Open Journal of
Clinical & Medical
Case Reports

Volume 2 (2016)
Issue 9

ISSN 2379-1039

Miliary Tuberculosis Manifesting as Acute Ischemic Stroke and Hypothermia in a Patient with Multiple Brain Tuberculomas

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Abstract

Tuberculosis (TB) is a widespread infectious disease caused by Mycobacterium Tubercle Bacilli. About 90 % of the affected individuals remain clinically asymptomatic (latent infection). In 15-20 % cases of active pulmonary TB, infection spreads to extrapulmonary foci, including the nervous system. A potentially more serious and usually deadly, widespread form of TB is called "disseminated" TB, commonly known as miliary TB making up 10% of extra pulmonary cases .

We report a 58-year-old African American female presented with rapid onset confusion and right hemiparesis. She had been recently diagnosed with military TB with central nervous system (CNS) involvement; her recent acute neurological manifestations began within 24 hours prior to admission in the hospital. A previous brain MRI had revealed multiple T1-weighted ring enhancing tuberculomas in the brain. She had already completed 2 months of intensive anti-TB treatment (ATT). A new MRI of brain revealed acute ischemic stroke involving left middle cerebral artery territory. Her core body temperature was recorded as 96◦ F and she remained hypothermic during the hospital course. This report describes an unprecedented case of a patient with known miliary TB and cerebral parenchymal tuberculomas who presented with acute ischemic stroke and hypothermia while ongoing ATT. Ischemic stroke and hypothermia are among less recognized manifestations of CNS TB.

Keywords

miliary TB; tuberculous meningitis; brain parenchymal tuberculomas; acute ischemic stroke; hypothermia

Introduction

Tuberculosis (TB) affects one-third of the world's population with an annual incidence of 1%. Tuberculosis (TB) is a top infectious disease killer worldwide. Globally, the most significant risk factor is AIDS and 13% of all people with TB are infected by the virus. TB is a leading killer of HIV-positive people: in 2015, 1 in 3 HIV deaths was due to TB. In addition, TB is closely associated with overcrowding and malnutrition. Over 95% of TB deaths occur in low- and middle-income countries, and it is among the top 5 causes of death for women aged 15 to 44 [1]. Miliary TB is the widespread dissemination of Mycobacterium tuberculosis via hematogenous spread. Classic miliary TB is defined as millet-like (mean, 2 mm; range, 1-5 mm) seeding of tuberculous bacilli in the lung, as evidenced by chest radiography. In the regions with low incidence rate, such as North America and Western Europe, extra

pulmonary TB is seen primarily in adults with reactivation of latent infection. Major neurologic manifestations of TB include meningitis, intraparenchymal tuberculoma and spinal arachnoiditis [2]. Small sub-ependymal tubercles spillage leads to hypersensitivity reaction which results in intracranial vasculitis with resultant aneurysm, thrombosis, and infarction [3]. Tuberculomas are granulomatous foci in brain parenchyma which can have mass effects resulting in headaches, seizures, and focal neurologic deficits depending on their location in the CNS. Tuberculomas may be seen in absence of meningitis and may regress with therapy [4]. We report an African American female with known brain tuberculomas and military TB presenting with unique combination of acute ischemic stroke and hypothermia.

Case Presentation

A 58-year-old African American female and nursing home resident was brought to the emergency department with new onset disorientation, right facial weakness, and right hemiparesis.

She was admitted a few months earlier for nocturnal fever and altered mental status of a few weeks duration. During her prior hospital stay, a comprehensive diagnostic work-up established a diagnosis of tuberculosis. The chest radiograph showed miliary TB pattern (Figure 1). Three separate sputum smear examinations did not reveal Acid Fast Bacilli. She had been a heavy smoker for the last 30 years. The patient was immune-competent with no obvious risk factors for immunosuppression. Past medical history did not reveal a history of alcohol abuse, diabetes mellitus, or HIV infection. Serum Quanti-FERON-TB Gold test was positive. Analysis of cerebrospinal fluid showed glucose 77 mg/dL, protein 201 mg/dL, nucleated cells 1/µL, red blood cells 4/ µL, while serological testing for neurosyphilis, herpes simplex virus, and cryptococcal antigen were non-reactive. Hepatitis and autoimmune panel were unremarkable. A definitive diagnosis of TB was established by detecting Mycobacterium Tubercle Bacilli utilizing nucleic acid probe from a tracheal aspirate. To see if there is central nervous system involvement; MRI brain with contrast was done which showed multiple ring enhancing lesions in both supra and infra tentorial regions (Figure 2). With inpatient anti-TB therapy (ATT), her condition slowly improved and the patient was discharged to the nursing home following completion of a two month intensive course of four ATT medications (Isoniazid, Rifampicin, Pyrazinamide and Moxifloxacin) with corticosteroids. She was treated with isoniazid and rifampicin for the past 10 months prior to her most recent admission.

