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# A case of anti-NMDA receptor encephalitis with thymoma

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## Abstract

*To explore the clinical characteristics, imaging examination, test characteristics, diagnostic ideas and treatment plans of anti-N-methyl-D aspartate receptor encephalitis, so as to better understand anti-NMAD receptor encephalitis.*

***Methods:*** *To analyze the diagnosis and treatment process of a case of anti-NMAD receptor encephalitis with thymoma admitted to the Department of Neurology of our hospital on May 31, 2021, and review the relevant literature.*

***Results:*** *In this article, the anti-NMAD encephalitis patients with pons as the main affected site also had thymoma, their disease progressed rapidly, clinical manifestations, imaging examinations were not typical, the effect of hormone therapy was not good, and the prognosis was poor.*

**Keywords:** Thymoma, Anti-NMAD receptor Encephalitis, Imaging, Pons.

## Clinical Information

A 35-year-old female patient was admitted to the Department of Neurology of our hospital on May 31, 2021, mainly due to "15 days of numbness in the distal end of the left upper extremity and 4 days of aggravated speech awkwardness". 15 days ago, the patient had a sudden numbness of the distal left upper extremity without obvious inducement, which was not paid attention to at that time. Before 6 days, he developed numbness of the left lower extremity. 4 days before admission, he developed unresponsiveness and awkward speech. He was able to understand other people's speech, but his speech speed decreased. Slow, laborious to speak. On the way to our hospital for treatment, I experienced twitching of the limbs, upturned eyes, foaming at the mouth, and tongue bite, which lasted for about 10 minutes and completely improved afterwards. The patient could not recall it afterwards. An outpatient head MRI showed that the brainstem was suspected to be space-occupying lesions, so he was admitted to the hospital with "convulsions pending investigation". Since the onset of the disease, the patient has had no fever or cough, has good sleep and eating conditions, has normal stools, and has no significant changes in body weight. On the second day after admission, the patient's condition worsened. He could only speak simple words, walk unsteadily, and frequently twitch the corners of his mouth to the left, which lasted about 5-10 seconds each time and got better.

**Physical examination on admission:** T36.7°C, P90 beats/min, R18 beats/min, BP 120/99 mmHg, Nervous system physical examination: slightly slow response, less speech, dysarthria, left tongue extension, muscle strength of limbs 5 Grade, needle tingling pain at the distal left upper limb and left lower limb is decreased, knee tendon reflex and Achilles tendon reflex are not elicited, bilateral calcaneal knee tibial test is not stable, bilateral Babinski's sign (-), and no positive signs are seen on other physical examinations.

Past history, personal history, and family history are normal.

## Auxiliary Inspection

Blood routine, biochemical routine, blood coagulation routine, antinuclear antibody spectrum, anti-O antibody combination, ANCA, and the first five items were not abnormal; the whole abdominal color Doppler ultrasound showed no abnormality; head MRI examination (Figure 1) showed T2 of the right pons FLAIR high signal, T1 low signal, suspected space-occupying lesions; enhanced MRI was performed (Figure 2), the results reported that the right pons T2, FLAIR high signal, incomplete enhancement, can not rule out the possibility of inflammatory demyelination and low-grade glioma sex. Lung CT showed anterior mediastinal space (Figure 3a), enhanced CT showed thymoma (Figure 3b); Lumbar puncture examination: the cerebrospinal fluid was clear and transparent, the pressure was 110mmH20, the white blood cells were 10*10^6, and the protein was 0.73 g/L. Protein is qualitatively positive, chloride and glucose are not abnormal, exfoliated cells

are negative, ink staining is negative, cerebrospinal fluid IgG-oligoclonal zone is positive, cerebrospinal fluid central nervous system demyelinating diseases such as anti- AQP4 antibody, anti-MOG antibody, anti-GFAP antibody, Anti-MBP antibodies were all negative, cerebrospinal fluid paraneoplastic syndrome antibodies were negative, and cerebrospinal fluid anti-NMAD receptor antibody IgG was 1:10 positive. Serum cerebrospinal fluid IgG 68.80 mg/L, IgM 1.38 mg/L. Electroencephalogram: extensive moderate-severe abnormal EEG, fully guided diffuse rhythmic delta activity, and occasional fast-rhythmic activity (occasionally brush delta wave), responding to painful stimuli. Although the antibodies of the patient's paraneoplastic syndrome were all negative, the patient's chest enhanced CT showed thymoma and anti-NAMD receptor antibody was positive, so the diagnosis was anti-NAMD receptor encephalitis related to thymoma.

