

# Guillain-Barre syndrome following cardiac surgery

## *Difficult diagnosis in the intensive care unit*

Hussein Algabani, MD, FRCPC, Dwight E. Moulin, MD, FRCPC, Charles F. Bolton, MD, FRCPC, Ahmad A. Abulaban, MBBS.

### ABSTRACT

ضعف الأطراف مع ضعف العضلات التنفسية الذي يحصل خلال وبعد العلاج في وحدة العناية المركزة عادة ما يكون بسبب الاعتلال العصبي المتعدد الحرج (من مضاعفات الإنتان) أو بسبب اعتلال العضلات الحرج (من مضاعفات استخدام أدوية حصار النهايات العصبية العضلية والستيرويد). من الممكن حدوث متلازمة غيلين بارييه في مثل هذه الظروف. قمنا بتسجيل حالتين لمريض ومريضة من وحدة العناية المركزة (ICU) تم رصدتهما خلال فترة العشرين سنة الماضية. كانت الجراحة السبب الواضح لكلا الحالتين وهي حالات معروفة سبق نشرها في أبحاث سابقة. كانت الحالة السريرية وتخطيط الأعصاب وخصائص السائل النخاعي لكلا المريضين متطابقة مع التشخيص. كلا المريضين استجابا للعلاج. تمت معالجة الحالة الأولى باستخراج البلازما والأخرى بجلوبين مناعي وريدي. إن حدوث مثل هذه الحالات يعتبر أمرا نادرا ومن المهم معرفة تشخيص المرض بشكل سريع في وحدة العناية المركزة لأن مثل هذه الحالات لها علاج خاص تستجيب له، وقد يكون علاجا شافيا.

Weakness of limb and respiratory muscles developing in the course of treatment in the intensive care unit (ICU) is commonly due to critical illness polyneuropathy, a complication of sepsis, or critical illness myopathy, a complication of the use of neuromuscular blocking agents and steroids. Guillain-Barre syndrome may rarely occur in this setting. We report 2 patients identified in our ICU in the last 20 years. Surgery was an apparent precipitating event in both patients. The clinical, electrophysiological, and cerebrospinal fluid features were consistent with this diagnosis. Both patients responded to treatment; the first case was treated with plasmapheresis while the other with intravenous immune globulin. Thus, while rare, it is important to identify this disorder in the ICU because of its response to specific treatment.

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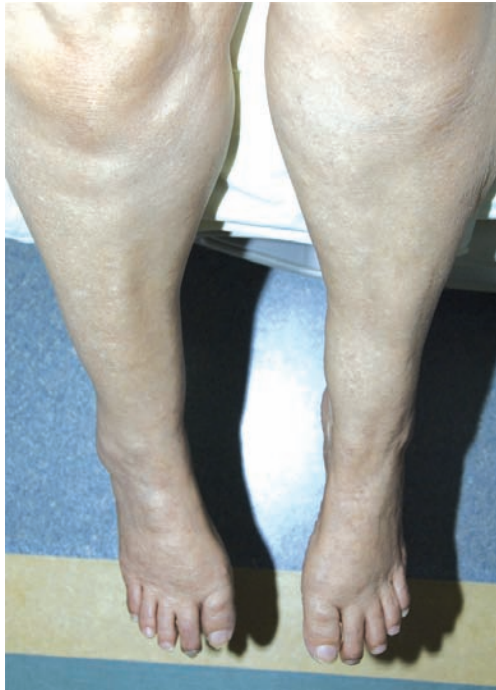
From the Department of Medicine (Algabani, Abulaban), King Abdulaziz Medical City, Jeddah, Kingdom of Saudi Arabia, and the Department of Clinical Neurological Sciences (Moulin, Bolton), University of Western Ontario, London, Ontario, Canada.

