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Development of recurrent facial palsy during plasmapheresis in Guillain-Barré syndrome: a case report

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Abstract

**Introduction** Guillain-Barré syndrome is an immune mediated polyneuropathy that is routinely initially treated with either intravenous immunoglobulin or plasmapheresis. No association between plasmapheresis treatment and acute onset of facial neuropathy is reported.

**Case presentation** A 35-year-old man, with no significant prior medical history, developed ascending motor weakness and laboratory findings consistent with a diagnosis of Guillain-Barré syndrome. Plasmapheresis was initiated. Acute facial palsy developed during plasma exchange that subsequently resolved and then acutely recurred during the subsequent plasma exchange.

**Conclusion** To our knowledge, no prior cases of facial palsy developing acutely during plasmapheresis treatment are known. Although facial nerve involvement is common in typical Guillain-Barré syndrome, the temporal association with treatment, near complete resolution and later recurrence support the association. The possible mechanism of plasmapheresis-induced worsening of peripheral nerve function in Guillain-Barré syndrome is unknown.
Introduction

Guillain-Barré syndrome (GBS) is an immune-mediated acute polyneuropathy typically characterized by ascending weakness and areflexia. An association with *C. jejuni* infection is most common; however, numerous associations are known [1]. Now recognized as a heterogeneous syndrome, different variants exist including demyelinating and axonal forms; the demyelinating variant is most common in the United States. Based on considerable clinical trial evidence, the American Academy of Neurology currently recommends treatment with either Intravenous immunoglobulin (IVIG) or plasmapheresis within two to four weeks [2]. Although the disease may continue to advance during treatment, acute focal worsening is not a recognized treatment complication. We report a case of facial palsy that acutely developed during plasma exchange, subsequently resolved, and then acutely recurred during the subsequent plasma exchange.

Case presentation

A 35-year-old Caucasian man, with no significant prior medical history, developed symmetric ascending weakness and paresthesia. Six days prior to admission he noted bilateral foot and then posterior leg numbness. Chiropractic manipulation provided no relief. Two days later progressively ascending lower extremity weakness and increasing leg and foot tingling and numbness developed. Hand weakness and paresthesia began two days prior to admission that spread to shoulder girdle involvement. His gait became unsteady prompting him to come to our emergency department. Prior to admission, he also noted shortness of breath with exertion but not at rest, feeling as though his heart was racing during exertion, and having night sweats, all of which were unusual for him. He was an avid runner prior to the onset of symptoms. His wife is a nurse practitioner and her home physical exam was described to show areflexia. He had no notable respiratory or gastrointestinal viral prodrome prior to the onset of neurological symptoms. However, he described a mild transient occipital, throbbing headache one morning at the start of his symptoms that resolved within two hours of onset. One day prior to admission he noted mid-tongue numbness. Sensation in his extremities seemed altered and he had difficulty distinguishing hot from cold objects. His weakness and numbness were progressively worsening on the day of admission. On the morning of admission, he also noted one period of blurry vision, which spontaneously resolved within two hours. He denied nausea, diarrhea, dysuria, presyncope, vertigo, hearing loss, rash, diplopia, facial asymmetry, tremor, dysphagia, or dysarthria. He also denied any recent vaccinations.

On admission he had normal orientation and cognition. Extraocular movements were full without nystagmus. Visual fields were full; no papilledema was evident. Pupils reacted briskly without afferent defect. Facial strength and sensation was full and symmetric. Despite the subtle symptoms, his face was symmetric upon smiling, eyebrow wrinkling, lip pursing, and eye closure. Light touch and cold perception in trigeminal nerve territories was normal. Hearing was intact. His palate elevated well although he had an odd sensation in the back of his throat. His tongue was midline on protrusion. No dysarthria was noted. Limb strength demonstrated bilateral weakness ranging from MRC
scale 4- to 4+/5 in his upper and lower extremities. Deep tendon reflexes were hypoactive in the arms and absent in both legs; he had decreased light touch, temperature, and pin-prick sensation bilaterally from his feet to the thigh, and in his hands ascending to the shoulder. No specific cerebellar abnormalities were evident. His gait was unsteady and wide-based with an inability to tandem walk.

Cerebral spinal fluid showed cytoalbuminologic dissociation with a protein of 51 mg/dL and 2 white blood cells/mm$^3$. His serology was negative for IgG anti-GQ1b and anti-GM1 ganglioside and related antibodies. No HIV human immunodeficiency virus antibodies were present. He had positive titers of CMV–cytomegalovirus IgG and IgM, and he had a borderline reactive CSF–cerebrospinal fluid Lyme antibody study though negative serum antibodies suggested a false positive result. Over the ensuing days the patient’s weakness continued to slowly progress in his arms and legs to a point that he was no longer able to walk or raise his arms without difficulty; however, his face remained uninvolved. No cranial sensory or motor deficits developed.

Plasmapheresis was initiated on day 9 of his symptoms following insertion of a vascular catheter. Towards the end of the first treatment, severe right-sided facial weakness with dysgeusia developed, and an obvious facial droop appeared. The remainder of his neurological exam including contralateral facial strength remained unchanged. MRI of the brain performed two hours later showed no restricted diffusion. This deficit completely resolved within thirty minutes and did not recur that day. Two days later a second round of plasmapheresis was initiated. Calcium gluconate was given prior to the procedure because of mildly low ionized calcium measures. About half-way into the second treatment, facial weakness reemerged, but this time without resolution and persistent right-sided facial droop, asymmetric smile, and weak right eye closure developed. The plasma exchange was discontinued mid-treatment and he was closely observed. His forehead was asymmetric but notably less involved; frontalis strength improved and was symmetric by the day following this second round of plasmapheresis though the remainder of his facial paralysis remained.

