Case Report

Giant Intracranial Tuberculoma Resembling a Brain Tumor: A Diagnostic Challenge

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Abstract

Despite being potentially remediable, central nervous system tuberculosis continues to be a major cause of morbidity and mortality in developing countries. Intracranial tuberculoma is one of the many presentations of CNS tuberculosis that can occur as solitary or multiple lesions. When tuberculomas are solitary and extremely large, they may cause increased intracranial pressure, compressive focal neurological deficits, or epileptic seizures mimicking a malignant lesion. Even using magnetic resonance imaging and spectrography, giant tuberculoma and brain tumors could be mistaken for one another, which warrants consideration of an infectious etiology as a diagnostic differential for prompt diagnosis and appropriate treatment plan. This case study demonstrates a 22-year-old woman who presented with headache, nausea and vomiting ,blurring of vision , weakness of the right side of the body, and features of frontal lobe syndrome with no particular clinical features of TB, and underwent craniotomy who had a preoperative diagnosis of brain tumor. Histopathology later revealed it to be a tuberculoma.

Key Words:
Giant intracranial tuberculoma, Brain tumor, Tuberculosis, Magnetic resonance spectroscopy (MRS).

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Introduction:

Involvement of the central nervous system in the form of meningitis, encephalopathy, tuberculous arteriopathy, tuberculoma, abscess, infarct, or miliary parenchymal lesions accounts for only 2–5% of patients with tuberculosis, and amongst these, cerebral tuberculoma is the least common presentation[1]. Intracranial tuberculomas still have a significant morbidity and mortality rate despite being potentially curable and having various contemporary modern approaches for early identification since the clinical signs are aberrant and non-specific frequently, and it has been reported that in 70% of cases, there may be no evidence of systemic tuberculosis or exposure to the disease[2]. When patients have single, large tuberculomas, they are frequently mistaken for brain tumors having non-specific neurologic deficits linked to features of increased intracranial pressure, local compression-related neurologic deficits, or epileptic seizures with no accompanying systemic signs and symptoms of infection[3]. Since there is significant overlap in imaging characteristics, conventional MRI sequences can not confidently diagnose tuberculomas in the majority of patients[4]. This report presents an interesting case of solitary giant intracranial tuberculoma located in the left frontal lobe, which presented with prolonged nonspecific symptoms and mimicked brain tumors in conventional MRI sequences and spectrography. The lesion was surgically removed, and the diagnosis of tuberculoma was confirmed by intraoperative findings and postoperative histo-pathological examination. The diagnostic challenge of solitary intracranial tuberculoma both clinically and radiologically poses a dilemma about the selection of the best treatment modality, either surgical or medical, as first line treatment, and thus the significance of a high index of suspicion and extensive preoperative workup, is highlighted here. In our opinion, considering tuberculoma

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in the differential diagnosis of cerebral lesions with such clinico-radiological features can help medical professionals with prompt diagnosis and treatment.

Case Report:

