

Infectious Lesion Simulating Malignant Neoplasm. Clinical Case and Literature Review

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The extrapulmonary manifestations of tuberculosis (TBC) that affect the Central Nervous System (CNS), by hematogenous dissemination, are an infrequent entity. Intracranial tuberculomas are the least common form of tuberculosis in CNS. Represent a granulomatous inflammatory process with cerebral involvement.

The prognosis is related to the early diagnosis, the degree of surgical resection and the complementary treatment with antituberculous drugs.

We describe an infrequent clinical case of cerebral tuberculoma that simulated a malignant neoplasm, and also performed a literature review.

A clinical case about a 31-year-old female with no relevant medical history. She described a sudden diplopia, without previous trauma. The patient was evaluated by Ophthalmology, which identified papillary edema, with no other alterations. In this context was performed a Brain CT/MRI, which showed an intra-axial, left frontobasal lesion with perilesional edema, ring contrast enhancement and a hypodense/hypointense central area. Spectroscopy showed a reduction in n-acetylaspartate (NAA) with a peak in creatine and choline, suggestive of a malignant tumor.

The patient underwent surgery, having performed a frontal left craniotomy and complete excision of a nodular, capsulated, avascular lesion with a spongy consistency. Subsequently, the histological diagnosis of tuberculoma was confirmed.

We describe an infrequent clinical case of cerebral tuberculoma which, due to the characteristics presented in the preoperative studies, was suggestive of a malignant tumor that was not confirmed, which is the particularity of this case. The patient presents a good clinical and imaging evolution during the follow-up period.

Keywords: Tuberculoma; Craniotomy; Microsurgery; Neuronavigation; Gross total resection**Introduction**

Tuberculosis (TB) is a transmissible disease that is a major cause of ill health and one of the leading causes of death worldwide. Until the coronavirus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS [1].

The causative agent of tuberculosis is Mycobacterium tuberculosis, it is aerobic and therefore affects primarily the respiratory system. Typically affects the lungs (pulmonary TB) but can affect other parts [1].

About 90% who develop this disease are adults, with more cases among men than women. About a quarter of the world's population

is infected with M. tuberculosis. TB is curable and preventable. The 85% of people who develop TB disease can be successfully treated with a 6-month drug regimen and regimens of 1–6 months can be used to treat TB infection [1].

In developing countries, TB has high incidence rate, however the diagnosis remains very difficult [1, 2]. The involvement of the central nervous system (CNS) by this infection accounts for 1% of all the TB cases and 5% of extrapulmonary TB cases [2]. The forms of presentation of tuberculosis in the CNS are tuberculoma, meningitis, cerebritis, abscess or miliary TB via the hematogenous spread [3].

Among these conditions, basal meningitis is a well-known sub-

type [4]. CNS tuberculoma is a rare disease but when present, it can cause neurological deficits that vary depending on the location of the lesion as well as its characteristics with severe neurological deficits such as altered mental status, hydrocephalus, cranial nerve palsies, hemiparesis, and seizures [5]. The tuberculoma is an anatomopathological concept that represents conglomerate with caseous necrosis focus located in the brain tissue that occurs because of hematogenous dissemination with tuberculosis bacillus.

Mainly are single lesions but in 15-34% appears multiple lesions. In 10% of the cases is associated with tuberculosis meningitis. In many cases, these lesions developed with similar behavior as high-grade malignant tumors as in our clinical case. In general, these lesions begin with focal signs or symptoms as neurological deficits depending where the lesion occur and without systemic disease and without meningeal inflammation reaction.

We describe a unusual clinical case of frontal lobe tuberculoma in an immunocompetent woman who developed suddenly diplopia. The intracranial lesion present similar aspects as malignant tumors. Was performed a surgical procedure, as described below, which allowed us to obtain a histological result and complement the medical treatment according to current guidelines.

