Intracranial Tuberculoma in Non-immunosuppressive State
—Two Case Reports—

Yoshihisa MATSUMOTO,1 Hiroshi AIKAWA,1 Sumito NARITA,1 Masanori TSUTSUMI,1 Hidenori YOSHIDA,1 Housei ETOU,1 Kimiya SAKAMOTO,1 Ritsuro INOUE,1 Kohei NII,2 and Kiyoshi KAZEKAWA1

1Department of Neurosurgery, Fukuoka University Chikushi Hospital, Chikushino, Fukuoka; 2Department of Neurosurgery, Fukuoka Kieikai Hospital, Fukuoka, Fukuoka

Abstract

The rise in the incidence of tuberculosis is generally related to human immunodeficiency virus infection. However, intracranial tuberculosis, a complication of tuberculosis considered to be a critical disease, can develop even in the absence of immunosuppressive state. Here, we describe 2 cases of intracranial tuberculoma occurring in patients with no evidence of immunosuppressive state or past history of tuberculosis. In Case 1, lesions were observed in the right lateral ventricle, with histological examination revealing granulomatous lesions. In Case 2, scattered lesions were observed in the cranium and the lung fields. In both cases, the QuantiFERON Test (QFT) was positive, and improvements were observed in the symptoms following administration of antituberculous drugs. Intracranial tuberculoma cannot be considered rare, and needs to be included in the differential diagnosis of intracranial lesions. Diagnosis can be tricky since this disease can develop in a patient in a non-immunosuppressive state or without a past history of tuberculosis. The QFT is an effective test to enable the diagnosis of tuberculomas in atypical patients.

Key words: intracranial tuberculoma, QuantiFERON Test, non-immunosuppressive state

Introduction

Tuberculosis continues to cause high rates of morbidity and mortality,1 although the incidence rates of its manifestations have changed with time. According to a report published in 1933, 34% of intracranial space-occupying lesions in England were tubercular lesions; this proportion decreased to 0.15% in Great Britain by 1972,6,12 indicating that the incidence of intracranial tuberculosis had rapidly decreased. However, in recent times, the number of reports linking tubercular lesions to human immunodeficiency virus (HIV) infection has increased.3 The incidence rate of tuberculosis in Japan has declined over the past few decades. However, in 1997, the number of new patients with tuberculosis and the associated incidence rate had increased. Subsequently, countermeasures for eliminating tuberculosis have been reinforced, and the trend has been reversed. In 2006, 26,384 new cases of tuberculosis were recorded; this incidence rate of 20.6 patients per 100,000 inhabitants was considered fairly high for a developed nation.20 Intracranial tuberculomas have attracted attention because of the high incidence in immunosuppressed patients,3 but patients in their 20s and 40s with no relevant medical history11,19 as well as patients in their 30s and 40s with no lung field lesions18,19 have been reported recently. Therefore, this disease may develop even in the absence of underlying disease or lung field lesions.

We encountered 2 cases of intracranial tuberculoma in the past year in our institution, with no immunosuppressive state or past history of tuberculosis. Here, we describe these cases with a review of the related literature.

Case Reports

Case 1: A 70-year-old male presented with loss of memorizing power. Cranial imaging revealed abnormal findings and this patient was referred to our hospital. No past or family history of tuberculosis was noted. On admission, higher brain dysfunction (Hasegawa dementia scale-revised score 18 points) and left homonymous hemianopsia were diagnosed. Peripheral blood test revealed white blood cell count of 4600/μl, and HIV antibody tested negative.

Cranial imaging revealed lesions in the posterior horn of the right lateral ventricle reaching the inferior horn. T2-weighted magnetic resonance (MR) imaging revealed central hyperintense lesions with isointense lesions in the
periphery. T1-weighted MR imaging with gadolinium confirmed the findings of the isointense lesions. The extensive hyperintense lesions had spread to the right occipital lobe with the presence of edema (Fig. 1A, B). Cerebral angiography did not show clear deep staining, with presence of avascular areas.

