



## Prodromal Infection Trigger Acute Onset Anti-DPPX Encephalitis without CNS Hyperexcitability Symptoms: A Case Report

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### Abstract

Dipeptidylpeptidase-like protein-6 (DPPX) antibody associated encephalitis can present with protracted encephalitis, symptoms of central nervous system (CNS) hyperexcitability, and cerebellar signs. Most of these patients onset subacutely and have diarrhea in the initial phase. We report a 26-year-old Chinese female, who had ten days history of upper respiratory tract infection, followed by headache, dizziness, gait instability suddenly. Neurological examination demonstrated prominent vertical nystagmus, ataxia and cognitive impairment. CSF testing for neuronal autoantibodies revealed DPPX antibody IgG titer of 1:1. After treatment with IV methylprednisolone combined with IV immunoglobulin, her neurological symptoms improved markedly. This case illustrated that anti-DPPX autoimmune encephalitis could be triggered by prodromal infection and onset acutely. Patients may only show cerebellar signs and cognitive impairment without CNS hyperexcitability. Performing an auto-antibody examination might aid differential diagnosis.

**Keywords:** Autoimmune encephalitis; Anti-dipeptidylpeptidase like protein 6 antibody; Nystagmus; Ataxia

### Introduction

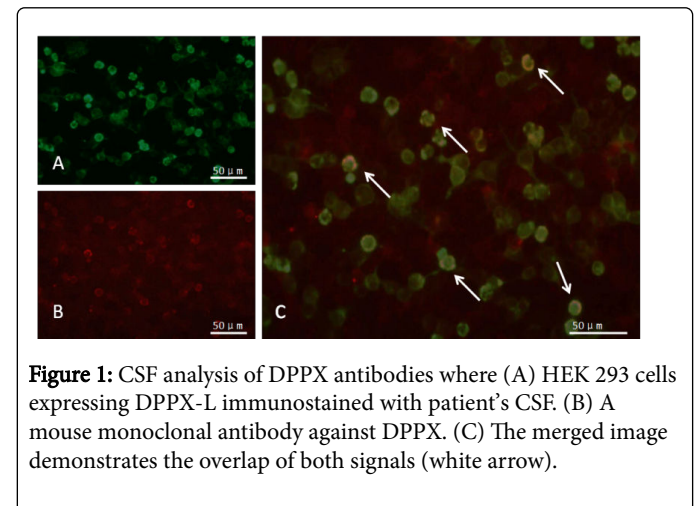
Dipeptidylpeptidase-like protein-6 (DPPX) antibody is a rare neuronal surface antigen that might cause autoimmune encephalitis (AE). Anti-DPPX encephalitis commonly affects elder people, and symptom onset is usually insidious. Most of the patients may have gastrointestinal signs before showing CNS manifestation. Neurocognitive deficits, sleep disturbance, central hyperexcitability, cerebellar signs are frequently observed [1]. Here, we describe a Chinese anti-DPPX encephalitis young patient presenting with acute onset, prominent vertical nystagmus and ataxia, who was triggered by prodromal infection.

### Case Presentation

A 26-year-old Chinese woman developed headache, dizziness, progressive gait instability, and fell over 5 days before admission to our hospital. On admission she also had vomiting, nausea, somnolence, slurred speech, and double vision. She caught a cold with mild fever, anginosis and cough 10 days before onset. She denied diarrhea in the

last three months. Family history revealed no abnormalities. Neurological examination demonstrated prominent vertical, horizontal, and torsional nystagmus components, obvious dysmetria by finger-to-nose test, and ataxia. The minimal state examination (MMSE) score was 20.

A brain MRI scan was performed and showed no abnormalities. Lumbar puncture revealed an opening pressure of 140 cmH<sub>2</sub>O, a leukocyte count of 281/mL (94% lymphocytes) and the protein level was 21 mg/dl (0–60 mg/dl). CSF testing for neuronal autoantibodies revealed a dipeptidylpeptidase-like protein-6 antibody IgG titer of 1:1 (Neuroimmunology Laboratory, Kingmed Diagnostics, using cell-based indirect immunofluorescence assay), providing evidence for immune-mediated encephalitis (Figure 1). Viral polymerase chain reaction (PCR) was negative. Assays for paraneoplastic antibodies were normal. Ultrasound of the uterine adnexa showed polycystic ovaries.



**Figure 1:** CSF analysis of DPPX antibodies where (A) HEK 293 cells expressing DPPX-L immunostained with patient's CSF. (B) A mouse monoclonal antibody against DPPX. (C) The merged image demonstrates the overlap of both signals (white arrow).

She was treated with IV methylprednisolone combined with IV immunoglobulin, and demonstrated a marked improvement after 10 days of therapy. Her nystagmus, ataxia, gait, and consciousness improved markedly. Before her check out from hospital, we performed another lumbar puncture. Her leukocyte count had decreased to 39/mL (96% lymphocytes) and the protein level was 31mg/dl (0–60 mg/dl). At her 6-month follow-up she was able to walk unassisted without any evidence of ataxia.

