Guillain-Barré syndrome following thoracic spinal cord trauma

[Syndrome de Guillain-Barré à la suite d'un traumatisme de la moelle épinière thoracique]

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Purpose: Guillain-Barré syndrome (GBS) is an acute immunologic attack of the peripheral nerves causing rapidly ascending weakness and areflexia. Occasionally, weakness is severe enough to leave patients paralyzed and without adequate respiratory function. In such patients, intensive care unit (ICU) admission is required. Infrequently, GBS occurs in patients already admitted to the ICU. When this occurs, it can be difficult to distinguish GBS from critical illness neuropathy (CIN). However, it is important to consider GBS in these cases, since treatment options are available, and early treatment is associated with significantly improved outcome.

Clinical features: A 28-yr-old man involved in a motor vehicle collision sustained multiple injuries, including T6-T7 thoracic vertebrae fracture. Magnetic resonance imaging identified spinal cord compression at T6-T7, without brain or cervical cord injury. Shortly after admission, the patient developed marked autonomic instability with fluctuating temperatures and severe hypotension. Lower extremity weakness rapidly worsened to paraplegia and new weakness developed affecting bilateral upper extremities and face. Electrodiagnostic studies showed severe axonal polyneuropathy, with denervation in all extremities. The cerebrospinal fluid protein concentration was 5.03 $g \cdot L^{-1}$. The patient was treated empirically for the possibility of GBS. Six months later, the patient recovered significant strength in his face and extremities, including his legs.

Conclusions: Guillain-Barré syndrome in trauma patients is rare and is limited to case reports following head trauma. This case also highlights the similarities and the subtle differences between GBS and CIN. Ultimately, definitive diagnosis of GBS may not be possible; however, an empiric course of intravenous immunoglobulins or plasma-exchange may be warranted, if GBS is a reasonable possibility.

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Objectif *: Le syndrome de Guillain-Barré (SGB) résulte d'une attaque immunologique aiguë des nerfs périphériques qui provoque de la faiblesse et une aréflexie ascendantes. Il arrive parfois que la faiblesse soit suffisamment grave pour que les patients deviennent paralysés et n'aient plus de fonction respiratoire appropriée. Dans de tels cas, une admission aux soins intensifs est de mise. Dans de rares situations, le SGB survient chez des patients déjà admis aux soins intensifs. Lorsque cela arrive, il peut être difficile de distinguer le SGB d'une neuropathie des états critiques (CIN). Il est toutefois crucial d'envisager le SGB dans ces cas-là étant donné qu'il existe des options thérapeutiques et qu'un traitement précoce est associé à des devenirs considérablement améliorés.*

Éléments cliniques *: Un homme de 28 ans impliqué dans un accident de la route a subi de multiples blessures, dont une fracture des vertèbres thoraciques T6-T7. L'imagerie par résonance magnétique a révélé une compression de la moelle épinière à T6-T7 mais sans lésion de la moelle épinière cervicale ou au cerveau. Peu après son admission, le patient a développé une instabilité autonome marquée accompagnée de fluctuations de température et d'une hypotension grave. La faiblesse des membres inférieurs s'est rapidement détériorée jusqu'à atteindre la paraplégie et une nouvelle faiblesse s'est développée, affectant les membres supérieurs bilatéraux et le visage. Des études électrodiagnostiques ont montré une polyneuropathie axonale grave avec dénervation dans tous les membres. La concentration de protéines dans le liquide céphalorachidien était de 5,03 $g \cdot L^{-1}$. Le patient a été traité pour un possible SGB de manière empirique. Six mois plus tard, le patient a recouvré une force considérable au niveau de son visage et de ses membres, y compris les jambes.*

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Conclusion *: Le syndrome de Guillain-Barré est rare chez les patients polytraumatisés et se limite à quelques cas à la suite de traumatisme crânien. Ce cas souligne les similarités et les différences subtiles entre le SGB et une neuropathie des états critiques. Un diagnostic définitif de SGB peut ne pas être possible en fin de compte ; toutefois, un traitement empirique à base d'immunoglobulines en intraveineuse ou de plasmaphérèse thérapeutique peut être justifié, si le SGB constitue une possibilité raisonnable.*

