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Intracranial tuberculoma masquerading as a brain tumor: A rare presentation in a healthy young adult with no prior history of tuberculosis

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Case presentation

An 18-year-old woman presented to the neurology clinic in May 2021 with a 9-month history of gradually worsening headaches with left-sided weakness and numbness. She reported recently experiencing several episodes of generalized tonic-clonic seizures, and her family added that she had become forgetful and irritable of late. She denied any illicit drugs use, and there was no history of fever or weight loss. Hematologic studies were non-contributory. A computed tomography (CT) scan of the head revealed unspecific findings. Cerebrospinal fluid (CSF) analysis demonstrated an opening pressure of 27 cm H2O, a colorless appearance, a lymphocytic pleocytosis (479/mm^3 total white cell count: 54 polymorphs, 425 lymphocytes), a red blood corpuscle count of 41/mm^3, a protein level of 2.09 g/L (209 mg/dl), a glucose level of 1.1 mmol/L (5.5 mmol/L blood), no visible organisms on Gram or Indian ink stains, and a negative acid-fast bacillus (AFB) testing. The patient was scheduled for a brain magnetic resonance imaging (MRI), which showed a well-circumscribed, ring-enhancing nodular lesion in the right thalamus, compressing the third ventricle without causing hydrocephalus (Fig. 1, **panel A**). Furthermore, the lesion demonstrated an accentuated hypointensity on T2-weighted imaging (T2WI) and mild perilesional edema on the fluid attenuation inversion recovery (FLAIR) sequence (Fig. 1, **panel B**). With susceptibility-weighted imaging (SWI), no presence of hemorrhage or calcification was evident, and the lesion content did not restrict the diffusion on diffusion-weighted imaging (DWI) (Fig. 1, **panel C**). The data obtained that far favored the diagnosis of tuberculoma [1,2], although being unconfirmed, with other possibilities such as a fungal abscess or a benign neoplasm included in the differential diagnoses list [3,4]. Therefore, the patient was scheduled for surgery, and due to the clear surgical cleavage plane, the mass was resected as a single piece measuring 3 cm in diameter (Fig. 1, **panel D**). Histopathological evaluation of the mass revealed a centrally necrotic caseating lesion surrounded by lymphocytes, epithelioid, and Langhans multinucleated giant cells, consistent with the diagnosis of tuberculoma, which was later confirmed by the visualization of acid-fast bacilli on Ziehl-Neelsen stain (Fig. 2). The patient stated no prior knowledge of