Case Report

We report a clinical case about a 31-year-old female, immunocompetent, with no relevant medical history, who was not complying with pharmacological treatments. The patient described a sudden diplopia, without previous trauma. Was evaluated by Ophthalmology, which aimed at papillary edema, without any other findings. No recent visit to tropical countries. No fever, no weight loss. No neurological deficits such as cognitive deterioration, absence of speech disturbances, or motor or sensitive dysfunction.

The blood count does not show signs of infection. In the study with radiology, the simple chest was normal, with no pleural effusion, without parenchymal alterations or adenopathies.

Taking into account the symptoms referred by the patient and the data collected during the evaluation was performed a Brain CT scan/MRI which showed an intra-axial, left frontobasal lesion with huge perilesional edema, without bone infiltration [Figure 1].

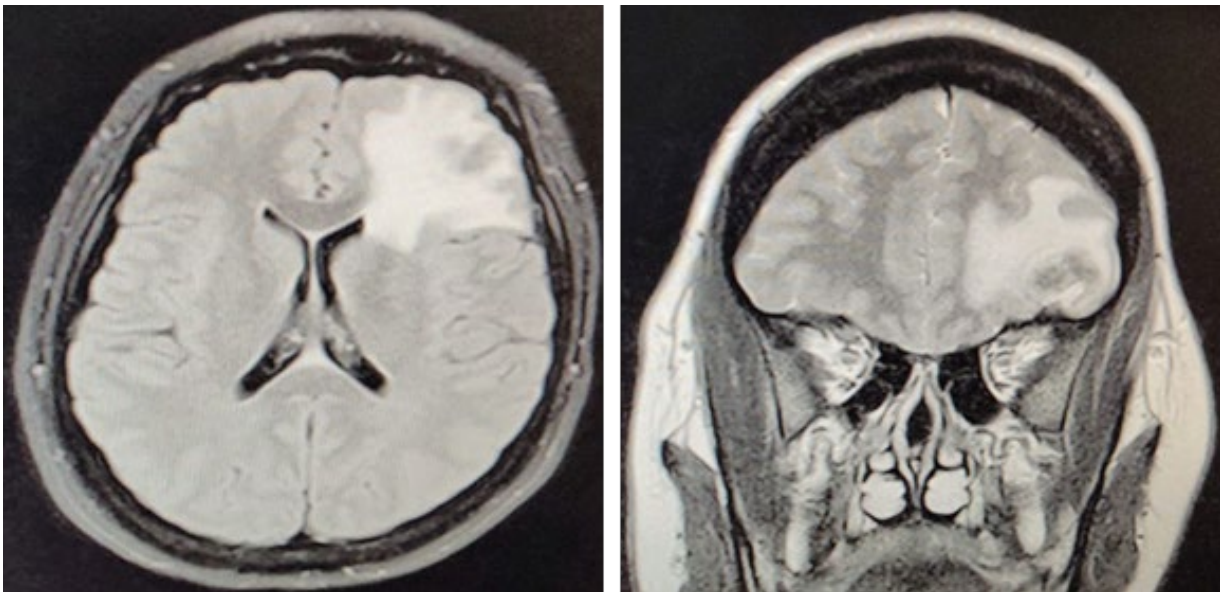


Figure 1: Axial (A) and coronal (B) slices; present a huge area of edema surrounding the intra-axial left frontobasal lesion.

After the administration of gadolinium the lesion present a ring enhancement and a hypointense area inside (Figure 2).

