A Patient of Neurocysticercosis Misdiagnosed as Tuberculous Meningitis for 26 Years: a Case Report

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Case Report

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Abstract

Background: Neurocysticercosis (NCC) is a neurological infection caused by the larval stage of the tapeworm Taenia solium (T. solium). The diagnosis of NCC can be challenging because of heterogeneity in clinical manifestation. Neurocysticercosis is easily misdiagnosed as tuberculous meningitis (TBM).

Case presentation: We describe a case of subarachnoid neurocysticercosis with 28 years illness course misdiagnosed as TBM for 26 years. The patient presented with symptoms of repeated headache, fever, serious low back and legs pain, and vomiting, occasional seizure and lose of consciousness. The neurological assessments revealed stiff neck and right plantar and saddle numbness. Lumbar puncture results revealed obvious intracranial hypertension, pleocytosis, elevated protein level, and decreased glucose level. Magnetic resonance imaging showed meningeal enhancement of brain, cystlike structure in the lumbosacral sac and the clumping of the nerve roots of the cauda equina. Five recurrent episodes occurred in twenty-eight years. TBM was considered as a probable etiology and was treated for tuberculosis empirically with adjunctive corticosteroids for 26 years. In the first three hospitalizations, During this period, the patient was hospitalized three times. In 2016, The local hypertrophic pachymeningitis were considered as a probable etiology. She was treated with steroid pulse therapy. At her fifth relapse, in 2018, next-generation sequencing of cerebrospinal fluid (CSF) identified the patient was NCC, T. solium infection. Her symptoms and CSF examination were relieved after etiological treatment.

Conclusions: Neurocysticercosis is easily misdiagnosed as TBM. Meanwhile, adjunctive corticosteroids therapy can alleviate the symptom of TBM and NCC. So we suggest that NCC should be considered in the differential diagnosis of TBM. NGS of CSF is a promising tool for the diagnosis of NCC.

Background

Human cysticercosis is caused by the accidental ingestion of T. solium eggs or via autoinfection. Neurocysticercosis (NCC) represents the most common helminthic infection of the central nervous system (CNS) [1]. NCC includes different forms including parenchymal NCC, ventricular NCC, and subarachnoid NCC. Because of heterogeneity in clinical manifestation, the diagnosis of NCC can be challenging, especially extraparenchymal NCC [2–3]. NCC is easily misdiagnosed as tuberculous meningitis (TBM). Meanwhile, the adjunctive corticosteroids accompanied with anti-tuberculous treatment can alleviate the symptom of NCC, which will delay the diagnosis. Here, we present a case of subarachnoid neurocysticercosis misdiagnosed as TBM for 26 years. The diagnosis of NCC was made 28 years after the initial symptoms onset.

Case Presentation

A 31-year-old woman in Hebei Province of China initially noticed headache with fever, nausea, diplopia, low back and legs pain in December 1990. Lumbar puncture (LP) revealed increased opening pressure

(600 mmH_2O), pleocytosis (20 cells/ml), elevated protein (1.1 g/L), and reduced glucose (1.83 mmol/L). The results of ink stain, acid fast stain and Mycobacterium tuberculosis culture of the cerebrospinal fluid (CSF) were negative. She was diagnosed with possible tuberculous meningitis (TBM) and started on empirical anti-tuberculous treatment and adjunctive corticosteroids therapy. The symptoms and CSF findings subsequently improved. The anti-tuberculous treatment lasted for more than one year. In 2004 and 2010 year, she was admitted with the same symptoms. LP revealed increased opening pressure with lymphocytic pleocytosis, elevated protein level, and reduced glucose. She was diagnosed with possible TBM and treated empirically for TBM again. Her symptoms and CSF findings improved significantly after treatment.