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Address correspondence and reprint request to: Dr. Hussein Algabani, King Abdulaziz Medical City, PO Box 12723, Jeddah 21483, Kingdom of Saudi Arabia, Tel. +966 (2) 6240000. Ext. 21298, 22070. Fax. +966 (2) 6240000. Ext. 22765. E-mail: neuroahmad@yahoo.com

Patients presenting with weakness of limb or respiratory muscles after admission to the intensive care unit (ICU) most commonly suffer from critical illness polyneuropathy (CIP), a complication of sepsis and multiple organ failure,<sup>1</sup> or critical illness myopathy, especially if large doses of steroids or neuromuscular blocking agents have been used (Figure 1).<sup>2</sup> Cachectic myopathy or disuse atrophy probably contributes to muscle weakness in the ICU. Less common are transient disorders of neuromuscular transmission due to neuromuscular blocking agents used to ease mechanical ventilation and necrotizing myopathy of intensive care. Early cases of CIP were initially attributed to Guillain-Barre syndrome (GBS). However, it was subsequently shown,<sup>3</sup> that, despite similar findings on clinical examination, the 2 conditions could be differentiated by precipitating events, cerebrospinal fluid (CSF) examination, electrophysiological features, and the morphology of peripheral nerves. While both CIP and GBS usually improve spontaneously, recently it has been demonstrated that recovery from GBS can be hastened by the administration of plasmapheresis or intravenous immune globulin. Thus, for practical reasons, it is important to diagnose GBS and distinguish it from the more common neuromuscular conditions that present while treatment for other primary conditions in the ICU. We, therefore, present 2 such cases of GBS diagnosed in our ICU during the last 20 years.

**Case Report. Patient 1.** A 71-year-old woman with a long-standing history of angina, hypertension, and hypercholesterolemia was admitted to hospital in January 1998, for elective coronary artery bypass surgery. The patient was an insulin-requiring diabetic, with mild chronic renal failure (baseline creatinine 210  $\mu\text{mol/l}$ , normal: 79-118  $\mu\text{mol/l}$ ). An angiogram



**Figure 1** - Bilateral foot drop with wasting of tibialis anterior in a patient with CIM who was diagnosed with TB lymphadenitis, adult respiratory distress syndrome, and pneumonia. Patient received high dose of steroid and she was mechanically ventilated for 12 days. She recovered completely after stopping steroid and when her multi system problems resolved. CIM - critical illness myopathy, TB - tuberculosis.

showed triple vessel disease, and the ejection fraction was 56%. There was no history of recent viral illness. During the procedure, the left anterior descending artery was found to be ungraftable and a double bypass was completed. On post-operative day 4, bilateral lower extremity weakness and severe right leg pain were noted. Neurological examination revealed her to be alert, with normal cranial nerves and symmetrical upper limb movement, with normal strength and tone. There was bilateral flaccid paralysis of the lower limbs and severe right lateral thigh tenderness to touch, with exacerbation on passive movement and straight leg raising. The sensory and cerebellar examinations were difficult to assess. By postoperative day 7, there was flaccid paralysis involving both legs and the right arm. The left arm withdrew only to pain. Deep tendon reflexes were absent. An MRI with views of the spinal cord and abdominal aorta was normal. A CT of the head was normal. A lumbar puncture revealed a CSF protein of 88 mg/100cc (normal 15-45 mg/100 cc), CSF glucose of 10.2 mmol/L (serum glucose 19.7mmol/L) (normal 50-60% of blood glucose), white blood cell count (WBC) of 44 cells/l (lymphocytes 41%, monocytes 43%, neutrophils 25%) (normal <5 cells) and red blood cell count (RBC) of 67 cells/l. On day 8,