GUILLAIN-BARRÉ syndrome (GBS) has rarely been reported following trauma. The exact mechanism remains unclear; however, immunologic attack of the peripheral nerves is likely. The characteristic presentation is rapidly ascending weakness and areflexia. Cerebrospinal fluid (CSF) studies typically show elevated protein without pleocytosis. Electrodiagnostic studies often reveal a demyelinating polyneuropathy; however, a more severe axonal form also exists. This axonal variant of GBS is often more severe and can frequently result in patients requiring aggressive supportive therapy in an intensive care unit (ICU) setting. Axonal GBS also shares many features seen in another frequently encountered polyneuropathy in the ICU.

Critical illness neuropathy (CIN) is an axonal polyneuropathy seen in ICU patients in the setting of severe illness and trauma. Distinguishing axonal GBS from CIN can be challenging; however, the presence of such features as autonomic dysfunction, bifacial weakness, and significantly elevated CSF protein may be important clues to a delayed presentation of GBS, as opposed to CIN. The ability to recognize the possibility of GBS is significant, since early treatment, in the form of plasma exchange and intravenous immunoglobulins (IVIG), has been shown to improve prognosis and to speed recovery. Although a definitive diagnosis of GBS may not be possible, an empiric course of IVIG or plasma exchange may be warranted if GBS is a reasonable possibility. We report an unusual case of thoracic spinal cord trauma to develop axonal GBS while in the ICU. While it is not entirely possible to exclude that this was an unusual case of CIN, the patient had clinical, laboratory, and electrodiagnostic features which were more consistent with GBS. Furthermore, his neurological status stabilized and quickly improved with empiric therapy for suspected GBS. Patient consent for publication of this case report was obtained.

Case report

A 28-yr-old male was admitted to the ICU following multi-trauma sustained in a motor vehicle collision. His injuries involved fractures of the seventh and eighth thoracic vertebrae, a flail chest, mediastinal hemorrhage, hemothorax, and multiple rib fractures. The patient's trachea had been intubated at the scene using a rapid-sequence technique, including succinylcholine, and he was transported to the receiving trauma centre. Initial neurological examination revealed movement of all extremities, although limited, as a result of his numerous injuries. He was observed to be strong and combative in his upper extremities, and bilateral movement of his lower extremities was documented. Rectal tone was intact. Magnetic resonance imaging (MRI) of the entire vertebral column and spinal cord identified vertebral body fractures of T6 and T7 causing thoracic spinal cord compression. There was no evidence of injury to the brain or to the cervical spinal cord.

The patient was admitted to the ICU. He was mechanically ventilated using a pressure-regulated volume-controlled mode. Surgical stabilization of the vertebral injury was deferred until the urgent medical issues were managed, including the hemothorax, a gastrointestinal hemorrhage, and acute renal failure secondary to rhabdomyolysis. Approximately one week after admission, the patient developed marked autonomic instability with fluctuating temperatures up to 41°C, and recurrent episodes of severe hypotension requiring inotropic support. A muscle biopsy, using the halothane-contracture test to investigate for malignant hyperthermia, was negative. The patient also began to develop new and progressive motor weakness in his upper extremities and face, which were previously unaffected by the trauma. Tone was decreased in all extremities and motor power testing revealed 3/5 strength, bilaterally, in the upper extremities and 1/5 strength, bilaterally, in the lower extremities. The motor weakness rapidly worsened over the following week. Sensory symptoms and deficits were present, but seemed less prominent than the rapidly evolving pattern of motor weakness. A repeat MRI of his head and spine did not identify any new lesions above the thoracic spinal cord.