The forth attack occurred in September 2016. The patient again developed fever, headache and severe, intolerable back and legs pain. In this attack, the patient developed symptoms of generalized tonic-clonic seizure and lose of conscious. The neurological evaluations indicated neck stiffness, decreased lower limbs muscle strength (MRC 4 degree), weakened bilateral patellar reflex, right plantar and saddle numbness, postive right Babinski sign and Kernig sign. LP results showed that opening pressure 300 mmH_2O, WBC 2 cells/ml, protein 0.3 g/L, glucose 9.6 mmol/L and CSF IgG index 2.41 (reference value: 0.26–0.62). The fasting blood glucose was 5.6 mmol/L, glycosylated hemoglobin was 5.8% on the same day. The results of ink stain, acid fast stain and Mycobacterium tuberculosis culture of CSF were still negative. CSF cytology for malignant cells was negative. The whole blood Interferon-Gamma Release Assays (IGRAs) was negative. The results of TB-antibody, Mycoplasma antibody, Chlamydia antibody and Legionella antibody of serum were all negative. Erythrocyte sedimentation rate (ESR) was 40mm/h (reference value: 0–20 mm/h) and C-reactive protein (CRP) was 17 mg/L (reference value: 0–8 mg/L). Antineutrophil cytoplasmic antibodies (ANCA) were negative, Antinuclear antibody (ANA) was 1:320, RNP/Sm antibodies were positive. Ophthalmic examination indicated papilledema, retina hemorrhage and exudation. Brain magnetic resonance imaging (MRI) showed white matter lesion without ventriculomegaly (Fig. 1A). Contrast-enhanced brain MRI showed linear pachymeningeal enhancement (Fig. 1B). Cervical spine MRI showed cervical spondylosis and spinal cord compression. Thoracic spinal meningeal reinforcement was found in contrast-enhanced MRI. Lumbar spine MRI showed a cystlike structure in the lumbosacral sac (Fig. 1C,1D) and the clumping of the nerve roots of the cauda equina (Fig. 1C). Contrast-enhanced lumbar spine MRI showed marked enhancement of the cauda equina and spinal meninges (Fig. 1E). The CT scan of chest, abdomen, and pelvis showed no abnormality. She was treated successively with cefatriaxone, fluconazol, anti-tuberculosis drugs and adjunctive steroids. Repeated LP results showed persistent increased intracranial pressure (ICP). CSF analysis results varied widely, WBC varied from 0–65 cells/ml, total protein varied from 0.06–1.4 g/L and glucose varied from 1.3–14.4 mmol/L. After 1.5 months, the clinical symptoms were relieved and CSF findings were improved. However, ICP remained higher than 300 mmH_2O. In the next examination, filling defect in superior sagittal sinus was found in magnetic resonance venography (MRV) of the head (Fig. 1f), In November 2016, after consultation in a higher level hospital, she was diagnosed as local hypertrophic pachymeningitis and was treated with high-dose pulse corticosteroid therapy. After treatment, ICP dropped to 150 mmH_2O.

Unfortunately, in July 2018, she was hospitalized for the fifth recurrent episodes and the highest body temperature was 39.1℃. LP showed ICP > 330 mmH_2O, WBC 6750 cells/ml (5% mononuclear cells, 95% multinuclear cells), total protein 1.88 g/L and glucose < 0.5 mmol/L. NGS of patients'CSF sample was performed and the result identified T. solium infection and the reads was 27729 (Fig. 2A). Meanwhile, the cysticercosis specific antibody of serum and CSF were positive by enzyme-linked immunosorbent assay (ELISA). Combined with imaging results,she was diagnosed as subarachnoid NCC and was treated with albendazole, prednisone. Her symptoms were relieved and CSF findings were improved significantly after treatment of 38 days. The result of CSF demonstrated reduced leukocytosis (48 cells/ml) with protein 1.14 g/L and glucose 1.0 mmol/L. The solium DNA sequence reads dropped to 814 (Fig. 2B). Antihelminthic therapy was not continued because of drugs-induced liver injuries. On February 2019, the patient developed episodic left upper limb weakness with involuntary paroxysmal shaking. Each attack lasted for about 10 seconds and symptoms could relieve completely. Brain MRI didin't revealed hyperintense lesions on DWI. She was hospitalized and treated with aspirin for transient ischemic attack (TIA) and albendazole for NCC. The symptoms relieved completely after treatment. Before discharge, LP results showed ICP was 150 mmH_2O, WBC 100 cells/ml (80% mononuclear cells, 20% multinuclear cells), total protein 1.92 g/L and glucose 0.9 mmol/L. The CSF solium DNA sequence reads dropped to 528 (Fig. 2C). The clinical timeline is presented in Fig. 3 and the results of LP are summarized in Table.1. She did not have a definite history of epidemiological contact. Follow up indicated that she has not had a severe symptom flare until now.

Discussion And Conclusions

NCC patients often present with non-specific findings and it has similarities with other CNS infections. Our patient presented with a recurrent headache, fever and progressive back and legs pain with CSF lymphocyte response and declined CSF glucose. TBM was considered as a probable etiology. Her symptoms and CSF findings were significantly improved after empirical anti-tuberculous treatment. Until 2018 year, 28 years after the initial symptoms onset, NGS of CSF samples identified T. solium infection. Positive anticysticercal antibodies and lumbar spine MRI further supported the diagnosis of subarachnoid NCC. NGS is an unbiased approach to identify pathogens of neuroinfectious disease. It is possible to identify the vast majority of known organisms, whether or not they are being considered as part of physician's differential diagnosis [4]. Because no reads corresponding to T. solium were present in background, while they were abundant in the NCC patient, the NGS results for NCC are readily interpreted compared with CNS bacterial infections [5]. NGS is promising in the diagnosis of NCC. According to the literatures, a woman with a 15-year history and a man with 8-year history of relapsing meningitis were diagnosed as extraparenchymal NCC by NGS eventually [3, 6].

