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# Staphylococcus Toxin-Mediated Motor Polyneuropathy

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**Background:** *Staphylococcus aureus* infection is known to cause a variety of neurologic complications, most involving the CNS, however, rarely have cases of *S. aureus* affecting the peripheral nervous system been reported in literature. We report a case of *S. aureus* toxin-mediated motor polyneuropathy in a patient presenting with acute flaccid quadriplegia.

**Case summary:** A 64-year-old female with mantle cell lymphoma on oral chemotherapy with ibrutinib presents with malaise and progressive ascending bilateral lower extremity weakness. Blood cultures resulted positive for methicillin-sensitive *S. aureus*, and she was initiated on antibiotics. Imaging studies and laboratory workup were negative for other causes of acute flaccid quadriplegia. Patient had complete resolution of her neurologic deficits with antibiotic therapy. It was determined that the likely diagnosis was *Staphylococcus* toxin-mediated motor polyneuropathy.

**Conclusions:** *Staphylococcus*-mediated motor polyneuropathy resulting in acute flaccid quadriplegia is a rare but treatable complication of bacteremia and should remain a diagnosis of exclusion.

**Key Words:** bacteremia; methicillin-sensitive *Staphylococcus aureus*; motor neuropathy; quadriplegia; septic shock; *Staphylococcus aureus* toxin

**S** *Staphylococcus aureus* infection is known to cause a variety of neurologic complications, most involving the CNS (1). Cases of *S. aureus* affecting the peripheral nervous system

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have been rarely reported in the literature. In this case report, we describe an instance of *S. aureus* toxin-mediated motor polyneuropathy presenting as flaccid quadriplegia

## CASE DESCRIPTION

A 64-year-old female with a history of mantle cell lymphoma on oral chemotherapy with ibrutinib for one and a half years, ulcerative colitis, hypertension, and hyperlipidemia presented to the emergency department with malaise and progressive ascending bilateral lower extremity weakness. Three days prior, the patient had started experiencing lower extremity weakness which became so severe that she could not get out of bed. As the lower extremity weakness progressed, she also began experiencing distal bilateral upper extremity weakness. On presentation, she was hypotensive, febrile, tachycardic, and hypoxic. Laboratory studies were notable for a leukopenia, thrombocytopenia, and acute kidney injury (Table 1), which were all new compared with laboratory findings 3 weeks prior to presentation. She was initiated on broad-spectrum antibiotics and vasopressors due to the concern for septic shock. Her neurologic examination was notable for preserved mentation, awake, alert, oriented with no aphasia and intact cranial nerves. She exhibited a flaccid bilateral lower extremity plegia (grade 0/5), and her bilateral upper extremities had minimal antigravity strength at the shoulders with grade 1/5 strength on finger flexion, grip, and wrist extension. She had absent deep tendon reflexes throughout her upper and lower extremities, and preserved sensation to light touch and pinprick with no sensory level at the thoracic or lumbar regions. Workup revealed no acute abnormalities on CT of the head or of the thoracic or lumbar spine, and blood cultures returned positive for gram-positive cocci. Although she could not undergo a lumbar puncture for cerebrospinal fluid analysis due to severe thrombocytopenia, MRI of the cervical, thoracic, and lumbosacral spine was negative for spinal epidural abscess or other intraspinal processes. Polyneuropathy laboratory workup showed no evidence of vitamin deficiencies or diabetes. A transthoracic echocardiogram did not show any vegetations and antibiotics were narrowed to oxacillin once methicillin-sensitive *S. aureus* bacteremia was confirmed. There was an initial concern for immune-mediated Guillain-Barré syndrome (GBS); however, within 2 days of antibiotic therapy, the patient had improvement to a strength of grade 5/5 in her upper and lower

**TABLE 1. Laboratory Studies**

Laboratory Studies	Results on Initial Presentation	Results on Follow-Up
Complete blood picture		
WBC, k/mm <sup>3</sup>	3.7	4.2
Hemoglobin, g/dL	8.6	11.4
Hematocrit, %	25.7	35.5
Platelet count, k/mm <sup>3</sup>	61	220
Mean corpuscular volume, femtoliters	74.3	85.3
Mean corpuscular hemoglobin, pg	24.9	27.4
Mean corpuscular hemoglobin concentration, g/dL	33.5	32.1
Neutrophil, %	45	49.2
Lymphocyte, %	37	27.7
Monocyte, %	10	10.3
Eosinophil, %	1	1
Basophil, %	1	0.4
Metamyelocyte, %	2	0
Band, %	1	0
Comprehensive metabolic panel		
Sodium, mmol/L	133	140
Potassium, mmol/L	3.7	4.1
Chloride, mmol/L	98	103
Bicarbonate level, mmol/L	15	25
Glucose level, mg/dL	197	223
Blood urea nitrogen, mg/dL	57	26
Creatinine, mg/dL	2.9	1.0
Alkaline phosphatase, U/L	114	214
Aspartate aminotransferase, U/L	175	25
Alanine aminotransferase, U/L	415	27
Total bilirubin, mg/dL	1.2	0.4

Initial laboratory studies notable for a leukopenia, thrombocytopenia, and acute kidney injury with resolution of her acute derangements on 4-wk follow-up after discharge.

extremities. Repeat blood cultures which were drawn 2 days after her presentation were negative which correlated with the timing of resolution of her paresis. In light of complete resolution of her motor deficits, nerve conduction studies were deferred, and it was determined that the likely diagnosis was Staphylococcus toxin-mediated motor polyneuropathy. The source of bacteremia was determined to be a central venous access device in her right chest which was placed 2 years prior to presentation when she was on IV chemotherapy with rituximab. Treatment with IV rituximab was discontinued after 4 months due to severe thrombocytopenia after which oral ibrutinib was initiated. Our patient's central

venous access device remained in place and was primarily used for blood draws. The port was removed prior to discharge and blood cultures remained negative. The patient subsequently followed up with her oncology office after 4 weeks from discharge and was noted to have resolution of laboratory derangements seen on initial presentation (Table 1) and continued to have 5/5 strength in her upper and lower extremities.