As the patient's hemodynamic and respiratory function stabilized, he was taken to the operating room for posterior thoracic instrumentation and fusion of T4-T10 vertebral bodies, with bone allograft and decompression of T6-7. Anesthesia was administered using volatile agents and opioid analgesics (isoflurane, fentanyl and morphine) in accordance with clinical parameters. His neck was maintained in the neutral

position during transfers. The procedure lasted five hours, and no neuromuscular blocking agents were administered. No complications occurred during the surgical procedure, and anesthesia was uneventful throughout. Postoperatively, his previously noted weakness progressed, and tracheal extubation was deemed inappropriate. The patient was flaccid in all four extremities, with no movement present. He also had bifacial weakness affecting his upper and lower face. No reflexes were elicited, and his plantar reflex response was equivocal. Sensation to pinprick was intact. A third MRI examination failed to identify any new lesions, particularly of the cerv ical spinal cord or brainstem. The patient continued to display autonomic instability, including very brief episodes of asystole during tracheal suctioning and bronchoscopy.

A nerve conduction study was performed, which revealed severe axonal polyneuropathy affecting motor and sensory nerve fibres. Needle electromyography studies demonstrated severe acute denervation in all limb muscles. No evidence of voluntary motor unit activation was observed, consistent with the patient's flaccid quadriplegia. A lumbar puncture was performed, revealing a protein concentration of 5.03 $g \cdot L^{-1}$, with two white blood cells, one red blood cell, and a glucose concentration of 3.8 $mmol \cdot L^{-1}$. Other investigations, including blood and CSF cultures, serology, and viral analysis, were all negative. A presumptive diagnosis of GBS was made, and a course of IVIG was initiated. As limited improvement in motor function was observed over the subsequent month, a course of plasma exchange was administered. The patient's trachea was extubated one month after the course of plasma exchange. Because of continuous gradual improvement, tracheostomy had been deferred. At this point, his strength had improved in all extremities, with upper extremities graded 3/5 bilaterally, and lower extremities 2/5 bilaterally. Within six months after his initial presentation, the patient showed considerable recovery of strength in his extremities and face. Although still requiring assistance with ambulation, he had regained much of his strength in his face and upper extremities, and he was displaying movement against gravity in both legs. No sensory level was present, and his bowel and bladder function were intact. He continues to make gradual improvement during rehabilitation.

Discussion

Although GBS following trauma of the head, face, and brachial plexus have been described, GBS following thoracic vertebral fracture has not been reported previously.[1–4] The characteristic clinical features of GBS include rapidly ascending weakness associated with areflexia. The weakness generally plateaus within four weeks of onset. Sensory features can occur, albeit to a milder degree; however a distinct sensory level is not present. Cerebrospinal fluid analysis typically shows an elevated protein with no pleocytosis. Electrodiagnostic studies generally reveal a demyelinating polyneuropathy; however, an axonal polyneuropathy can occur in patients with severe demyelination or in axonal variants of GBS.

Critical illness neuropathy is a more common cause of axonal polyneuropathy in trauma patients, particularly in patients admitted to the ICU. Critical illness neuropathy is a distinct entity from GBS and is thought to be caused by impaired microcirculation.[5] Distinguishing CIN from axonal GBS can be difficult. Critical illness neuropathy generally occurs in ICU patients with critical illness, and is often associated with sepsis, systemic inflammatory response syndrome and multi-organ failure. However, such a history does not exclude a diagnosis of GBS, as shown by a case report of a patient with campylobacter sepsis who developed GBS.[6] Certain features of acute axonal polyneuropathy can be used to distinguish GBS from CIN (Table I). Cranial nerve involvement, such as associated with bifacial weakness, is uncommon in CIN, and should prompt a search for an alternate diagnosis such as GBS. Dysautonomia is also a feature suggestive of GBS; however, sepsis associated with CIN can produce similar symptoms and needs to be ruled out. Both motor and sensory nerve fibres can be involved in axonal GBS. An exception is the axonal motor variant of GBS, often referred to as acute motor axonal neuropathy (AMAN). This variant of GBS can have striking similarities to CIN, in regards to clinical presentation and electrodiagnostic studies.

Electrodiagnostic studies can be very similar for axonal GBS and CIN.[7] The presence of sensory involvement, in addition to motor impairment, is well described in the axonal variant of GBS, known as acute motor-sensory axonal neuropathy (AMSAN). However, sensory involvement can also be seen in CIN. The degree of sensory symptoms and sensory nerve involvement seen in CIN is mild, and to a much lesser degree compared to the motor nerve involvement in CIN. The sensory nerve involvement seen in CIN tends to be much less severe than that encountered in AMSAN, the motor-sensory variant of axonal GBS. Although clinical sensory deficits were mild in our patient, electrodiagnostic examination revealed significant, diffuse, sensory involvement as well, supporting a diagnosis of the AMSAN variant of GBS.

