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Atypical cause of stroke in a 27 year old male

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Summary

Background:

Central nervous system (CNS) Tuberculosis (TB) meningitis is a progressive disease that can present in many forms. CNS TB is encountered frequently in areas of high prevalence of tuberculosis and dissemination is common, but TB meningitis is a disease that has a relatively low prevalence in North America.

Case Report:

27 year-old African American male presented with complaints of headache, altered mental status (AMS), and seizure activity. He was found to have fever, encephalopathy, and leukocytosis. Work up of his AMS revealed cerebral spinal fluid (CSF) consistent with acute lymphocytic meningitis and magnetic resonance imaging (MRI) revealed right basilar meningeal enhancement with acute right basal ganglia infarction. Given the characteristic CSF and MRI finding for Tuberculosis (TB) a computed tomography (CT) of the chest was performed which revealed right upper lobe nodules with central cavitations. Biopsy results revealed Tuberculosis. The patient showed significant improvement once empiric tuberculosis therapy was begun.

Conclusions:

CNS TB is a treatable disease that will be fatal if not recognized early. It is imperative to be aware of the key clinical features of TB meningitis, and maintain a high level of suspicion when dealing with CNS infection if the cause is unknown.

key words:

meningitis • *Mycobacterium tuberculosis* infection • basilar stroke • extrapulmonary tuberculosis • purified protein derivative

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BACKGROUND

CNS TB is a treatable disease that will be fatal if not recognized; therefore, it is imperative to be aware of the key clinical features of TB meningitis.

CASE REPORT

A 27 year-old African-American male was brought in by his family for altered mental status and possible seizure activity. The family stated that the patient had been complaining of a headache for one to two months. The family noted some mild behavioral and cognitive changes that had progressed over the last month. The week prior to presentation to our facility, the patient had an episode of slurred speech, facial droop, drooling, and seizure-like activity in the left upper extremity. The patient was taken to outlying emergency department (ED) but on arrival to the outside facility his symptoms had resolved. He was evaluated with basic labs and a non-contrasted computed tomography (CT) of the brain. He was discharged from the outside ED with a prescription for naprosyn and doxycycline. Over the next week, he had further behavior changes and became very lethargic. The family brought the patient to our facility for further evaluation at this time. The patient had no known past medical history and no prior surgeries. Current medications included naprosyn and doxycycline that he had received one week prior, no other home medications. Social history was significant for alcohol misuse for 10 years, tobacco use of 1 pack per day for 10 years and occasional marijuana use. The patient had just recently moved back to Tennessee to seek help from his family in quitting alcohol, after living in Texas and working as a bank teller for 7 years. No known travel outside of the country and no known contact with persons with communicable diseases. On physical exam he was well developed, well nourished, profoundly encephalopathic and diaphoretic. Temperature was 103°F, heart rate 87 beats/min, blood pressure 154/84 mmHg, respiratory rate 16 /min, and oxygen saturation 99% RA. His cardiovascular, pulmonary, and abdominal exams were unremarkable, skin was notable for significant diaphoresis without rash. He was unable to follow commands for a full neurologic exam but was confused and combative, moved all extremities spontaneously and with equal strength, and did exhibit significant photophobia or nuchal rigidity.

Investigations

Initial laboratory data revealed leukocytosis of 11.7 th/mm^3 with 92% neutrophils otherwise hemoglobin, hematocrit, and complete metabolic panel were within normal limits. Cerebral spinal fluid evaluation revealed WBC count of 302/ mm^3 with 98% lymphocytes, glucose 14 mg/dl, protein 144 mg/dl, and was clear in character. Chest x-ray and non-contrast CT of head were without significant pathology. After blood cultures had been obtained and initial CSF studies sent, the patient was placed in the neurologic intensive care unit and started on broad spectrum antibiotics with vancomycin and piperacillin/tazobactam. Over the next twelve hours the patient was closely monitored and supportive care was continued as initial results began to return. Gram staining of CSF and blood was negative for bacteria and HIV, RPR, Cryptococcal antigen, HSV PCR were negative. The patient showed minimal mental status improvement within the first 24 hours and an MRI of the brain and Neurologic

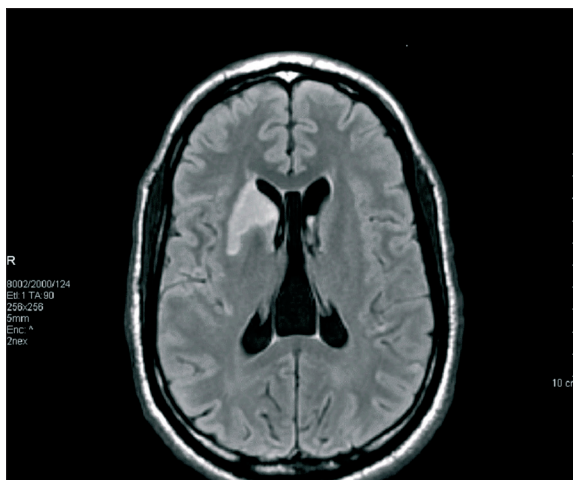


Figure 1. MRI revealed right basilar meningeal enhancement concerning for meningitis and acute infarction of the right basal ganglia.