Neurocysticercosis is easily misdiagnosed as TBM. Meanwhile, adjunctive corticosteroids had been recommended to alleviate the symptom of TBM [7]. Corticosteroids can also suppress inflammation in subarachnoid and ventricular NCC [8]. Therefore, the diagnosis of NCC could be delayed by empirical anti-tuberculous treatment. As we known, NCC is the most common zoonotic disease, so we suggest that

clinicians should take NCC into consideration in differential diagnosis of chronic meningitis. ELISA for serological diagnosis of cysticercosis had a specificity of 93% and a sensitivity of 93% [9], which is accessible and rapid and can be used as a regular laboratory test in the diagnosis of chronic meningitis. There is a correlation between tests positivity and the cysticercosis location and count [10]. Subarachnoid NCC is commonly associated with very high titer antibodies and thus a negative or weak result should raise questions about the diagnosis. Subarachnoid NCC is frequently accompanied by a profuse inflammatory reaction characterized by pleocytosis and increased protein in the CSF [11]. The most common CSF findings are a moderate mononuclear pleocytosis, with a cell count rarely exceeding 300 cells/ml [12]. On the patient's fourth attack, CSF analysis showed neutrophilic pleocytosis which was infrequent and found in severe forms. Long illness course and a high parasite load appear to be seen in these patients [13].

Above all, we suggest that clinicians should take NCC into consideration in differential diagnosis of chronic meningitis especially of TBM. NGS of CSF samples is a promising tool for the diagnosis of neurocysticercosis.

Abbreviations

NCC: neurocysticercosis; T. solium: Taenia solium; NGS: Next-generation sequencing; CSF: cerebrospinal fluid; WBC: white blood cell; LP: Lumbar puncture; IGRAs: Interferon-Gamma Release Assays; ICP: intracranial pressure; MRI: magnetic resonance imaging; ELISA: enzyme-linked immunosorbent assay

Declarations

Ethics approval:

This study has been approved by Ethics Committee of Tianjin Haihe Hospital. Committee's reference number:2020HHWZ-007

Consent to participate:

Not applicable.

Consent for publication:

Not applicable.

Availability of data and material:

All data generated or analysed during this study are included in this published article.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yiyi Wang,YuanLiu, Liandi Lu, Qian LI, Xiaohan Zhen, Yu Zhao. The first draft of the manuscript was written by Yiyi Wang and Hongzhi Guan. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Table

Table 1

Laboratory features of the patient with subarachnoid neurocysticercosis.

Time	Pressure (mmH2O) (80–180)	WBC (x106cells/L) (< 8)	LYM(%) (60–70)	Protein (g/L) (0.15–0.45)	Glucose (mmol/L) (2.5–4.5)	Lactic acid (mmol/L)	ADA (U/L) (0–8)
1990.12	250	20	-	1.1	1.83	--	-
2004.07.23	300	106	-	1.79	1	-	-
2016.09.21	300	2	-	0.3	9.6	5.95	0.1
2016.09.27	320	65	70	1.07	3.5	6.82	2.1
2016.10.06	320	11	-	0.11	14.4	7.84	0.6
2016.10.18	320	6	-	0.08	12.9	5.78	0.8
2016.10.26	310	-	-	0.06	11.9	5.81	0.2
2016.11.07	320	55	80	1.4	1.3	6.41	2.7
2017.04.20	Unsuccessful puncture						
2018.07	> 330	6750	5	1.88	< 0.5	-	-
2018.10.08	> 330	175	50	4.85	0.9	10.79	4.9
2018.10.25	280	80	95	1.87	1.9	10	2.7
2018.10.29	320	80	95	1.48	1.7	9.46	2.6
2018.11.19	280	50	90	1.86	0.7	10.05	1.9
2018.12.03	250	47	95	1.14	1.0	8.71	2.8
2019.02.25	150	100	80	1.92	0.9	8.85	3.9