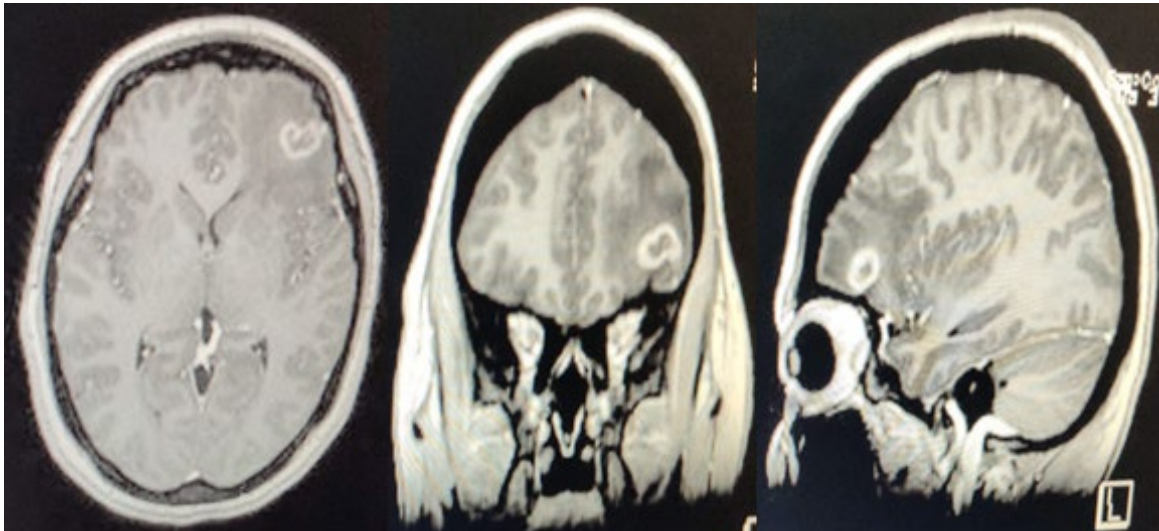


Figure 2: axial (A), coronal (B) and sagittal (C) slices; Intra-axial lesion without bone invasion. Ring enhancement after gadolinium administration.

Due to the findings, it was decided to carry out a study of Spectroscopy that showed a reduction in n-acetyl-aspartate with a peak in creatine and choline, suggestive of a malignant tumor lesion [Figure 3].

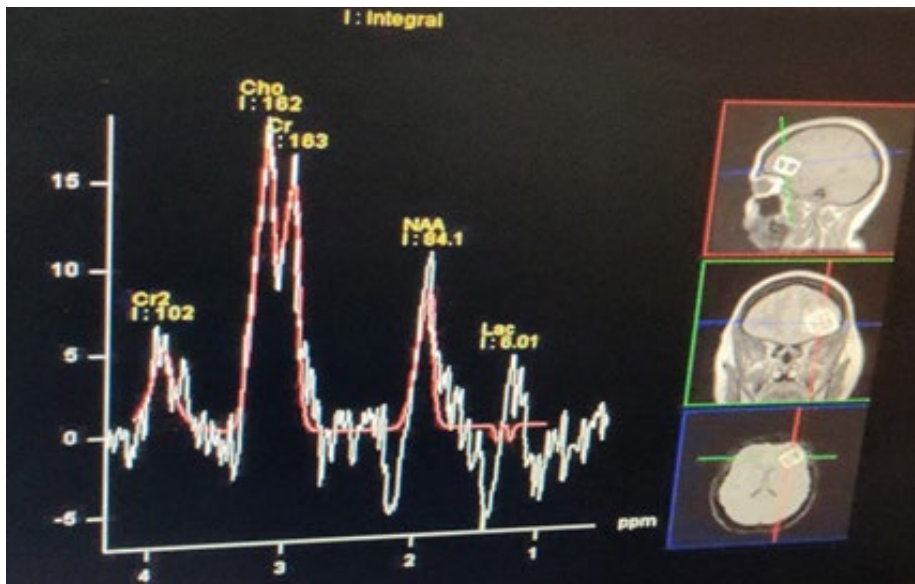


Figure 3: Spectroscopy advanced MRI Study, peak in creatine and choline, reduction of n-acetyl-aspartate.

The patient underwent surgery, under general anesthesia, supine, head clamped with a Mayfield device. Aseptic protocol. With Neuronavigation System we proceed to localize the lesion. We chose to carry out a curvilinear incision. Left frontal craniotomy, centered on the lesion with the help of the navigation system. Dural suspension like in all cases to prevent epidural hematoma. With a microscopical view proceeded to a dural open. Small corticectomy and localization and identification of the lesion again with the support of the navigator. Used microsurgical dissection techniques

to released a complete excision of a nodular, capsulated, avascular lesion with a spongy consistency.

