

Received: 2019.09.29
Accepted: 2020.02.27
Available online: 2020.04.14
Published: 2020.06.05

Ischemic Stroke and Disseminated Tuberculosis in Intensive Care: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G





ABCDEF 1,2,3 Killen H. Briones-Claudett
 ABCDEF 2,3 Mónica H. Briones-Claudett
 ACDEF 4 Killen H. Briones Zamora
 ABCDEF 3 Rubén D. Nieves Velez
 ABCDEF 3 Marlon E. Martinez Alvarez
 ABCDEF 5,6 Michelle Grunauer Andrade

1 Faculty of Medical Sciences, Universidad de Guayaquil, Guayaquil, Ecuador
 2 Physiology and Respiratory Center Briones-Claudett, Guayaquil, Ecuador
 3 Intensive Care Unit, Ecuadorian Institute of Social Security (IESS), Babahoyo, Ecuador
 4 Faculty of Medical Sciences, Universidad Espíritu Santo, Samborondón, Ecuador
 5 School of Medicine, Universidad San Francisco de Quito, Quito, Ecuador
 6 Pediatric Critical Care Unit, Hospital de los Valles, Quito, Ecuador

Corresponding Author: Killen H. Briones Claudett, e-mail: killenbrio@hotmail.com, killen.brionesc@ug.edu.ec, kyllebrio@yahoo.com
Conflict of interest: None declared

Patient: Male, 73-year-old
Final Diagnosis: Ischemic stroke and disseminated tuberculosis
Symptoms: Aphasia • deterioration of the level of consciousness • deviation of the labial commissure
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine
Objective: Unusual clinical course
Background: Tuberculosis (TB) continues to be a major public health problem worldwide. Extrapulmonary tuberculosis at the level of the central nervous system is the most devastating and deadly form of tuberculosis.
Case Report: We present the case of a 73-year-old male Ecuadorian patient with no history of contact with tuberculosis and with a clinical picture of 4 days of evolution characterized by aphasia, deviation of the labial commissure, and deterioration of the level of consciousness with a Glasgow coma score of 7/15. A brain tomography showed evidence of indirect signs of cerebral ischemia; the patient was therefore diagnosed with non-specific cerebrovascular disease. Due to the critical nature of his clinical picture, the patient entered the Intensive Care Unit (ICU), where a chest x-ray was performed and bilateral perihilar alveolar opacities with a reticular and nodular pattern were visualized. These results, combined with the bronchoalveolar brushing, evidenced the presence of *Mycobacterium tuberculosis*. Adenosine deaminase (ADA) was also detected in the cerebrospinal fluid with 30.7 μL and a molecular biology technique was used with high-multiplex real-time polymerase matrix MALDI-TOF mass spectrometry (Bruker Daltonics) for rapid identification of the causative agent. DNA/polymerase chain reaction (PCR) analyses were used for detection of *M. tuberculosis*, subsequently confirming the presence of cerebral tuberculosis.
Conclusions: This case illustrated an infrequent form of disseminated tuberculosis in a critically ill patient. Timely diagnosis and appropriate management are essential to reducing mortality.
MeSH Keywords: Brain Infarction • Glasgow Coma Scale • Intensive Care Units • Mycobacterium Infections, Nontuberculous • Stroke
Abbreviations: ICU – Intensive Care Unit; MTB – Mycobacterium tuberculosis; ACI – acute cerebral infarction; ARF – acute respiratory failure; ABB – acid-base balance; Tv – tidal volume; Vmin – ventilator delivered minute volume; RR – respiratory rate; HR – heart rate; Ph – the negative logarithm of concentration of hydrogen ions; pCO₂ – concentration of carbon dioxide; PO₂ – partial pressure of arterial oxygen; SaO₂ – arterial oxygen saturation; FiO₂ – fraction of inspired oxygen; EB – excess base; ABG – arterial blood gases; HCO₃ – sets the concentration of buffer or blood bicarbonate; OTI – orotracheal intubation; M_{cg} – micrograms; SpO₂ – partial oxygen saturation; PA – systolic/diastolic blood pressure; IMV – invasive mechanical ventilation; ADA – adenosine deaminase; CSF – cerebrospinal fluid; TB – tuberculosis; HIV – human immunodeficiency virus