Figures

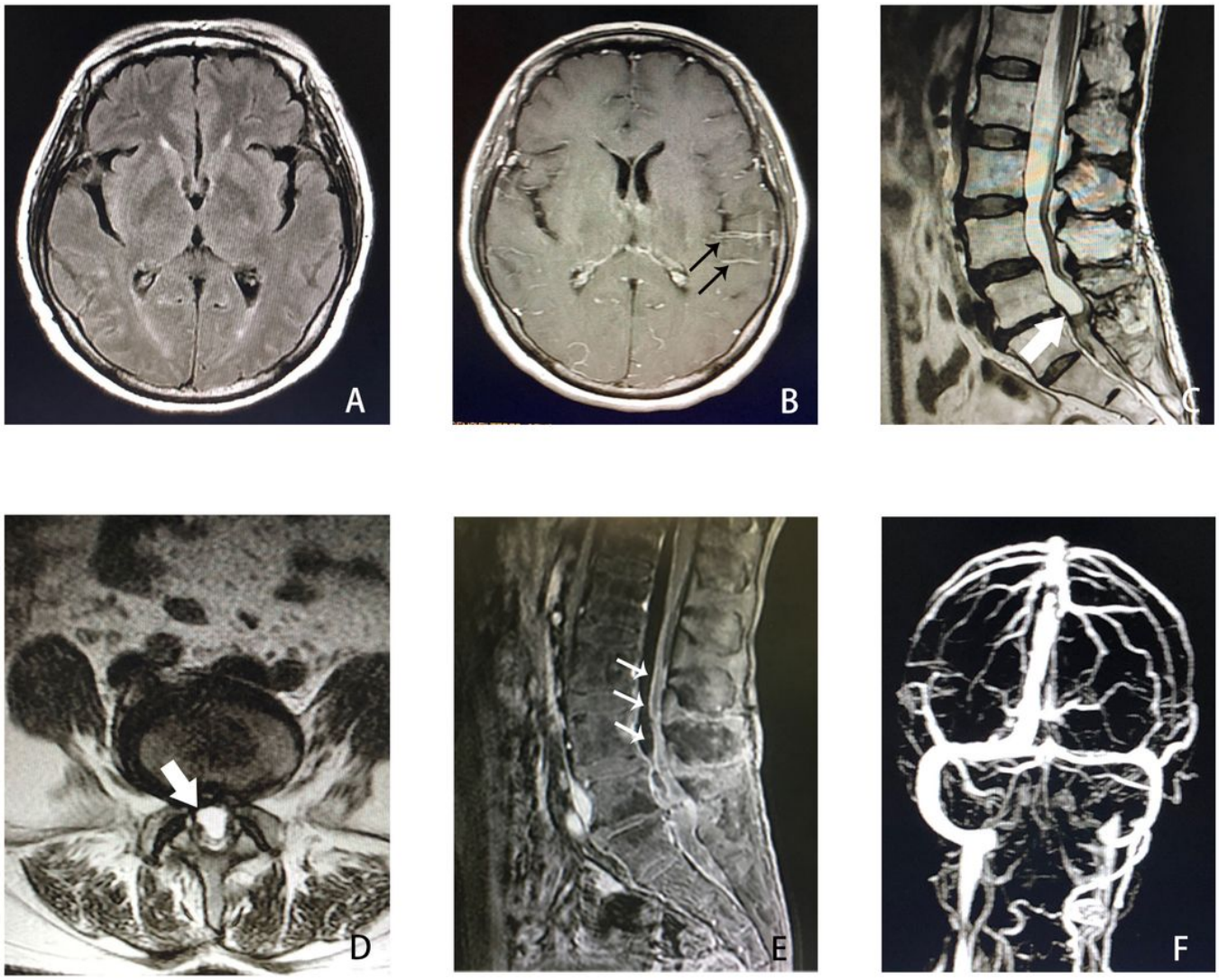

Figure 1

Magnetic resonance imaging (MRI) findings of brain and lumbar spine. (A). Brain MRI in 2016 showed white matter lesion without ventriculomegaly. (B). Contrast-enhanced brain MRI showed linear pachymeningeal enhancement (black arrows).C-D the lumbar spine MRI showed a cystlike structure in the lumbosacral sac (thick white arrow) seen on sagittal (C) and axial (D) T2-weighted images. The clumping of the nerve roots of the cauda equina was seen on sagittal (C) T2-weighted images. E. Contrast-enhanced lumbar spine MRI showed enhancement of the cauda equina and spinal meninges. F. Filling defect in superior sagittal sinus in magnetic resonance venography (MRV) of the head.