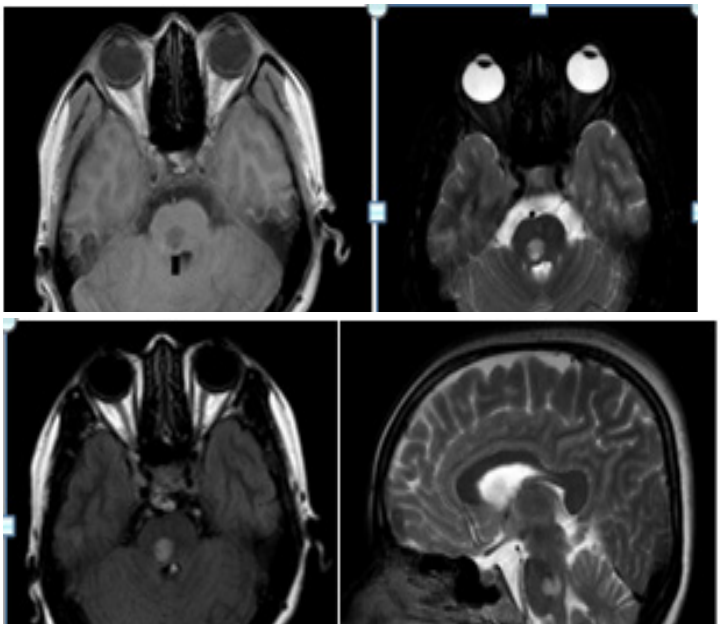


**Figure 1:** A) The patchy T1WI image of the pons can be seen with a slightly low signal shadow; B) The patchy T2WI image of the pons can be seen with a slightly high signal shadow; C) The patchy FLAIR image of the pons can be seen with a slightly high signal shadow; D) There is a patchy T2WI image with slightly high signal shadow in the pontine axial position.

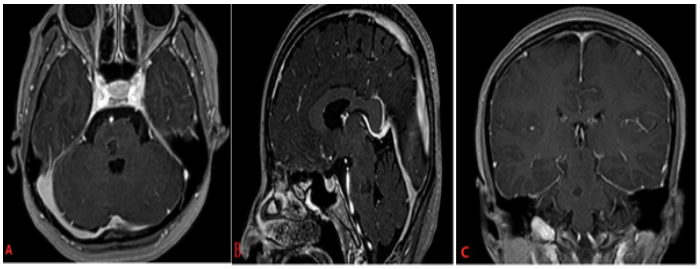
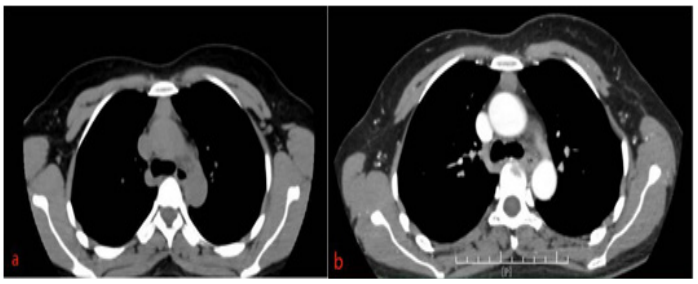


**Figure 2:** Right pons T2, FLAIR high signal, incomplete enhancement.



uneven enhancement, which is considered to be a thymoma.

The Course Of Treatment And The Evolution of the Condition

The patient was given symptomatic treatment such as anti-epilepsy for the first 5 days after admission. The condition did not improve and continued to aggravate, with difficulty speaking, unsteady walking, and twitching of the corners of the mouth. On the 6th day of admission, the cerebrospinal fluid autoimmune encephalitis-related antibody, namely anti-NMAD receptor antibody IgG was 1:10 positive, and he was given a 1000mg methylprednisolone sodium succinate injection once a day as an impulse treatment, and it was planned to be halved after 3 days. However, the patient experienced further aggravation after the second hormone treatment, unable to speak, and had difficulty swallowing. I can't walk, and my mouth ticked frequently. Considering that the patient's condition progressed rapidly, the head and cervical spine MRI showed no enlarged lesions and no abnormalities in the cervical spine. The family members requested to be transferred to the Affiliated Hospital of Harbin Medical University for further treatment. After transfer, the patient continued to be given hormone therapy, and at the same time adjuvant immunoglobulin, vitamin B12, vitamin B1 and other treatments, but the patient's condition continued to aggravate and developed a coma during the 16 days of treatment. After 16 days of treatment, the patient was confused, aphasia, cognitive decline, and pain No response to stimulation, level 4 muscle strength of both upper limbs, and level 2 muscle strength of both lower limbs, were transferred to our hospital to continue recovery. During the period, the patient was unable to undergo thymoma resection due to his poor physical condition and was given conservative treatment.

## Discussion

Paraneoplastic neurologic syndrome (PNS) is a neurological disease caused by a tumor, but not caused by direct tumor growth, metastasis, metabolism, or infection complications. The incidence of PNS in patients with malignant tumors is 0.01% [1].

