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Case Report

18F-FDG PET/CT findings in fatal *Balamuthia Mandrillaris* encephalitis in brain stem: A case report ☆,☆☆

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ABSTRACT

We presented a case of a 66-year-old female whose initial symptom was headache without obvious inducement. The patient's condition progressed rapidly to a semi-coma state after symptomatic treatment. The ^{18}F-FDG PET/CT scan revealed circular FDG hypermetabolism and central metabolic defect of the pons and left frontal lobe lesions. The combination of clinical findings, MRI, and Metagenomic next-generation sequencing (NGS) of cerebrospinal fluid led to the diagnosis of Balamuthia mandrillaris encephalitis. The patient died 5 days after discharge.

Introduction

Balamuthia mandrillaris encephalitis is a sporadic infectious disease of the central nervous system with a mortality rate of up to 90% [1]. There is no exact incidence of the disease, and most patients have an insidious onset and rapid progression to death with a course of 2 weeks to 2 years [2]. Not only immunocompromised but also immunocompetent people can be infected, especially children and older adults [3]. More than 300 cases of this disease have been reported worldwide, with about 200 cases concentrated in South America and the United States and 30 cases in China [4]. The clinical manifestations of cases reported in different countries are also different. The imaging examination of this disease mainly relies on CT and MRI, but no specific manifestations

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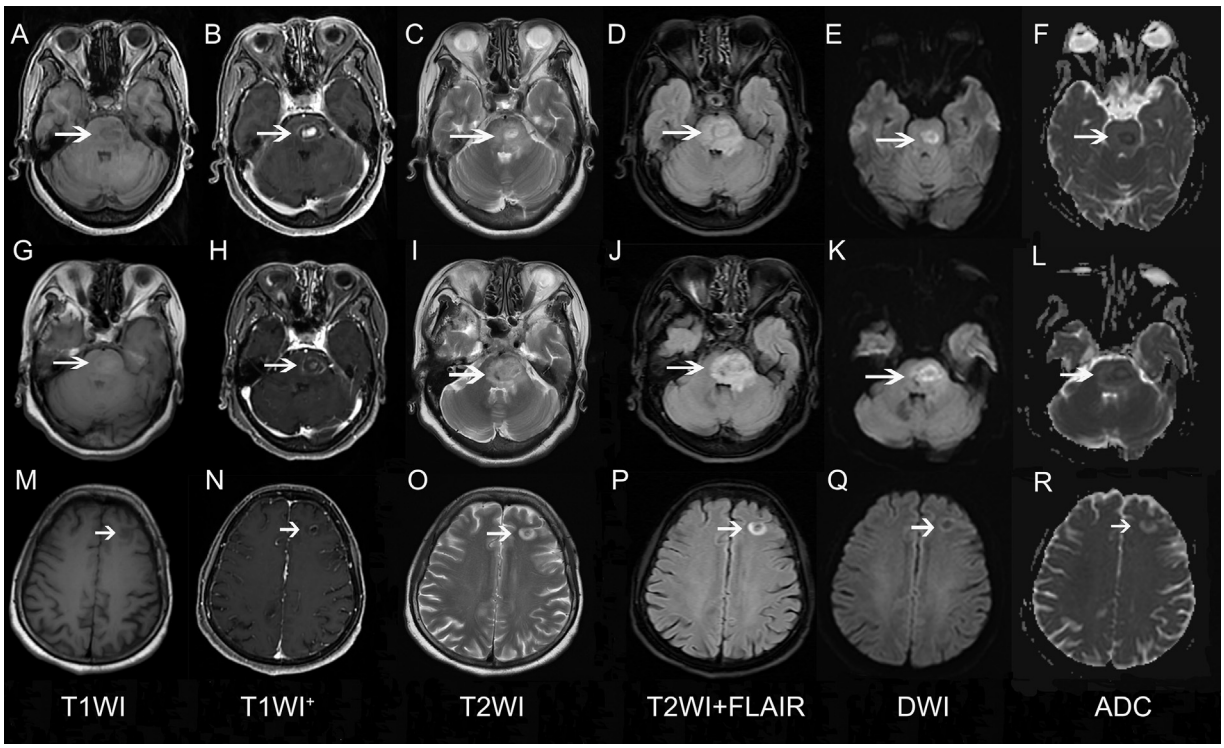