Present Hospital Course

Due to her recent, acute onset of right hemiparesis and confusion, she was assessed by the neurology consultant physician. Neurological examination revealed a disoriented female with nuchal rigidity and right central seventh nerve paresis along with severe right hemiparesis. Her pupils were symmetrical and reactive to light. Extra ocular movements were present. Her visual fields were full on visual threat. She was able to localize the pain on left side of her body. Stat non-contrast CT of brain did not show any hemorrhage. Blood and urine cultures were negative. Her core body temperature was 96◦ F. Brain MRI revealed areas with restricted diffusion involving the left basal ganglia and internal capsule in the territory of lenticulostriate artery, a major branch of middle cerebral artery (Figure 3). In addition, several T1-weighed ring enhancing lesions were present in thalamus, hypothalamus, left temporal and insular cortex, with marked regression of many lesions observed in prior brain MRI (Figure 4).

MR spectroscopy of brain with focus on areas of restricted diffusion demonstrated neuronal loss, supportive of a diagnosis of acute ischemic stroke. CT angiography of head and neck, ultrasonography of carotid system and brain MRAngiogram were all unremarkable. Continuous cardiac monitoring for next 2 weeks did not reveal any paroxysmal cardiac arrhythmias. EEG was interpreted as normal. Infectious disease consultant recommendation of treatment with a combination of isoniazid, rifampicin, and intravenous dexamethasone were followed. Her repeat chest X-ray CAR also showed resolving TB.

During the hospital course, she remained hypothermic with core body temperature 94-96 F. Her hypothermia was managed by warm blankets. Gradually, her clinical condition improved and she had mild improvement in verbal expression upon discharge. Patient underwent physical and occupational therapy with some improvement of the right hemiparesis. A percutaneous endoscopic gastrostomy tube was placed for long term enteral nutrition. Later, she was discharged to inpatient rehabilitation service with continuation of ATT.

Discussion

Over the last two decades incidence of TB in developed countries has been on the rise, mainly, due to high rates of immigration from areas where TB is endemic [5]. Infection with HIV and the resultant immunosuppression is another significant reason for development of new TB cases [1, 5]. Miliary TB is a malignant form of extra-pulmonary TB and CNS involvement has been reported in 10-30 % cases of miliary TB [6]. Tuberculous meningitis and tuberculomas are major complications of CNS TB. One of the most serious and established complications of miliary TB with CNS involvement is ischemic stroke. It is presumed that the ischemic stroke associated with CNS TB stems from TB-induced or immune activation-induced CNS vasculitis. Such devastating complications of CNS TB carries high morbidity and mortality rates. Other neurovascular complications of CNS TB consist of aneurysmal dilatation, ruptured mycotic aneurysms, septic embolisms, and inflammatory exudates [7]. In one autopsy series study of 27 cases, phlebitis and varying degrees of arteritis were demonstrated in 22 cases, including eight patients with associated hemorrhagic cerebral infarction [8].

CNS TB can cause ischemic strokes in 15-57 % of affected individuals; however, the majority of patients may remain clinically asymptomatic. These ischemic lesions are usually multiple, bilateral, and sometimes symmetric, involving the basal ganglia, anterior thalamus, anterior limb, and/or the genu of internal capsule. Cortical, subcortical white matter, brainstem, and hindbrain involvement are less frequent. Lehrer, in 1966, described an angiographic triad in TB meningitis consisting of a hydrocephalic pattern, narrowing of the vessels at the base of the brain, and narrowed or occluded small and medium sized vessels with scanty collaterals [9].

Extensive review of literature review shows that only one case has been reported where an adult patient with miliary TB presented with acute ischemic middle cerebral artery stroke and the patient passed away from the disease complications [10]. We present the first ever case of CNS TB manifesting with acute ischemic stroke and persistent hypothermia in the context of miliary TB with multiple brain parenchymal tuberculomas. The ischemic stroke in our patient was most likely from transient vasculitis or vasospasm or possibly pressure effects from tuberculomas. The hypothermia most likely originated from the hypothalamic tuberculous lesions.

We propose that early diagnosis and aggressive treatment of miliary TB with CNS involvement should be instituted to avoid life threatening complications. It is also important to see if acute stroke in such patients originates from CNS TB or co-existing intracranial atherosclerotic disease utilizing advanced neuroimaging or conventional angiographic approach as the further management may differ.

Figures

Figure-1: Chest x-ray, standard AP view, which showed miliary pattern bilateral nodular opacities within the lungs.

