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Clinical Observations

# Voltage-Gated P/Q-Type Calcium Channel Antibodies Associated With Cerebellar Degeneration

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ABSTRACT

**BACKGROUND:** Paraneoplastic cerebellar degeneration is a rare neurological condition characterized by diffuse cerebellar dysfunction and magnetic resonance imaging evidence of progressive cerebellar atrophy. It has been associated with several autoantibodies and malignancies in adults. To date, only six cases have been described in male children. **PATIENT DESCRIPTION:** We describe an eight-year-old girl with a prodrome of abdominal pain and vomiting followed by acute onset diplopia, dysarthria, dysmetria, and ataxia. She was found to have cerebellar degeneration in association with P/Q-type calcium channel antibodies. **CONCLUSION:** This is the first child with documented paraneoplastic cerebellar degeneration in association with P/Q-type calcium channel antibodies.

***Keywords:*** paraneoplastic, cerebellar degeneration, voltage-gated calcium channel antibodies, child, female

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## Introduction

Paraneoplastic cerebellar degeneration (PCD) is a rare neurological syndrome associated with numerous cancers, most commonly small-cell lung cancer (SCLC), gynecological and breast cancers, and Hodgkin lymphoma. It is thought that paraneoplastic antibodies are produced as the body's immune reaction to an underlying and usually yet undetected malignant process. The resultant syndrome is a by-product of the antibodies' effect on normal structures.[1] PCD is clinically characterized by a prodromal phase of dizziness, nausea, and vomiting which can last weeks or months. This is followed by relatively acute onset of ataxia, diplopia, dysarthria, and at times dysphagia.[1,2]

This syndrome occurs predominantly in adults, although six boys with Hodgkin lymphoma have been documented.[3-8] In three of these individuals autoantibodies were isolated, one with anti-PCAb[6] and two with anti-Tr.[7,8] Although up to 41% of adult patients with SCLC and PCD have voltage-gated calcium channel antibodies (VGCC Ab),[9] no pediatric patients have been documented.

## Patient Description

This eight-year-old girl with a two-month history of intermittent abdominal pain and occasional diarrhea experienced several episodes of vomiting after eating five days before admission. Two days before presentation, she had increasing difficulty with walking and had fallen several times with no loss of consciousness. The day after admission, she complained of double vision and kept her left eye preferentially closed. Over the next three days, vomiting and double vision persisted. She complained that she was dizzy, describing intermittent "room spinning." Her speech became slurred. She denied headache, weakness or numbness, fevers, chills, trauma, cough, or recent travel.

On examination, her vital signs were normal. She was irritable but cooperative. She had nystagmus in all directions of gaze, and although extraocular movements appeared full, she had horizontal diplopia in all directions. She had dysarthria with a scanning speech pattern, truncal ataxia, and severe bilateral, symmetric dysmetria. She was unable to stand or walk unsupported. Strength and sensation were normal;

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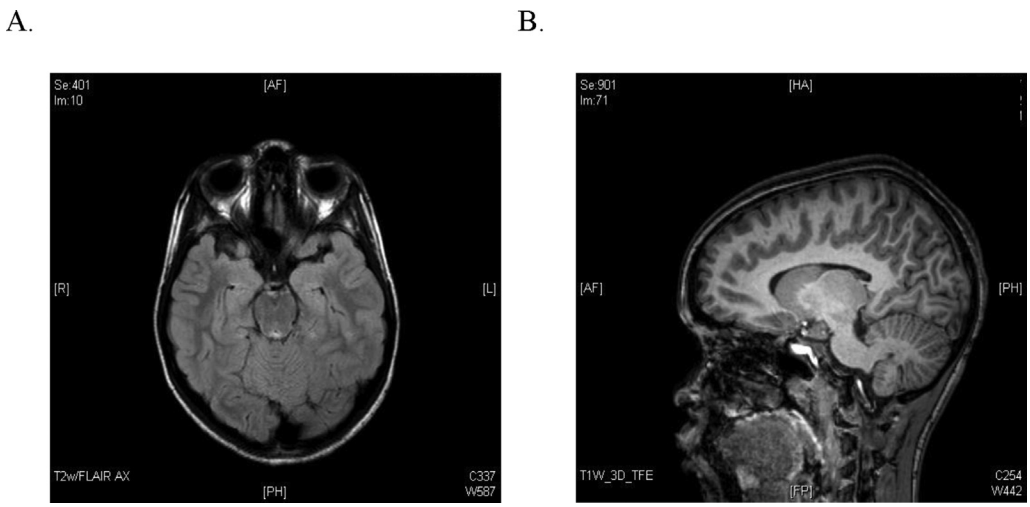


