

Anti-GABA_B Receptor Encephalitis in China

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Description

Autoimmune encephalitis (AE) refers to the inflammatory disease of the central nervous system caused by autoimmune reaction [1]. AE is associated with antibodies against γ -aminobutyric acid B receptor (GABA_B R) in patients with limbic encephalitis (LE), which was first described in 2010 [2]. It is with the features of seizures, memory loss, and confusion, ataxia and status epilepticus. The available treatments included steroids, intravenous immunoglobulins (IVIg), or plasma exchange and oncologic therapy. The long-term prognosis is dictated by the presence of a tumor. The early recognition of syndromes associated with GABA_B R antibodies is vital because they usually respond to treatment [3]. Here, we present a series of Chinese patients with anti-GABA_B R encephalitis.

As known, AE accounts for about 10% to 20% of all the encephalitis patients. And the relative frequency of the GABA_B autoantibodies is 5.6% in patients with AE [4]. AE associated with autoantibodies against GABA_B R often presents with limbic syndrome, such as, epilepsy, short-term memory loss, and some psychiatric symptoms. The pathogenesis remains unclear, which may be attributed to that anti-GABA_B R antibodies can influence receptor function and block the inhibitory effects of baclofen on the spontaneous firing of cultured neurons [2].

To the best of our knowledge, there were 48 cases [5-7] reported in China, and the average age was about 56 years old, which was smaller than that reported in 2010 (62 years) [2]. And most of them were middle-aged and old men (about 65%). All patients were acute or subacute onset. About 82% of the patients had seizures as the initial symptoms, and also with memory function decline and mental and behavioral abnormalities. Among them, one female patients had headache and fever initially, which was similar to the manifestations of viral encephalitis. So, it was easy to be misdiagnosed and delay the treatment.

Severe and intractable seizures are the main features of anti-GABA_B R encephalitis, mainly with generalized tonic-clonic seizures. As reported, 22 Chinese patients had generalized tonic-clonic seizures, and 10 progressed to status epilepticus quickly. The antiepileptic drugs were ineffective at most time.

The anti-GABA_B R encephalitis is always associated with tumors, especially the small cell lung cancer (SCLC). SCLC was identified in 10 (50%) patients, all with LE [3]. In addition, esophageal carcinoma and malignant melanoma were also reported [8,9]. Among the 48 patients reported in China, 14 were diagnosed with lung cancer, nine of whom were SCLC. There were two patients with previous history of cervical cancer and renal clear cell carcinoma respectively.

The imaging findings of anti-GABA_B R encephalitis are often atypical. An American study reported that magnetic resonance imaging (MRI) of the brain showed increased Fluid-Attenuated Inversion Recovery (FLAIR) signal in the medial temporal lobe of both hemispheres, compatible with limbic encephalitis in 66% patients with anti-GABA_B R encephalitis [2]. In China, 26 patients had similar head MRI findings. In the cerebrospinal fluid (CSF) there were 5 patients with oligoclonal bands. And some were accompanied by additional autoantibodies such as anti-Hu antibodies, anti-NMDAR antibody, and anti-Yo antibody. The electroencephalogram (EEG) did not have high specificity in the diagnosis of anti-GABA_B R encephalitis. Seventeen Chinese patients showed mild-to-moderate abnormal EEGs. As for 18F-FDG PET/CT four patients showed abnormal results from PET, including three unilateral temporal hyper metabolisms and one bilateral temporal hyper metabolism.

During treatment in hospital, seizures and psychiatric symptoms were not controlled with only antiepileptic drugs or antiviral treatment until starting IVIg and/or steroids. Most patients showed complete or partial neurological relief with improved mRS to immunotherapy, antiepileptic therapy, and other symptomatic treatment.

At follow-up, six Chinese patients died, and five of whom died of lung cancer. It has been reported that patients with SCLC might have unfavorable treatment outcomes if using the immunotherapy. And the main causes of death in patients with anti-GABA_B R encephalitis were lung tumor progression and chemotherapy related complications [2,6,10]. Therefore, it is necessary to attach great importance to the detection of tumor or paraneoplastic biomarkers.

In summary, the early detection, diagnosis and treatment of anti-GABA_B R encephalitis is very important to improve prognosis. So, it's necessary to test for anti-GABA_B R antibodies in patients with possible LE or new-onset epilepsy with unknown etiology.

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