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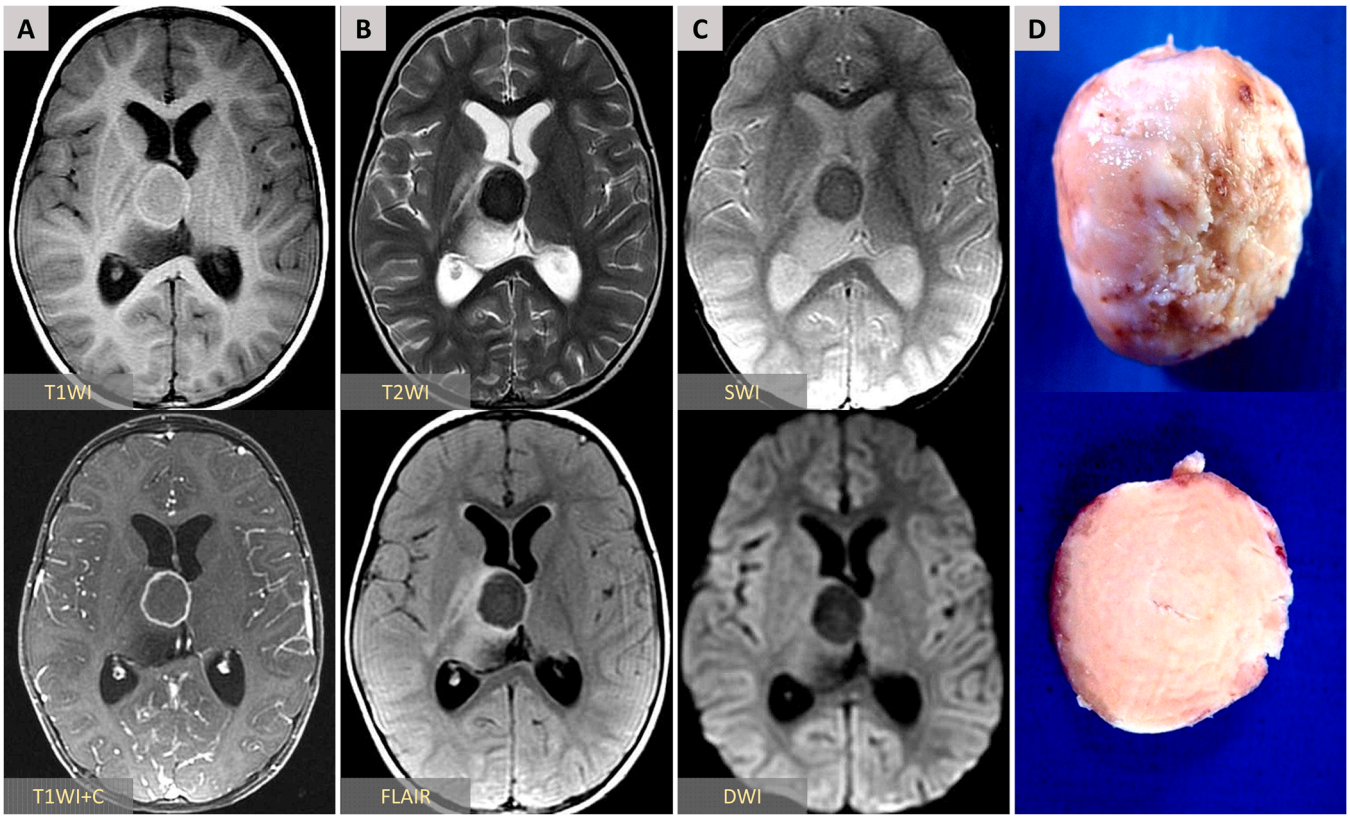

Fig. 1. Axial brain MRI through the level of basal ganglia and thalami revealing a well-circumscribed, ring-enhancing nodular lesion in the right thalamus, compressing the third ventricle without causing hydrocephalus (**panel A**). The lesion demonstrates an accentuated hypointensity on T2WI and mild perilesional edema on the FLAIR sequence (**panel B**). No presence of hemorrhage or calcification is evident on susceptibility-weighted imaging (SWI), and the lesion content shows no diffusion restriction on diffusion-weighted imaging (DWI) (**panel C**). A gross image of the resected mass (**panel D**) shows a discrete smooth mass with a diameter of 3 cm, with no observed areas of hemorrhages or necrosis.