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/920410>

 1805   3  14



Background

Tuberculosis (TB) continues to be a major public health problem worldwide. It is estimated that one-third of the global population is infected with tuberculosis bacillus [1,2]. According to World Health Organization (WHO) data, tuberculosis represents one of the top 10 global causes of mortality. In 2016, 10.4 million people became ill with tuberculosis and 1.7 million died because of it [3]. The WHO estimated that there were approximately 8400 new cases of TB (51.6 per 100 000 inhabitants) in Ecuador in 2016, including those infected with the potentially lethal tuberculosis bacteria and human immunodeficiency virus (HIV) coinfection (TB/HIV) [4].

Extrapulmonary tuberculosis at the level of the central nervous system is the most devastating and deadly form of tuberculosis. This presentation represents approximately 1% of the total cases of tuberculosis and 6–10% of the extrapulmonary forms in immunocompetent patients [5]. For this reason, tuberculosis at the brain level represents a significant challenge at the time of diagnosis.

Stroke is considered a vascular epidemic in developed countries and a major public health problem. In recent decades, it has been identified as the second most frequent cause of death globally [6]. However, there are no data in the literature that report an association between ischemic stroke as an initial manifestation of cerebral tuberculosis in patients in intensive care units (ICUs).

The objective of this article was to report a case of ischemic stroke as an initial manifestation of cerebral tuberculosis in a critically ill patient.

Case Report

The patient was a 73-year-old male who came to the emergency department presenting clinical symptoms of aphasia accompanied by deviation of the labial commissure and further deterioration of the level of consciousness with a Glasgow score of 10/15. (Motor: 5; Ocular: 3; Verb: 2), without fever and blood pressure was 130/80 mmHg.

He had a personal history of spondyloarthropathy, arterial hypertension (20 years ago, treated with losartan 50 mg per day); gout (7 years ago, treated with allopurinol 30 mg per day); recurrent respiratory disease beginning approximately 6 months prior to admission (on more than 3 occasions), and blindness in the right eye due to glaucoma diagnosed 2 years ago. The patient's relatives denied any possible contact and family/occupational history with tuberculosis.

The patient's relatives reported the patient's history of weight loss, evening fever, and occasionally non-productive cough with frequent respiratory infections during the last 3 months. The patient only attended the first examination by the general practitioner without performing the relevant laboratory tests requested by the health provider.

Tracing

The first day of being admitted to the Emergency Department, the patient presented with leukocytosis and signs of infection. Regarding blood biometry, the following results were reported. Laboratory tests consisted of complete blood count with leukocytes at $12\,400\text{ mm}^3$; hemoglobin at 13.4 g/dL; hematocrit at 40.2%; monocytes (%) at 4.2%; eosinophils (%) at 4.5%; lymphocytes (%) at 18.5%; neutrophils (%) at 66.8%; basophils (%) at 6%; and platelets at $285\,000\text{ mm}^3$. Biochemistry tests consisted of glucose at 95 mg/dL; electrolytes were sodium at 135 meq/L; potassium at 4.3 meq/L; chlorine at 105 meq/L; calcium at 8.8 meq/L; and quantitative PCR at 42.9 mg/L. A urinalysis showed leukocytes: 25 cells/ μL , thus the presence of a urinary tract infection was suspected. The brain computed tomography (CT) demonstrated indirect signs of cerebral ischemia and therefore nonspecific cerebrovascular disease was diagnosed.