Cerebrospinal fluid examination can also help iden-

TABLE I Distinguishing axonal GBS from CIN in patients with axonal polyneuropathy in the ICU

	Axonal GBS	CIN
History	Onset post infection as patient is improving, rarely post surgery, rarely post trauma, very rarely post vaccination Develops prior to ICU admission	Onset at peak of critical illness, sepsis, SIRS Develops during ICU admission
Clinical	Motor changes predominate in AMAN variant Motor and sensory changes in AMSAN variant Autonomic instability	Mostly motor changes, with mild sensory involvement No autonomic involvement
Examination	Cranial nerves involved: bifacial weakness	Cranial nerves rarely involved
Electrodiagnostic testing	Motor axonal polyneuropathy Sensory nerves less often involved	Sensory-motor axonal polyneuropathy Myopathy
Lumbar puncture	Significantly elevated protein Elevated IgG antibodies to GM_1,GM_{1b}, GD_{1a}, and $Ga_1Nac\text{-}GD_{1a}$	Normal-mildly elevated protein Normal IgG antibodies to GM_1,GM_{1b}, GD_{1a}, and $Ga_1Nac\text{-}GD_{1a}$
Nerve biopsy	Axonal polyneuropathy with inflammation	Axonal polyneuropathy without inflammation
Prognosis	< 5% Mortality 75% None-mild deficits	> 50% Mortality Majority of survivors have persisting deficits

GBS = Guillain-Barré syndrome; CIN = critical illness neuropathy; ICU = intensive care unit; SIRS = systemic inflammatory response syndrome; AMAN = acute motor axonal neuropathy; AMSAN = acute motor-sensory axonal neuropathy; IgG = immunoglobulin G; GM_1 = ganglioside GM_1; GM_{1b} = ganglioside GM_{1b}; GD_{1a} = ganglioside GD_{1a}; $Ga_1Nac\text{-}GD_{1a}$ = N-acetylgalactosaminyl GD_{1a}.

tify patients with GBS. Guillain-Barré syndrome characteristically has a significantly elevated CSF protein, whereas CIN has a normal, or slightly elevated, CSF protein. The presence of certain CSF antibodies also supports a diagnosis of GBS, including anti-GM_1 ganglioside antibody (anti-GM_1), anti-GM_{1b} ganglioside antibody (anti-GM_{1b}), anti-GD_{1a}, ganglioside antibody (anti-GD_{1a}) N-acetylgalactosaminyl GD_{1a} ganglioside antibody ($Ga_1Nac\text{-}GD_{1a}$), anti-GQ_{1b} ganglioside antibody (anti-GQ_{1b}).[8] A nerve biopsy can also be used to differentiate GBS from CIN. Guillain-Barré syndrome is characterized by significant inflammation, whereas CIN shows sensory and motor axonal degeneration with little inflammation.[9] Finally, GBS generally responds to IVIG and/or plasma exchange, whereas CIN does not.[10] Despite these features, many cases of acute axonal polyneuropathy that develop in the setting of critical illness or trauma, remain a diagnostic challenge in regards to distinguishing GBS from CIN. This has prompted some authors to suggest an overlap syndrome comprising certain features of both GBS and CIN.[11]

The mechanism of GBS occurring in trauma patients remains unclear. Guillain-Barré syndrome is typically caused by an autoimmune attack of peripheral nerves. In two-thirds of patients, a bacteria or virus provokes an immune response that cross reacts with self-antigens on peripheral nerves, a process known as molecular mimicry. In trauma patients with GBS, a similar immunologic attack directed against peripheral nerves may occur. Trauma patients are exposed to infections via open wounds, aspiration, and invasive instrumentation, which could, in turn, trigger an immune response directed towards peripheral nerves. Alternatively, traumatized tissues, including peripheral nerves, may lead to the exposure of antigens such as myelin proteins, with subsequent generation of autoantibodies against the peripheral nerves. The presence of antibodies to myelin basic protein has been identified in trauma patients and in surgical patients.[1] Myelin proteins P0, P2, and PMP22 have been shown in humans to induce a CD4 T-cell attack of the endoneurium, leading to demyelination.[12] Exposure to other antigens, including glycolipids (galactocerebroside) and gangliosides (GM1, GD1), has also been shown to cause a demyelinating neuropathy.[13]

