

Mixed brain abscess due to *Streptococcus* and Tuberculosis in a pregnant woman with favorable evolution. A case report

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Abstract

Tuberculosis is a global public health problem and is among the top ten causes of mortality in the world. We present the unusual case of a 37-year-old woman, referred for fever, progressive headache, nausea, vomiting and change in mental status. Brain imaging studies showed a left frontal brain abscess with subfalcine herniation. As an urgent procedure, surgical drainage of the brain abscess was performed, and in the culture of pus there was growth of an anaerobic Streptococcus. The histopathological study of the abscess wall showed data on tuberculosis. The patient was pregnant at surgery, for about five weeks and received anti-tuberculous medications with close maternal fetal follow-up. Pregnancy came to term and was resolved by an elective cesarean section, both mother and child had a favorable evolution.

Keywords: tuberculosis, pregnancy, mixed brain abscess, mycobacteria

Introduction

Tuberculosis (TB) is a global public health problem and according to the World Health Organization it is among the top ten causes of mortality in the world [1]. Central nervous system disease caused by TB represents 5% to 10% of extrapulmonary forms of TB and is its most lethal form [1]. TB in pregnancy poses difficulties for early diagnosis, and treatment with anti-tuberculous drugs in pregnant women and their possible repercussions on the product require careful considerations [2].

Case report

A 37-years-old woman was referred to our institution with a history of four weeks of mild headache. Two days prior to admission, the headache worsened, accompanied by fever, nausea, vomiting, photophobia and mild confusion. She denied respiratory or urinary symptoms and history of contact with persons with TB. Her gynecological-obstetric history included a pregnancy with a normal delivery 18 years earlier, she did not use contraception and had irregular periods and was unable to specify the date of her last period. Upon admission, her vital signs indicated blood pressure 110/80, heart rate 88 per minute, respiratory rate 18 per minute, and temperature 37°C. On physical examination, she was found awake, inattentive, with a long latency verbal response, and moderately confused. Examination of the cranial nerves showed no abnormalities. Sensitivity and motor exam were normal, with bilateral plantar flexor response and without meningeal signs. Laboratory studies reported normal cell blood count and blood chemistry and a negative HIV test. A non-contrasted computed tomography of the head revealed an hypointense lesion in the left frontal cerebral lobe, with significant mass effect and extensive perilesional brain edema, which produced subfalcine herniation. A brain magnetic resonance imaging (MRI) study with contrast (Figure 1A and 1B), corroborated the left frontal mass with intense contrast enhancement in annular pattern, without uptake in its

internal portion in the perfusion phase, MRI Spectroscopy showed lipid and lactate peaks compared to normal tissue, these findings were compatible with a brain abscess in late capsular stage. The patient was rushed to surgery approaching the lesion through a left frontotemporal craniotomy, a transcortical puncture of the abscess was performed, and 20 cubic centimeters of thick non-fetid greenish purulent material was obtained, and the medial and rostral abscess walls were partially resected. The Gram stain of pus showed polymorphonuclear leukocytes and necrotic material. In culture, an obligate anaerobic *Streptococcus* species was isolated, fungal and mycobacterial cultures were negative up to six weeks. She received intravenous ceftriaxone and metronidazole and was discharged with improvement on oral antibiotics. In the follow-up consultation two weeks after discharge a scheduled pregnancy test was found positive. The report of histopathological study of the abscess wall with special stains, then available, revealed a dense acute and chronic inflammatory infiltrate and newly formed vessels with abundant macrophages and plasma cells, vasculitis, and occasional multinucleated giant cells. Some macrophages showed scarce bacillary structures in the cytoplasm, Grocott's stain, periodic acid Schiff and Gram stain were negative, and the Ziehl-Neelsen staining was positive (Figure 2). She was referred to an obstetrics gynecology center, where she began the intensive phase of anti-tuberculous treatment with a combination of isoniazid, rifampin, ethambutol and pyrazinamide (PZA) in fixed dose combination tablets according to her body weight, plus pyridoxine, starting in the 5th postoperative week for two months, followed by the continuation phase with isoniazid and rifampin up to one year. The pregnancy resolved at term by ultrasound estimation by elective caesarean section, obtaining a healthy baby with a weight of 2,860 g at birth. A new MRI study was performed 19 months after her cranial surgery (Figure 1C and 1D), it showed resolution of the abscess, with an area of left frontal gliosis and no abnormal contrast uptake. The patient son was healthy at the age of two years.