Fig. 1 – (A-F) Brain magnetic resonance imaging (MRI) at admission showed a 2.1 x 1.4 x 1.1cm area of low signal intensity on T1WI (A) and ADC (F), high signal intensity on T2WI (C), FLAIR sequence (D) and DWI (E) with peripheral edema. The lesion showed moderate ring enhancement with a central enhancement nodule on T1WI (B) and involved the mesencephalon and left cerebellar peduncles, with compression of the fourth ventricle. A repeat brain MRI one week after admission showed a slightly enlarged pontine lesion (G-L) and a new lesion in the left frontal lobe (M-R).

on images. Therefore, this disease remains poorly understood by clinicians and radiologists and is easily misdiagnosed as a primary glial tumor of the brain. Its diagnosis depends on the presence of amoeba trophozoites in histopathological and etiological examinations [5]. The essential pathological manifestations of the disease are necrotizing granulomatous encephalitis with infiltration of inflammatory cells dominated by lymphocyte and plasma cells and considerable coagulation necrosis or focal hemorrhage [6]. At present, there are no definitive treatments available for this disease. Unlike other reported cases, this is the first PET/CT examination of Balamuthia mandrillaris encephalitis, hoping to provide clinical practice to improve diagnostic accuracy.

Case report

A 66-year-old female was admitted to our hospital with a 1-week history of headache without obvious inducement on March, 2023. The patient denied the history of living in the epidemic area and had no nausea, vomiting, fever, or other discomfort on admission. Laboratory tests indicated 9.85 $\times$ 10^9/L of white blood cell (normal range: [3.5-9.5] $\times$ 10^9/L) and 7.76 $\times$ 10^9/L of neutrophile granulocyte (normal range: [2-7] $\times$ 10^9/L). Brain magnetic resonance imaging (MRI) (Fig. 1A-F) showed a 2.1 $\times$ 1.4 $\times$ 1.1cm area of low signal intensity on T1-weighted imaging (T1WI) (Fig. 1A) and apparent diffusion coefficient (ADC) (Fig. 1F), high signal intensity on T2-weighted imaging (T2WI) (Fig. 1C), fluid-attenuated inversion recovery (FLAIR) sequence (Fig. 1D) and diffusion-weighted imaging (DWI) (Fig. 1E) with peripheral edema. The lesion showed moderate ring enhancement with a central enhancement nodule on T1WI (Fig. 1B) and involved the mesencephalon and left cerebellar peduncles, with compression of the fourth ventricle. With symptomatic treatments such as lowering intracranial pressure and anti-infection, the patient's condition progressed rapidly to a semi-coma state. One week later, a repeat brain MRI performed revealed a slightly enlarged pontine lesion (Fig. 1G-L) and a new lesion in the left frontal lobe (Fig. 1M-R) similar to the original lesion. A stereotactic tissue biopsy was not performed because the patient's family could not agree.

The patient subsequently underwent whole-body Fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) on the 13th day of admission. Except for the physiological retention of both kidneys and bladder, there was no abnormal FDG hypermetabolism lesion in the body on the maximum-intensity projections (MIP) imaging (Fig. 2A). While the lesions in the pons and left frontal lobe showed irregular low-density shadows on computed tomography (CT) imaging (Fig. 2D and E), and circular FDG hypermetabolism on PET imaging (Fig. 2B and C) and fusion imaging (Fig. 2F and G) with central