During the first 24 hours in the post-operation period, the patient was under neurological monitoring in intensive care unit (ICU). Postoperative control CT was performed without complications associated with the procedure. Small pneumocephalus without tension. Good coaptation of the craniotomy bone flap [Figure 4].

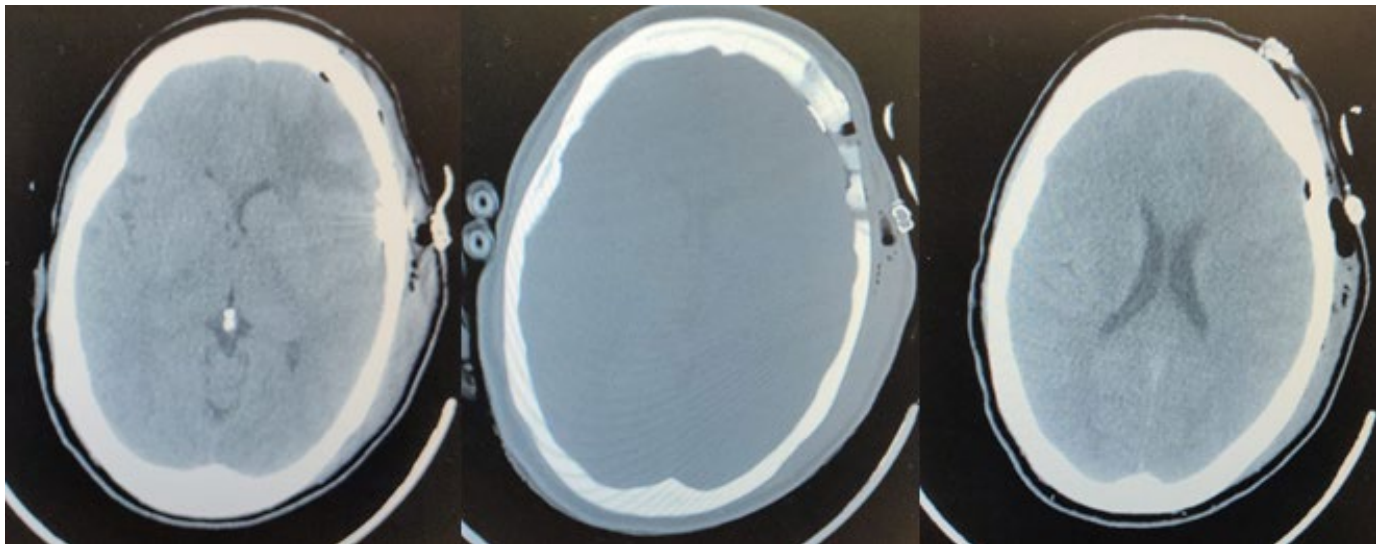


Figure 4: Brain ct-scan after surgery. Status post left frontal craniotomy. Good coaptation of the craniotomy bone flap with craniofix plate. Without complications associated with the procedure.

During follow-up MRI was performed, for exclusion complications associated with the procedure or discard lesion recurrence [Figure 5].