Lumbar puncture revealed total leukocyte count of 11 cells/mm³, protein content of 86 mg/dl, chloride content of 126 mg/dl, and glucose content of 60 mg/dl. Culture of the cerebrospinal fluid (CSF) was negative for tuberculosis. The observed lesions were suspected to be either neoplastic or granulomatous. The rapid progress of the symptoms necessitated early diagnosis for commencing appropriate therapy. Therefore, craniotomy was performed and the lesions were biopsied. Histological examination indicated granulomatous lesions, with a high probability of cerebral tuberculoma (Fig. 2). The tuberculin skin test was negative, and polymerase chain reaction (PCR) of sputum and biopsy specimens was negative for tuberculosis. The QuantiFERON test (QFT) was positive, so the diagnosis was cerebral tuberculoma. A course of antituberculous drugs was administered to the patient. Gradual improvement was noted in his symptoms, and the patient was able to return home on his own at discharge. The left homonymous hemianopsia disappeared by the third month after discharge. Follow-up MR imaging revealed reduction in the size and extent of the lesions (Fig. 1C).

Case 2: A 30-year-old male presented with a history of lower back pain persisting for 4 months, with loss of appetite and increased back pain necessitating bed rest for 1 month. He came to the emergency department for multiple bouts of vomiting and an episode of vertigo. No relevant medical history or family history of tuberculosis was noted.

On arrival, his Glasgow Coma Scale score was E3V4M6, with mild disturbance of consciousness along with frequent hiccups. Hypoglycemia was observed, but the disturbance of consciousness persisted even after regulating his blood sugar levels. Peripheral blood test revealed white blood cell count of 8100/μl, and HIV antibody tested negative. Cranial computed tomography (CT) revealed multiple cerebral parenchymal lesions. Fluid-attenuated inversion recovery MR imaging revealed hyperintense lesions scattered throughout the cerebral parenchyma, including in the medulla oblongata. T2-weighted MR imaging revealed hypointense lesions surrounded by the hyperintense le-
sions assumed to be edema. CT with contrast medium revealed enhanced lesions scattered in the cerebral parenchyma (Fig. 3).

Small scattered lesions were also observed in the lung field. However, the patient experienced no coughing, and sputum samples could not be collected even by forced expiration. Imaging findings revealed the possibility of miliary tuberculosis. Culture samples were collected from the gastric juice, urine, and CSF, and QFT was performed. Lumbar puncture revealed total leukocyte count of 46 cells/mm³, protein content of 94 mg/dl, chloride content of 110 mg/dl, and glucose content of 27 mg/dl. Culture of the CSF was negative for tuberculosis. On the second day of hospitalization, the disturbance of consciousness aggravated and the patient became drowsy. Subsequently, antituberculous and steroid therapy was initiated. On the third day of hospitalization, the disturbance of consciousness improved. The QFT results were obtained after the commencement of the treatment, and were positive. PCR testing of urine and gastric juice was positive for tuberculosis. The gastric juice samples were positive on the Gaffky scale, so the patient was immediately transferred to a hospital specializing in tuberculosis.

Discussion

The present 2 cases of intracranial tuberculosis manifested no indications of immunosuppressive state or past history of tuberculosis, making the initial diagnosis considerably difficult to establish.

Diagnostic imaging for intracranial tuberculomas is related to the pathological characteristics of this disease entity, as the imaging characteristics change with the progressive stages of intracranial tuberculomas. Large ring-enhanced, solid lesions on CT appeared as hypointense on T₁-weighted and isointense on T₂-weighted MR imaging, whereas small ring-enhanced lesions on CT appeared with hyperintense centers on T₂-weighted MR imaging. The lesion component with complicated histopathological changes in tuberculomas. The Langhans giant cells and granulation tissue consisting of epithelioid cells in the second layer appeared isointense on T₁-weighted and hypointense on T₂-weighted MR imaging. The Langhans giant cells and granulation tissue consisting of epithelioid cells in the second layer appeared isointense on T₁-weighted MR imaging and hyperintense on T₂-weighted MR imaging. The lesion component with increased collagen fibers forming the third layer appeared isointense on T₁-weighted and hypointense on T₂-weighted MR imaging. Therefore, these heterogeneous diagnostic imaging appearances are known to accord with the complicated histopathological changes in tuberculomas. Cerebral angiography may reveal avascular areas or dense staining, varying from case to case. Avascular areas were observed in our Case 1.