### Discussion

Antibody-associated encephalitis characterized by specific autoantibodies has been recognized in the last ten years. It is a diverse group of syndromes that include two groups: classic paraneoplastic disorders (PNDs) and autoimmune encephalitis [2]. The latter is caused by the direct interaction between antibodies and their target antigens on neuronal surfaces and synapses [3]. Our case was a 26-year-old Chinese woman who presented with acute onset ataxia, vertigo, and cognitive impairment. CSF examination showed she was DPPX-antibody positive and she had a good response to immunotherapy. Therefore, we diagnosed her as autoimmune encephalitis caused by DPPX-antibody.

AE associated with antibodies to DPPX was first identified in 2013[4]. Most patients are middle-aged adults with insidious and subacute symptom onset. Severe diarrhea may occur at the initial

episode of neurological manifestation. Prominent clinical symptoms include encephalopathy affecting the cortical, cerebellar, and brainstem regions of the CNS. Cortical hyperexcitability has been observed, including myoclonus, rigidity, and stiffness [4]. Cerebellar and brainstem regions targeted by DPPX antibodies may cause ataxia and eye movement disturbances [5]. Tobin et al. reported 40% of 20 seropositive patients had diplopia, oscillopsia, blurred vision, and upbeat-torsional nystagmus [5,6]. The clinical findings of our case are different from reports in the original series. She had a prodromal viral infection 10 days before admission, and her CSF showed increase in leucocytes. Although systemic infections are frequently considered a potential trigger of AE, it is only reported in several subtypes with antibodies against NMDA receptor, GABA<sub>A</sub> receptor, mGluR5, Neurexin3 and dopamine-receptor-2 antibodies [7]. Prodromal-infection-like symptoms were rare reported in patients with anti-DPPX symptoms. This may be due to the diversity of the immune activation pathways of the AE subtypes. But our case may indicate that viral infection could also trigger anti-DPPX encephalitis while the mechanism still needs further study.

The patient showed obvious vertical and torsional nystagmus and ataxia. Cognitive impairment of short-term memory was also observed, but she did not have any gastrointestinal symptoms or progressive encephalomyelitis with rigidity and myoclonus (PERM)-like presentation. DPPX is a regulatory subunit of the Kv4.2 potassium channel complex, which is expressed in neuronal dendrites and soma. Its function is to increase the surface expression and channel conductance of Kv4.2 channels [6]. The different organic expression of DPPX is responsible for the diverse clinical manifestations. In our opinion, anti-DPPX AE may also occur in young adults, and some patients show acute onset disease. The combination of obvious nystagmus, ataxia, and cognitive impairment should indicate testing for anti-DPPX antibodies.

In this report, the patient was treated with IV methylprednisolone and immunoglobulin, her nystagmus, ataxia, and cognitive impairment improved markedly without any. In the original reports, most patients had good responses to immunotherapies, but some required additional treatment with plasma exchange and rituximab. Patients with a long-term history of AE might have lengthy hospitalizations and multiple relapses [4-6]. Therefore, an early diagnosis and initiation of therapy is very important for a good long-term outcome.

## Conclusion

Overall, our case verified that prodromal infection may trigger acute onset anti-DPPX encephalitis. Prominent vertical nystagmus, ataxia, cognitive impairment without PERM may occur in anti-DPPX encephalitis. Early immunotherapy is important for the positive long-term outcomes of patients.

## Authors' Contributions

CXH, CJJ contributed to the initial development of the research, and WJ, LA, HJ to its further development and completion. All authors

contributed to the development of the outline and all stages of drafting and revision of the manuscript. CJJ is the corresponding author and takes responsibility for its overall content.

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## Competing Interests

The authors declare that they have no competing interests.

## Consent for Publication

Written informed consent was obtained from the patient for the publication of this Case Report and any accompanying images.

## Ethics Approval and Consent to Participate

Not applicable.

## References

1. Piepgras J, Hölting M, Michel K (2015) Anti-DPPX encephalitis: pathogenic effects of antibodies on gut and brain neurons. *Neurology* 85: 890-897.
2. Dalmau J, Rosenfeld MR (2014) Autoimmune encephalitis update. *Neuro Oncol* 16: 771-778.
3. Dalmau J (2016) NMDA receptor encephalitis and other antibody-mediated disorders of the synapse: The 2016 Cotzias Lecture. *Neurology* 87: 2471-2482.
4. Boronat A, Gelfand JM, Gresa-Arribas N (2013) Encephalitis and antibodies to dipeptidyl-peptidase-like protein-6, a subunit of Kv4.2 potassium channels. *Ann Neurol* 73: 120-128.
5. Doherty L, Gold D, Solnes L (2017) Anti-DPPX encephalitis: prominent nystagmus reflected by extraocular muscle FDG-PET avidity. *Neurol Neuroimmunol Neuroinflamm* 4: e361.
6. Tobin WO, Lennon VA, Komorowski L (2014) DPPX potassium channel antibody: frequency, clinical accompaniments, and outcomes in 20 patients. *Neurology* 83: 1797-803.
7. Joubert B, Dalmau J (2019) The role of infections in autoimmune encephalitis. *Rev Neurol* 175 :420-426.