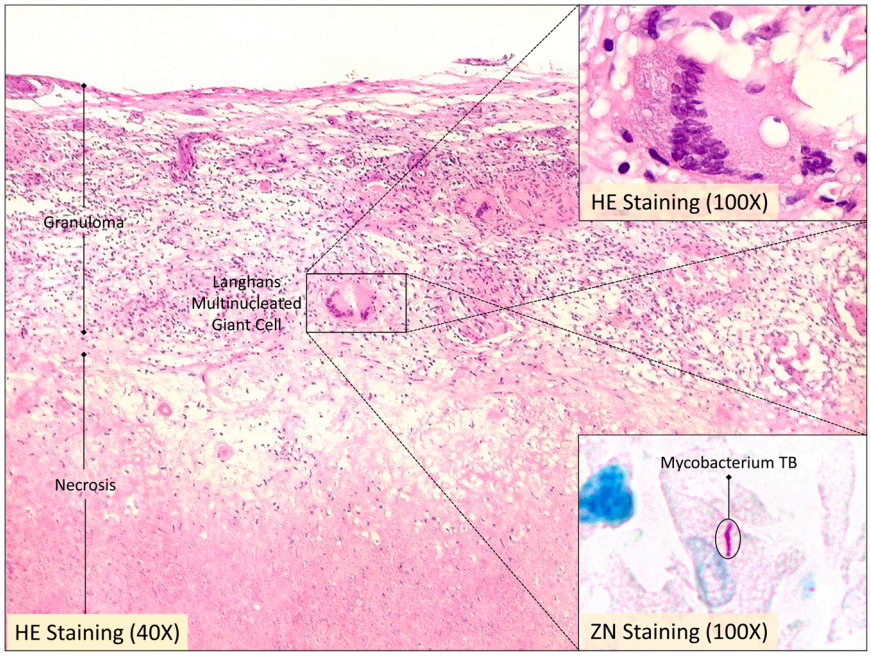

Fig. 2. Histopathological images of the resected mass demonstrating a centrally necrotic caseating lesion surrounded by lymphocytes, epithelioid, and Langhans multinucleated giant cells. An acid-fast bacillus was detected on the Ziehl-Neelsen stain, consistent with Mycobacterium tuberculosis. [Of note, the microbiology lab stated that visualizing the bacilli in this sample was technically challenging compared to other specimens they had previously dealt with].