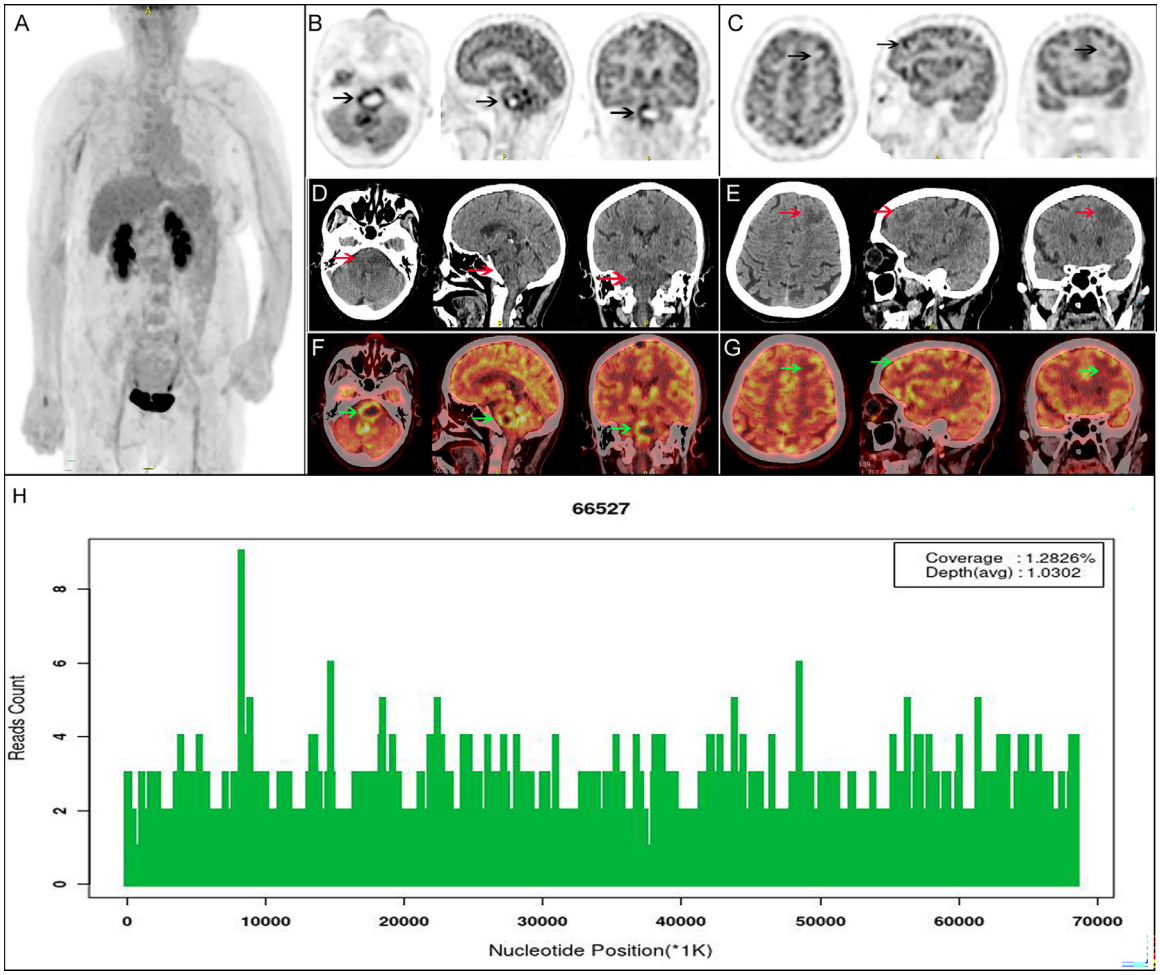

Fig. 2 – (A-G) The ^{18}F-FDG PET/CT showed no abnormal FDG hypermetabolism lesion in the body on the MIP imaging (A). The lesions in the pons and left frontal lobe showed irregular low-density shadows on CT imaging (D, E), circular FDG hypermetabolism on PET imaging (B, C) and fusion imaging (F, G) with central metabolic defects. (H) The metagenomic next-generation sequencing result of cerebrospinal fluid revealed 12,036 copy reads with 1.2826% of coverage and 1.0302X of average depth.

metabolic defects. We reviewed the literature and found that ^{18}F-FDG PET/CT findings of amoebic encephalitis are rarely reported.

