Multiple Meningeal Tuberculomas Recurring After 18-Month Anti-tuberculous Chemotherapy
—Case Report—

Hideo TAKESHIMA, Takashi KAWAHARA, and Jun-ichi KURATSU

Department of Neurosurgery, Faculty of Medicine, Kagoshima University, Kagoshima

Abstract

A 26-year-old man with multiple intracranial masses widely attached to the dura presented with hypopituitarism and sexual impotence. Magnetic resonance imaging showed the lesions were isointense on the T1-weighted and hypointense on the T2-weighted images, and involved the bilateral sphenoid ridges, the convexity, and tentorial incisura. The lesion was partially removed via the right pterional approach. Histological examination identified tuberculoma associated with giant cells and caseous necrosis. Although his neurological and radiological signs worsened paradoxically during anti-tuberculosis therapy, he recovered spontaneously upon continuation of the anti-tuberculous treatment. However, he suffered recurrence as tuberculous meningitis, after administration of anti-tuberculous therapy for 18 months. Additional anti-tuberculous treatment for 12 months stabilized the disease. Tuberculoma should be included in the differential diagnosis of enhanced intracranial mass lesions. Anti-tuberculous therapy may require extended periods of up to 36 months to stabilize the disease.

Key words: meningeal tuberculoma, paradoxical worsening, recurrence

Introduction

Intracranial tuberculoma continues to be a common neurosurgical disease in underdeveloped countries, but accounts for less than 0.2% of intracranial space-occupying lesions treated in developed countries. Fewer than 50% of patients present with extraneural disease or a past history of tuberculosis, so the diagnosis of brain tuberculosis may be delayed. Furthermore, since most intracranial tuberculomas manifest as intraaxial lesions and very seldom as dural-based masses, the diagnosis of meningeal tuberculomas is usually established at the time of surgical excision. We treated a patient with multiple meningeal tuberculomas, which manifested with unusual clinical and neuroradiological features, including recurrence as tuberculous meningitis despite 18-month administration of anti-tuberculous therapy.

Case Report

A 26-year-old man presented to the Department of Urology of Kagoshima University Hospital with a 2-year history of mild headache and a 1-year history of sexual impotence. Computed tomography (CT) demonstrated multiple intracranial mass lesions. He was referred to our department in June 2000.

At the time of his first admission, he had no significant previous medical history. He had intermittent mild fever. Physical examination showed decreased body hair but no signs of respiratory infection. Neurological examination disclosed no abnormalities and no signs of meningeal irritation. Laboratory evaluation revealed slight elevation of C-reactive protein (0.7 mg/dl, normal 0 to 0.4 mg/dl), but normal result of blood counts (white blood cell count 6300/μl). Hormonal study disclosed that the levels of luteinizing hormone, follicle-stimulating hormone, cortisol, and testosterone were suppressed and that of prolactin was slightly elevated. Magnetic resonance (MR) imaging demonstrated multiple meningeal-based, extraaxial masses in the bilateral sphenoid ridges, left tentorial edge, and
convexity, which appeared isointense on the T1-weighted and hypointense on the T2-weighted images (Fig. 1A, B). There was minimal perifocal edema. The masses were homogeneously enhanced after intravenous administration of gadolinium-diethylenetriaminepenta-acetic acid (Fig. 1C). In addition, there were a number of spotty or fused enhanced lesions in the hypothalamus, basal ganglia, and subarachnoid space (Fig. 1D). Bilateral carotid angiography revealed hypovascular masses without vascular compression of major vessels. The tentative preoperative diagnosis was multiple meningiomas.

For histological verification, he underwent right frontotemporal craniotomy using the pterional approach. The tumor at the right sphenoid wing was partially extirpated. The intraoperative pathological diagnosis based on frozen sections was granuloma, so further surgical removal was halted. Histological examination of the surgical specimen identified epitheloid and giant cell (multinucleated and Langhans-type) inflammatory granuloma associated with caseous necrosis (Fig. 2). These findings were compatible with tuberculoma. Staining and culture of the cerebral mass and cerebrospinal fluid (CSF) were negative for fungi and acid-fast organisms. Polymerase chain reaction of the surgical specimens demonstrated no evidence of tuberculous infection. He had no history or family history of tuberculosis and no symptoms of concurrent extracranial tuberculosis. Chest radiography and chest CT found no abnormalities.

Based on the specific pathological findings of tuberculoma, he was treated postoperatively with a course of anti-tuberculous chemotherapy that included isoniazid (300 mg/day), ethambutol (750 mg/day), rifampicin (450 mg/day), and pyrazinamide (1.5 g/day). He responded well, his headache resolved, and he was discharged 6 weeks after the operation. However, he developed paradoxical worsening of his clinical condition after 4 months of anti-tuberculous therapy. MR imaging showed extension of the enhancement along the dura (Fig. 3A, D). Anti-tuberculous chemotherapy was continued and he recovered spontaneously. Twelve months after the start of drug therapy he was able to lead a normal life that included surfing. Residual enhanced lesions persisted (Fig. 3B, E), but the
anti-tuberculous chemotherapy was stopped after a total of 18 months because the enhanced lesion had remained stable for 1 year and he returned to his previous job.

