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Case Report

CASE REPORT

Guillain–Barré syndrome mimics primary biliary cirrhosis-related myopathy

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Abstract

Guillain–Barré syndrome (GBS) is an immune-mediated disorder characterized by acute polyneuropathy, ascending paralysis and post infectious polyneuritis. Two-thirds of patients present with a history of recent upper respiratory tract or gastrointestinal infection. The clinical history, neurologic examination and laboratory assessment allow for a straightforward diagnosis in the majority of cases. However, primary biliary cirrhosis (PBC) is known to cause clinically detectable muscular weakness. It is therefore critical to differentiate between PBC-associated muscular weakness and GBS-induced paralysis. Here, we report a patient with a longstanding history of PBC who developed progressive weakness and respiratory failure due to GBS, which clinically mimicked PBC myopathy. This is the first reported association between GBS and PBC.

INTRODUCTION

Guillain–Barré syndrome (GBS) is characterized by acute polyneuropathy, ascending paralysis and post-infectious polyneuritis [1]. The incidence rate of GBS is reported to affect between 1 and 3 per 100 000 [1]. The disorder is thought to be immune-mediated, predominantly targeting motor fibers [1, 2]. A typical presentation involves acute flaccid paralysis, with maximum weakness occurring approximately 4 weeks after disease onset [1]. Two-thirds of patients present with a history of recent upper respiratory tract infection or recent gastrointestinal infection [3]. Although the majority of patients recover, the mortality rate from Guillain–Barré ranges between 3 and 5% [1, 4]. The clinical history, neurologic examination and laboratory assessment allow for a straightforward diagnosis in the majority of cases. However, primary biliary cirrhosis (PBC) is known to cause muscular weakness. It is therefore critical to differentiate between PBC-associated muscular weakness and GBS in these patients. Here, we report a PBC patient who developed progressive weakness and respiratory failure due to GBS, which clinically mimicked PBC myopathy.

CASE REPORT

A 51-year-old woman with end-stage liver disease secondary to PBC presented with a 6-week history of rapid progressive weakness following an episode of bronchitis. Her medical history included type 2 diabetes mellitus, hypertension and hyperlipidemia. The past surgical history was significant for splenectomy during childhood. Medications included atorvastatin and metformin. The patient worked full time as an operator of heavy

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machinery. She had no history of smoking, alcohol consumption or illicit drug use. The patient's sister was also affected by PBC.

Physical examination was notable for proximal muscular weakness more prominent in the lower extremities. No abnormal movements, tremors or fasciculations were noted. Sensation to light touch and pinprick were intact. Deep tendon reflexes were absent in the lower extremities and intact in the upper extremities. Plantar reflexes were down going bilaterally. Owing to the lack of strength, cerebellar assessment and gait could not be assessed. Rectal tone was intact.

Laboratory investigations revealed an elevated creatine kinase (CK) of 608 U/l (24–170 U/l). Serum myoglobin was significantly elevated at 3850 µg/l (<30 µg/l). Nerve conduction studies showed evidence for a myopathy and no evidence for a neuropathy or disorder of the neuromuscular junction. Cerebrospinal fluid protein was not elevated. Muscle biopsy revealed fibers with decreased calibers including angulated fibers and occasional fascicular atrophy (Fig. 1A). There was occasional fiber necrosis and myophagocytosis (Fig. 1B). CD68 immunostain highlighted the myophagocytosis of necrotic muscle fibers (Fig. 1C), whereas CD3 showed scattered positive T cells (Fig. 1D) suggesting a limited inflammatory process. There was muscle fiber splitting and occasional fiber regeneration.

The patient progressed to respiratory failure and an autopsy was requested. At autopsy, the brain and spinal cord did not show pathologic changes. The spinal root ganglia and para-ganglion nerve roots, however, revealed marked acute demyelination and axonal degeneration (Fig. 2A–F). Infiltrating lymphocytes and macrophages extensively involved the dorsal root ganglia and proximal peripheral nerves as highlighted by CD68 and CD45 immunostains, respectively (Fig. 2G–I). By light microscopy, the musculature showed similar morphology to that of the prior muscle biopsy (Fig. 1E and F).

DISCUSSION

Our patient presented with a history of infection followed by progressive weakness. Physical examination revealed proximal weakness and absent patellar reflexes. These features together are suggestive of GBS. The unusual clinical characteristics of this case are, however, highlighted by the patient's elevated serum CK and myoglobin with concomitant electromyogram (EMG) findings indicative of myopathy. Serum CK is only rarely elevated in GBS [5]. Myositis is, however, known to occur in PBC patients [6–8]. Circulating anti-mitochondrial antibodies (AMAs) in PBC patients are thought to induce muscular injury [9]. Therefore, although our patient's recent clinical history of upper respiratory tract infection followed by weakness was suggestive of GBS, the laboratory findings, nerve conduction studies and past medical history elicited the differential diagnosis of PBC-related myopathy. The muscle biopsy showed limited myocyte necrosis, which cannot account for the patient's progressive weakness; however, it could account for the elevated serum CK and myoglobin and EMG findings. Angulated fibers were present and support a neurogenic origin of the patient's weakness.