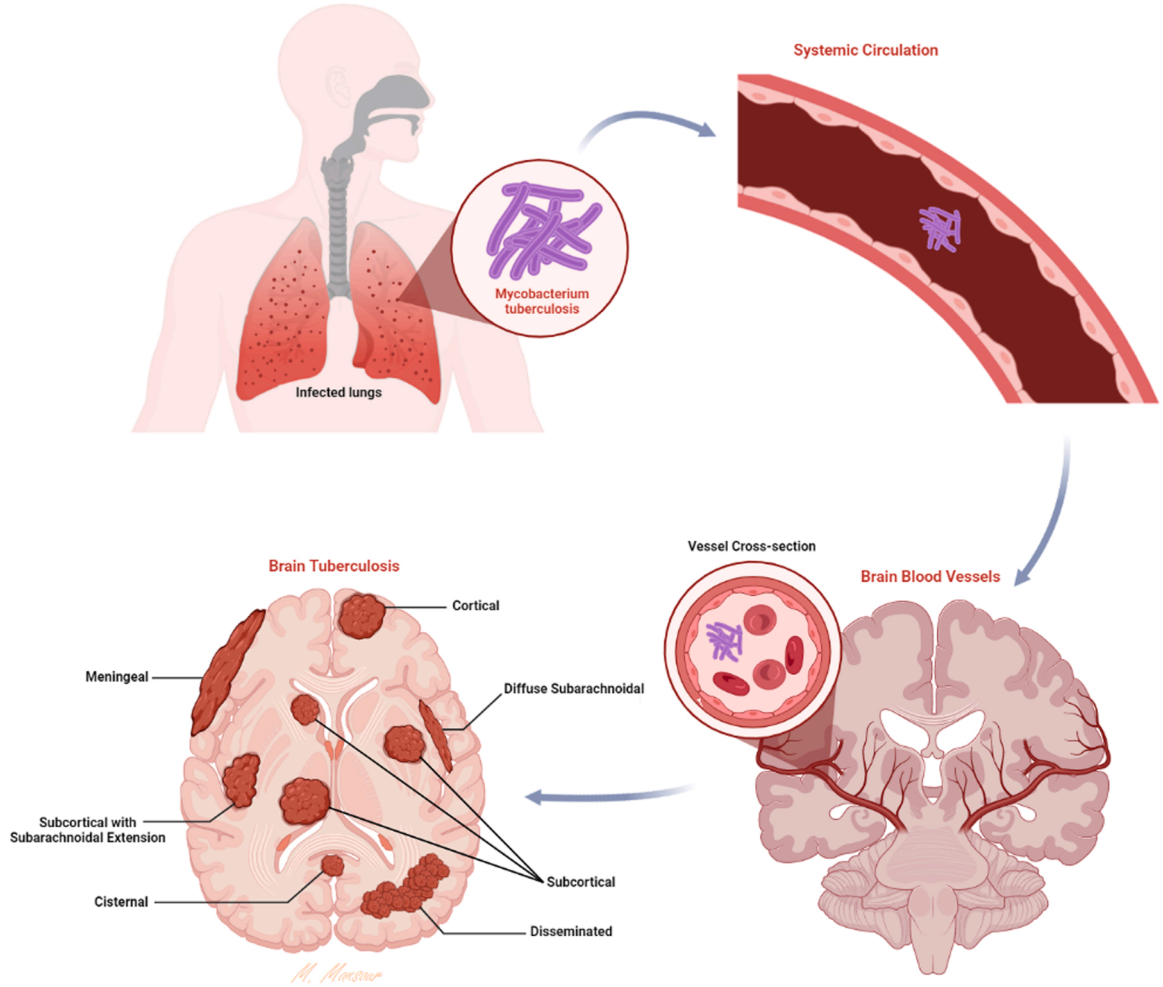

Fig. 3. Schematic illustration of the underlying pathophysiologic route of brain tuberculosis as a consequence of pulmonary infection. Potentially affected areas in intracranial tuberculosis are outlined.

Table 1
Classification of intracranial tuberculosis based on axial locations.

Location	Examples	Predominant Manifestations
Extra-axial	- Tuberculous leptomeningitis. - Tuberculous pachymeningitis.	Meningism (headache, neck stiffness, and photophobia).
Intra-axial	- Intracranial tuberculoma/ abscess. - Focal tuberculous cerebritis - Tuberculous rhombencephalitis. - Tuberculous encephalopathy.	Focal Neurologic Deficit (+/- seizures).

having tuberculosis (TB) and denied any contact with TB patients. Interestingly, her chest and abdominal CT scans were unremarkable and she tested negative for human immunodeficiency virus (HIV) antibodies. Negative testing also included polymerase chain reaction (PCR) for TB in blood and CSF, as well as mycobacterial culture. The patient was then treated for 18 months with rifampicin, isoniazid, pyrazinamide, and ethambutol, along with 60 mg daily prednisone for the first 2 months as well as levetiracetam 500 mg twice daily for seizure prophylaxis. On November 2022, during her follow-up in the 18th month of therapy, the patient showed marked improvement in her headache, behavior, seizures, sensory and motor symptoms, with no evidence of tuberculoma recurrence on repeated MRI studies.

Case discussion

Neurotuberculosis generally results from hematogenous dissemination, mostly from a pulmonary origin as outlined in (Fig. 3), and constitutes approximately 1% of all tuberculosis, with 5–10% of cases presented with extrapulmonary tuberculosis in immunocompetent patients, and up to 50% in immunocompromised patients [5]. The common spectrum of CNS involvement includes tuberculous meningitis, tuberculoma(s), focal cerebritis, and tubercular abscess(es) [6]. For clinical and anatomical purposes, and based on our clinical experience, intracranial tuberculosis can also be classified as intra-/extra-axial based on the presenting symptoms (Table 1), and localized/non-localized based on the anatomical location(s) involved as outlined in (Fig. 4).