In our Case 1, T₂-weighted MR imaging demonstrated hyperintense areas with isointense periphery, and edema as hyperintensity in the cerebral parenchyma. Based on this appearance, we identified a type of intracranial tuberculoma that had developed to some extent. In our Case 2, T₂-weighted MR imaging showed that the edema had spread around the hypointense lesions, so the lesion was considered to be intracranial tuberculoma in the initial stage. Based on these findings, we suggest that if layered structures are noted in imaging studies, even as isolated lesions, or if scattered intracranial lesions are observed, intracranial tuberculoma must be considered in the differential diagnosis.

In our Case 1, the diagnosis was based on the pathological findings and QFT. In our Case 2, the diagnosis was based on the QFT results, together with the gastric juice culture results. In both cases, QFT provided a valid diagnosis. The tuberculin skin test is known to be not very accurate because false-positive reactions are generated due to bacillus Calmette-Guérin (BCG) vaccination. The QFT does not generate false-positive reactions due to BCG, and has high sensitivity (86%) and specificity (97.7%) for tuberculosis. Other reports have stated the specificity to be 94%. However, QFT has limitations in immunosuppressed patients. QFT stimulates peripheral blood lymphocytes in vitro through Mycobacterium tuberculosis-specific protein, and this infection is identified by measuring the interferon-gamma released. In immunosuppressed subjects, the function of immunocompetent cells is suppressed, resulting in low production of interferon-gamma. Interpretation of QFT results is therefore difficult in these patients.

PCR may have low sensitivity for the detection of CSF tuberculosis. The sensitivity and specificity of nucleic acid amplification tests for tuberculous meningitis have been reported to be 0.56 and 0.98, respectively. The sensitivity has been reported to be as low as 48%. In one case, the PCR test for CSF was negative but the patient was diagnosed with intracranial tuberculoma from the histology of lesions. Various reports have discussed the limitations of detecting CSF tuberculosis by PCR, but other studies report that PCR is a very useful method for detecting tuberculosis. The sensitivity was 98% and specificity was 70% using patient sputum samples. Recently, another study that performed PCR using primers directed against the IS6110 gene reported the sensitivity of 91.4% and specificity of 75.9% for the diagnosis of tuberculous meningitis.

Both QFT and PCR have advantages and limitations. Given their advantages and non-invasive nature, we consider that QFT and PCR should be performed whenever intracranial tuberculoma is suspected. The need for early diagnosis often necessitates histopathological testing for which minimal invasive guided stereotactic brain biopsy is often selected. However, valid specimens cannot always be collected, so open brain biopsy is often required. Antituberculous drugs are used to treat intracranial tuberculomas. Early diagnosis and initiation of therapy is par-
ticularly critical in the presence of rapidly progressing symptoms. In such cases, antituberculous treatment, which also acts as a diagnostic therapy, should be initiated while waiting for definitive diagnostic results.

The present 2 cases of intracranial tuberculoma were identified in the absence of immunosuppressive state or past history of tuberculosis. QFT was an effective diagnostic test in both cases. Administration of antituberculous drugs improved the symptoms in both the patients. Although the incidence of intracranial tuberculoma continues to decrease, we consider that it should be included in the differential diagnosis of relevant space-occupying lesions, even in the absence of immunosuppressive state or history of tuberculosis.

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Conflicts of Interest Disclosure

The authors declare that they have no conflict of interest. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

References


Address reprint requests to: Prof. Kiyoshi Kazekawa, Department of Neurosurgery, Fukuoka University Chikushi Hospital, 1–1–1 Zokumyoin, Chikushino, Fukuoka 818–8502, Japan. e-mail: kazekawa@xb3.so-net.ne.jp