Metagenomic next-generation sequencing (NGS) of cerebrospinal fluid was performed on the 17th day of admission. The total covered length of the genome sequence of Balamuthia mandrillaris was 867,740 base-pairs (bp) with 1.2826% of coverage and 1.0302X of average depth. The NGS result of the patient revealed 12,036 copy reads in cerebrospinal fluid (Fig. 2H).

Discussion

Balamuthia mandrillaris was first isolated in 1986 during an autopsy of a baboon brain that had died of encephalitis at the San Diego Zoo in California [7]. It can reside in hot springs, water parks, chlorinated pools, rivers, or soil and enter the body through skin or respiratory tract wounds to cause severe amoebic encephalitis [8]. Most reported cases in China start with a chronic granuloma of the maxillofacial skin and then gradually develop into a fatal granulomatous encephalitis (GAE) within 6 months to nine years [9]. On repeated questioning, our patient consistently denied any history of cutaneous involvement, which may manifest rapid progression to encephalitis and death without skin lesions [10]. Combined with her occupational characteristics, this patient's infection may be related to her long-term exposure to soil through agricultural work.

The clinical manifestations of GAE have specific regional distribution characteristics [4]. Cases with skin lesions as the initial symptom were mainly concentrated in China and Peru, which were relatively weak pathogenic and could be rapidly diagnosed and treated in time. In comparison, cases with encephalitis as the initial symptom were mainly distributed in the United States, with death occurring within days to months [1,9,10]. In the reported cases, the skin lesions most commonly involved the maxillofacial region, especially around the nasal alar, and presented as localized red plaques [9,11]. The

main clinical symptoms of central nervous system invasion include fever, headache, vomiting, epilepsy, altered consciousness, and speech disorder [9].

Due to the lack of specific manifestations, the clinical diagnosis of this disease is still challenging. Conventional and enhanced CT or MRI scans are the main methods to diagnose this disease, while PET/CT examination is rarely reported in all cases. Typical Balamuthia mandrillaris encephalitis shows single or multiple abnormal signals in different brain locations on MRI, usually a low-intensity signal on T1WI and increased intensity on T2WI, most of which are accompanied by ring enhancement and peripheral edema [9,12]. As the first case to perform PET/CT, the patient's PET images showed annular FDG hypermetabolism with a central metabolic defect corresponding to the lesions' peripheral granulomatous inflammation and central necrosis. Because not every patient can undergo a biopsy of brain lesions, diagnosing this disease still requires a combination of serological, skin, and molecular biology results.

At present, the treatment of this disease is mainly for the symptomatic treatment of skin lesions and central nervous system symptoms. Although various antiamoebic drugs have been developed and put into clinical practice in succession [4], the treatment effect on the disease is still not exact and ideal, and the outcome of most patients is death with different duration. Considering the existence of the blood-brain barrier, multiple drugs are often used in combination in the literature. For example, the combination of fluconazole, pentamidine, macrolides, sulfadiazine or fluorocytosine, miltefosine, and albendazole can produce a better frequency and efficacy of drug usage [13].

Conclusion

We presented a case of Balamuthia mandrillaris encephalitis that occurred in the brain stem and progressed rapidly to death without warning skin lesions. We were fortunate to have the first PET/CT images of this disease but unlucky not to have the pathological information of the brain lesion tissue. Although rare, this disease should be considered when diagnosing intracranial infectious lesions.

Patient consent

I declared that written informed consent has been obtained from the patient's family for publication of this case report and accompanying images. A copy of the written consent is available for review.

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