The ELISA (enzyme-linked immunosorbent assay) test was not reactive for HIV

On the second day after admission, the patient presented with sudden deterioration of the sensorium, right brachioradial hemiplegia, and a decrease in Glasgow score from 10 to 7; hence, endotracheal intubation was carried out and the patient was transferred to the ICU. Ventilatory support was initiated in IPPV (intermittent positive pressure ventilation) mode assisted with the following: tidal volume (V_t) at 400 mL (8 mL/kg ideal body weight [IBW]); inspiratory time at 1.2 seconds; flow at 45 L/minute; positive end expiratory pressure (PEEP) at 5 CMH_2O ; respiratory frequency at 14 RR; and FIO_2 at 35%. The patient's ventilatory parameters included minute ventilation at 9.7 L/minute; exhaled tidal volume at 415 L; maximum airway pressure at 19 CMH_2O ; plateau pressure at 13 CMH_2O ; average pressure at 9 CMH_2O ; and airway resistance and compliance at 54 mL/ CMH_2O .

The formula for the calculation of tidal volume and referenced tidal volume defined that 460 mL (V_t) should be used by calculating: 8 mL/kg IBW, using the following formula: 55.5 ± 2.3 (height in inches – 60) for males and 45.5 ± 2.3 (height in inches – 60) for females.

The patient's arterial blood gas analysis (ABG) was pH at 7.44; pCO_2 at 34.9 mmHg; PO_2 : at 262 mmHg; HCO_3 at 23.2 mmol/L;

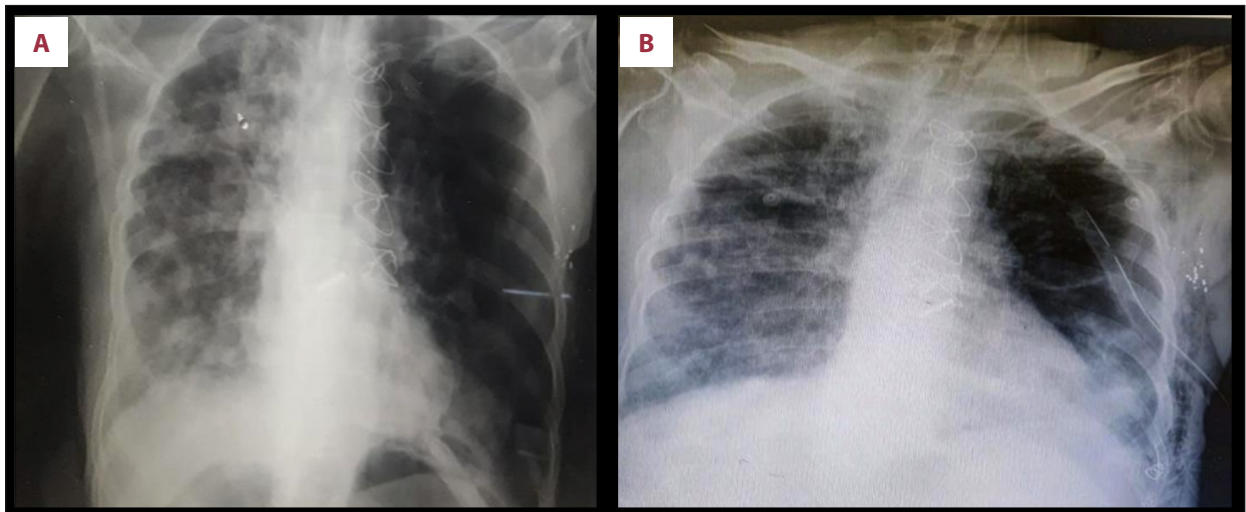


Figure 1. Chest x-ray showing fibrotic infiltrates in the right vertex. (A) Anteroposterior chest radiograph shows bilateral diffuse opacities, predominantly in the right lung field, with left pneumothorax. (B) The pleural drainage tube is observed on the left side.