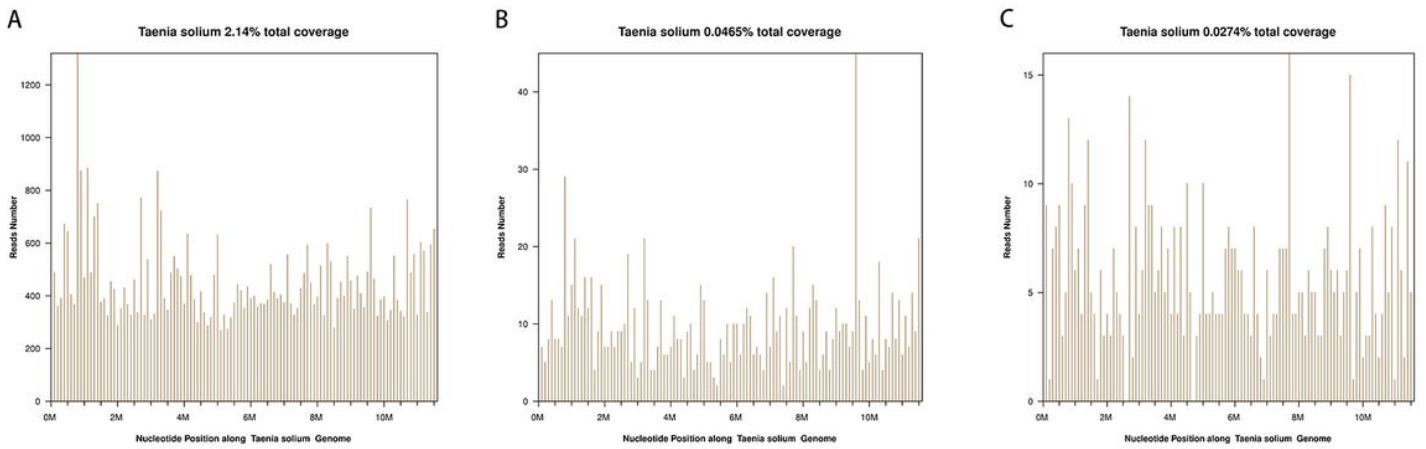

Figure 2

The results of Next-generation sequencing (NGS) of of cerebrospinal fluid (CSF). (A) NGS of CSF identified T. solium DNA sequences and the reads were 27729 before anti-helminth therapy. (B) After 38 days of treatment , the CSF solium DNA sequence reads dropped to 814. (C) The last results of NGS indicated the CSF solium DNA sequence reads dropped to 528.

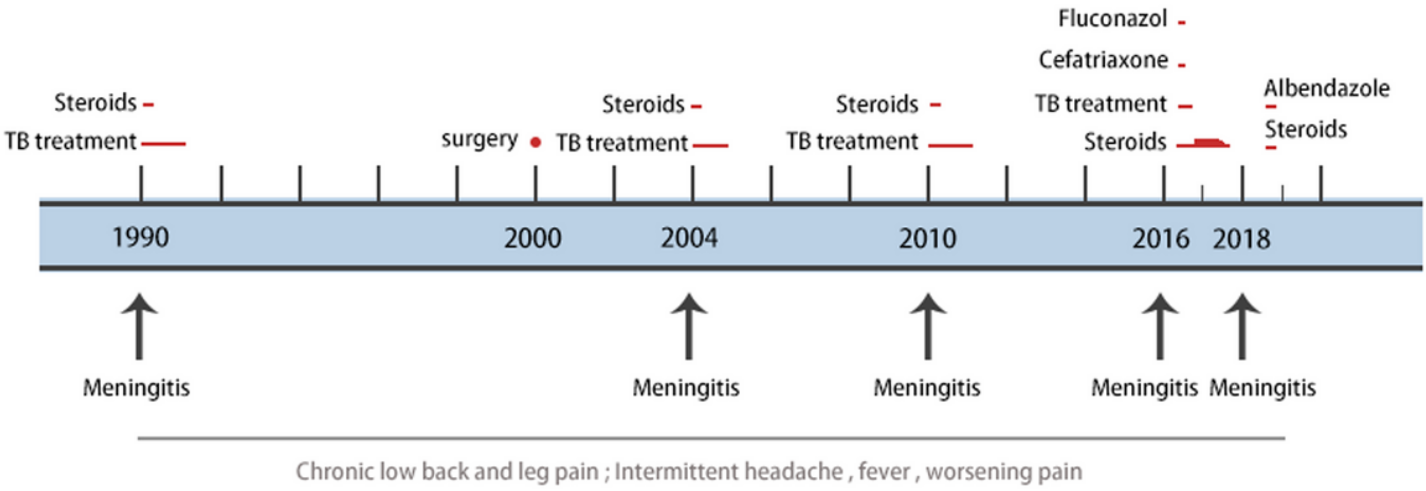

Figure 3

Timeline representing the clinical disease course. TB = Mycobacterium tuberculosis.