motor and sensory nerve conduction studies and needle electromyography (EMG) were performed in the upper and lower limbs. These revealed marked reductions or absences in compound muscle and sensory nerve action potential with only mild prolongation of distal latencies and mild reduction in conduction velocities. However, F-wave latencies were either absent or markedly prolonged (69 and 85 ms for the tibial and peroneal nerves, normal <58 ms). Moderate conduction block was present for motor fibers of the left ulnar nerve, with a distal amplitude of 4 mV and an absent response on stimulation at the axilla. Needle EMG revealed only the occasional positive sharp wave, and motor unit potentials were markedly reduced in number. The remaining ones were normal except for very rapid firing. These findings were consistent with an acute demyelinating motor and sensory polyneuropathy. On post-operative day 9, plasmapheresis was initiated and this treatment was performed daily for 5 days. Movement was regained slowly with most improvement seen early in the course of treatment. On the second day of treatment, the patient was denying pain in the legs and she was able to move her toes, as well as internally and externally rotate her feet on command. By day 3 of treatment, the patient had regained spontaneous movement in all limbs, although she was still weak. Neurologically, the patient continued to improve over the rest of her course in the hospital. Repeat electrophysiological studies on day 30 revealed mild improvement in the amplitude of compound muscle and sensory nerve action potentials, with improvement of the conduction block in the ulnar nerve. The F-waves returned, although they remained somewhat prolonged and dispersed. Needle EMG showed more denervation potentials in the lower limbs, but in general, there was a better recruitment of motor unit potentials, consistent with the clinical improvement. Thus, overall electrophysiological findings indicated improvement in the demyelinating polyneuropathy, but with the development of some axonal degeneration, as is often observed in GBS. The patient came off the ventilator on day 42, and she was transferred out of the ICU. The patient was discharged in March 1998, after a 21/2 month course in the hospital, and transferred to a local center for rehabilitation.

**Patient 2.** A 77-year-old man with a long-standing history of chronic obstructive lung disease and mitral valvular disease presented to the referring hospital in January 1992 with a 5-day history of dry cough and dyspnea. He also had a known history of coronary artery disease, a 6-month history of mild congestive heart failure and atrial flutter requiring anticoagulation. He had a previous uncomplicated transurethral resection of the prostate. In hospital, he rapidly decompensated, became hypotensive, febrile and required intubation

with assisted ventilation. Blood and urine cultures were negative. He was kept stable on a ventilator, requiring verapamil for intermittent supraventricular tachycardias. He was transferred for urgent cardiac investigation on day 8. Subsequent cardiac catheterization primarily revealed severe aortic valvular disease, with mild mitral stenosis and insufficiency. The left ventricular angiogram showed slight global hypokinesis, inferior akinesis, and an ejection fraction of 45%. The coronary arteries were normal. After the procedure, he became cyanotic with hypotension. He developed tension pneumothoraces, which were treated with chest tubes. An emergency aortic valve replacement was performed on day 9 without complication. He required inotropes postoperatively, but was hemodynamically stable. On day 11, bilateral ascending paralysis was noted. On neurological examination, he was alert, and obeyed simple commands. There was no evidence of cranial nerve involvement. Deep painful stimuli evoked full facial grimacing, but no movement in either leg. Deep tendon reflexes were absent. A CT of the head was negative for acute infarction. The motor and sensory conduction study and needle EMG were performed in the upper and lower limbs. These showed a marked reduction or absence in compound muscle and sensory nerve action potentials. There was a moderate reduction in conduction velocities of the median nerve (motor 40 m/s, normal >47 m/s) and tibial nerve (motor 25 m/s, normal >41 m/s). There was also mild prolongation of motor distal latencies. Conduction velocities in the median and ulnar nerve sensory fibers were 44 m/s (normal >53 m/s) and 35 m/s (normal >51 m/s). The F waves could not be recorded from any nerve. There was a mild conduction block in motor fibers of the ulnar nerve. A needle EMG showed small numbers of fibrillation potentials and positive sharp waves, with no firing of motor unit potentials on attempted voluntary contractions. These findings were consistent with an acute demyelinating motor and sensory polyneuropathy. Lumbar puncture revealed CSF protein of 55 mg/100cc, glucose 5.2 mmol/L, WBC count 0, and RBC count 3 cells/l. On day 15, he was started on a course of treatment with 35 grams per day intravenous immune globulin for 5 consecutive days, and he made gains neurologically. On day 18, treatment day 4, he was moving both arms, though they were still weak. Two days after the completion of the treatments, he was moving the lower limbs. Follow-up electrophysiological studies on day 21 revealed some improvement. The patient was sent for a rehabilitation program for cardiac, respiratory, and neurological functions.