A 22-year-old lady presented with progressive headache with nausea and vomiting for 4 months and a 2-month history of blurred vision and right sided hemiparesis. Her weakness was more marked on the right upper limb than the right lower limb. She had features of positive frontal lobe syndrome, including disinhibition, poor judgment, emotional lability, and poor abstract thoughts. She reported no history of convulsions of epileptic fits,trauma, significant weight loss, chronic cough, or low grade fever. She had no documented history of tuberculosis. She is immunized with BCG vaccine. On general examination, her vitals were recorded within normal limits. Concerning the neurological examination, the patient was alert, oriented to time, place, and person, with a Glasgow of 15/15. MMSE (score-23/30) indicated mild cognitive impairment. She had bilateral 6th nerve palsy (Lt>Rt) & fundoscopy revealed bilateral papilledema. On motor examination of the right upper limb, tone was increased with muscle power G-3 in the right lower limb and muscle power G-4 in MRC grade with increased deep tendon jerks. The plantar response was extensor on the right and equivocal on the left. The blood cell profile, including CBC with ESR, was within normal limits, showing no signs of infection. Other routine investigations revealed no significant abnormalities. The MT test concluded as negative. CSF analysis was not done because of papilloedema. Chest X-ray revealed normal (Fig 1). Magnetic resonance imaging (MRI) scan of the brain with spectrography was done. The contrast enhanced MRI shows a well-defined ring enhancing lesion measuring(3.4×3.3) occupying the left frontal region with mass effects including midline shift, rim is thick and irregular with adjacent convexity dural enhancement(Fig-2). T2 weighted axial plane MRI shows the lesion is isointense with massive perilesional edema and mass effects. There are no major flow voids within or around the lesion(Fig. 3). MRI Flair axial plane shows massive perilesional edema, effacement of the ipsilateral lateral ventricle, obliteration of sulci/gyri demarcation, and midline shift(Fig. 4). Diffusion-weighted MR Imaging shows no restriction of diffusion(Fig. 5). MR spectrography shows choline peak is high with low NAA and creatine peak, lipid and lactate level is significantly high consistent with neoplastic lesion most possibly high grade glioma (Fig-6). Magnetic resonance venography(MRV) revealed normal patent dural venous sinuses(Fig-7). A clino-radiological diagnosis of high-grade glioma was established. The neurosurgery team opted for a plan of surgical excision. The patient underwent left frontal craniotomy and complete surgical resection of the left frontal lesion with the aim of cytoreduction, relief of mass effect, tissue for histopathological diagnosis, and preservation and improvement of neurological function. Intraoperatively, the mass lesion was pale, minimally vascular, and had variable consistency with some areas of caseation. There was a well-demarcated interface between the mass and the brain parenchyma. The gross specimen shows multiple irregular pieces of grayish-brown tissue(Fig. 8). The final histopathology confirmed epithelioid granuloma with caseation necrosis suggestive of tuberculoma(Fig-9a,9b). Upon recovering from postoperative stress, the patient commenced on Anti-TB chemotherapy, liaising with the oncologist. At her follow-up visits, the patient started to improve both clinically and radiologically (Fig. 11). She is on anti-TB chemotherapy and is in our regular follow-up.