Tuberculoma begins as a non-caseating granuloma consisting of a necrotic center surrounded by lymphocytes, epithelioid macrophages, and Langhans giant cells encircled by a richly vascular zone as illustrated in (Fig. 5). These lesions can further evolve into caseating abscesses or may continue to grow to form a giant tuberculoma [7]. The caseating center is initially solid and is composed of a cheesy material with a high lipid content, macrophage infiltration, fibrosis/gliosis, free radicals, and may contain few bacilli. The center is surrounded by a thick collagenous capsule, epithelioid cells, multinucleated giant cells, and macrophages. Tuberculomas are commonly accompanied by extensive perilesional edema [8].

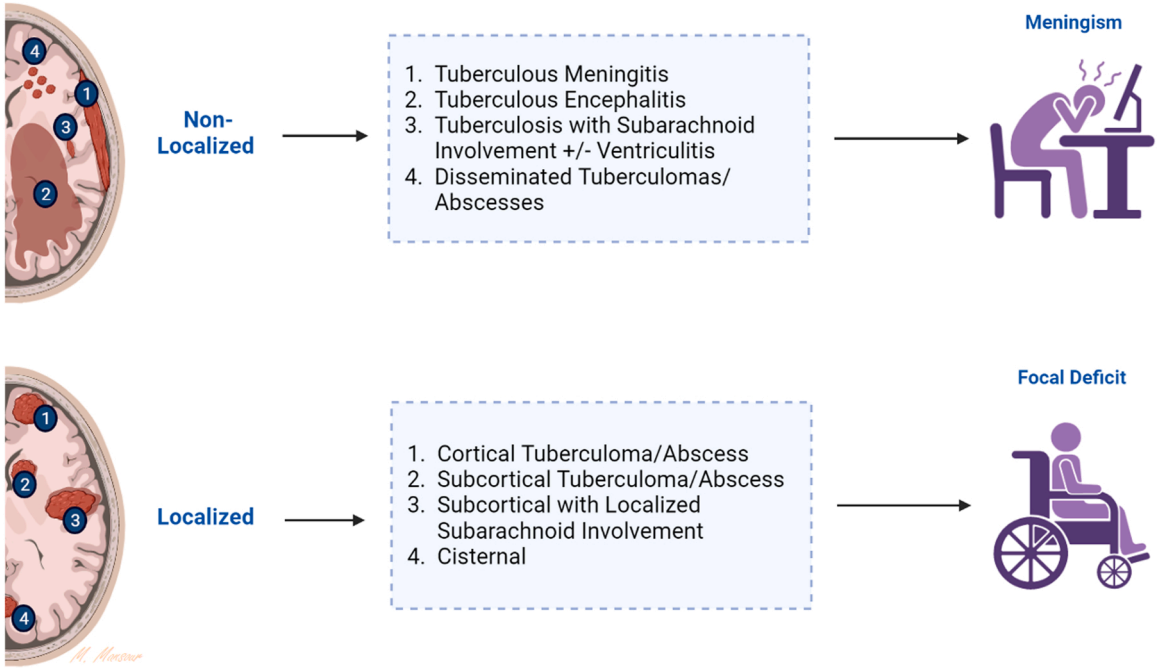

Fig. 4. Schematic illustration of the authors' proposed classification of intracranial tuberculosis based on the affected region(s) and the predominant manifestation(s).

On imaging, giant tuberculoma can be a diagnostic dilemma and can mimic tumoral lesions. Imaging features vary according to the caseating or non-caseating contents [9]. Non-caseating tuberculomas are usually isointense to hypointense on T1-weighted images, hyperintense on T2-weighted images, and hyperintense on FLAIR. Nodular or ring enhancement may be seen with diffusion restriction. Caseating tuberculomas possessing a solid center demonstrate relatively isointense to hypointense signals on both T2- and T1-weighted images. These lesions are surrounded by a rim of variable thickness that may appear hyperintense on T1- and T2-weighted images with ring enhancement; evidence of diffusion restriction is noticeably absent [2,10,11] as perfectly demonstrated in our patient.

