

Diffuse leptomeningeal tuberculoma masquerading as leptomeningeal gliomatosis: a case report and review of literature

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ABSTRACT:

- **Introduction:** Tuberculoma limited to the meninges as a result of mycobacterium tuberculosis infection is very rare and few cases have been reported on this clinical entity. Although some authors have described solitary forms of this presentation, no one reported a case on this diffuse occurrence. This diffuse pattern made the lesions mimic leptomeningeal gliomatosis on imaging studies.
- **Case presentation:** We present a case of a 72-years old man with a two (2) months history of right lower limb weakness and slurred speech which he initially did not take into a great deal of consideration. He had no cough, fever or chills, syncopal episodes. He has a past medical history of splenectomy and cholecystectomy as a result of a car accident 8 years before. Contrast enhanced MRI performed at our facility showed left diffused temporo-parieto-occipital meningeal thickening with multiple parenchymal nodules.
- **Conclusions:** Leptomeningeal tuberculomas should be suspected in patients who present with diffuse lesions of meninges although solitary or multiple forms of this kind of presentation frequently occur. The progress of the lesions or pathology from the time of first contact with mycobacterium depends on the immune response of the patient as well as the number and type of virulent strains involved. Open surgical biopsy to confirm the diagnosis is a very critical diagnostic step. The main treatment option is anti-TB medication and patients must be followed for a long time with series of imaging studies.
- **Keywords:** Leptomeningeal, Tuberculoma, Tuberculosis, Diffuse, Gliomatosis.

INTRODUCTION

Tuberculosis (TB) of the central nervous system (CNS) is symptomatic in 10-20% of patients with extra pulmonary TB, and merely 1% of patients advance into intracranial tuberculoma^{1,2}. Tuberculomas of the leptomeninges are rarer than the intracranial localizations²⁻⁴. It is very important to note that the immune system influences the different types of presentation of TB lesions. The pathological progression of the lesions from the time of first contact with mycobacterium depends on

the immune response of the patient⁵. Tuberculoma can be found in any part of the intracranial space and most often leads to increase intracranial pressure. The lesion may be solitary or multiple and may be seen with or without meningitis⁶. To the best of our understanding, only a few authors have reported cases of leptomeningeal tuberculoma and almost all the cases were solitary or multiple presentations and not diffused. We, therefore, present a rare case of diffuse leptomeningeal tuberculoma masquerading as leptomeningeal gliomatosis and review of literature.

CASE REPORT

We present a case of a 72-years old man with a two-month history of right lower limb weakness and slurred speech, which initially did not take seriously. His right limb weakness and slurred speech progressed gradually until they became worst and he decided to be seen at a local hospital in his community. He had no cough, fever or chills. He had no syncopal attacks. He has a past medical history of splenectomy and cholecystectomy as a result of motor accident eight years before. The family, however, denied past history of pulmonary tuberculosis or other infectious disease. On physical examination, his nutrition was satisfactory, no palpable lymph nodes, no abnormalities on the scalp. Chest examination was unremarkable.

Abdominal examination revealed right longitudinal incisional scar of about 15 cm. There were no obvious spinal deformities. Neurological examination revealed bilateral dilated pupils that react to light. No neck stiffness. The muscle bulk on the lower limbs was normal. Power was 5/5 on the left limb and 3/5 on the right limb with normal Babinskis reflexes. Routine preoperative laboratory investigations were all normal.

Chest computer tomographic scan (CT-Scan) done at our facility revealed interstitial involvement, signs of lung emphysema, and opacities at the right lower lobe with bilateral pleural effusion, potentially of infectious origin. We did not perform a diagnostic tap. Abdominal CT-scan was unremarkable except for prostate calcification, while Spinal CT-scan revealed degeneration of the lumbar vertebrae with bone hyperplasia. Magnetic resonance imaging (MRI) showed left diffused tempo-

ro-parieto-occipital meningeal thickening with multiple parenchymal nodules on contrast enhanced MRI. (Fig.1 A-D) The parenchyma of the occipital lobe was edematous with mild ischemia. The left lateral ventricle was constricted and the brain shifted to right. There were associated sinusitis and bilateral otitis media. A working diagnosis of inflammatory disease and tuberculoma was made to rule out leptomeningeal gliomatosis.

The aim of surgery in this patient was to get biopsy for substantive diagnosis and possible resection of the lesions if frozen section confirms that the lesion was leptomeningeal gliomatosis. After opening the skull bone, *dura mater* was opened and normal brain tissue was observed. A cauliflower-like lesion was seen at left parietal lobe, the boundary between the brain tissue and the lesion was seen clearly. The lesion was hard and tough with rich blood supply. After controlling perivascular and brain tissue bleeding, careful dissection of the surrounding tissues and the lesion, a sample of the lesion was finally obtained for frozen section examination. Intraoperative frozen section revealed "inflammatory granulation tissue". After performing total hemostasis, the excised *dura mater* was replaced with artificial *dura mater* and the bone flap was placed back and was secured with titanium plates and screws. The skin was closed in layers and wound was dressed with sterile gauze. The patient was sent to the recovery room.