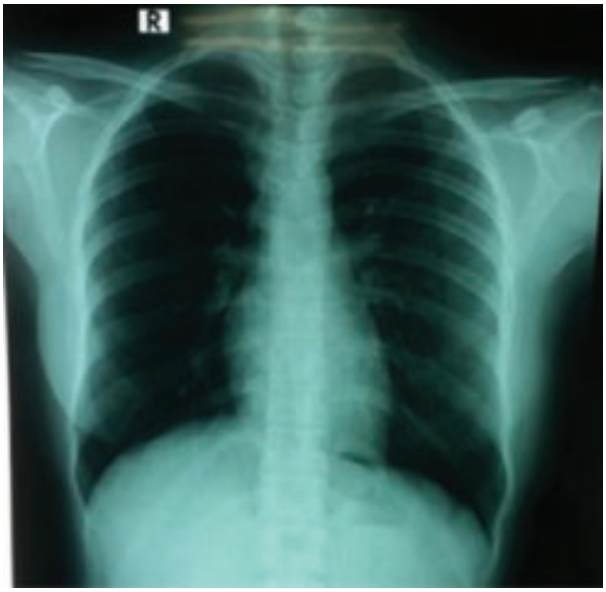

Figure 1: *Chest X-ray normal*

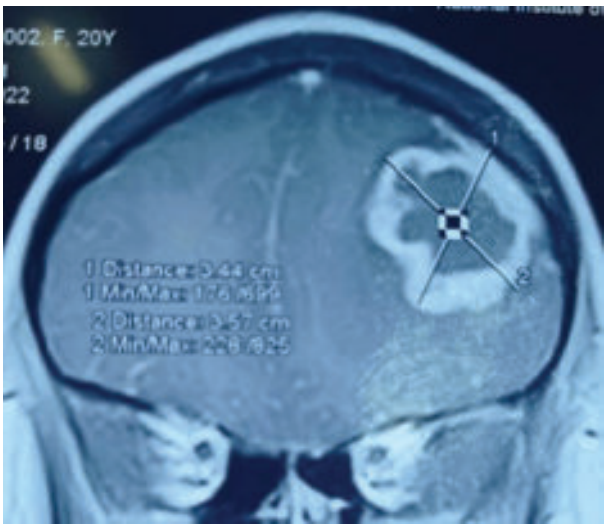

Figure 2: *Contrast enhanced MRI coronal plane of the brain shows a well-defined ring enhancing lesion measuring(3.4 3.3) occupying the left frontal region with mass effects including midline shift, rim is thick and irregular, with adjacent convexity dural enhancement present.*

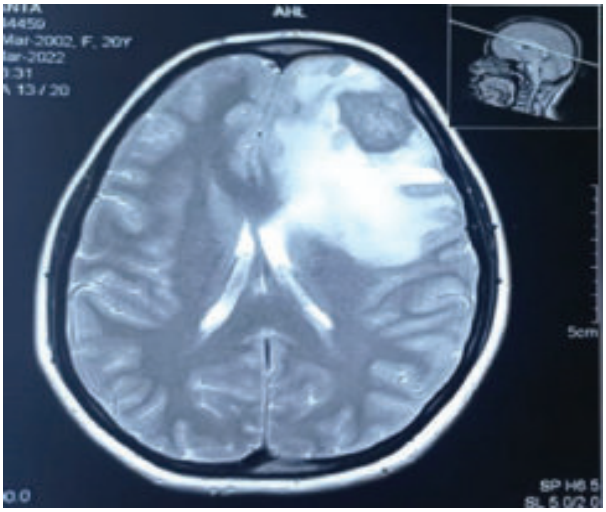

Figure 3: *T2 weighted axial plane MRI shows the lesion is isointense. There are no major flow voids within or around the lesion. massive perilesional edema with mass effects*

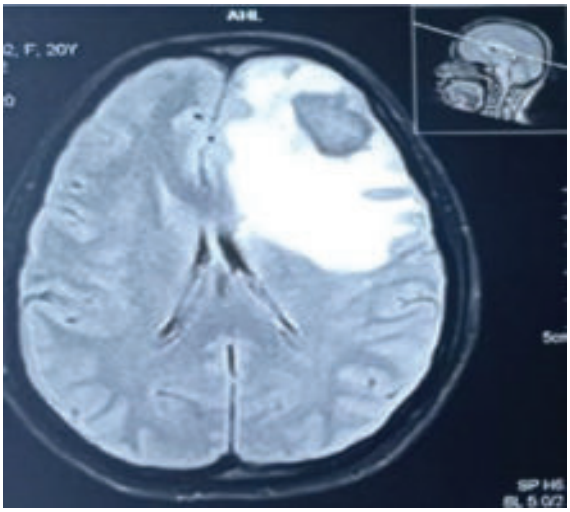

Figure 4: *MRI Flair the axial plane shows massive perilesional edema. Effacement of the ipsilateral lateral ventricle, obliteration of sulci/gyri demarcation, and midline shift*