Several strikingly similar cases have been previously reported. A 57-year-old woman with PBC experienced a rapid and fatal weakness with respiratory insufficiency, similar to our patient [6]. EMG studies indicated a myopathic process with evidence for myonecrosis, while muscle biopsy showed a myopathy with variable fiber size in the absence of inflammation. In yet another case series, two women with PBC experienced progressive weakness resulting in hypoventilation and death [8]. In all cases, death was attributed to PBC-related myopathy. The overlap between these cases and our case is extraordinary. All patients were women with PBC in the fifth and sixth decades of life. All four patients experienced progressive weakness and respiratory

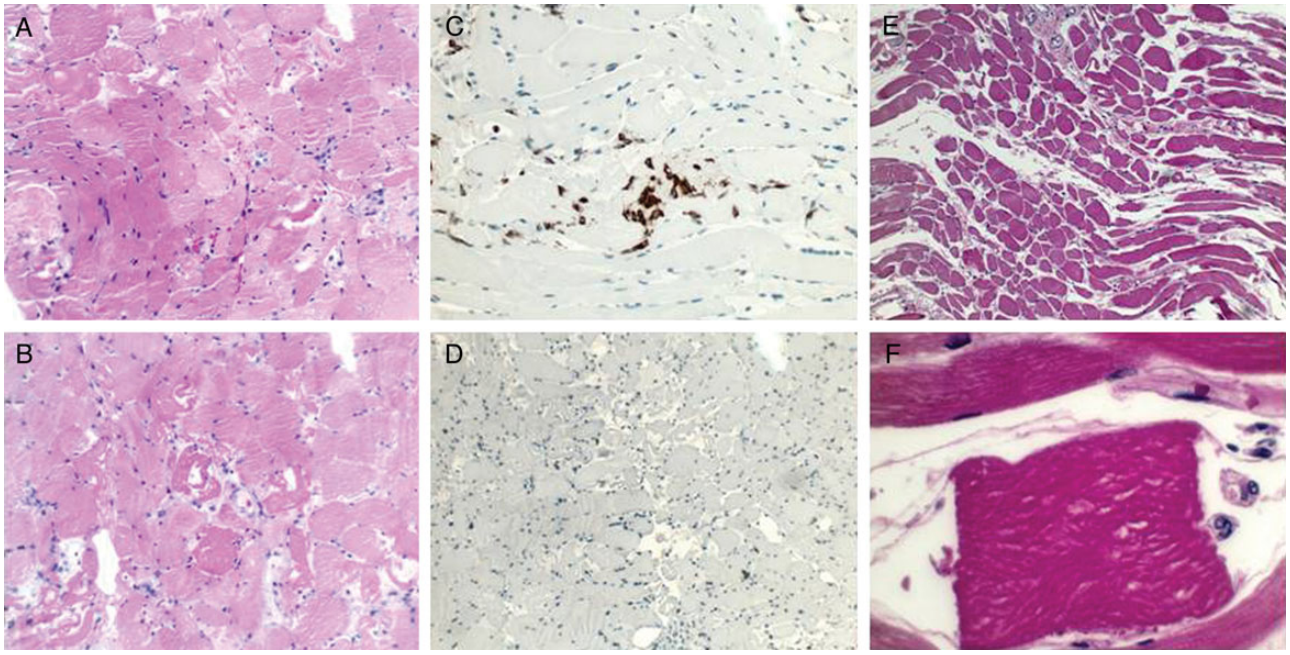

Figure 1: Muscle biopsy during life (**A–D**) and at autopsy (**E** and **F**). (A) Anterior thigh biopsy shows numerous fibers with decreased caliber and angulated fibers (H&E, ×10). (B) Individual myocyte necrosis and myophagocytosis are evident (H&E, ×20). (C) CD68-positive macrophages engulfing necrotic myocytes (×20). (D) CD45 immunostain is negative, illustrating the absence of myositis (×10). (E) Angulated fibers with decreased caliber are seen in the diaphragm (H&E, ×10). (F) High power view of individual myocyte undergoing myophagocytosis (×40).