Histological and immunohistochemical phenotypic evaluation of the specimen collected during surgery revealed a mycobacterium tuberculosis infection. After freezing the specimen with paraffin frozen section, we observed tumor necrosis microstructure with granulomatous inflammation (Fig. 2 A-B). Acid-fast bacilli were

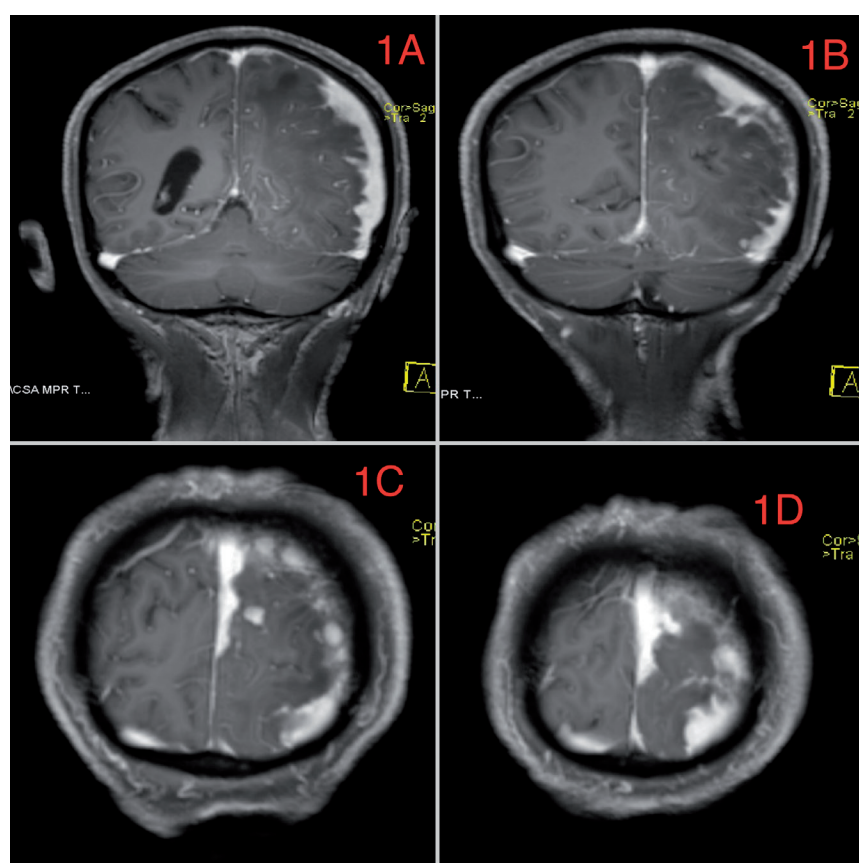


Figure 1. A-D, are MRI showing left diffused temporo-parieto-occipital meningeal thickening with multiple parenchymal nodules.

detected with the ziehl-Nelson staining (Fig. 2 C-D) while PAS and methenamine silver staining were negative. DNA fragment of tuberculous bacillus (*Mycobacterium tuberculosis*) was detected by polymerase chain reaction (PCR). The patient had a good post-operative recovery and was referred to the TB Department of our hospital where he was treated with anti-TB medications. He was subsequently referred back to his community hospital to continue his anti-TB medication.

DISCUSSION

Tuberculomas of the leptomeninges, without evidence of pulmonary or miliary tuberculosis is a very rare occurrence even in endemic areas of tuberculosis^{3,4}. We present a case of diffuse leptomeningeal tuberculoma mimicking leptomeningeal gliomatosis. Our case may also have pulmonary involvement, as well as pleura effusion, which we believe could also be pulmonary TB. We, however, did not do diagnostic tap to confirm the diagnosis. Hematogenous or contiguous spread from juxtameningeal foci, choroid plexus foci or osseous infection is almost always the route of spreading secondary TB infection of the CNS⁵. The hematogenous seeding of the leptomeninges and brain parenchyma ends in is the formation of enlarged tubercles, with a fibrous capsule. In most instances, the leptomeningeal tubercles remain attached or infiltrates the meninges, forming fibrous masses enclosed to the *dura mater* such as tuberculoma en-plaque or rupture into the subarachnoid space developing a Rich's foci^{1,7}.