## DISCUSSION

The differential diagnoses list for diffuse weakness in the setting of bacteremia is broad and includes generalized malaise/fatigue, spinal epidural abscess, meningitis, ischemic or hemorrhagic stroke, myelitis, exacerbation of underlying benign polyneuropathies, postinfectious autoimmune demyelinating neuropathies, and medication/antibiotic-induced neuropathies. Generalized malaise does not typically present with a flaccid para- or quadriplegia, however, and one would expect deep tendon reflexes to be preserved. Spinal epidural abscesses may present with progressive ascending weakness and may cause a flaccid quadriplegia if present in the cervical spine; however, patients typically complain of neck or back pain, and lower extremities may actually be hyperreflexic with clonus or upgoing toes. Cerebral complications such as meningitis or stroke may also present with upper motor neuron findings, but level of consciousness is not usually preserved, as it was in our patient. Workup of any patient with bacteremia and any focal neurologic deficits including coma should always begin with a plain CT of the head to rule out subacute ischemic strokes or hemorrhages, although this will not rule out an acute infarct. Although infectious myelitis is more frequently virally mediated, some bacteria such as mycoplasma, *Streptococcus pneumoniae*, and *Neisseria meningitidis* have been described to cause direct spinal cord infection (2). Patients with profound diabetic or vitamin deficiency-associated polyneuropathies may experience exacerbation of their symptoms in the setting of any acute illness, but these tend to be mixed sensory-motor neuropathies and decreased sensation in a stocking/glove distribution is usually found on examination. Antibiotic-induced neuropathies, including from linezolid, have been previously described, but these tend to occur after prolonged administration of the medication rather than upon presentation to the emergency department (3). Our patient was not on antibiotic therapy prior to admission.

Although a rare cause for acute quadriplegia, tick-borne illnesses need to be considered in the Northeastern United States. Tick Paralysis is a neurotoxic poisoning which occurs after tick attachment and injection of potent salivary toxins. After approximately 4–7 days, symptoms begin with generalized weakness and malaise with ascending paralysis ensuing in a mean of 1.4 days (range, 1–10 d). Other symptoms include diplopia, dysphagia, dysarthria, ataxia, and it is frequently misdiagnosed as GBS (4, 5). Over 40 tick species have been implicated in causing paralysis in humans and animals. The most common species are *Dermacentor andersoni* in Western Canada and the Pacific Northwest, and *Dermacentor variabilis* in the Southeastern United States. After removal of the tick rapid neurologic recovery is typically noted with full recovery in approximately 1–2 days (4). Our patient lived

in the North East, but she had not spent significant time outdoors and denied any recent tick or mosquito bites. After a meticulous skin examination, she was not found to have any ticks attached to her body. West Nile virus has been associated with neurologic manifestations, typically limb paresis, and paralysis due to viral involvement of the lower motor neurons of the spinal cord (anterior horn cells). However, presentation is usually asymmetric and often results in monoplegia (6). Our patient had ascending bilateral motor polyneuropathy.

Patients with a history of cancer, such as in our case, are at risk for bacteremia in the setting of immunocompromise and are also at risk for chemotherapy-induced neuropathy (7). Chemotherapy-induced neuropathies typically exhibit sensory deficits along with motor impairment, and the classes associated with polyneuropathy include vinca alkaloids, platinum drugs, taxanes, procarbazine, alkylating agents, and antimetabolites (8). Our patient was on oral chemotherapy for mantle cell lymphoma and was being treated with ibrutinib, a Bruton's tyrosine kinase inhibitor. Common neurologic side effects of ibrutinib include spontaneous bleeding notably into the subdural space. However, sudden paralysis or significant sudden neurologic compromise is not seen with patients on ibrutinib. (9)

*S. aureus* bacteremia has been recognized to cause CNS complications such as meningitis, septic cerebral emboli, spinal epidural abscess, or intracerebral hemorrhage; however, it is not frequently associated with peripheral nervous system involvement (1). There are only six published cases describing patients experiencing motor polyneuropathy as a result of *S. aureus*. Caksen et al (10) reported a 13-year-old boy who experienced peripheral sensorimotor neuropathy as well as a 65-year-old woman who developed quadriparesis from an acute motor axonal neuropathy. Karmakar et al (11) also described three other cases of staphylococcal bacteremia complicated with polyradiculoneuropathy. These cases, like ours, improved shortly after antibiotic therapy and likely represented a direct toxin-mediated attack on the peripheral nervous system. Cases of secondary autoimmune-mediated syndromes such as GBS have also been published, although symptoms did not subside until 1 month following the infection, consistent with its usual course (12).

The pathophysiology underlying these cases is not well understood; however, direct axonal damage and demyelination may be implicated. Studies conducted on mice and rabbits have shown

staphylococcal  $\alpha$ -toxins to cause severe damage to the myelin sheath and injury to nerve axons (13). Anti-staphylococcal beta-hemolysin antibodies have also been linked to neurologic complications in humans (14).

## CONCLUSIONS

Staphylococcal-mediated motor polyneuropathy resulting in acute flaccid quadriplegia is a rare but treatable complication of bacteremia and should remain a diagnosis of exclusion.

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