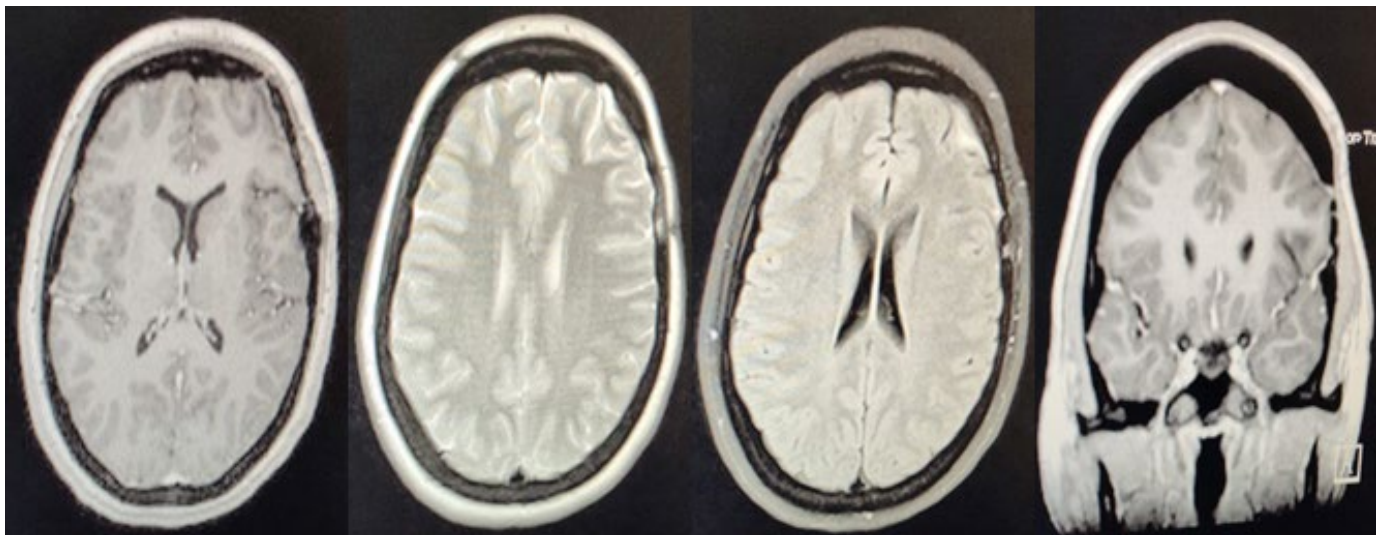


Figure 5: postoperative mri without residual lesion, recurrence or complications associated with the surgical procedure.

In the histological study with Hematoxylin-eosin (H&E), granulomas were seen in the brain parenchyma, with central caseous necrosis, multinucleated giant cells Langerhans type, epithelioid cells and lymphocytic infiltrate perilesional [Figure 6]. Sample was also sent for study with PCR obtain-ing confirmation diagnosis of *Mycobacterium tuberculosis* infection.

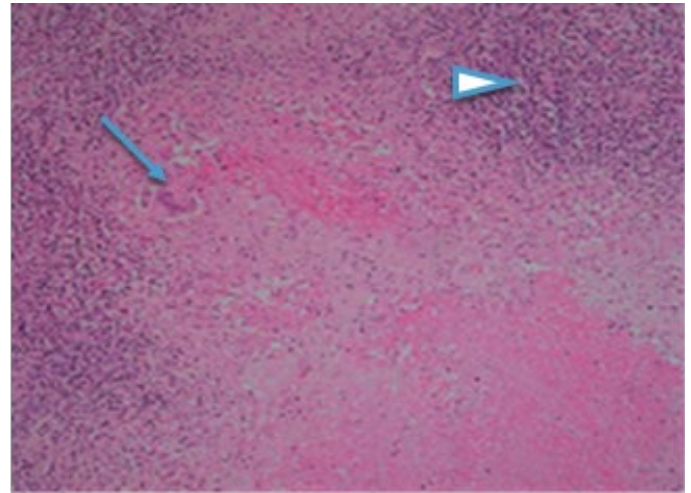
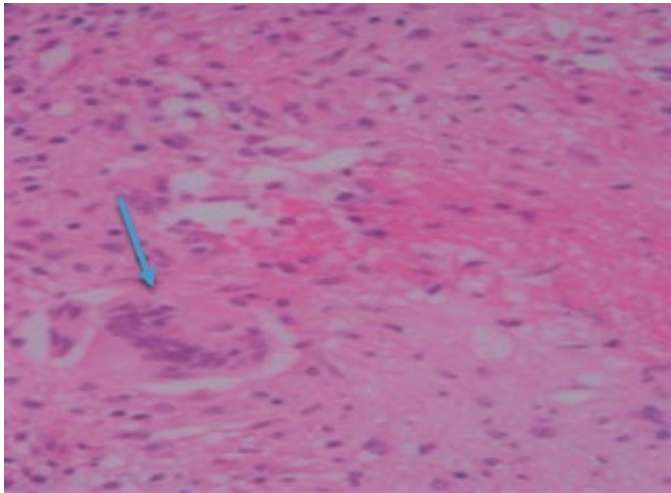