Trauma, itself, can alter immune function. Severe head injury is associated with impaired cell-mediated immunity.[14] Such an alteration in immune function may predispose to T-cell dysregulation and lead to the development of GBS.[13] Surgery can also alter T-cell function, and has been reported in several cases of GBS, as a precipitant for autoimmune attack against peripheral nerves.[1,14,15] Certain human leukocyte antigen subtypes have been associated with the development of Campylobacter jejuni related GBS. Similarly, certain trauma patients may be more susceptible to the development of GBS.

Regardless of etiology, patients with GBS benefit from early treatment with IVIG and/or plasma exchange, in terms of reduced illness severity and disability duration.[10] As a result, it is important to

TABLE II Differential diagnosis of weakness in a trauma patient

CNS Disorders		PNS Disorders	
Brain	Ischemic stroke, Intracerebral hemorrhage, subdural, encephalitis, inflammatory	*Ventral root*	Traumatic avulsion, ALS, West Nile virus Other: paraneoplastic, poliomyelitis, Hodgkins lymphoma
Brainstem	Stroke, demyelination	*Nerve*	GBS, critical illness neuropathy Other neuropathy: compressive, toxin, drug, vasculitis, lymphoma, porphyria, diphtheria
Spinal cord	Compressive myelopathy Transverse myelitis Spinal infarction, hematoma Spinal abscess	*NMJ*	Myasthenia gravis, neuromuscular blocking agents Other: botulism, Lambert-Eaton syndrome, hypermagnesemia
		Muscle	Critical illness myopathy, rhabdomyolysis Other: myotonic dystrophy, muscular dystrophy hypokalemia, hypophosphatemia, pyomyositis, inflammatory myopathy, mitochondrial myopathy

Organized by disorders affecting the central nervous system (CNS) and peripheral nervous system (PNS). ALS = amyotrophic lateral sclerosis; NMJ = neuromuscular junction.

recognize the possibility of GBS for prompt treatment and optimal outcome. Identification of peripheral nerve impairment in trauma patients requiring intensive care, is not always obvious. Communication with patients is limited in the setting of head injury, intubation, sedation, and encephalopathy. Strength testing is also limited relating to effort, associated injuries, restraints, and indwelling catheters. Weakness, or recognition of muscle wasting and flaccidity, is often identified during attempts to wean patients from ventilatory support. As a result, the precise onset of peripheral nerve injury is often unclear. Approaches to weakness in the ICU have been previously described, and etiologies that need to be considered are presented in Table II.[16] A peripheral nervous system disorder should be suspected in any patient with weakness and areflexia, especially if hypotonia or muscle atrophy is present. There are other features that are characteristic of certain peripheral nervous system disorders, for example, autonomic instability and bifacial weakness in GBS, ptosis and fatigability in myasthenia gravis, and myotonia, in myotonic dystrophy.

In summary, weakness following severe trauma can arise secondary to a variety of etiologies. Although an uncommon cause, GBS should be a consideration in trauma patients with weakness and areflexia, particularly if autonomic instability and bifacial weakness are present. Electrodiagnostic testing and CSF studies can facilitate diagnosis; however, results in CIN can be very similar to axonal GBS. As in our case, definitive diagnosis may not be possible, and in cases where GBS is a reasonable possibility, a course of IVIG or plasma exchange may be warranted, since early treatment reduces disability and duration of illness in GBS. We report a case of a young male who developed a severe, acute axonal polyneuropathy following a thoracic vertebral fracture, and multiple skeletal and soft tissue injuries sustained in a motor vehicle collision. The presentation and investigations were highly suggestive of axonal GBS; however, CIN remained a consideration. Following treatment with IVIG and plasma exchange, the patient stabilized and showed gradual improvement.

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