**FIGURE 1.**
Normal magnetic resonance imaging of the brain at presentation. (A) Axial T2 flair; (B) sagittal T1.

**TABLE 1.**
Negative/Normal Diagnostic Evaluations

| Category | Test |
|---|---|
| Inflammatory | ESR, CRP, CSF oligoclonal bands and myelin basic protein |
| Autoimmune | Anti-SM, anti-Ro, anti-La, RF, anti DNA, celiac panel, comprehensive immunoglobulins, Gq1b, serum autoantibodies (Hu, Ma2, Yo, Ri, CAR, CV2, Zic4, VGKC, Ampiphysin, AChR, NMDA) |
| Infectious | EBV (IgG/IgM), HCV (IgG/IgM), HIV, lyme, parvo, VZV IgM, mycoplasma IgM, ASLO, HepA IgM, RPR, CSF culture and viral panel |
| Endocrine | TFTs, urine HVA, AFP |
| Nutritional | B12, ferritin, lipid panel |
| Metabolic/genetic | Lactate, pyruvate, CPK, ceruloplasmin, urine electrolytes, fritaxin |
| Neoplastic | Abdominal and pelvic ultrasound, abdominal and pelvic MRI, CT chest, urine metanephrines, serum AFP, HCG, LDH |

Abbreviations:
AChR = acetylcholine receptor
AFP = alpha fetoprotein
Anti-DNA = Anti-deoxyribonucleic acid
Anti-SM = Ant-smooth muscle
ASLO = anti-streptolysin O
CAR = cancer associated retinopathy
CPK = creatine phosphokinase
CRP = C reactive protein
CSF = cerebrospinal fluid
CT = Computed tomography
EBV = Epstein Bar Virus
ESR = erythrocyte sedimentation rate
HCG = human chorionic gonadotropin
HCV = Hepatitis C virus
Hep A = Hepatitis A
HIV = Human immunodeficiency virus
HVA = homovanillic acid
LDH = lactate dehydrogenase
MRI = Magnetic resonance imaging
NMDA = N-Methyl-D-aspartate
RF = rheumatoid factor
RPR = rapid plasma regain
TFT = thyroid function tests
VGKC = voltage gated potassium channel
VZV = Varicella zoster virus

reflexes were diminished with flexor plantar responses. Routine serum studies and urine toxicology were negative.

Magnetic resonance imaging (MRI) of the brain with and without contrast (Fig 1) was normal. Cerebrospinal fluid examination revealed 14 leukocytes/μL with lymphocytic predominance, 34 red blood cells/μL, protein of 15 mg/dL, and glucose of 56 mg/dL. Electroencephalography was normal. An extensive serologic evaluation performed in search of inflammatory markers, infection, rheumatologic markers, endocrine function, vitamin levels, heavy metals, and genetic and metabolic etiologies was negative (Table 1). The only significant positive value was an elevated antinuclear antibody (ANA) titer at 1:80. Screening for occult malignancy with extensive serum and urine testing and imaging was negative (Table 1). A course of intravenous methylprednisolone 250 mg every six hours for three days did not improve the symptoms. After a five-day (2 g/kg total) course of intravenous immunoglobulin (IVIG), she had marked improvement in vision, speech, coordination, and gait. At discharge, she had no visual complaints, was able to feed herself with only very mild dysmetria, and was able to walk with assistance. After discharge, serum paraneoplastic examination showed elevated VGCC Ab (433 pmol/L, normal range <71 pmol/L).

She was readmitted approximately three months later with symptoms similar to time of presentation, although milder. She reported "dizziness" and was found to have nystagmus. Her gait became more ataxic, and she required full assistance to ambulate. She received another five-day course of IVIG at 2 g/kg total, with modest improvement. Her dizziness resolved, and nystagmus and ataxia improved significantly. She was able to walk with only minor assistance at the time of discharge.

As of 17 months after presentation, her speech retained a scanning quality, and although she walked unsupported with a narrow-based gait, she was unsteady. She had mild bilateral finger to nose dysmetria, which did not affect her ability to perform most tasks, with improvement in handwriting. Despite the continuing clinical improvement, repeat serum antibodies were elevated (0.59 nmol/L, normal <0.02 nmol/L). Repeat MRI revealed diffuse cerebellar atrophy (Fig 2). Because of the stable nature of her deficits and overall clinical improvement, further immunomodulatory therapies have not been prescribed. Repeat screening for malignancies with MRI abdomen and computed tomography scan of chest was negative.

## Discussion

PCD is a rare neurological syndrome which occurs mainly in adults with malignancies. Clinically, patients present with a subacute course of pancerebellar dysfunction