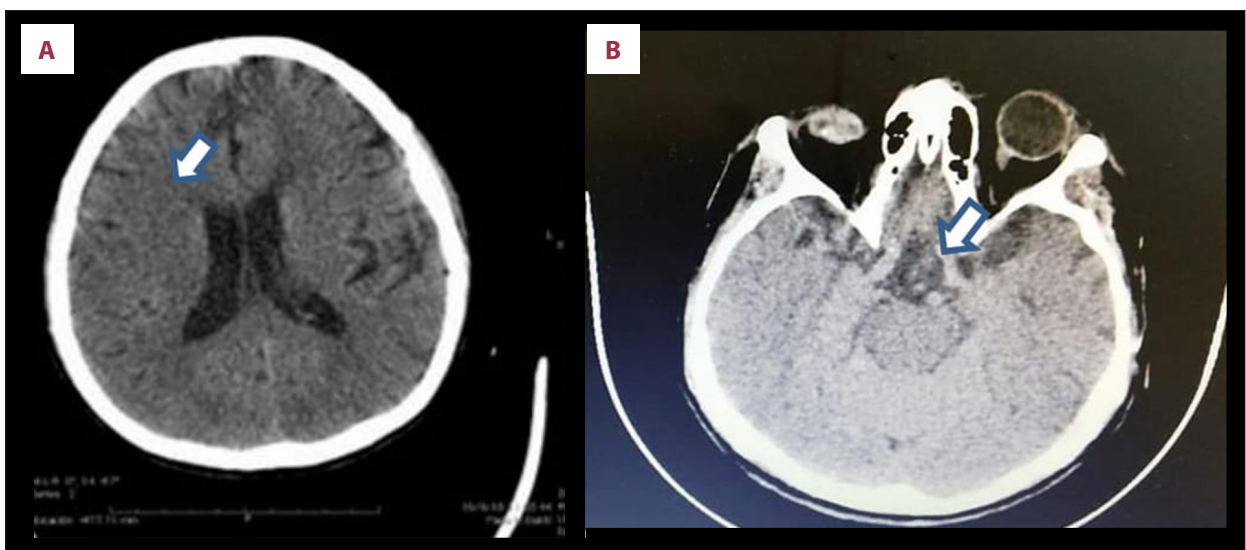


Figure 2. (A, B) Brain computed tomography. Periventricular hypodensities were evidenced at the level of the left lenticular nucleus in relation to the ischemic event.

base excess at -0.4 ; and SO_2 at 96%. The patient received sedation and analgesia with propofol at a dose of 1 mg/kg/hour and fentanyl at a dose of 1 mcg/kg/hour.

New imaging studies were performed and bilateral perihilar alveolar opacities with reticular pattern and nodules in both lungs were visualized on the chest radiograph (Figure 1); the brain CT showed moderate cerebral atrophy and a hypodense image (Figure 2).

The patient presented with tonic-clonic seizures, and he was treated with phenytoin at a dose of 18 mg/kg. He remained

hemodynamically unstable with metabolic acidosis and respiratory alkalosis; his condition became critical.

Several days later, the patient did not show improvement. A chest x-ray demonstrated a pattern consistent with pulmonary fibrosis, pulmonary condensation at the upper and middle lobes, presence of bronchiectasis, and signs of pulmonary emphysema.

Bronchoscopic procedure

Bronchoscopy was performed on the ninth day of admission, visualizing a reddish-colored carina with reddened mucosa and