PNS that may be associated with thymoma include limbic encephalitis, subacute cerebellar degeneration, Morwan syndrome, and peripheral neuropathy. These PNSs are mostly mediated by anti-neuronal antibodies or participate in the pathogenesis. Positive anti-neuronal antibody is also the main basis for diagnosing PNS related to thymoma. At present, anti-neuronal antibodies are mainly divided into two categories: one is anti-intracellular antigen antibodies, including anti-GAO antibodies and anti-CV2. It is generally

believed that anti-neuronal antigen antibodies are mainly involved in cellular immune responses, and neuronal damage is severe and difficult. recover. The other type is anti-neuronal cell surface antigen antibodies, such as anti-AMPAR antibody and anti-NMMDAR antibody, which mainly cause reversible neurological dysfunction through humoral immune mechanism, and the immunotherapy effect is good [2].

Anti-NAMD receptor encephalitis associated with thymoma is a type of PNS and a rare cancer complication. In previous research reports, tumors related to anti-NAMD receptor encephalitis were mainly teratomas [3-6], followed by lung cancer [7], and thymoma was very rare. Although thymoma is often associated with autoimmune diseases such as myasthenia gravis, it is a relatively rare cause of anti-NAMD receptor encephalitis. Because the clinical symptoms of patients often appear before the tumor is found, and the clinical manifestations are diverse, it brings certain difficulties to clinical diagnosis.According to reports by Gultkin and others [8], only 60% of patients with paraneoplastic encephalitis have anti-neuronal antibodies, and the remaining 40% have negative antibodies. The patient in this article was diagnosed with thymoma-related anti-NAMD encephalitis because of the positive anti-glutamate receptor antibody in the cerebrospinal fluid, lung CT and enhanced CT suggesting thymoma.

Glutamate is a neurotransmitter. Its receptors are divided into ion channel type and metabolite type. Ion channel types are divided into NMDA type and non-NMDA type [9]. Anti-NMDA receptor antibodies are directed against nerve cell surface receptors. Of antibodies. In 2007, Dalmau et al. [10] first discovered specific autoantibodies against NMDAR NR1 subunit in a cohort of 12 female patients, 11 of whom had ovarian teratomas. Studies have found that anti-NMDA receptor encephalitis mostly occurs in adolescents, and the incidence is higher in women than in men [11]. The symptoms caused by anti-NMDA receptor encephalitis can be improved by adding anti-tumor therapy and immunotherapy early in the course of the disease. It is reported that about 25% of patients have some sequelae, and the acute mortality rate is 7% [10].

Patients with anti-NMDA encephalitis usually present with mental symptoms, cognitive dysfunction, seizures, speech disorders, movement disorders, decreased levels of consciousness, and autonomic dysfunction or hypoventilation. At the same time, some patients also have prodromal symptoms such as headache, fever, nausea and upper respiratory symptoms [12]. The clinical manifestations of children and adults may be different. Children usually have neurological impairment symptoms such as behavioral problems, seizures, speech disorders, and movement disorders [13]. In addition, children's mental disorders are mostly tantrums, hyperactivity, or irritability, while adults usually exhibit anxiety, partial behavior, and delusions.

Since anti-NAMD receptor antibodies are mainly diagnosed by cerebrospinal fluid and serum antibody testing, many hospitals do not have the testing conditions and the testing takes a long time. Therefore, the diagnosis of the disease is difficult and cannot be completely dependent on antibody testing. Cerebrospinal fluid abnormalities are often seen in patients with anti-NMDA encephalitis, including mild to moderate increase in lymphocytes, mild increase in protein concentration, and positive cerebrospinal fluid-specific oligoclonal bands [14]. In the early stage of the disease, the oligoclonal zone of cerebrospinal fluid can be negative, but the positive rate gradually increases as the disease progresses [15]. About 30%-50% of patients with anti-NMDAR encephalitis have abnormal head MRI results[14,16,17]. Usually in the cortex, subcortex, hippocampus, basal ganglia, medial temporal lobe and posterior cranial fossa, high signals of FLAIR and T2 sequences can be observed, and T1 low signals. Some patients can also observe multifocal or extensive demyelination changes, which suggests that patients with anti-NMDAR encephalitis may also develop demyelinating diseases at the same time [15]. In the acute phase of the disease, more than 90% of patients have abnormal EEG, and one third of them can show extreme delta brush, which is an electrographic pattern considered to be characteristic of patients with anti-NMDAR encephalitis [18]. In addition, it is also necessary to actively look for the presence of tumors.

The reasons for the poor prognosis of the patients in this article after being diagnosed with high-dose glucocorticoids and immunoglobulins are considered: First: the first symptoms of the patient and the lesion site are atypical, which may be confusing in the early diagnosis of the disease, Failed to give hormone shock therapy immediately after admission. Second: The patient had a thymoma and could not be treated with surgery due to his physical condition. Therefore, when encountering such diseases, it is necessary to combine various aspects with early and rapid diagnosis, timely administration of hormones, immunoglobulin and other treatments, and combined surgery to remove the tumor to improve the patient's prognosis.

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