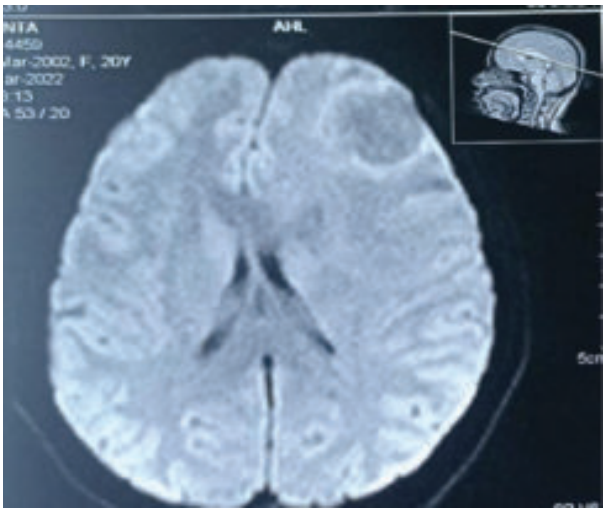

Figure 5: *Diffusion-weighted MR Imaging shows no restriction of diffusion*

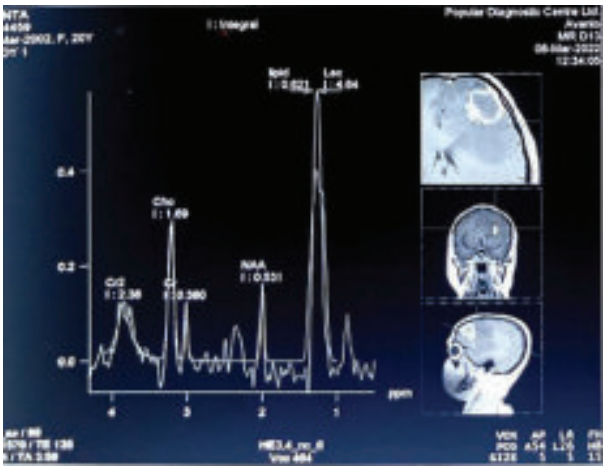

Figure 6: *MR spectrography shows choline peak is high with low NAA and creatine peak, lipid and lactate level is significantly high.*

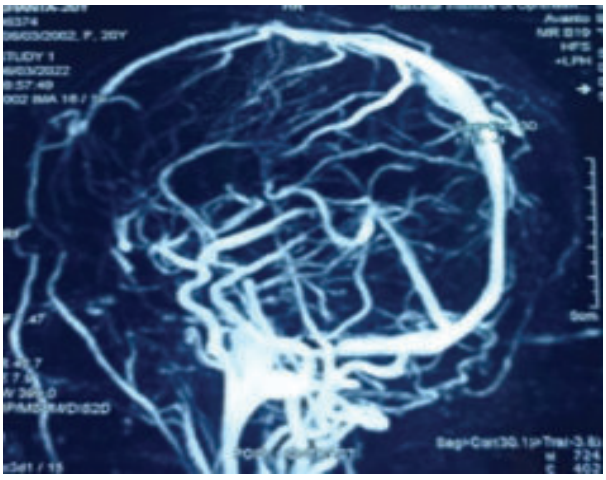

Figure 7: *Magnetic resonance venography(MRV) revealed normal patent dural venous sinuses.*

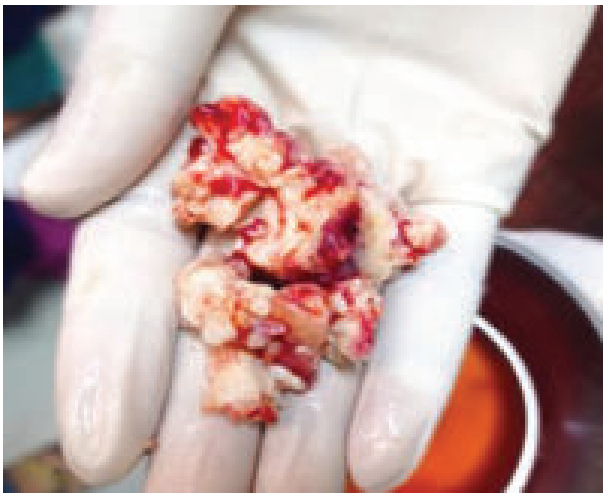

Figure 8*: The gross specimen shows irregular pieces of grayish-brown tissue with multiple caseation foci.*