When encountering a case of brain tuberculosis, it is of high importance to analyze the patient's clinical course and any associated risk factors that might have predisposed to an immunosuppression status, and hence acquiring an opportunistic infection such as Mycobacterium tuberculosis (MTB). However, it is not a must to find any [12–14]. CSF analysis plays a major role in the diagnosis of brain tuberculosis, which typically demonstrates normal-high opening pressure, lymphocytic pleocytosis, elevated protein, and low-normal glucose levels; however, it might be unspecific especially when brain tuberculoma is the only demonstrated lesion. Furthermore, it has been reported that Ziehl-Neelsen staining and culture of the CSF for MTB can be negative when only brain parenchyma is involved as the patient we present in our case [15–17]. MTB antigen- and cell-free-DNA-based PCR assays of the patient's CSF can be useful to diagnose brain tuberculoma; however, they might not be useful for a rapid diagnosis and treatment [18,19].

The followed management regimen for cases with brain tuberculoma, including the duration of treatment, and whether or not surgery is favored, is an area of major debate [20]. Although Rajeswari et al. showed that a 9-month course of antituberculous treatment (ATT) was effective in 88% of the patients involved in their study [21], Nair et al. demonstrated that some patients may require longer periods of treatment (>24 months) [22]. Although the treatment of brain tuberculomas is generally medical, surgery might be required in uncertain diagnoses to obtain a tissue specimen for culture and sensitivity, or to reduce a raised intracranial pressure or local mass effects [23]. Furthermore, surgery was found to decrease the duration of ATT and achieve earlier resolution of the lesions compared to ATT alone [24].

Conclusions and take-home points

1. Intracranial tuberculomas can often be a diagnostic imaging dilemma and can mimic tumoral pathologies.
2. The imaging features vary according to the caseating or non-caseating contents.
3. Solo parenchymal involvement in intracranial tuberculomas might report negative results of CSF analysis.
4. Antituberculous treatment for a prolonged period of time is the mainstay of management of cases with intracranial tuberculomas.
5. Neurosurgical intervention is required when ATT fails, or when there is a significant mass effect produced by the tuberculoma (i.e., manifestations of high intracranial pressure, diameter >20 mm).

Ethics approval

The approval was obtained from the Ethics Committee of Al-Azhar University Hospitals, reference number HSUZ-21-0004521.

Consent

The patient gave written informed consent to publish the case and any related data.

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CRediT authorship contribution statement

M.M. was responsible for the conception of the work, data collection, drafting the article, critical revisions, illustrating the figures, and obtaining approval of the final version of the manuscript. Z.A. contributed by drafting the article, and critical revisions. A.A. and H.A. contributed by critical revisions of the article. All authors read the final

