

## CASE REPORT:

# SENSORY-ONLY GULLAIN-BARRÉ SYNDROME ASSOCIATED WITH COXSACKIEVIRUS B4 INFECTION

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## INTRODUCTION

Guillain-Barré syndrome (GBS) is classically defined as a disorder of motor neurons but several variants that include sensory deficits have also been described. Variants that are primarily sensory, with little to no motor dysfunction, have been reported rarely. In most cases, an antecedent infection is identified. Here we present a case of sensory-only GBS associated with coxsackie virus B4 infection in a 79 year-old male. There have been rare reports of coxsackie viruses causing classic GBS or peripheral neuropathy, but to our knowledge this is the first reported association with sensory-only GBS.

## CASE REPORT

A 79 year-old male presented to the emergency department in August 2013 with a one-week history of fever, chills, generalized myalgia's, and a maculopapular rash on his trunk and upper and lower extremities (Fig 1). He was febrile (38.6°C) and tachycardic (109 bpm). Laboratory studies showed leukopenia (3,400 WBC/ $\mu$ L) and elevated liver enzymes (AST of 101 U/L, ALT of 191 U/L). He was suspected of having a tick-borne illness such as ehrlichiosis or Rocky Mountain spotted fever (RMSF) and was started on a ten-day course of doxycycline. He showed clinical improvement and was discharged after three days. Ehrlichia PCR and RMSF antibody titers drawn at admission were subsequently found to be negative.

Four days later he returned to the ED with worsening unsteadiness which he described as difficulty coordinating his hands and feet. Physical examination revealed dysmetria, dysdiadochokinesia, and gait ataxia. Vibration sense was absent in his lower extremities as well as distal to and including his proximal interphalangeal joints. Bilateral Achilles reflexes and his left patellar reflex were absent. Strength was 5/5 in all extremities and light touch and pinprick sensation were preserved. He was oriented and had no memory deficits.

Laboratory studies revealed hyponatremia (120 mmol/L). The patient's white blood cell count had normalized since his first admission and his liver enzymes were trending downward. A lumbar puncture showed mildly elevated protein (58 mg/dL) and glucose (82 mg/dL) in his cerebrospinal fluid. A head CT scan was negative for any acute changes. Electromyography revealed a sensory neuropathy involving both the upper and lower extremities with preserved motor function. There was no evidence of axonal damage or neuromuscular junction dysfunction.

Many tests trying to determine the etiology of his neurological symptoms were ordered. Infectious agents assessed for included HSV, *Burellia burgdorferi*, *Mycoplasma pneumoniae*, VZV, HIV, syphilis, EBV, CMV, hepatitis viruses, West Nile virus, coxsackie viruses, echoviruses, adenoviruses, and repeat RMSF titers. Other tests evaluated TSH, folate, vitamin E, ceruloplasmin, a paraneoplastic panel, and a GBS-associated antibodies panel.

The patient's neurological symptoms failed to improve after correction of his hyponatremia. Given his neurological deficits following an acute, likely infectious illness, the patient was presumed to have a sensory-only variant of GBS. He was started on a five-day course of IV immune globulin (IVIg) therapy. His dysmetria and dysdiadochokinesia showed improvement, and he was discharged after two weeks in the hospital to a rehabilitation facility.

A send-out titer for antibodies to Coxsackie virus B4 returned positive at a  $\geq 1:640$  titer ( $<1:10$ ). All other previously-mentioned tests were negative or normal. As of March 2014, the patient ambulates without issue and has resumed his previously active lifestyle. His only lingering symptom is a tingling sensation he feels in his feet when he first arises in the morning.

### **DISCUSSION:**

GBS is classically a disorder characterized by predominantly motor nerve demyelination with corresponding progressive muscle weakness. It usually follows an antecedent infection such as *Campylobacter jejuni*. However, there are well-known variants of GBS that involve autonomic, sensory, and cranial nerve pathways. Some of these have been well-characterized such as Miller-Fisher syndrome [1]. Other less-defined conditions with ataxia due to peripheral loss of proprioception have fallen under the umbrella of sensory-only GBS. Asbury put forth criteria that have since been used to define these sensory-only GBS variants [2-4]. These criteria include:

1. The onset must be rapid.
2. The distribution of neuropathic findings must be widespread and symmetrical.
3. Recovery must be complete or nearly so.
4. CSF protein should be elevated without elevation in cells (albumin-cytologic dissociation).
5. Electrodiagnostic results should be consistent with a demyelinating peripheral neuropathy.

Our patient fulfilled all of these criteria, with his neuropathy mainly affecting the large-diameter peripheral nerves involved in proprioception and vibration sense.

GBS is believed to be an autoimmune disease with evidence suggesting a molecular mimicry mechanism. Subtypes of GBS have different autoantibodies associated with them; in Miller-Fisher syndrome, antibodies to GQ1b are positive in 90% of cases [5]. Our patient did not have a positive titer for these antibodies or other antibodies associated with GBS.

Coxsackie viruses are implicated in hand-foot-and-mouth disease, viral meningitis, myocarditis, and pleurodynia. Our patient's presentation of fever, myalgia, rash, and liver enzyme elevation was more consistent with a tick-borne illness or mononucleosis, though tests for these were found to be negative. However, there is a case report of Coxsackie virus associated with a mononucleosis-like syndrome [6]. There have been reports of coxsackie viruses associated with classic GBS but to our knowledge this is the first report of Coxsackie virus associated with sensory-only GBS [7]. There is a previous report of Coxsackie virus B associated with autonomic neuropathy and some sensory impairment in a pregnant woman, but in this case the neuron damage was axonal and not demyelinating as in our case [8].

One limitation in tying Coxsackie virus B4 to this case is that only a single antibody titer was obtained weeks after the patient had his initial febrile illness. To diagnose a recent infection, ideally an acute titer is obtained at the onset of symptoms and then a convalescent titer is obtained weeks later, looking for

a several-fold rise in the titer. However, given that his titer for Coxsackie virus B4 was 64-times higher than the reference range and many other potential causes of his condition had been ruled out, Coxsackie virus is the most likely cause of his febrile illness and what provoked the development of sensory-only GBS.

## CONCLUSION

This case demonstrates the importance of recognizing variant forms of GBS that include sensory deficits. The index of suspicion should be high when a patient presents with confusing sensory deficits following a recent infectious illness. Diagnosis can be made clinically by following the criteria put forth by Asbury. Prompt recognition facilitates early treatment which may hasten recovery.

## REFERENCES

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Fig 1: Maculopapular rash seen on patient's right lower extremity during his acute febrile illness.