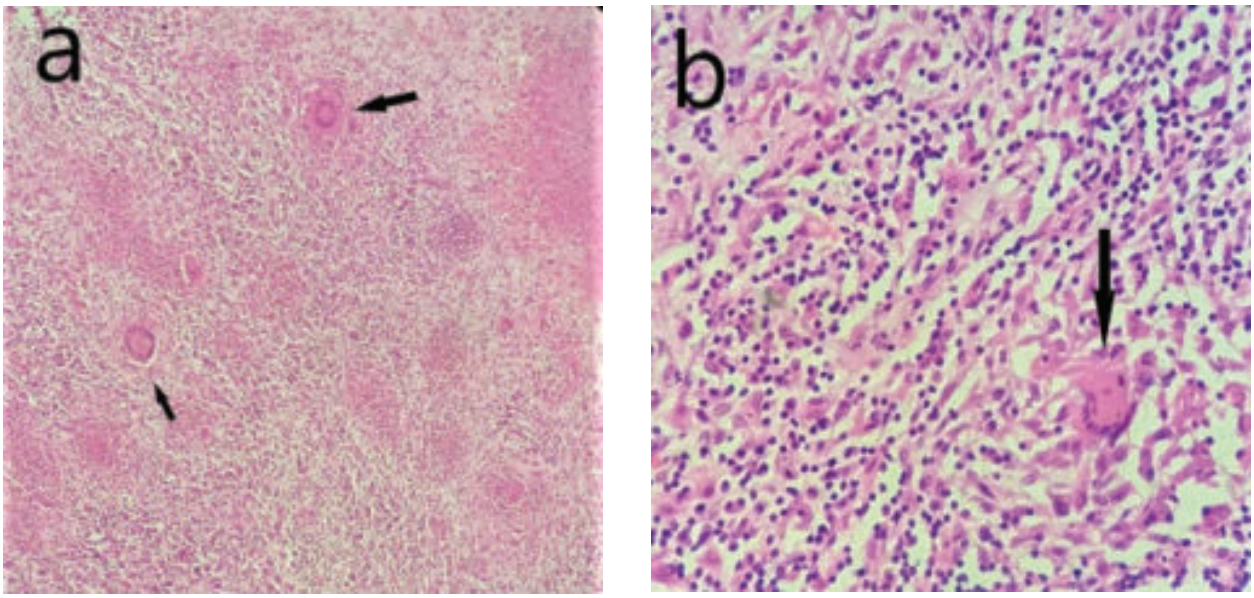

Figure 9(a,b): *Microscopic examination shows epitheliod granuloma with caseous necrosis and langhans type giant cells(marked by arrow). H&E stain*

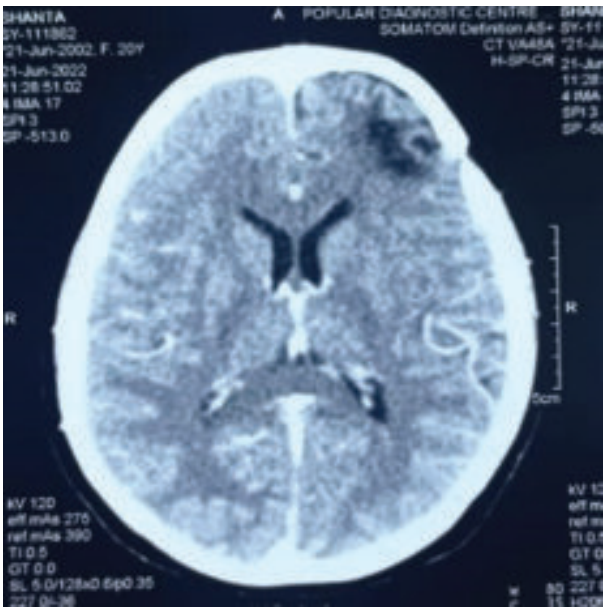

Figure 10*: Postoperative contrast CT scan axial shows no residual lesion, mild encephalomalacic change at operated site.*

Discussion:

Multiple CNS tuberculomas are more commonly associated with meningitis, whereas solitary CNS tuberculomas, in particular, are associated with less or atypical clinical manifestations[5]. Solitary large tuberculoma is frequently mistaken for a brain tumor and removed surgically[6], as in our case. Our patient presented with a headache for 4 months, a 2-month history of blurred vision and progressive weakness of the right side of her body, and characteristics of frontal lobe syndrome without any specific clinical signs or symptoms of TB. Risk factors for CNS TB are HIV, malignancy, immunosuppressive agents, age (children > adults), and alcoholism; With the increase in HIV patients, there is an increase in TB cases with increased CNS manifestations[6]. Our patient was immunocompetent and didn't have any significant risk factors for TB except her age and endemic geography, and therefore, we considered intracranial tuberculoma as a remote possibility. Constitutional symptoms, a history of current or known TB elsewhere in the body, and a history of intimate contact with a patient who has an open case of TB are clinical characteristics that may be helpful in differentiating tuberculomas from other brain tumors[4]. The patient in our case had no history of previous exposure, and there were no symptoms of systemic tuberculosis. She had clinical features including headache with nausea vomiting, blurring of vision, and weakness of the right side of the body that pointed to a slowly progressive mass lesion causing worsening of neurological deficits. Currently, a method for diagnosing tuberculoma is possible using diagnostic techniques based on clinical symptoms, such as cerebrospinal fluid (CSF) study, imaging, and biopsy characteristics[7]. Brain tuberculomas usually occur in isolation, with only 30% of patients having a positive chest radiograph[2], whereas the chest X-ray was normal in our patient. Other tests including CBC with ESR and MT test revealed normal. CSF analysis with smear, culture, and conventional and real-time PCR was not done due to papilloedema, no signs of meningism, and considering the cost-benefit ratio. Moreover, those are still too insensitive to confidently exclude the diagnosis on

laboratory grounds[8]. Regarding imaging, MRI cannot confidently diagnose tuberculomas in many cases as substantial overlap is known to occur with other focal brain lesions. However, non-invasive diagnosis of tuberculomas would obviate the need for biopsy, an invasive procedure fraught with risks[12]. Advanced imaging techniques, including MRS, perfusion MRI, diffusion weighted imaging (DWI), and susceptibility weighted imaging (SWI) are thought to increase diagnostic precision and eliminate the need for tissue biopsy[4]. A study reported that DWI offers no clear advantage in differentiating tuberculomas from metastasis and gliomas; the presence of a complete and regular peripheral hypointense ring in SWI favors the diagnosis of tuberculoma[9]. We carried out an MRI with MRS on our patient, which did not provide us with SWI sequences in our setting. Clino-radiologically, the patient was diagnosed as a suspected high-grade glioma. The indistinct radiological findings of intracranial tuberculoma can be due to the different stages of maturation[10]. A caseating tuberculoma with a solid center shows ring and central heterogeneous enhancement and is iso-to hypointense on T1-and T2-weighted MRI, whereas a caseating lesion with a liquid center shows ring enhancement and is hypointense on T1-and hyperintense on T2-weighted MRI[11]. In our case, the T1-weighted coronal plane magnetic resonance imaging (MRI) of the brain with contrast shows a well-defined ring enhancing lesion measuring(3.43.3) occupying the left frontal region with mass effects including midline shift, rim is thick and irregular, with adjacent convexity dural enhancement present . MRI Flair axial plane shows massive perilesional edema. Effacement of the ipsilateral lateral ventricle, obliteration of sulci/gyri demarcation, and midline shift . T2 weighted axial plane MRI shows the lesion is isointense. There are no major flow voids within or around the lesion. massive perilesional edema with mass effects . Diffusion-weighted MR imaging shows no restriction of diffusion. Tuberculomas may be differentiated from high-grade gliomas by their unique metabolite pattern on MRS[9]. The impact of combining MRI with MRS in improving the radiologist's ability to offer a single imaging diagnosis was significant[12]. Dissimilar aetiologies of the intracranial ring-enhancing lesions appear similar on conventional MRI whereas, the differential diagnosis of the neoplastic and non-neoplastic lesions is better diagnosed by MRS because of its higher specificity (93.3%) and sensitivity (87.5%) that produced varying success rates[13]. Tuberculomas may be differentiated from metastases and gliomas by their metabolite pattern consisting of elevated Cho/Cr ratio, reduced NAA/Cr and NAA/Cho ratios with presence of prominent lipid peak. Markedly elevated Cho/Cr ratio, reduced NAA/Cr and NAA/Cho ratios with/without lipid or lactate peak favors a diagnosis of neoplastic brain lesion[4]. MR spectrography in our patient shows choline peak is high with low NAA : creatinine peak, lipid and lactate level is significantly high. Choline peak along with lipid lactate elevation is a puzzle in MRS as it is found in a variety of conditions like high-grade gliomas, metastases, lymphomas, tuberculomas, demyelinating disorders, and to solve this puzzle, one should read spectra under the light of conventional MR imaging and clinical history and, if in doubt, should not hesitate to perform biopsy, especially in an endemic zone[14]. Therefore,in general, it appears to generate doubt and can make it difficult to differentiate between high grade glioma and tuberculoma in a case like ours because of some overlapping findings . Note: The presence of a lipid peak within it has long been thought to be a distinguishing feature of tuberculoma[15]. Although the presence of lipids is non-specific and can be present in high-grade gliomas and lymphomas, its absence makes the diagnosis of tuberculoma less likely[12]. However, recent studies have demonstrated a singlet peak at 3.8 ppm as another supportive feature of CNS tuberculomas. This peak is conspicuously absent in most high-grade gliomas and metastases. Its presence appears promising to help differentiate tuberculomas from malignant tumors[16]. In our case, there was no singlet peak at 3.8 ppm. CT-guided stereotactic methods have long been used for the diagnosis and treatment of intracranial masses. One study concluded that CT-guided stereotactic surgery of intracranial tuberculomas has advantages over other methods, with a potential to become the first-line modality, particularly as a diagnostic tool, in the management of these lesions[17]. Another case study recommended that the CT-guided stereotactic brain biopsy does not always yield the correct diagnosis, as the needle is not able to penetrate the dense capsule of the tuberculoma ,and therefore, open biopsy of the lesion is advised in these circumstances[18]. CT guided stereotactic biopsy did not seem to be a practical option in a setting with limited resources like ours. Depending on the MRI and MRS findings, a diagnosis of suspected high grade glioma is made in our patient.The management of brain tuberculomas is mainly pharmacological with different first-line antituberculous drugs; while some authors advocate empirical medical treatment without requiring histological confirmation, others believe that such treatment should be administered until a confirmatory diagnosis is obtained[19]. Giant tuberculoma is usually mistaken for other intracranial mass lesions, including malignant pathologies and taken up for surgery to find out to confirm the histopathological diagnosis as well to reduce the mass effect and reduce raised intracranial pressure. However, the management of giant tuberculoma