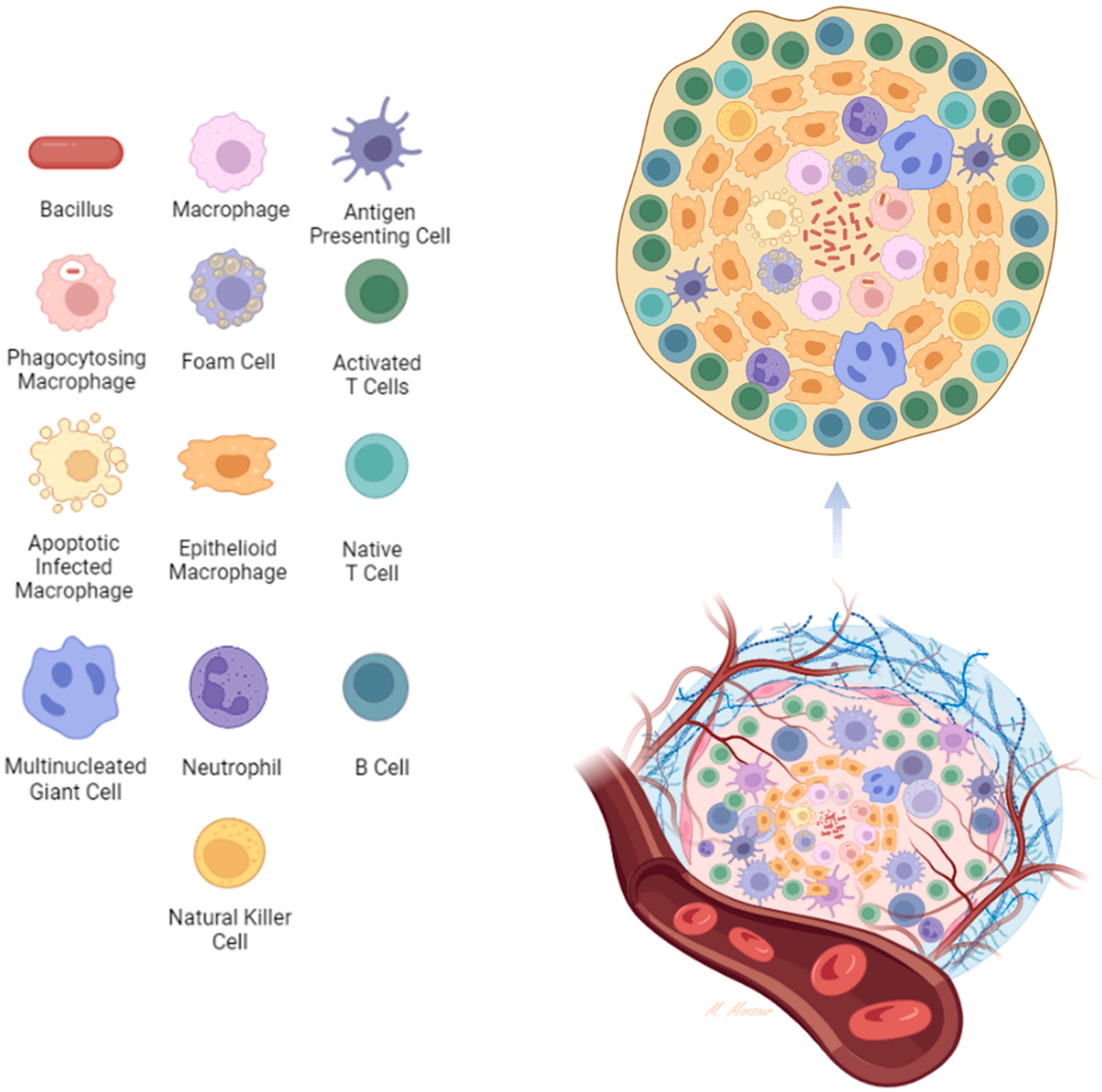

Fig. 5. Schematic illustration demonstrating histopathologic orientation and cellular organizations of brain tuberculous granuloma.

manuscript and were involved in direct patient care.

Acknowledgments

Not applicable.

Competing Interests

None declared.

