimens (to at least 12 months), as well as improvements in surgical techniques, converted this fatal clinical scenario into a curable one. Other than one patient who presented with acute respiratory distress syndrome, suspected myocardial involvement, and an atrioventricular block whose diagnosis was significantly delayed, all patients survived with proper management.[15] In conclusion, early diagnosis of TBE, an appropriate treatment strategy, and close follow-up can deliver a favorable outcome. To the best of our knowledge, this is the first reported case of successfully treated TBE complicated with septic cerebral embolization.

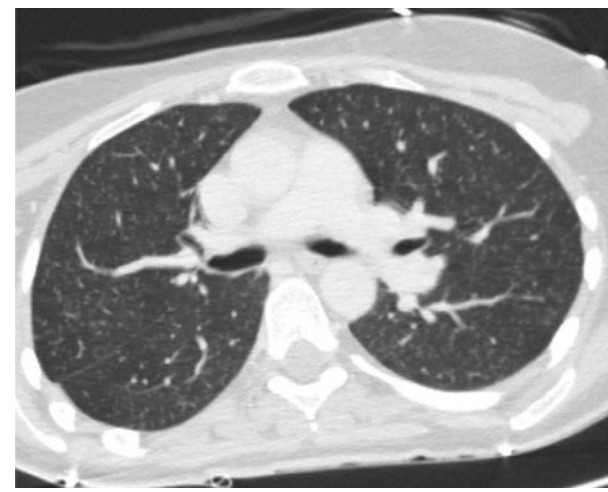

FIGURE 2. Lung window of contrast-enhanced chest CT depicts multiple centrilobular nodules randomly distributed in both lungs. Cavity with surrounding consolidation and macrocalcification is also present in apex of both lungs. The mediastinum is unremarkable.

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TABLE 1. Clinical and Laboratory Features of Valvular Tuberculosis Endocarditis Cases

Patient No/Reference	Age/Gender/Health Status/ Clinical Condition	Clinical Presentation	Thorax CT	Echocardiographic Findings	TB Culture Positivity	TBARB Positivity	TB PCR	Histopathology of Vegetation	Cardiac Surgery	Medical Therapy and Duration	Outcome
1 (6)	78/M İmmunocompetant Miliary TB	Long-lasting fever Heart failure	Miliary pattern	Thickened aortic cusp	Liver biopsy Sputum Gastric washings Urine	None	None	NA	Not done	R, I, P, E NA	Alive
2 (8)	64/M İmmunocompetant Concominant bacterial endocarditis	Bacterial endocarditis	NA	Mitral valve vegetation	Mitral valve vegetation	Negative	None	Calcified nodule with multiple granulomas	MVR	Anti-TB 1 year	Alive
3 (5)	35 /M AIDS Subacute endocarditis	Long-lasting fever	NA	Tricuspid valve vegetation	Hemoculture	None	None	None	Not done	R, I, P, E NA	Alive
4 (9)	63/M İmmunocompetant ASVLA	Long-lasting fever Heart failure	NA	Thickened right aortic cusp	None	None	None	Epithelioid cells and Langerhans giant cells	AVR	R, I, E 9 months	Alive
5 (10)	30/M Immunocompetent Subacute endocarditis and tuberculoma	FUO Progressive dyspnea Heart failure	NA	29 × 10 mm vegetation (mitral) Tricuspid valve regurgitation	Mitral valve vegetation Right atrial tuberculoma	None	None	Nondiagnostic	MVR Right atrial mass resection	R, I, P, E	Alive
6 (14)	17/F Immunocompetent Subacute endocarditis	FUO Foot gangrene Hemiparesis	NA	32 × 15 vegetation (Mitral valve)	None	None	None	Granuloma with focal necrosis and calcification	AVR MVR	Anti-TB NA	Alive
8 (15)	61/F Immunocompromised Subacute endocarditis	Hemiplegia AV block ARDS	ARDS	Mitral valve vegetation	None	Vegetation	None	Granuloma showing central caseous necrosis	Not done	NA	Died
9 (12)	21/F Immunocompetent Disseminated TB	Recurrent FUO Hepatitis Splenomegaly	Interstitial involvement in both lungs	15 × 10 mm vegetation (Aortic valve)	BM	BM Vegetation	BM	Granulomatous infiltration	AVR MVR	R, I, P, E 1 year	Alive
10 (7)	50/M Subacute endocarditis (paradoxical reaction)	Intermittent fever Aortic insufficiency Culture positive lung TB	"Tree in bud" opacification in upper lobes	Mitral valve thickening (paradoxically involved valve)	None	None	None	Small epithelioid granulomas with fibrinoid necrosis (aortic)	AVR	Anti-TB Prednol	Alive
Present case	36 /F Immunocompetent Disseminated TB	FUO Meningoencephalitis Brain abscess	Atypical miliary pattern with small cavitations and calcification	0.4 × 0.5 cm mobile vegetation (mitral valve)	CSF	CSF	CSF	NA	MV repair	R, I, P, E 6 months	Alive

F indicates female; M, male; CT, computed tomography; CSF; cerebrospinal fluid ; FUO, fever of unknown origin; BM, bone marrow; ARB, acid-resistant bacillus; PCR, polymerase chain reaction; TB, tuberculosis; AVR, aortic valve replacement; MVR, mitral valve replacement; AV, atrioventricular; ARDS, acute respiratory distress syndrome; NA, nonavailable; ASLVA, annular subvalvular left ventricular aneurysm; R, rifampicin; I, isoniazid; P, pyrazinamid; E, ethambutol.

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