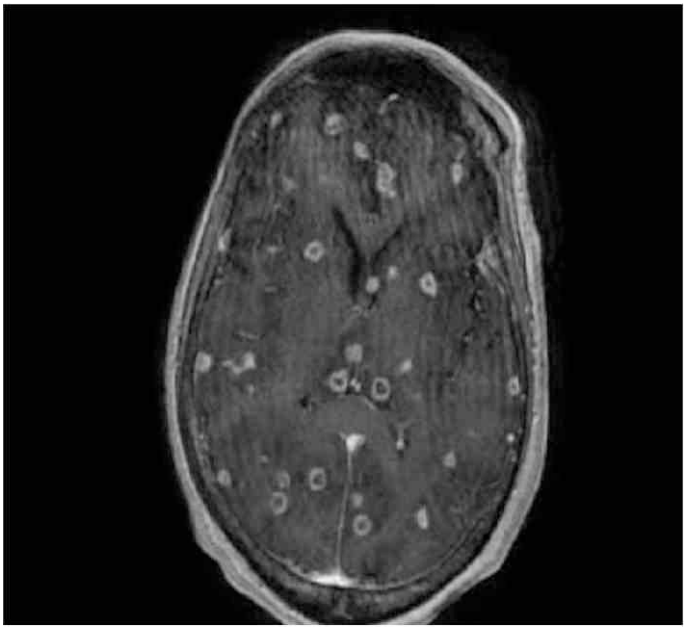

Figure-2: T1-weight post-contrast axial images of brain which shows widespread and multiple contrast-enhancing ring lesions.

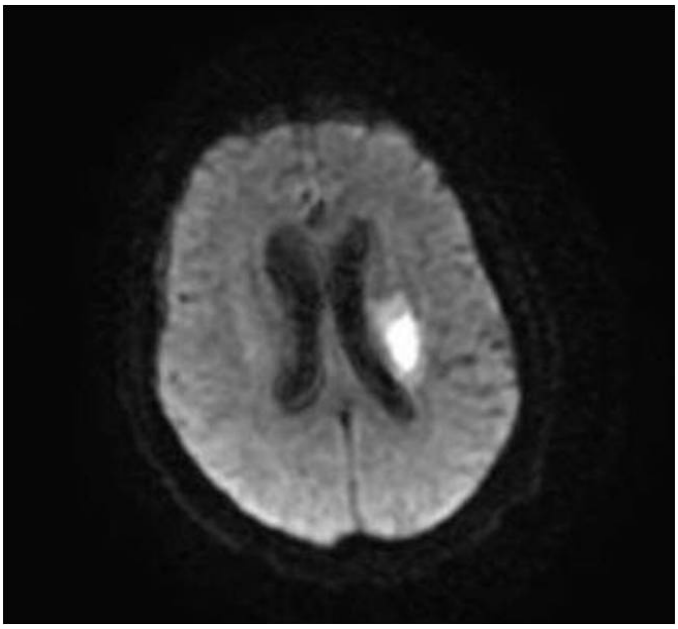

Figure-3: Diffusion weighted image axial view which shows restricted diffusion of the area including posterior limb of left internal capsule.

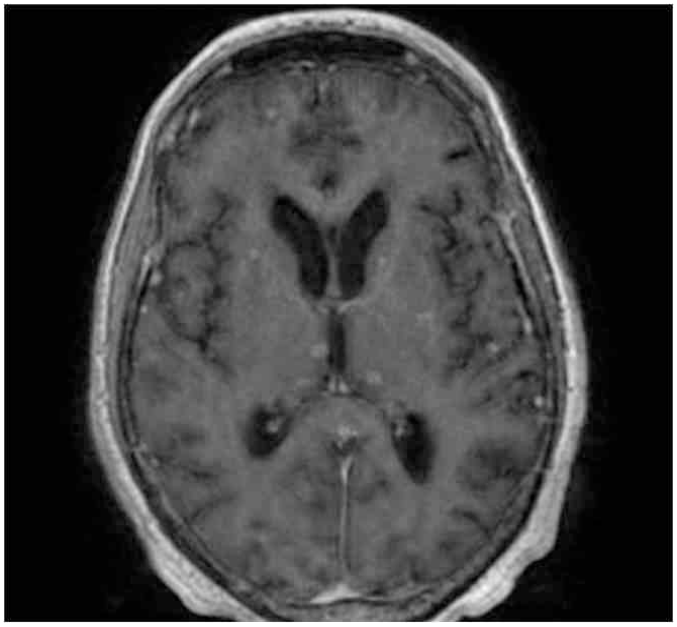

Figure-4: T1-weighted post-contrast axial view of the same patients, three months after anti-TB therapy, which shows significant resolution of ring-enhancing lesions.

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Manuscript Information: Received: December 28, 2015; Accepted: May 06, 2016; Published: May 10, 2016

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Citation: Abbas SW, Rodriguez Jreynolds C, Minagar A, Gonzalez-Toledo E. Miliary tuberculosis manifesting as acute ischemic stroke and hypothermia in a patient with multiple brain tuberculomas. Open J Clin Med Case Rep. 2016; 1111

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