Because of the association of recurrent acute facial weakness during plasmapheresis, the therapy was discontinued and a decision was made to substitute a five-day course of IVIG. He received a conventional dose of IVIG, which was a total dose of 2.0 mg/kg given as a 5-day treatment course (0.4 mg/kg/day of 6% IVIG). He tolerated the infusions without complication.

Despite treatment, weakness in his extremities continued to slowly progress and he later slowly developed left-sided facial weakness first noted four days subsequent to his second plasmapheresis treatment. Additionally, on day 12 of his symptoms chewing difficulty prompted a change to a soft mechanical diet; on day 14 of his course he failed a swallowing evaluation indicating probable pharyngeal weakness. The patient’s symptoms continued to progress and seemed to nadir by week five of his course.

Facial motor nerve conductions were performed on the day of the second plasmapheresis (day 11 of symptoms). Normal distal latencies and normal and symmetric evoked
amplitudes were found from common facial nerve stimulation and recording from bilateral orbicularis oculi, nasalis, and orbicularis oris muscles. In all likelihood insufficient time had elapsed for Wallerian degeneration to occur. Blink reflex studies demonstrated an increased R1 latency (16.1 ms) and absent ipsilateral and normal contralateral R2 responses following right-sided supraorbital stimulation. Left sided stimulation demonstrated a mildly increased R1 latency but normal ipsilateral and absent contralateral R2 responses.

Nerve conduction studies of the right median, ulnar, peroneal, and tibial nerves were performed on days 9, 18, and 26 of his course and showed a demyelinating pattern with axonal involvement that progressively worsened with each examination. Increased distal motor latencies, serially reduced evoked motor amplitude, reduced sensory responses, and loss of F-waves ensued; conduction velocity remained relatively unaffected. Focal conduction block or significant temporal dispersion was not evident at any point. Abundant fibrillations were evident in multiple muscles on study #3.

His facial droop improved by the third week of his course, which continued through week four; his face became symmetric. His clinical course was complicated by pneumonia, respiratory failure requiring intubation, and a tracheotomy. He was discharged on day 46 in stable condition to an acute rehabilitation facility. At that point he had mild facial weakness, was able to symmetrically produce a small smile and could fully but not forcefully close his eyes. One year later he recovered almost fully, following extended rehabilitation and physical therapy, and he has returned to work. He continues to report numbness in his great toes, and partial numbness in his second and third toes bilaterally, with sporadic neuropathic pain occurring 2-3 times per week but not requiring the use of pain medications. His facial symptoms ultimately resolved.

**Conclusion**

Guillain-Barré Syndrome typically produces relatively symmetric ascending weakness and depressed deep tendon reflexes or areflexia [3]. Plasmapheresis and IVIG are the mainstays of acute GBS treatment [2]. Conventional plasmapheresis is not recognized to induce acute worsening including facial neuropathy. Only one previous similar report, of two clinical cases, was identified. Chida and colleagues reported in 1998 two cases of bilateral facial palsy developing in Miller Fisher syndrome, a GBS variant associated with GQ1b antibodies, occurred in the setting of immunoadsorption plasmapheresis (IAP) therapy. In these cases bilateral facial palsy developed after either 3 of 3 or 3 of 5 IAP treatments while other neurological deficits were improving [4]. IAP is a newer form of plasmapheresis that selectively removes IgG without removal of significant albumen and other blood components. Of note the process does not remove notable amounts of IgM antibodies. This process has been shown to be efficacious in Miller Fisher Syndrome [5].

In the present report, the patient twice developed acute onset right-sided facial weakness during conventional plasmapheresis for GBS, with resolution of his symptoms in the first
incidence and persistence of them in the latter. This close temporal association of his facial weakness onset is supportive of a direct relationship with the plasma exchange treatment. The remainder of his symptoms continued to gradually and slowly progress over days without acute changes. Plasmapheresis is proven to decrease the duration and severity of deficits [6]. It is believed that antecedent infection leads to the production of humoral and cellular immune effectors that cross-react with certain nerve or myelin epitopes [7]. More recent work involving immunoadsorption, which selectively removes specific antibodies, show that IAP is also an efficacious treatment which removes specific antimyelin antibodies associated with GBS [8, 9]. Our case is highly suggestive of a direct relationship between plasma exchange and development of facial palsy. It is conceivable that protective antibodies were removed by this treatment leading to the acute facial neuropathy. Additionally, other unknown large molecular weight proteins serving to modulate the immune response may have been removed. The etiology of the peripheral nerve dysfunction is unknown at this stage. The mildly low ionized calcium during the first exchange and calcium gluconate infusion during the second treatment is not likely a significant factor. Sudden improvement of neurological function is reported in some cases associated with plasma exchange, such improvement is thought to occur faster than that explicable by neuroregenerative processes such as remyelination. In these settings antibody-mediated changes in ion channel function that restores neural transmission is proposed. Ultimately the affected side of the face had the same outcome as the later more conventionally affected side. Plasmapheresis units should be watchful for acute changes in strength during exchange treatments that may be exacerbated by further treatment.

Consent
Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interests
The authors declare that they have no competing interests

Authors Contributions
MS, IB, and LW reviewed the current literature and patient presentation to compile this case report. LW analyzed the nerve conduction studies. All authors read and approved the final manuscript.

References