Figure 6: hematoxylin-eosin granulomas in brain parenchyma, central caseous necrosis, multinucleated giant cells Langerhans type (arrow) A and B, epithelioid cells and lymphocytic infiltrate perilesional (arrowhead), B.

The clinical course during the postoperative period was favorable, the patient starting antituberculous treatment with good tolerance, without neurological deficits and no recurrence during the follow-up as described and showed previously.

Discussion

Tuberculosis is a major health concern in developing countries where prevalence is high. There is obviously an overall decrease in the number of peoples newly diagnosed with TB and notified. Comparing the data for 2019 and 2020 there is a decrease from 7,1 million to 5,8 million respectively. Provisional data up to June 2021 shows continued declines. The most obvious impact on TB of disruptions caused by the COVID-19 pandemic is a large global drop in the number of people newly diagnosed with TB and reported in 2020 compared with 2019 [6].

In certain areas where the diagnosis is late and the difficult access to TB treatment resulted in an increase in the number of deaths from this pathology. The best estimates for 2020 are 1.3 million TB deaths among HIV-negative people (up from 1.2 million in 2019) and an additional 214 000 among HIV-positive people (up from 209000 in 2019), with the combined total back to the level of 2017. Declines in TB incidence (the number of people developing TB each year) achieved in previous years have slowed almost to a halt. These impacts are forecast to be much worse in 2021 and 2022 [6].

Although tuberculosis is a primary infectious with lung involvement that progresses and can affect many organs and systems, including de Central Nervous System (CNS) [7].

Infection by *M. tuberculosis* occurs during the inhalation of particles that contain the bacillus, with subsequent deposition in the pulmonary alveoli. After this period, the bacillus initiates an interaction with alveolar macrophages using different types of receptors releasing cytokines that intervene in the immune response medi-

ated by T-helper lymphocytes, forming the granuloma. In the initial phases of this process, before the infection is contained, some bacilli can filter into the lymphatic drainage system and from there spread hematogenously to different regions of the body, generally highly oxygenated areas such as the brain. In the CNS, the disease begins with the development of small tuberculous foci called Rich foci, in the brain, spinal cord or meninges [8].

Usually, the tuberculomas appears as small tumor-like lumps in large quantities, can be seen in all organs. Intracranial tuberculomas are mostly seen in the basal section of the brain. Major gross features of tuberculomas are small round or oval shaped nodules, ranging from 2-12 mm in size. The tuberculomas as all intracranial lesions may present different clinical symptoms depending on their location and size. The most frequently symptoms include headache, seizures, neurological deficits, and papilledema. It's a rare pathology that could be included in the differential diagnosis of intracranial lesions [9]. Early diagnosis and treatment are important in this pathology to reduce morbidity as neurological deficits and mortality. In cases of patients without signs of meningitis, the clinical features are nonspecific and indistinguishable when compared with any other space-occupying injury [9, 10].

Intracranial tuberculosis can be broadly divided into meningeal and parenchymal patterns of involvement any combination of the patterns can also occur. Diagnosis is usually made by evaluating the clinical presentation, epidemiology, and imaging studies and sometimes fine needle biopsy. Cranial CT and MRI and histopathologic examinations are used for diagnosis, some cases needed biopsy or gross total resection also to obtain diagnosis and reduce in these cases de intracranial pressor.