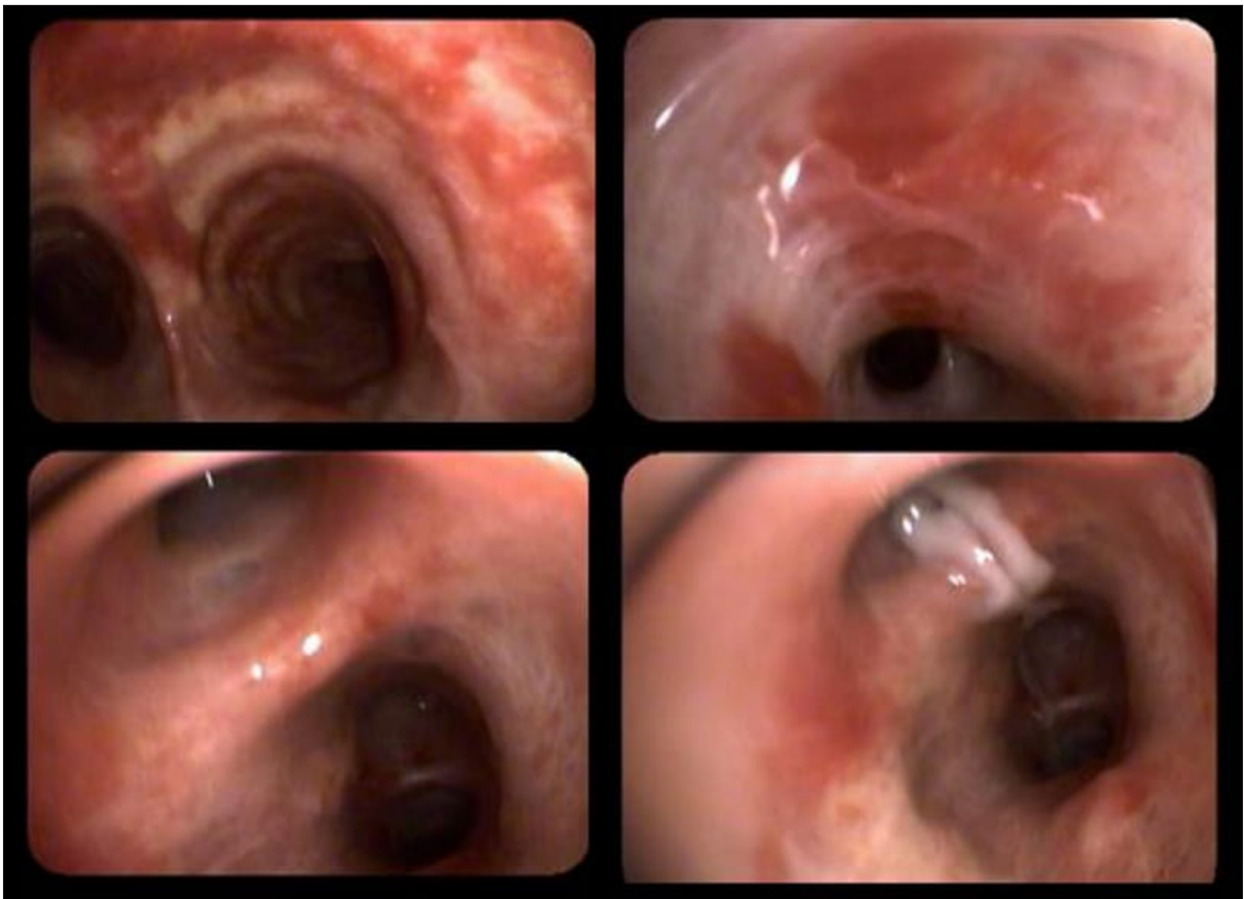


Figure 3. Video-bronchoscopy. Evidenced active pulmonary lesions, hemorrhagic stippling, erosion in the bronchial mucosa with whitish secretions and a cavitory lesion.

areas of erythematous punctuations along the airway with a cavitory image in the right upper lobe. Bronchial lavage was performed, also alveolar bronchiole lavage, bronchial brushing of the lesion and samples for microbiological cultures.

