International Journal of Infectious Diseases 24 (2014) 37–39

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Importance of contrast-enhanced fluid-attenuated inversion recovery imaging to detect paradoxical expansion of tuberculoma

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ARTICLE INFO

Article history:
Received 25 February 2014
Received in revised form 12 March 2014
Accepted 17 March 2014

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Tuberculous meningitis
Paradoxical tuberculoma
Contrast-enhanced fluid-attenuated inversion recovery imaging

SUMMARY

Tuberculosis is a significant public health problem that continues to be a major cause of morbidity and mortality worldwide. Tuberculous meningoencephalitis (TM) is the most common extrapulmonary lesion in tuberculosis. A 41-year-old female was thought to have TM. Tests to confirm the TM diagnosis were initially negative, including tuberculosis PCR and adenosine deaminase level in serum and cerebrospinal fluid (CSF). Anti-tuberculous medication and intravenous steroids were administered to her on the basis of brain imaging and lactate dehydrogenase electrophoresis in CSF, suggestive of the diagnosis of TM. Her neurological problems improved rapidly following treatment. Serologic and CSF markers were positive in PCR and culture after 60 days. Radiological findings are often nonspecific and TM is difficult to diagnose without an increased index of suspicion. The detection of paradoxical expansion of tuberculoma is very important in the maintenance of medication. Magnetic resonance imaging was used to detect paradoxical expansion of the tuberculoma using various methods, such as contrast-enhanced fluid-attenuated inversion recovery (CE-FLAIR) imaging. CE-FLAIR imaging conspicuously showed paradoxical expansion of the tuberculoma. If patients present with clear meningitis, without any identified pathogen, there is a need to constantly and scrupulously check for TM, including with the use of CE-FLAIR brain imaging.

1. Introduction

Tuberculous meningoencephalitis (TM) is the most common extrapulmonary lesion in tuberculosis, presenting with various symptoms. It occurs particularly in developing countries, affecting up to 15% of the population in such countries.[1] The serological and radiological findings are often nonspecific, and TM is difficult to diagnose without an increased index of suspicion. Serial serological diagnosis is not specific for TM. Follow-up magnetic resonance imaging (MRI) may suggest a paradoxical expansion of the tuberculoma, providing a clue for the treatment of TM.

Here we report findings from a patient with TM, which was confirmed by abnormal signals on contrast-enhanced fluid-attenuated inversion recovery (CE-FLAIR) MRI; this suggested paradoxical tuberculoma.

2. Case report

A 41-year-old female was admitted with mild Parkinsonism, presenting with involuntary movements of her left side and aggressive behavior, which she had been experiencing for 1 month. Her vital signs were stable. Upon neurological examination, she exhibited right upper and lower limb weakness (grade IV/grade IV) with intermittent clonic movements on the left side. She was mentally alert, but appeared disorientated and irritated.

Initial cerebrospinal fluid (CSF) findings showed leukocytosis with lymphocyte dominance, without protein elevation (white blood cell count 220×10^6/l, red blood cell count 6×10^6/l, and protein 46 mg/dl). Tests to confirm the TM diagnosis were initially negative, including tuberculosis PCR and adenosine deaminase (ADA) level in serum and CSF.

The involuntary movements and hemiparesis on the left side became worse in the 7 days after admission. There were high signal changes on CE-FLAIR imaging in the right temporo-parietal regions (Figure 1A). Contrast-enhanced T1-weighted imaging showed a lack of enhancement in the same area (Figure 1B). Anti-tuberculous medication and intravenous steroids were administered to her on the basis of the brain imaging and lactate dehydrogenase (LD) electrophoresis in CSF, suggestive of the diagnosis of TM (increased total LD up to 47 IU/l (normal value 28 IU/l), increased LD3 and LD4 fractions, and decreased LD1). Her neurological problems had resolved completely 30 days after starting medication.