**Discussion.** In patients presenting for the first time with limb and respiratory weakness in the ICU, the main differential diagnosis involves CIP,<sup>1</sup> and critical illness myopathy (CIM), acute myopathy of intensive care, and

acute quadriplegic myopathy. The CIP is a complication of sepsis and multiple organ failure in 70% of patients, and presents as difficulty in weaning from the ventilator and varying degrees of limb weakness.<sup>1</sup> Morphological studies indicate the presence of a primary axonal motor and sensory polyneuropathy. Recovery from the neuropathy occurs in approximately 50% of the patients provided the sepsis and multiple organ failure can be successfully treated.<sup>1</sup> Critical illness myopathy may occur in the similar clinical setting of sepsis and multiple organ failure, but most patients have had large doses often over prolonged periods of time of both neuromuscular blocking agents and steroids. Electrophysiological studies point to a primary myopathy and muscle biopsy often reveals loss of thick myosin filament and milder, nonspecific changes. Guillain-Barré syndrome usually presents before admission to the ICU with a minor infection and, less commonly, trauma being the precipitating events. Electrophysiological studies show a demyelinating polyneuropathy. Morphological study of the nerve may reveal inflammation. Improvement may be hastened by the use of either plasmapheresis or intravenous immune globulin. An axonal form of GBS, either purely motor or motor and sensory, may be more difficult to distinguish from CIP due to the similar electrophysiological signs of axonal degeneration. However, axonal GBS, as in the demyelinating form, commonly presents before admission to the ICU and usually has infection with *Campylobacter jejuni* as a precipitating event. Studies have shown no relationship between a specific type of bacterial, fungal, or viral infection associated with sepsis and CIP. Table 1 describes the main differentiating features of CIP and the demyelinating and axonal forms of GBS. We believe our 2 patients had Guillain-Barré syndrome distinct from either CIP or myopathy for several reasons. First, neither the patient had evidence of sepsis or the systemic inflammatory response syndrome (SIRS) postoperatively when limb weakness was first observed. Moreover, both patients were alert and had no evidence of septic encephalopathy. Sepsis, SIRS and septic encephalopathy are common accompaniments of CIP, but not GBS. Acute diabetic neuropathy is unlikely to explain the first case because of the symmetrical weakness and recovery within a few days. Second, both patients developed limb weakness suddenly within 4 days of cardiac surgery, a known precipitant of GBS.<sup>7</sup> The interval between time of surgery and onset of symptoms can occur from a few days to a few weeks with the average being one to 2 weeks. Both patients in the 2 cases reported here experienced the first symptoms within a few days of surgery. The reason for the comparatively short interval between surgery and onset of symptoms in these patients is unknown. Third, while mild elevation in CSF protein is typical of CIP, it is often seen in the early stages of

**Table 1** Features of polyneuropathies in the ICU.

Type of polyneuropathy	CIP	AIDP	AMSAN	AMAN
Precipitating factor	Sepsis	<i>C. jejuni</i> , EBV, CMV, HIV, vaccine, trauma	<i>C. jejuni</i>	<i>C. jejuni</i>
Clinical feature	Onset of polyneuropathy after ICU admission	Onset of polyneuropathy before ICU admission (except our 2 patient )	Feature of AIDP unusually severe course	Feature of AIDP, motor only
CSF	Near normal	Albumino-cytologic dissociation. May be normal early on	As with AIDP	As with AIDP
Microbiology & immunology	Non-specific	Serology IgA, IgM to <i>C. jejuni</i> anti-GM1 anti-CD1B, stool culture	As AIDP	As AIDP
Electrophysiology	Evidence of axonal motor & sensory polyneuropathy	Evidence of demyelinating polyneuropathy	Unresponsive nerves, abundant spontaneous activity	
Morphology	Primarily axonal degeneration of distal peripheral nerves without inflammation	Primarily demyelinating process with inflammation	Motor & sensory axonal degeneration	Motor axonal degeneration
Treatment	Treat sepsis	Plasmapheresis, intravenous immune globulin	Plasmapheresis, intravenous immune globulin	plasmapheresis, intravenous immune globulin
Course	Recovery	75% complete recovery, 30% require ICU admission	Worse than AIDP	somewhat worse than AIDP