The CT scan is the imaging exam performed initially. Not showing characteristics for these injuries. Lumbar Puncture (LP) are typically avoided due to fear of brain herniation, but when performed, they usually reveal normal and nonspecific results. MRI

present greater sensitivity and specificity than CT scan, and when performed for suspected intracranial tuberculosis should include axial pre-contrast T1W, T2W, FLAIR (fluid attenuated inversion recovery sequence), DWI (diffusion-weighted imaging sequence), and GRE (gradient echo sequence)/SWI (susceptibility-weighted imaging sequence) sequences and postcontrast T1W scans in all three planes. The noncaseating granulomas are usually hypointense on T1-weighted images and hyperintense on T2-weighted images, with homogenous contrast enhancement. The caseating solid granulomas, on the other hand, are relatively isointense or hypointense on T1- and T2-weighted images. Although MRI is useful for diagnosing tuberculoma, histopathologic examination is the gold standard for a final diagnosis [9, 11].

The H proton spectroscopy and magnetisation transfer imaging may be additionally performed in cases where the morphology or distribution of the lesions are atypical, presenting a diagnostic challenge. Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) may be used in cases with suspected vascular complications [11]. A primary treatment method is the medical approach and surgery is not usually recommended, are recommended particularly in cases with symptoms caused by intracranial hypertension. When the histopathologic result indicated tuberculosis, screening was carried out during which cervical lymphadenopathy, and the microbiological examination of this revealed Tbc DNA positivity.

For the cases of tuberculosis that progress with CNS involvement, quadruple treatment is recommended for the first two months and then a dual anti-tuberculosis treatment should be completed in 9-12 months. While clinical recovery takes place within a few weeks, radiological shrinkage or elimination of lesions lasts from 6-12 months. A quadruple anti-tuberculosis treatment consisting of rifampicin, ethambutol, isoniazid, and pyrazinamide [11]. Surgical intervention is indicated if the lesions are at risk of causing obstructive hydrocephalus or mass effect [12]. Surgical removal must include decompression and excision as much as possible preventing additional neurological morbidity followed by intensive treatment with antitubercular drugs as the biopsied of the partially excised lesion may exhibit persistent lesions even after a full course of treatment [13].

These lesions are often misdiagnosed as primary or secondary tumors. Many authors, especially Bauer et al. emphasize the need for biopsy to obtain material for histopathological study and thus obtain a definitive diagnosis of tuberculoma. In conclusion, in regions where tuberculosis is endemic as in our country, tuberculomas should be considered in the differential diagnosis of lesions that occupy space in the CNS. Intensive treatment with antitubercular drugs for an adequate duration (6–9 months) is sufficient for tuberculoma but may need to be prolonged to 1 year or more depending on the radiological state of the lesion [11-14]. In our case, as described in many works, we decide to release a gross total resection, without any complication, and complete pharmacological treatment with good results during the follow-up.

Conclusions

Intracranial tuberculosis is a unique disease with many possible presentations in the image's appearance, and produces a wide spectrum of patterns. The involvement of the CNS by tuberculosis, with or without extracerebral manifestations, can occur as a lesion than on imaging studies resemble a malignant neoplasm as described in our case. The detailed analysis of preoperative imaging is mandatory in all cases and identifies suspected aspects and including the tuberculoma among the diagnostic possibilities especially in immunocompromised patients. The early diagnosis and treatment can be lifesaving, and improve the neurological status. The histopathologic analysis is required for a definitive diagnosis, the study with PCR in the extracted material in the extracted material during the surgery/biopsy or even in CSF can help us make a certain diagnosis. The role of surgery should be considered in cases with accessible lesions with intracranial hypertension, doing complete resection of the lesion and complemented the treatment with adequate antituberculosis drugs. The selection and the duration of the medical treatment must be adjusted to each patient. In conclusion, in regions where tuberculosis is endemic as in our country, tuberculomas should be considered in the differential diagnosis of lesions in the CNS.

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