is still debated and a few authors advocate surgical resection of giant tuberculoma[2]. In the published literature, the majority of giant tuberculomas are treated surgically, both in adults and children[2] and our case is no exception to that. When a brain tuberculoma is more than 20 mm in size or causes a mass effect on the brain, surgery is required. Similar to other space-occupying lesions, it becomes surgically urgent when intracranial pressure is raised or when conventional therapy has entirely failed[19]. In our case, we promptly opted for surgery as clino-radiologically it was diagnosed as a malignant lesion. Though giant intracranial tubercula was our diagnostic differential given the patient's age and endemic demography, we were convinced to choose surgery in either possibility for its huge sige to reduce mass effect. However, a case report of giant intracerebral tuberculoma with significant mass effect (98.6cm) showed complete disappearance on antitubercular therapy alone in an 11-year-old boy[20]. It emphasizes the importance of a preoperative definitive confirmatory diagnosis to choose an appropriate treatment plan for better prognosis.

Conclusion

In an endemic region like Bangladesh, tuberculoma should always be included in the differential diagnosis of ICSOL. Giant tuberculoma may pose a diagnostic challenge due to variations in clinical and imaging presentations mimicking a brain tumor, non-specific initial work-up, disputed biopsy role, and economic constraints. Although many studies have shown that advanced MRI sequences and MRS can distinguish intracranial tuberculoma from malignant lesions, they sometimes mislead diagnosis and treatment plans. Therefore, a high index of suspicion, rational use of diagnostic investigations, and clinical and epidemiological correlation are necessary for an accurate diagnosis.

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