In our patient, the leptomeningeal tubercles infiltrated the meninges resulting in a diffuse form of the disease. It is already known that the brain parenchyma round the tuberculomas evolves into a thick fibrous capsule around the lesion, which may enlarge sizably before the manifestation of symptoms. Andreula et al⁵ indicated that the type, severity and extent of the lesions depend on the number and virulence of acid fast bacilli as well as the immune status of the patient. We believe that the age of our patient as well as the immunological status could be predisposing factors. The patient also had splenectomy seven years ago, which further compromises his immune system and hence predisposes him to tuberculosis infection and the formation of tuberculoma.

Andreula et al⁵ further stated that the hypersensitivity to mycobacterium progresses into severe diffuse inflammation such as miliary infection, while, on the other hand, acute localized caseous infection is usually due to adequate immune response, and acute meningitis is typical of immunocompromised patients. Our patient, however, did not have human immunodeficiency virus (HIV) infection. Clinical diagnosis of leptomeningeal TB is very challenging especially when the patient does not have active systemic manifestation of the disease or past medical history of the disease³. The clinical manifestations of leptomeningeal tuberculomas depend on the localization of the lesions and nature of the lesion (solitary, multiple or diffuse), as well as the progressing of the disease which usually generates a mass effect with signs and symptoms of increased intracranial pressure³. The clinical presentation can advance gradually or quickly with or without fever³.

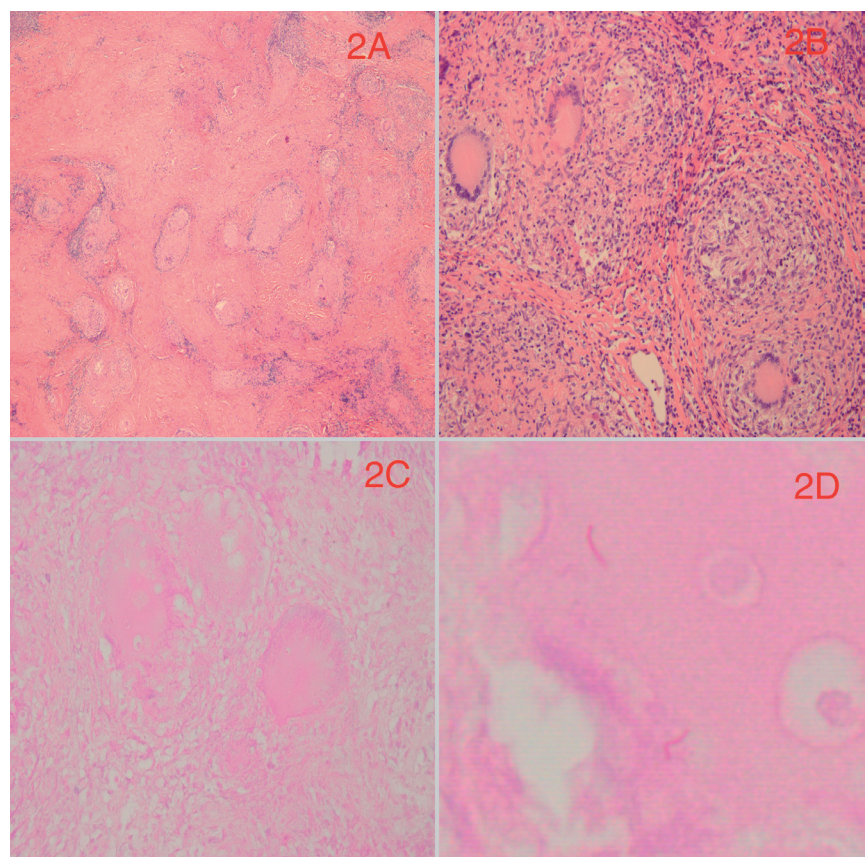


Figure 2. A-B, are HE staining while; C-D, are ziehl-Nelson staining. 2A is HEx40 while 2B is HEx200 both showing necrotic caseous center enclosed by a capsule that contains fibroblasts, epithelioid cells, Langhans giant cells, and lymphocytes. 2C is ziehl-Nelson x 400 while 2D is a magnification of 2C showing acid-fast bacilli.

The radiological findings of leptomeningeal muddling are not specific of TB, and a number of diseases, such as leptomeningeal carcinomatosis, intracranial fibromatosis, lymphoma, meningioma, sarcoidosis, and syphilis, need to be considered in the differential diagnosis^{6,8}. On non-enhanced CT scans, tuberculoma may be isodense, hyperdense, or of mixed density while on contrast enhanced CT, it may be associated with ring-like enhancement or infrequently, as an area of nodular or irregular nonhomogeneous enhancement. The diagnosis is usually prompted by a central calcification with surrounding ring-like enhancement, known as the 'target sign'^{6,9}. On MRI, however, non-enhanced studies indicate a mixed and largely low signal intensity lesion with a central zone of high signal intensity and surrounding high signal intensity edema on T2-weighted or FLAIR images⁶. The central high-signal intensity zone matches with caseation and necrosis and the low signal intensity of the capsule may be associated with a layer of collagenous fibrosis with high protein concentration and low water content^{6,10}.