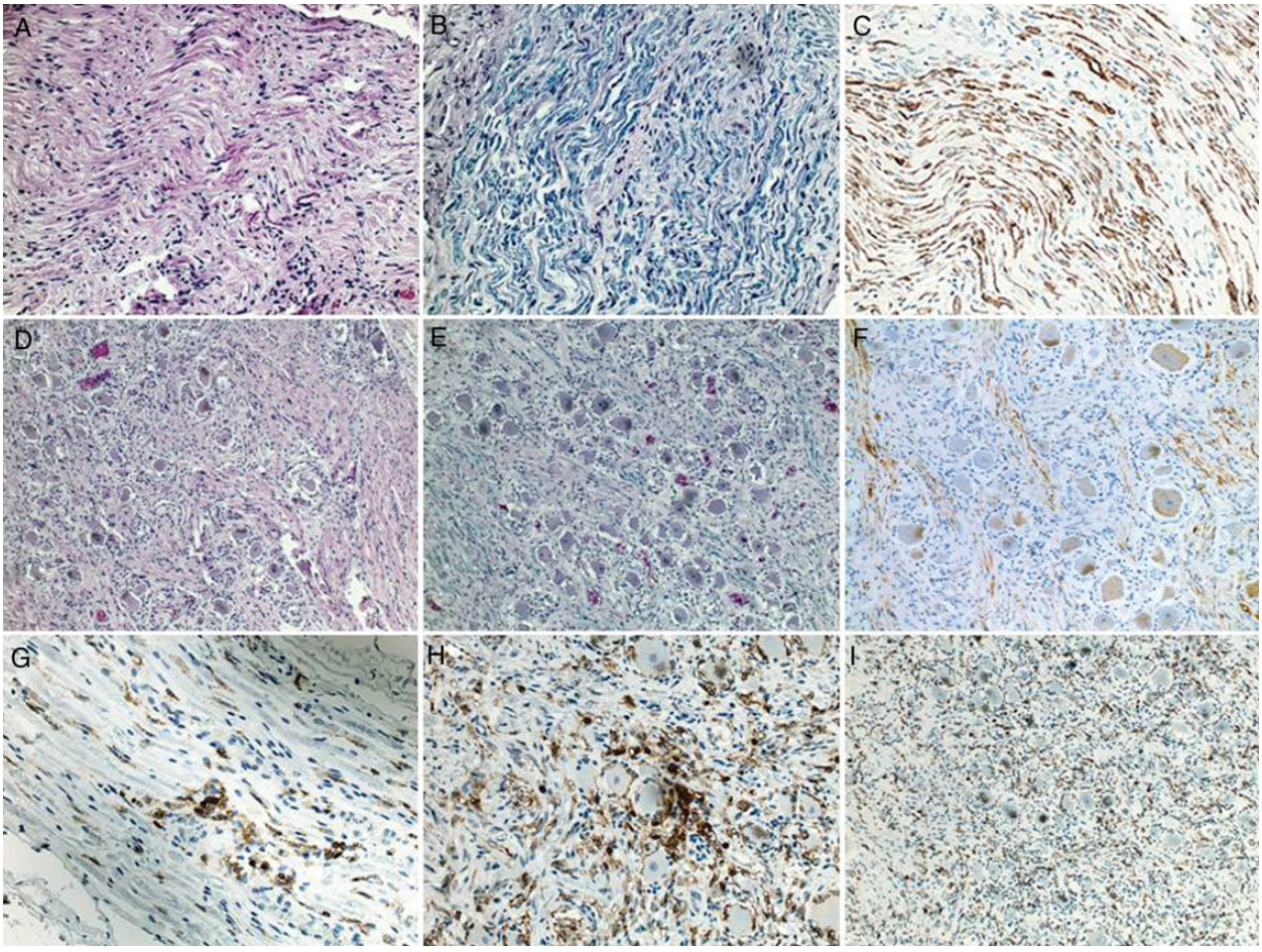

Figure 2: Spinal root ganglia and nerve roots showing marked acute demyelination and axonal degeneration. (**A**) Nerve root showing axonal degeneration (H&E, ×20). (**B**) LFB stain demonstrates reduced myelination (×20). Neurofilament immunostain highlights axonal loss and degenerative changes (×20). (**D**) Spinal ganglia with abundant acute inflammation. (**E**) LFB stain shows severe loss of myelination (×20). (**F**) Neurofilament immunostain highlights severe axonal degeneration (×20). (**G**) CD45-positive lymphocytes infiltrating the nerve root are seen. (**H**) Extensive CD45-positive lymphocytes involving the spinal ganglia. (**I**) Macrophages extensively involving the dorsal root ganglia (×20).

insufficiency. All patients had EMG findings suggestive of myopathy, yet in each case muscle biopsy showed minimal myocyte necrosis. In the previously reported cases, however, peripheral nerves were not evaluated at autopsy. Our case is the first to provide data on the examination of the spinal ganglia and peripheral nerves where GBS was discovered.

Although the differential diagnosis of muscular weakness in the setting of PBC includes GBS, there is currently no recognized association. First, as previously discussed, the clinical signs and symptoms of weakness are likely to be interpreted as PBC myopathy. Second, background AMA-induced muscular damage may be detectable by EMG studies, reinforcing the clinical impression of a primary myopathy. The AMA-induced muscular damage will also interfere with the characteristic EMG pattern in GBS further obscuring its recognition. Furthermore, it is well described that the cytoalbuminologic dissociation and classic electrophysiological abnormalities associated with GBS often lag behind the clinical picture [10]. The diagnosis of GBS in patients with PBC may be extraordinarily challenging.

PBC patients presenting with weakness should elicit GBS in the differential diagnosis which we have shown can mimic PBC-related myopathy. Furthermore, AMA-mediated myopathy can interfere with EMG studies, which should be interpreted carefully. In summary, the two entities—PBC myopathy and GBS—may present similarly. In the setting of rapidly progressive weakness, the diagnosis of GBS should not be excluded based on nerve conduction studies or additional testing that may suggest a primary myopathy.

CONFLICT OF INTEREST STATEMENT

None declared.

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