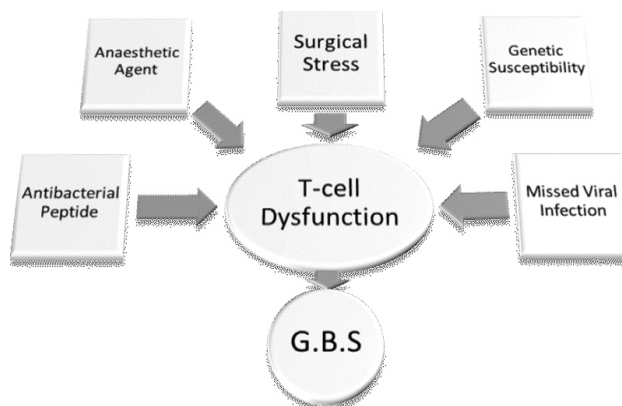
ICU - intensive care unit, *C. jejuni* - campylobacter jejuni, EBV- Epstein-Barr virus, CMV – cytomegalovirus, HIV - human immunodeficiency virus, CSF - cerebrospinal fluid, CIP - critical illness polyneuropathy, AIDP - acute inflammatory demyelinating polyneuropathy, AMSAN - acute motor sensory axonal neuropathy, AMAN - acute motor axonal neuropathy.

GBS. The mild increase in WBC in patient one and no cells in patient 2 is consistent with either GBS or CIP. As noted below, cases of post-surgical GBS may have typical albuminocytologic dissociation (Table 1). Fourth, the electrophysiological features pointed to a demyelinating polyneuropathy. These features included prolonged or blocked F-waves, evidence of conduction block or dispersion of compound muscle action potentials, a relative lack of fibrillation potentials and positive sharp waves and the presence of a reduced number of motor unit potentials, which fired at an abnormally high rate. Finally, both patients responded to the use of either intravenous immune globulin or plasmapheresis, which would have had little effect in the setting of CIP.

While uncommon, GBS is a well-documented complication of several surgical procedures. In a report of 97 cases from the Mayo Clinic in 1964,<sup>16</sup> 5 cases were post-operative, but the details of each of these cases were not described. The traumatic event presumably triggers the immune response. Cases have been reported following spinal,<sup>4</sup> cranial,<sup>5,6</sup> gastrointestinal,<sup>8,10</sup> genitourinary, maxillofacial,<sup>11</sup> orthopedic, pulmonary, eye,<sup>12</sup> and cardiac<sup>7</sup> surgery. Many cases of GBS following solid organ and bone marrow transplantation were reported. However, most were associated with cytomegalovirus infection.<sup>9,13,14</sup> The exact mechanisms

by which GBS develops following surgery is not well-known. However, there are many postulated mechanisms, including missed viral infection, surgical stress, genetic susceptibility, anesthetic drugs, and finally an antibacterial peptide, which is generated following surgery in one immunological research<sup>15</sup> (Figure 2).

In conclusion, many patients are admitted to the ICU because of major surgery. Thus, the occasional instance of GBS might be expected to occur. The diagnosis should



**Figure 2** - Postulated mechanism of Guillain-Barre syndrome (GBS) following surgery.

be suspected especially if electrophysiological studies indicate a primary demyelinating polyneuropathy. The CSF should be examined, a typical albuminocytologic dissociation helping to confirm the diagnosis. Then, treatment with plasmapheresis or intravenous immune globulin may hasten recovery.

