

Commentary

In this Journal issue, the authors describe an 11-year-old boy presenting with a solitary ring enhancing lesion in the midbrain with pronounced perifocal edema.^[1] Magnetic resonance spectroscopy (¹H-MRS) was notable for increased lipid peak that led to a diagnosis of central nervous system (CNS) tuberculoma. Empirical antituberculosis (TB) treatment resulted in clinical improvement that was sustained at 18 months follow-up. The case illustrates an increasing importance of noninvasive radiological techniques for diagnosis and treatment guidance of CNS tuberculoma.

TB remains among the leading causes of morbidity and mortality with CNS involvement occurring in up to 5% of patients.^[2] In endemic regions, CNS tuberculomas comprise up to 30% of all intracranial mass lesions. Therefore, CNS tuberculoma should be included in the differential diagnosis in anyone presenting with intracranial mass lesion with or without TB risk factors. However, the diagnosis of CNS tuberculoma can be difficult if based solely on clinical presentation and routinely available imaging methods. For example, tuberculin skin test and chest radiographic are often negative and should not be used to rule out CNS TB. Routine brain imaging modalities, such as computed tomography (CT) and magnetic resonance imaging, usually demonstrate nonspecific findings that are similar to other CNS infections, CNS lymphoma, and brain metastases.^[3]

A constantly increasing body of evidence suggests that ¹H-MRS can be valuable noninvasive imaging tool with high diagnostic yield for CNS tuberculoma. Elevated lipid peak is the most specific ¹H-MRS findings for CNS tuberculoma because cell wall of mycobacteria is predominantly composed of lipids. For example, Santy *et al.* demonstrated lipid peak on ¹H-MRS in four pediatric patients presenting with presumable CNS tuberculoma.^[4] However, infection with *Mycobacterium tuberculosis* was not confirmed by the means of culture or molecular methods in the latter study. Another study from Peru in patients presenting with single

enhancing brain lesions demonstrated that ¹H-MRS reliably distinguished between CNS tuberculoma and neurocysticercosis, with tuberculomas demonstrating high lipid peak, more choline, and less N-acetylaspartate and creatine.^[5] However, another study for China that included 19 patients with intracranial tuberculomas and 22 patients with high-grade gliomas (HGGs) found significantly lower choline/creatinine and choline/N-acetylaspartate ratio in CNS tuberculomas relative to HGGs, while lesion-to-normal brain lipid ratio was similar between the two patient groups.^[6] These findings suggest that ¹H-MRS is a promising diagnostic tool for CNS tuberculoma that provides with pathogenically specific biochemical information for *M. tuberculosis* infection. However, further research in larger patient populations validating the clinical utility of ¹H-MRS for differentiating CNS tuberculoma from other ring enhancing mass lesions should be performed. There should be efforts to combine currently existing raw ¹H-MRS data from smaller case series and case reports into a larger dataset to identify ¹H-MRS fingerprints of CNS tuberculoma.

Albeit ¹H-MRS is becoming increasingly used for diagnosis and treatment guidance of CNS tuberculoma patients, but it should be recalled that definitive diagnosis of TB requires isolation of *M. tuberculosis* or positive acid-fast stain in tissue biopsy.^[2] The major advantages of definite tissue diagnosis are expedited initiation of effective treatment interventions and avoidance of side effects associated with potentially ineffective empirical therapy. Furthermore, due to a high prevalence rate of drug resistance, universal drug susceptibility testing of *M. tuberculosis* is strongly recommended by the World Health Organization.^[1] It is estimated that 3.3% of new TB cases are multidrug-resistant TB (MDR-TB), and of these, 9.7% of patients have extensively drug-resistant TB defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable medication.^[2] Therefore, drug susceptibility of *M. tuberculosis* should be considered when choosing treatment regimen.

Toward this end, a stereotactic CT-guided biopsy is safe and accurate diagnostic intervention for lesions located in eloquent brain areas and deep-seated locations, such as brainstem, thalamus, and basal ganglia. It is recommended that biopsy should be considered in all suspected CNS tuberculoma cases.^[7,8] For example, a study in 20 patients presenting with CNS tuberculomas based on CT scan results reported that stereotactic biopsy was diagnostic in 17 cases, and nonspecific inflammatory changes were found in 3 patients. There was no procedure-related morbidity or mortality.^[8] Similarly, a recent systemic review of stereotactic biopsy procedures for brainstem tumors that included 38 studies with a total of 1480 biopsy procedures found high diagnostic success rate (96.2%) with low rates of overall morbidity (7.8%), permanent morbidity (1.7%), and mortality (0.9%).^[9] The experience of the center was the only factor significantly associated with diagnostic success rate. These findings strongly suggest that stereotactic biopsy of brainstem lesion is valuable and safe procedure in experienced hands.

Despite continuously increasing accuracy and availability of noninvasive diagnostic imaging modalities, such as ¹H-MRS, it should be recalled that tissue biopsy remains the golden standard that provides with an important diagnostic information and can significantly alter the treatment plan. It can be performed safely and with high diagnostic accuracy in experienced hands and should be considered in all patients.

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