Microbiological diagnostics

Results were obtained 2–4 hours after performing the bronchoscopy using a molecular biology technique with MALDI-TOF mass spectrometry (Brucker Daltonics) for rapid identification of the causative agent and by additional phenotypic tests (e.g. optochin, Vitek 2). These tests involved a disc diffusion method as specified by CLSI [6] recommendations for detection of *Pseudomonas aeruginosa* with resistance to ESBL (extended-spectrum beta-lactamases) and GeneXpert MTB/RIF (DNA-PCR) for detection of *M. tuberculosis* without resistance to rifampicin.

The results were positive for acid-alcohol resistant bacilli, GeneXpert MTB/RIF (DNA-PCR) for detection of *M. tuberculosis* without resistance to rifampicin and for *P. aeruginosa* with resistance to ESBL in bronchoalveolar lavage (Figure 3).

Lumbar puncture and cerebrospinal fluid analysis

Lumbar puncture was performed and xanthochromic cerebrospinal fluid (CSF) recovered. The cytochemical study revealed a clear rock water coloration and transparent aspect. Subsequently, an ADA study was performed, and 30.7 μL reported. A GeneXpert MTB/RIF molecular biology technique (DNA-PCR) was used for *M. tuberculosis* detection. Tuberculosis of the brain was subsequently diagnosed, thus initiating treatment as follows: 4 tablets of rifampicin 600 mg+isoniazid 300 mg+pyrazinamide 1500 mg+ethambutol 800 mg every day by nasogastric tube.

On the eleventh day of admission, the patient remained in a critical condition with poor adaptation to mechanical ventilation, hemodynamic instability, and non-palpable pulse with pulseless electrical activity and asystole. Thus, advanced cardiac life support was initiated and adrenaline plus atropine administered; there was an adequate response within 10 minutes of reanimation. However, the patient's heart rate was 150 beats per minute and his blood pressure was 190/78 mmHg. An electrocardiogram demonstrated an elevation of the J point

in the posterior inferior face. The patient died after 25 minutes of ineffective resuscitation. Unfortunately, an autopsy was not performed.

Discussion

Among the different presentations of disseminated tuberculosis, meningeal tuberculosis is the most infrequent clinical form in developing countries. Particular clinical features are not characteristic, making it extremely difficult to identify and complete a timely diagnosis. Such difficulties are intrinsically associated with increased morbidity and mortality in those who suffer from it [7] as was the case presented here. Our patient presented with brain and pulmonary tuberculosis, with cerebral stroke as an initial manifestation of the spread of the infection. He ultimately died from the disease.

The etiological diagnosis of cerebral stroke was determined using the classification criteria Trial of ORG 10172 in Acute Stroke Treatment (TOAST classification) with neuroimaging support and laboratory tests [8]. Our case corresponds to the infarction group of indeterminate etiology (TOAST 5), due to infection of the central nervous system [6].

The unusual presentation of this case highlights the importance of gathering information related to epidemiological background and primary pulmonary infections. The diagnosis of the present case was confirmed by different analyses including bronchoscopy, which allowed us to visualize the caverns produced by the primary tuberculosis infection, and GeneXpert MTB/RIF analysis [9] of the sample obtained by bronchoalveolar lavage and brushing and of the cerebrospinal fluid.

CFS analysis evidenced lymphocyte pleocytosis, an increase in the number of proteins, and a decrease in glucose. ADA levels were above 9.5–10.5 U/L, this result evidences a sensitivity of 81–87% and specificity of 80–90%. The results of the GeneXpert MTB/RIF (ADN-PCR) analyses for detection of *M. tuberculosis* and ADA were 30.7 μ /L, which allowed us to confirm brain tuberculosis.

Although tuberculosis may be present from admission, these cases do not typically evolve until the consolidation phase of treatment [10].

Central nervous system tuberculosis (CNS TB) is associated with high mortality, it can occur in 1% to 5% of all patients with TB and 10% of those with AIDS-related TB [11].