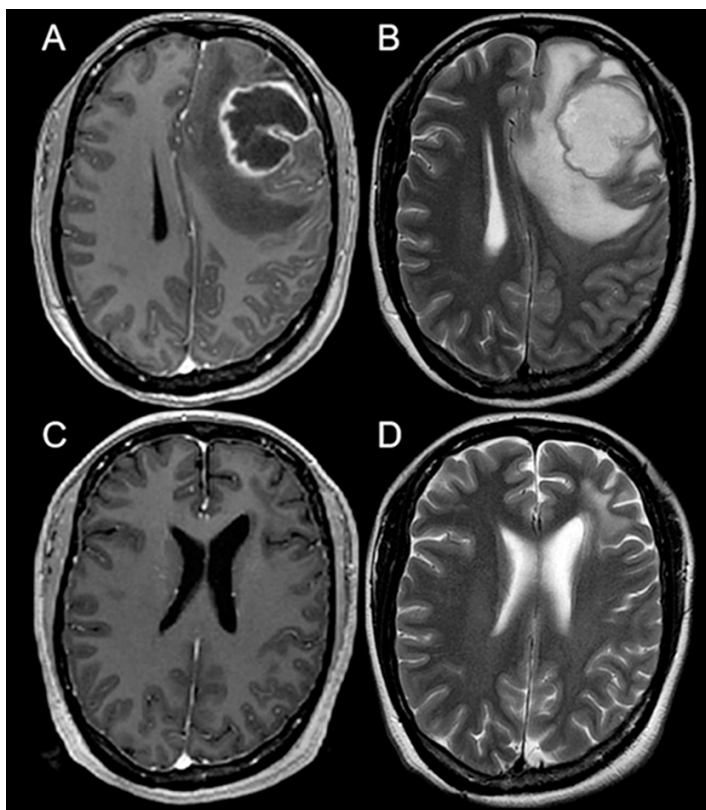


Figure 1. A) Preoperative magnetic resonance imaging (MRI), axial section in FSGPR (3D fast spoiled gradient-echo dual-echo) sequence with contrast, shows a left frontal abscess with significant mass effect, with midline deviation and obliteration of the right ventricle, the wall is irregular with intense contrast uptake. B) Axial image in T2 sequence, frontal perilesional edema and subfalcine herniation are more clearly seen. C) MRI obtained after 19 months of surgery shows complete resolution of the abscess, and ventricular asymmetry due to traction of the anterior portion of the left ventricle due to cicatricial gliosis. D) in the T2 sequence, left frontal subcortical hyperintensity due to gliosis.

Discussion and conclusion

Our patient was in serious neurological condition at presentation, with mild confusion, inattentive, and with extensive frontal cerebral edema in the brain image studies, which indicated the urgent need to drain a life-threatening brain abscess. Surgical drainage of the abscess was carried out, with growth of an anaerobic *Streptococcus* in the pus culture, and negative cultures for fungi and mycobacteria. Antibiotic treatment was given, and as an outpatient, with a positive pregnancy test and an ultrasound estimation of seven weeks of gestation she was referred for anti-tuberculous treatment and antenatal care, once the results of the histopathological study were found to be compatible with a TB brain abscess.

The treatment modalities for brain abscess are a simple puncture that reduces intracranial pressure and allows the bacteriological study and guides the specific treatment. The abscess puncture is usually followed by partial or complete resection of the abscess wall, which provides detailed information on the histological structure and with special stains, immunohistochemistry or polymerase chain reaction, it increases the sensitivity to detect other pathogens. This situation was fortunate for our patient, because the biopsy made possible to identify TB and give treatment. Globally, an estimated 10.0 million people fell ill