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http://dx.doi.org/10.1016/j.ijid.2014.03.1383

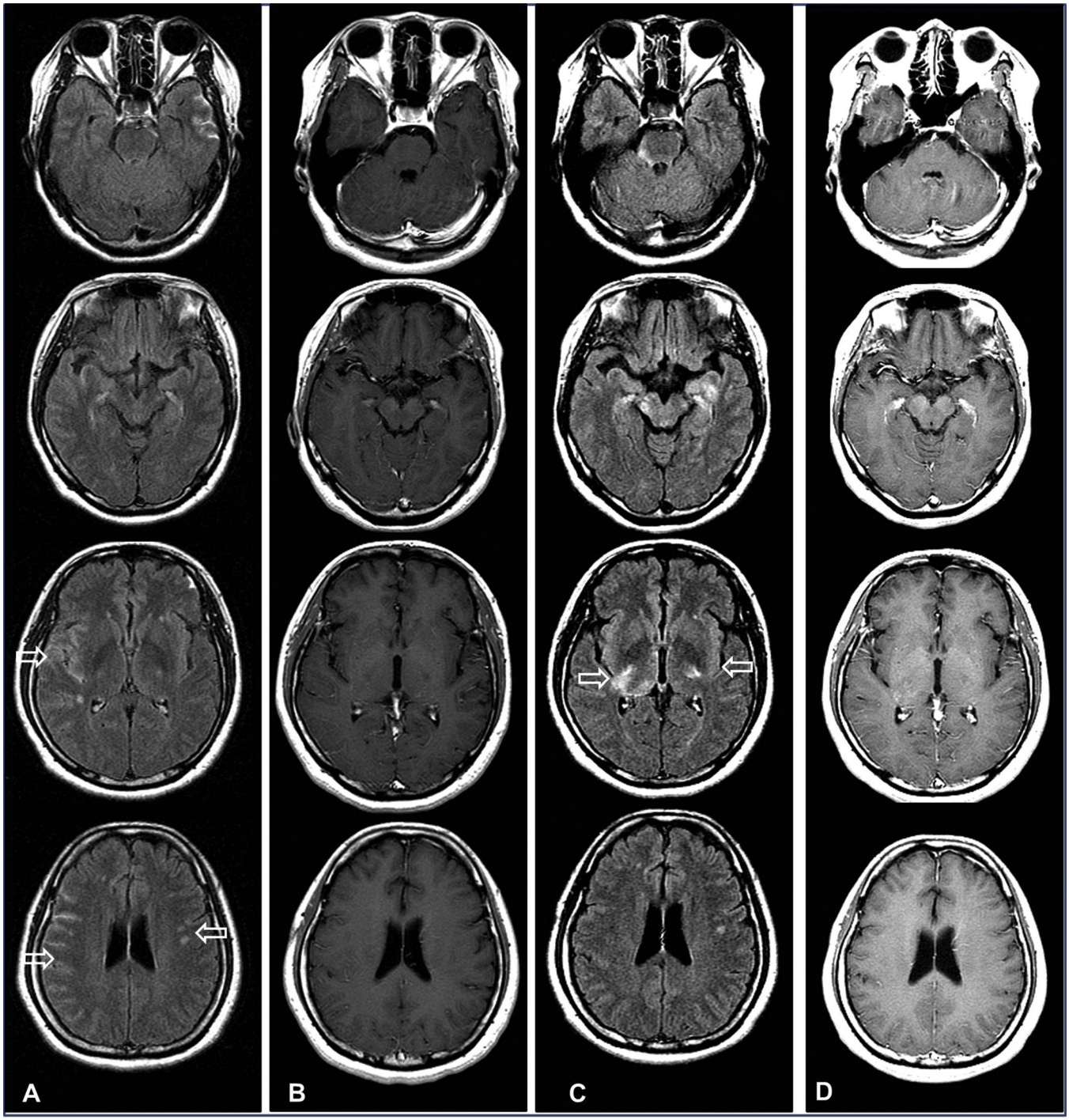

Figure 1. (A) Hospital day 1: Contrast-enhanced FLAIR images showing slight leptomeningeal enhancement in the right temporo-parietal region (arrows). It is difficult to differentiate tuberculosis meningitis from other diseases showing high signal intensity within the sulci. (B) Hospital day 1: Contrast-enhanced T1-weighted images. (C) Hospital day 60: Contrast-enhanced FLAIR images conspicuously showing high signals in right peripontine and left medio-temporal regions (arrows). (D) Hospital day 60: Contrast-enhanced T1-weighted images. The contrast-enhanced T1-weighted images showed no evidence in the same areas.