References

[1] Patkar D, Narang J, Yanamandala R, Lawande M, Shah GV. Central nervous system tuberculosis: pathophysiology and imaging findings. Neuroimaging Clin N Am 2012;22(4):677–705.
[2] DeLance AR, Safaee M, Oh MC, Clark AJ, Kaur G, Sun MZ, et al. Tuberculoma of the central nervous system. J Clin Neurosci 2013;20(10):1333–41.
[3] Luthra G, Parihar A, Nath K, Jaiswal S, Prasad KN, Husain N, et al. Comparative evaluation of fungal, tubercular, and pyogenic brain abscesses with conventional and diffusion MR imaging and proton MR spectroscopy. AJNR Am J Neuroradiol 2007;28(7):1332–8.
[4] Huisman TA. Tumor-like lesions of the brain. Cancer Imaging 2009;9 Spec No A (Special issue A):S10–3.
[5] Thakur K, Das M, Dooley KE, Gupta A. The global neurological burden of tuberculosis. Semin Neurol 2018;38(2):226–37.
[6] Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. Ann Intern Med 2008;149(3):177–84.
[7] Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev 2008;21(2):243–61.
[8] Murthy JM. Management of intracranial pressure in tuberculous meningitis. Neurocrit Care 2005;2(3):306–12.
[9] Khatri GD, Krishnan V, Antil N, Saigal G. Magnetic resonance imaging spectrum of intracranial tubercular lesions: one disease, many faces. Pol J Radio 2018;83:e524–35.
[10] Gupta RK, Kumar S. Central nervous system tuberculosis. Neuroimaging Clin N Am 2011;21(4):795–814 (vii-viii).
[11] Kumar D, Sheoran RK, Bansal SK, Arora OP. Revisiting the CNS tuberculosis with emphasis on giant tuberculomas and introducing the "outer rim excrescence sign". Neuroradiol J 2011;24(3):357–66.
[12] Guler SA, Bozkus F, Inci MF, Kokoglu OF, Ucmak H, Ozden S, et al. Evaluation of pulmonary and extrapulmonary tuberculosis in immunocompetent adults: a retrospective case series analysis. Med Princ Pr 2015;24(1):75–9.
[13] Kang W, Yu J, Du J, Yang S, Chen H, Liu J, et al. The epidemiology of extrapulmonary tuberculosis in China: A large-scale multi-center observational study. PLoS One 2020;15(8):e0237753.
[14] Sunnetcioglu A, Sunnetcioglu M, Binici I, Baran AI, Karahocagil MK, Saydan MR. Comparative analysis of pulmonary and extrapulmonary tuberculosis of 411 cases. Ann Clin Microbiol Antimicrob 2015;14:34.
[15] Gómez B, Zarco LA. Tuberculomas cerebrales reporte de un caso. Univ Méd Bogotá 2010;51:220–7.

[16] Calderón-Garcidueñas AL, Peña-Rúelas CI, Ríos-Sarabia NI, Rodríguez-de la Rosa R. Tuberculosis cerebral y espinal en una paciente inmunocompetente sin daño pulmonar. Rev De Esp Méd-Quir 2012;17:235–8.
[17] Talamás O, Del Brutto OH, García-Ramos G. Brain-stem tuberculoma. An analysis of 11 patients. Arch Neurol 1989;46:529–35.
[18] Singh KK, Nair MD, Radhakrishnan K, Tyagi JS. Utility of PCR assay in diagnosis of en-plaque tuberculoma of the brain. J Clin Microbiol 1999;37:467–70.
[19] Perez-Malagon CD, Barrera-Rodriguez R, Lopez-Gonzalez MA, Alva-Lopez LF. Diagnostic and Neurological Overview of Brain Tuberculomas: A Review of Literature. Cureus 2021;13(12):e20133.
[20] Ramachandran R, Muniyandi M, Iyer V, Sripriya T, Priya B, Govindarajan TG. Dilemmas in the diagnosis and treatment of intracranial tuberculomas. J Neurol Sci 2017;381:256–64.
[21] Rajeswari R, Sivasubramanian S, Balambal R, et al. A controlled clinical trial of short-course chemotherapy for tuberculoma of the brain. Tube Lung Dis 1995;76:311–7.
[22] Nair BR, Rajshekhar V. Factors predicting the need for prolonged (>24 months) antituberculous treatment in patients with brain tuberculomas. World Neurosurg 2019;125:e236–47.
[23] Rajshekhar V. Surgery for brain tuberculosis: a review. Acta Neurochir (Wien) 2015;157(10):1665–78.
[24] Chandra Vemula R, Prasad BCM, Koyalmantham V, Hanu G. Role of surgery in intracranial tuberculomas and proposal of a novel diagnostic criteria for diagnosis (Sri Venkateswara Institute of Medical Sciences Criteria). World Neurosurg 2020;138:e52–65.