Anti-TB medications are the main treatment for TB patients regardless of whether it is a symptomatic or asymptomatic presentation^{1,3,5,6}. Close follow-up with suitable neuroimaging is advised in cases of CNS tuberculomas because the relapse rate is high after anti TB medication and the radiological resolution of the lesions takes a long time, particularly in immunocompromised patients^{1,3}. A radiological resolution study piloted by Poonnoose et al with histologically proven tuberculomas treated with anti-TB therapy revealed that more than two thirds of patients with partially excised or biopsied intracranial tuberculomas demonstrated persistent lesions on CT scans up to 18 months after therapy. They, therefore, suggested that some patients with intracranial tuberculomas might require prolonged anti-TB therapy depending on the radiological resolution of their lesions^{1,7}. Histologically, the mature tuberculoma is made up of a necrotic caseous center enclosed by a capsule that contains fibroblasts, epithelioid cells, Langhans giant cells, and lymphocytes^{1,11}.

CONCLUSIONS

Leptomeningeal tuberculomas, although very rare, should be suspected in patients who present with diffuse lesions of meninges; however, solitary forms of the leptomeningeal tuberculomas frequently occur. The progression of the lesions from the time of first contact with mycobacterium depends on the immune response of the patient as well as the number and type of virulent strains involved. Open surgical biopsy to confirm the diagnosis is very crucial in this kind of presentation. The main treatment option is anti-TB medication and patients must be followed for a long time with series of imaging studies.

AUTHORS' CONTRIBUTIONS:

SAR and YL conceived the project and SAR designed the study. SAR and RL collected patient's data. CL pro-

vided the pathology report and pictures. YL provided technical assistance in the study. SAR analyzed the data, prepared the illustrations and wrote the paper. All authors approved the paper for the submission.

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All the authors have no competing interest to disclose.

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CONSENT FOR PUBLICATION:

The patient and his relatives were dually informed about our intention to publish his case and he/they fully consented to the use of his documents. The hospital also consented to the use of this information for publication.

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REFERENCES

- Kocaeli H, Taşkapılıoğlu Ö, Başaran E, Karaoğlu A, Bekar A. Multiple dural tuberculomas presenting as leptomeningeal carcinomatosis. *Case reports in Neurological Medicine* 2011; pp.4.
- Lindner A, Schneider C, Hofmann E, Soerensen N, Toyka KV. Isolated meningeal tuberculoma mimicking meningioma: case report. *Surg Neurol* 1995; 43: 81-83.
- Tseng MY, Kao MC, Chiu CT. Isolated leptomeningeal tuberculoma. *Journal of the Formosan Medical Association Taiwan Yi Zhi* 1999; 98: 361-364.
- Tseng SH, Chen Y, Shun CT. Isolated dural tuberculoma. *Acta Neurochir (Wien)* 1997; 139: 263-264.
- Andreula C, Recchia-Luciani A. Isolated leptomeningeal spinal tuberculosis: case report. *Rivista di Neuroradiologia* 1998; 11: 211-214.
- Sanei Taheri M, Karimi MA, Haghighatkah H, Pourghorban R, Samadian M, Delavar Kasmaei H. Central nervous system tuberculosis: an imaging-focused review of a re-emerging disease. *Radiol Res Pract* 2015; 2015: 202806.
- Dastur DK, Manghani DK, Udani P. Pathology and pathogenetic mechanisms in neurotuberculosis. *Radiol Clin North Am* 1995; 33: 733-752.
- Berenguer J, Moreno S, Laguna F, Vicente T, Adrados M, Ortega A, González-LaHoz J, Bouza E. Tuberculous meningitis in patients infected with the human immunodeficiency virus. *N Engl J Med* 1992; 326: 668-672.
- Whiteman M. Neuroimaging of central nervous system tuberculosis in HIV-infected patients. *Neuroimaging Clin N Am* 1997; 7: 199-214.
- Ku B, Yoo S. Extensive meningeal and parenchymal calcified tuberculoma as long-term residual sequelae of tuberculous meningitis. *Neurol India* 2009; 57: 521-522.
- Kim TK, Chang KH, Kim CJ, Goo JM, Kook MC, Han MH. Intracranial tuberculoma: comparison of MR with pathologic findings. *AJNR Am J Neuroradiol* 1995; 16: 1903-1908.