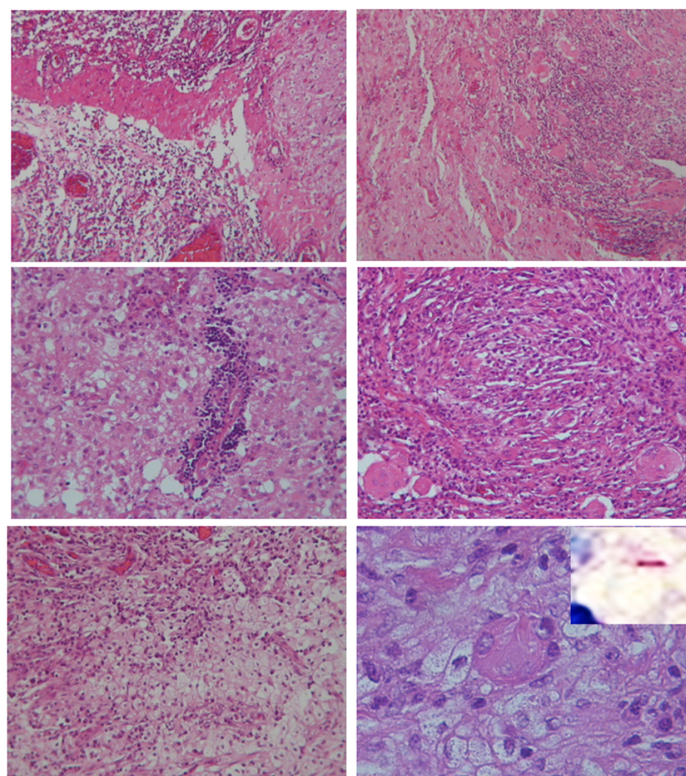


Figure 2. Histologically, brain tissue with necrosis and dense inflammatory infiltrate is observed in A) and B) Better preserved areas show an inflammatory infiltrate with hyalinized vessels and reactive gliosis. C) with formation of granulomas (H & Ex100). D and E) Mononuclear infiltrate of perivascular distribution indicating vasculitis, and abundant macrophages with “dirty” cytoplasm interspersed with inflammatory cells and elongated histiocytes (H & Ex200) and in F) at a closer zoom we observe foci of necrosis, histiocytes, dirty macrophages and necrotic multinucleated giant cells (H & Ex400). The insert shows a bacillus with positive acid-fast stain (Ziehl-Neelsen x 1000).

with TB in 2018, women accounted for 32% of all cases [1]. A study using publicly accessible country-level estimates concluded that approximately 216 500 active tuberculosis cases existed in pregnant women worldwide in 2011 [2]. In a systematic review and meta-analysis to evaluate pregnancy outcomes associated with TB that was published in 2017, they included 3384 pregnancies of women with active TB and 119 448 without TB. Compared with pregnant women without TB, pregnant women with active TB was associated with increased odds of maternal morbidity, anemia, caesarean delivery, preterm birth, low birth weight, newborn asphyxia, and perinatal death [3]. TB brain abscess is a rare manifestation of CNS TB, accounting for 4 to 7.5% of all patients presenting with CNS TB [4]. TB brain abscesses usually present acutely, often in the third and fourth decades, commonly have a supratentorial location, frequently present with focal neurologic signs, and are associated with historical and laboratory evidence of TB, and it may be difficult to differentiate from pyogenic brain abscesses or tuberculomas on the basis of clinical, laboratory, and roentgenographic information. Appropriate therapy includes adequate anti-tuberculous chemotherapy and surgical excision [5]. An association of TB with another pathogen in a brain abscess is rare, however, a TB brain abscess can be over-infected by a bacterial source. Four cases of TB co-infections with pyogenic

bacteria were reported in a joint series of two institutions in Mexico City [6], two occurred in immunocompromised patients, one with leukemia and the other with HIV infection, and two in patients without concomitant disease. Bacteria associated with TB were *Streptococcus pneumoniae* in two cases, *Staphylococcus coagulase negative* in one case, and *Enterobacter* spp. in one. In that report a literature review until the year 2017 found nine patients reported with TB and bacterial co-infection with CNS TB, the most frequently associated bacterium was *Streptococcus pneumoniae* in five patients [6].

In relation to TB and pregnancy, the American Thoracic Society Guidelines [7] recommend initiate treatment for TB whenever the probability of maternal disease is moderate to high because of the risk of untreated TB to a pregnant woman and her fetus. Although antituberculosis drugs cross the placenta, they do not appear to have teratogenic effects in humans. However, the inclusion of PZA in the treatment regimen for pregnant women is controversial in the United States. The FDA previously classified all 4 first-line drugs, INH, RIF, PZA, and EMB, as having equal potential for teratogenicity (all assigned to category C according to the previous FDA letter-based classification). The guidelines suggested that clinicians evaluate the risks and benefits of prescribing PZA on a case-by-case basis, allowing the patient to make an informed and, educated decision, recognizing that for all first-line drugs, risk cannot be ruled out as there are no adequate and well controlled studies in humans, but potential benefits warrant use of the drug in pregnant women despite potential risks. It is also important to recognize that PZA has been used extensively in high burden countries and expert opinion is that in pregnant women with extrapulmonary or severe TB or HIV, it is more beneficial to include PZA in the treatment [7]. Whenever TB resistant strains are present so-called multi-drug resistance, the patients should only be treated in consultation with infectious disease specialist, microbiologists and obstetrician, taking into account the individual risks of TB vs. adverse drugs reactions [8]. Breastfeeding should not be discouraged in women receiving first-line drugs against TB, because the concentrations reached in it are insufficient to generate drug toxicity in the infant. For the same reason, drugs that are

present in breast milk are not an effective treatment for a baby with TB or latent TB [8].

Conclusion: In geographic areas with a high prevalence of tuberculosis, the routine processing of bacteriological samples of brain abscesses should include the identification of mycobacteria. The histopathological study of the wall of brain abscesses is an important complementary diagnostic process that may provide information to identify possible causes missed by standard bacteriological study. Pregnant women in whom TB disease is diagnosed should be treated as soon as TB is detected. Although the anti-tuberculous drugs used in treatment cross the placenta, these drugs do not appear to have harmful effects on the baby, and appropriately treated pregnant women with TB may have successful outcomes.

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