Figure 2. Coronal section MRI showing right basilar enhancement.

consult where obtained. MRI with and without contrast revealed right basilar meningeal enhancement with an acute right basal ganglia infarction (Figures 1,2). Given the characteristic finding of the CSF and MRI a PPD was placed and Infectious disease was consulted. PPD was read as negative at 48 hours by nursing staff and re-read as positive at 72 hours by an infectious disease physician. Initial direct smears of two separate samples of CSF were negative for acid fast bacilli, and PCR of the CSF was negative for TB on two different occasions. CT of the chest was obtained to look for possible source of infection and revealed right upper lobe nodules with central cavitations (Figures 3,4). Biopsy of the lung was performed and pathology revealed necrotizing granulomatous inflammation with acid fast bacilli (Figures 5,6). Initial concentrated direct smears for acid fast bacilli from the lung biopsy were negative, but *Mycobacterium tuberculosis* was isolated and identified by DNA probe with High Performance Liquid Chromatography at 32 days.

Treatment

Treatment should be initiated on the basis of strong clinical suspicion. As mentioned previously it may take several

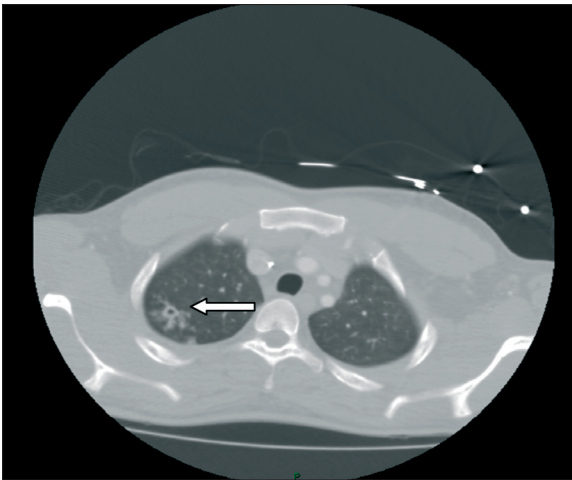


Figure 3. CT Thorax findings consist of right upper lobe cluster of nodules with central cavitations.

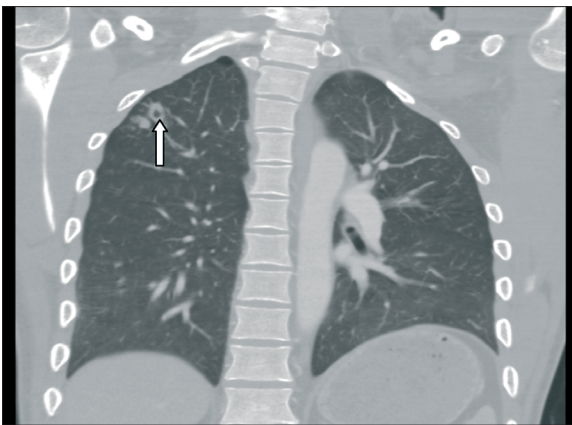


Figure 4. Coronal section from CT with right upper lobe cavitary nodules.

repeated studies before obtaining positive proof of tuberculous infection and delay in treatment often leads to irreversible deficits or death. Recommended treatment is for 9–12 months and is divided into two phases. The intensive phase is four drug therapy with isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (STM) for two months followed by a continuation phase of INH and RIF for 7–10 months depending on clinical response and sensitivity of the specimen [1–3].

Outcome and follow-up

Once empiric TB coverage was started the patient showed significant clinical response with improvement of his mental status, but at the time of discharge still had prominent personality, memory, and functional impairment.

DISCUSSION

Our patient is a young, relatively healthy, male with no known prior exposure to TB that presented with a complicated case of *Tuberculosis Meningitis* leading to stroke and long term residual functional deficit. Central nervous system (CNS) TB is encountered frequently in areas that

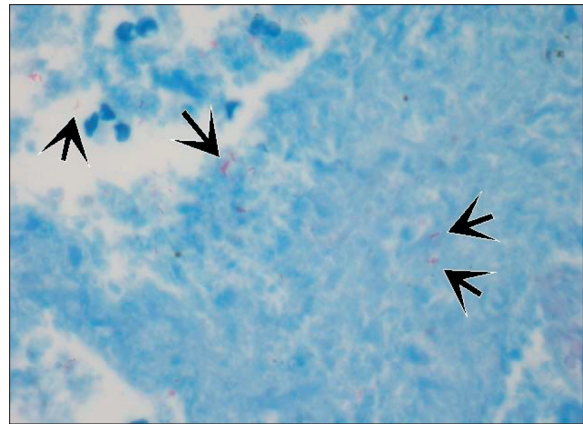


Figure 5. CT guided biopsy right lung nodule reveals acid fast bacilli (arrows).