## References

1. Zifko UA, Zipko HT, Bolton CF. Clinical and electrophysiological findings in critical illness polyneuropathy. *J Neurol Sci* 1998; 159: 186-193.
2. Lacomis D, Giuliani MJ, Van Cott A, Kramer DJ. Acute myopathy of intensive care: clinical, electromyographic, and pathological aspects. *Ann Neurol* 1996; 40: 645-654.
3. Bolton CF, Laverty DA, Brown JD, Witt NJ, Hahn AF, Sibbald WJ. Critically ill polyneuropathy: electrophysiological studies and differentiation from Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry* 1986; 49: 563-573.
4. Riebel GD, Heller JG, Hopkins LC. Guillain-Barré syndrome after an operation on the spine. A case report. *J Bone Joint Surg* 1995; 77: 1565-1567.
5. Foubert-Samier A, Penchet G, Yekhelef F, Lemasson G, Sibon I. [Guillain-Barre syndrome secondary to cranial surgery: direct or fortuitous relationship?] *Neurochirurgie* 2005; 51: 604-606. French
6. Puertas-Muñoz I, Miranda-Lloret P, Lagares A, Ramos-González A. [Guillain-Barre syndrome following resection of glioblastoma multiforme] *Rev Neurol* 2004; 39: 1137-1139. Spanish
7. Hogan JC, Briggs TP, Oldershaw PJ. Guillain-Barre syndrome following cardiopulmonary bypass. *Int J Cardiol* 1992; 35: 427-428.
8. Chouillard E, Fingerhut A. Guillain-Barré syndrome following oesophagectomy. *ANZ J Surg* 2004; 74: 915-916.
9. Janssen JJ, Tissingh G, Ossenkoppele GJ. Guillain-Barre syndrome after autologous peripheral blood stem cell transplantation for CML. *Eur J Haematol* 1999; 63: 358-359.
10. Orringer D. Gastrectomy complicated by the Guillain-Barre syndrome. *AMA Arch Surg* 1958; 76: 447-450.
11. Shuert GT, Gamble JW. Guillain-Barre syndrome after mandibular surgery: report of case. *J Oral Surg* 1972; 30: 913-915.
12. Ben Simon GJ, McCann JD, Barth N, Goldberg RA, Glasgow BJ, Straatsma BR. Partial resolution of acute ascending motor polyneuropathy after enucleation of an eye with metastatic melanoma. *Br J Ophthalmol* 2004; 88: 847.
13. Fujisaki G, Kami M, Murashige N, Kishi Y, Hori A, Chizuka A, et al. Guillain-Barre syndrome associated with rapid immune reconstitution following allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant* 2006; 37: 617-619.
14. Bouza-Piñeiro P, Pego R, Alonso A, de la Fuente R, Martul EV. Guillain-Barré syndrome after renal transplantation: a case of clinical success with intravenous immunoglobulin therapy. *Nephron* 1996; 74: 223-224.
15. Tasiemski A, Salzet M, Benson H, Fricchione GL, Bilfinger TV, Goumon Y, et al. The presence of antibacterial and opioid peptides in human plasma during coronary artery bypass surgery. *J Neuroimmunol* 2000; 109: 228-235.
16. Wiederholt WC, Mulder DW, Lambert EH. The Landry-Guillain-Barre-Strohl syndrome or polyradiculoneuropathy: Historical review, report on 97 patients, and present concepts. *Mayo Clin Proc* 1964; 39: 427-451.

### Related topics

Alzaidi MA, Nouri KA. Guillain-Barre syndrome: Pattern of muscle weakness. *Neurosciences* 2002; 7: 176-178.

Koul RL, Nair PM, Chacko A, Venugopalan P. Myoclonic seizures in a young girl with Fishers variant of Guillain-Barre syndrome. *Neurosciences* 2002; 7: 188-190.

Qutub HO. Acute respiratory failure revealing Guillain-Barre syndrome. *Neurosciences* 2002; 7: 191-193.