The CNS TB can be characterized as follows: 1) diffuse, as in tuberculous meningitis, 2) localized, as in tuberculoma, 3) as a tuberculous abscess, or 4) as extradural and intradural spinal infections. In any case, CNS TB can occur nonspecifically in the early stages of disease [12].

The measures to manage the patient's cerebral infarction were appropriate for this case; however, it was necessary to establish antifimic treatment early. Recommendations specify the use of the same antibiotic regimens for primary tuberculosis, with a duration that lasts 12 months in the case of tuberculosis with involvement of the central nervous system [13].

Conclusions

It is very important to establish the diagnosis of this subtype of acute cerebral infarction; due to the acute cerebrovascular event, it may constitute the first manifestation of a systemic disease that could have different prognosis and treatment than the remaining subtypes of cerebral infarctions. We illustrate an infrequent form of disseminated tuberculosis in a critical patient [14]. An acute cerebrovascular event may occur in the course of an underlying disease, and in this scenario, the infection may be the etiological cause of cerebral infarction when associated with other underlying infectious conditions. This case reminds us that it is vital to consider the different possible presentations and clinical manifestations of *M. tuberculosis* infection. Timely diagnosis and appropriate management are essential to reducing mortality.

Department and Institution where work was done

Intensive Care Unit, Ecuadorian Institute of Social Security (IESS), Babahoyo, Ecuador.

Conflict of interest

None.

References:

1. World Health Organization: Global TB report 2018. WHO; 2018. <https://www.tballiance.org/why-new-tb-drugs/global-pandemic>
2. World Health Organization report 2004. Global tuberculosis control surveillance, planning, financing. https://apps.who.int/iris/bitstream/handle/10665/144567/9241563141_eng.pdf;jsessionid=BBE3386DC8C7EA78AA58823670A510E6?sequence=1
3. World Health Organization: Global TB report 2017. WHO; 2017. <http://apps.who.int/iris/bitstream/10665/259366/1/9789241565516-eng.pdf?ua=1>
4. World Health Organization: Global TB report 2016. WHO; 2016. <http://apps.who.int/medicinedocs/documents/s23098en/s23098en.pdf>
5. Gropper MR, Schulder M, Sharan AD et al: Central nervous system tuberculosis: Medical management and surgical indications. *Surg Neurol*, 1995; 44(4): 378–84
6. Gutierrez J, Elkind MS, Virmani R et al: A pathological perspective on the natural history of cerebral atherosclerosis. *Int J Stroke*, 2015; 10(7): 1074–80
7. Maheswari EU, Bhoopathy RM, Bhanu K et al: Clinical spectrum of central nervous system tuberculosis and the efficacy of revised national tuberculosis control program in its management. *J Neurosci Rural Pract*, 2011; 10(1): 71–77
8. Arsava EM, Helenius J, Avery R et al: Assessment of the predictive validity of etiologic stroke classification. *JAMA Neurol*, 2017; 74(4): 419–26
9. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 2011; CLSI M100-S21
10. Pauranik A, Behari M, Maheshwari MC: Appearance of tuberculoma during treatment of tuberculous meningitis. *Jpn J Med*, 1987; 26(3): 332–34
11. Raviglione MC, Snider DE Jr., Kochi A: Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. *JAMA*, 1995; 273(3): 220–26
12. Bernaerts A, Vanhoenacker FM, Parizel PM et al: Tuberculosis of the central nervous system: overview of neuroradiological findings. *Eur Radiol*, 2003; 13(8): 1876–90
13. Das KK, Jaiswal S, Shukla M et al: Concurrent cerebellar and cervical intramedullary tuberculoma: Paradoxical response on antitubercular chemotherapy and need for surgery. *J Pediatr Neurosci*, 2014; 9(2): 162–65
14. Duro RP, Figueiredo Dias P, Ferreira AA et al: Severe tuberculosis requiring intensive care: A descriptive analysis. *Crit Care Res Pract*, 2017; 2017: 9535463