At 4 months after the termination of chemotherapy he gradually noted increasing general fatigue. He was admitted again because he complained of increased headache. MR imaging demonstrated remarkable enhancement in the subarachnoid space (Fig. 3C, F). CSF analysis disclosed elevated protein (1400 mg/dl) and decreased glucose levels (36 mg/dl), and lymphocytic pleocytosis (171 cells/ml). The diagnosis was meningeal tuberculosis. He received a second course of anti-tuberculous therapy. He recovered clinically and the disease remained stable after 12 months of additional drug treatment.

Discussion

This case of intracranial tuberculoma presents an extraordinary array of unusual characteristics, including the unusual neuroradiological findings and clinical course. At first, multiple dura-based lesions were identified without symptoms of systemic tuberculosis infection such as pulmonary tuberculosis or tuberculous meningitis. Most intracranial tuberculomas manifest as intracerebral lesions. Various MR imaging features of intracerebral tuberculoma are useful for differentiation from other ring-enhancing brain lesions.9 On T1-weighted images, granulomas typically appear as isointense–hyperintense masses with single or multiple ring enhancement, accompanied by a slightly hyperin-
tense rim that was surrounded by a rim of slight hypointensity. The hyperintense and hypointense rims corresponded with layers of collagenous fibers and inflammatory cell infiltrates, respectively. On T2-weighted images, granulomas appear as isointense–hypointense masses surrounded by a hypointense rim.

In the present case, the tuberculoma manifested as dura-based skull base lesions without the MR imaging features of intracerebral tuberculoma except for appearing hypointense on T2-weighted images. Instead, the lesions exhibited radiologic features similar to those of meningioma, except for multiplicity and slight parenchymal enhancement. Excisional biopsy was required to obtain the correct diagnosis. Even in India, where systemic tuberculosis is widespread, the presentation of tuberculoma as a dural-based mass is rare.\textsuperscript{21} In previously reported cases with meningeal tuberculoma, CT and MR imaging were unable to differentiate the lesions from meningioma and surgery was required for diagnosis.\textsuperscript{1,3,4,8,12,14}

Our patient manifested paradoxical worsening that was overcome by the continuation of anti-tuberculous treatment. Paradoxical worsening of clinical and laboratory findings despite appropriate anti-tuberculous therapy has been described in both pulmonary and extrapulmonary tuberculosis.\textsuperscript{7,10,11} Review of 34 cases of intracranial tuberculoma with a paradoxical response to anti-tuberculous chemotherapy found that most patients were children or young adults with inoperably located intracranial tuberculomas that developed a few weeks or months after the start of appropriate chemotherapy.\textsuperscript{71}

Despite 18 months of anti-tuberculous therapy, our patient suffered recurrence as tuberculous meningitis. Administration of anti-tuberculous therapy for 12 months is generally considered adequate to resolve intracranial tuberculomas.\textsuperscript{15} When we stopped drug therapy, our patient manifested no evidence of new intracranial tuberculomas or expansion of older existing lesions. Our experience indicates that any persistent enhanced lesions may regrow after the termination of anti-tuberculous chemotherapy. Therefore, drug treatment should be continued for as long as 12–30 months in patients showing paradoxical expansion,\textsuperscript{71} because anti-tuberculous chemotherapy for 14 months after the manifestation of paradoxical worsening was insufficient in our patient.

Tuberculomas of the brain continue to be prevalent in developing countries and seem to be making a comeback in developed nations, which may be at least partially attributable to population movements, and may result in increased exposure to such pathogens in developed countries. Our experience suggests that tuberculoma should remain a part of the differential diagnosis for enhanced mass lesions even in the absence of any active extracranial tuberculous lesion. Recognition of this unusual presentation may facilitate the appropriate diagnosis and management of patients with intracranial tuberculoma.

References

14) Shindo A, Honda C, Baba Y: A case of an intracranial...
multiple meningeval tuberculomas, mimicking meningioma, that developed during treatment with anti-tuberculcous agents. No Shinkei Geka 27: 837–841, 1999 (Jpn, with Eng abstract)


________________________
Address reprint requests to: H. Takeshima, M.D., Department of Neurosurgery, Faculty of Medicine, Kagoshima University, 8–35–1 Sakuragaoka, Kagoshima 890–8520, Japan. e-mail: m2040k@m3.kufm.kagoshima-u.ac.jp