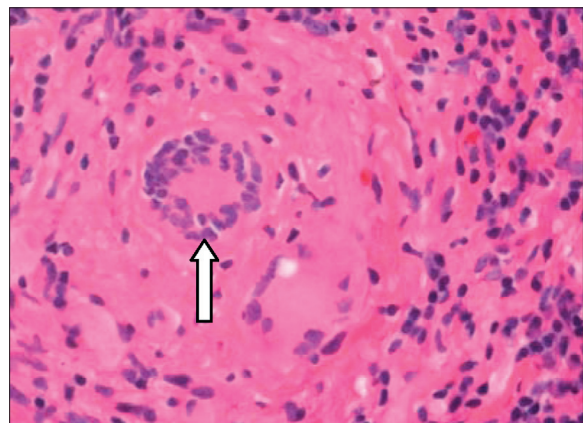


Figure 6. CT guided biopsy right lung with necrotizing granulomatous inflammation.

continue to have high prevalence of tuberculosis and dissemination is very common in children and young adults. CNS TB is a disease that has a relatively low prevalence in North America. It accounts for around 1 percent of all cases of TB and 6 percent of extrapulmonary infections in immunocompetent individuals [4,5]. Tuberculous meningitis develops most commonly from chronic reactivation in patients with immune deficiency secondary to aging, malnutrition, alcoholism, malignancy, or HIV infection. Clinical features of TB meningitis commonly consist of a series of phases, beginning with sub acute fever, malaise, and personality changes. This may last for two- three weeks and if unrecognized will progress to a meningitic phase. Meningitic phase has more pronounced neurologic features such as confusion, headache, lethargy, and focal cranial nerve deficits. The final phase, which our patient presented with, is the paralytic phase consisting of stupor, coma, seizures, and possibly stroke [4–8]. If left undiagnosed and untreated majority of patient will die within five to eight weeks from onset of illness [4,5,7,8].

Diagnosis can be difficult as standard culture methods are quite slow, often taking as much as four to eight weeks for growth and are highly dependent on the number of organisms in the inoculum.10 Typical CSF shows elevated protein usually greater than 100, low glucose (80% less than 45),

and elevated WBC (between 100 and 500 cells/microL) with lymphocytic pleocytosis [6,8–10]. Serial CSF bacterial examination is critical in diagnosing CNS TB. One series of patients showed an increase in diagnosis with positive smears from thirty-seven percent to eighty-seven percent when four specimens were evaluated. If clinical suspicion is high and initial smears remain negative it is recommended that a minimum of three CSF specimens be obtained [6,8]. Rapid detection assays for *M. tuberculosis* in the CSF and pulmonary samples include nucleic acid-based amplification test (NAAT) that rely upon polymerase chain reaction (PCR). The qualitative assay performed by our Tennessee state laboratory uses PCR to amplify the IS6110 gene and the 16SrRNA gene. The IS6110 and 16SrRNA genes are specific for the *M. tuberculosis* complex and this assay detects as few as 10 cells per sample. The sensitivity of this assay is 95% for *M. tuberculosis* [11,12]. Many laboratories are now also using High Performance Liquid Chromatography (HPLC) with either fluorescence or ultra violet detection of mycolic acids, which has proven to be highly sensitive for *M. tuberculosis* [13]. These tests should be used in conjunction with standard culture and smears as was done in our patient to increase sensitivity and specificity. Tuberculin skin test is used to identify latent TB by testing cell mediated immunity to mycobacterial antigens. Purified protein derivative is injected intradermally causing a delayed type hypersensitivity reaction that causes induration. Test should be read by measuring the induration, not the erythema, in millimeters. There can be significant variation in measurement and reliability of results depending on the time from skin testing and the expertise of the interpreter. Results should be read by a qualified practitioner within 48 to 72 hours, after 72 hours test results become less reliable [1,14].

Spillage of tubercular protein into the subarachnoid space causes an inflammatory reaction most commonly seen in the base of the brain. If the inflammation goes unchecked it will produce a fibrous mass that may encase cranial nerves and penetrate into vessels leading to vasculitis and resulting in infarction. Multiple lesions may be common allowing for a variety of stroke like symptoms most commonly in the basal ganglia, pons, and cerebellum [7,10]. Given the pathogenesis and predilection for intense inflammation at the base of the brain, CT and MRI tend to have characteristic findings of basilar enhancement and edema with possible infarction and hydrocephalus [7,11,15,16]. Hydrocephalus results from extension of the inflammatory process to the basilar cisterns causing CSF impedance.

CONCLUSIONS

Central nervous system TB is a progressive disease that can present in many forms. Although, in general TB is relatively rare in immunocompetent individuals in North America it is something to keep on the differential when dealing with atypical presentations of infection. CNS TB is a treatable disease that will be fatal if not recognized. Therefore, it is imperative to be aware of the key clinical features of TB meningitis, and maintain a high level of suspicion when dealing with CNS infection if the cause is unknown

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