After 60 days, a serial brain MRI showed diffuse abnormal signals within the right hemispheric region that were conspicuously present in the right peripontine and left medial temporal regions on CE-FLAIR; this was suggestive of paradoxical expansion of the tuberculoma (Figure 1C). There were no abnormal signals on contrast-enhanced T1-weighted images of the same regions (Figure 1D). Serologic and CSF markers were positive by PCR and culture at the same time. We decided to continue medication for 1 year, based on the paradoxical granuloma in the brain CE-FLAIR images of the left peripontine area.

3. Discussion

A diagnosis of definite TM is only made when acid-fast bacilli (AFB) are seen, or when *Mycobacterium tuberculosis* is cultured or detected by a reliable molecular method from the CSF in someone

with symptoms or signs suggestive of the disease.[2] Some studies have reported the detection of AFB and culture isolation of *M. tuberculosis* from the CSF to be easily detected, but most are exceptional.[3]

The rapid diagnosis of TM is very important because most affected patients die, and any delay in treatment results in significant morbidity.[2] The mortality rates vary from 7% to 45%, and the optimum therapeutic regimen for various presentations of central nervous system tuberculosis have not yet been determined.[4] The CSF PCR assay represents a significant advance in the diagnosis of microbial diseases, and TM is no exception. The results of PCR studies in the CSF have shown a specificity of 94–100%, but sensitivities range from 75% to 100%.[3] MRI can aid in the diagnosis of TM. The detection of secondary resistance, atypical mycobacterial infection, and paradoxical spread of the tuberculoma have come to the fore in TM.

A paradoxical response after anti-tubercular therapy is defined as a transient worsening of disease at a pre-existing site, or the development of new tuberculous lesions in a patient who initially improved on anti-tubercular therapy. This phenomenon is more commonly associated with extrapulmonary tuberculosis.[1] Initially, the explanation for the paradoxical expansion of the tuberculoma was that it could be indicative of a blood–brain barrier (BBB) breakdown, drug resistance, enhanced anti-tuberculous immune response, or irregular medication.[2] The detection of this phenomenon is necessary for treatment maintenance. The enhancement is much more conspicuous on CE-FLAIR images. Additional enhancement is present in several inferior and lateral sulci in the right temporo-parietal and left frontal regions. CE-FLAIR can be more conspicuously detected in a BBB breakdown, increased protein content, or CSF outflow disturbance than in routine contrast-enhanced T1-weighted imaging.[5]

This patient started anti-tuberculous medication without any evidence from laboratory tests to support this action. TM serological markers, including PCR, were negative 60 days after treatment. Only the abnormal signals in the CE-FLAIR images had important implications for the commencement and ongoing treatment with anti-tuberculous medication in this patient. Standardized diagnostic criteria for TM have not been established, and most reports have used different case definitions. Since there are no standardized criteria, there is a limit in using existing data to apply to diagnosis and treatment.[2] If patients present with clear meningitis, without any identified pathogen, there is a need to constantly and scrupulously check for TM, including with the use of CE-FLAIR brain imaging.

Acknowledgement

This work was supported by the research fund of Hanyang University (HY-2014).

Patient consent: Informed consent was obtained from the participant in accordance with the regulations of the Institutional Review Board of Hanyang University Medical Center.

Conflict of interest: The authors report no disclosures. The authors have no potential conflicts of interest to report concerning this article.

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