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Guillain-Barré syndrome mimicking brain death pattern: a poorly reversible condition

Violaine Bernard[1], Vincent Van Pesch[2] and Philippe Hantson[1]

[1]Department of Intensive Care; [2]Department of Neurology, Cliniques St-Luc, Université catholique de Louvain, Brussels, Belgium

Abstract

A 73-year-old man developed a fulminant form of Guillain-Barré syndrome with abolition of brainstem reflexes. Antibodies to GQ1b were positive (1:180). The clinical findings mimicked a "brain death" pattern for a period of 12 days. In contrast, the EEG showed remaining cerebral electrical activity. Brainstem auditory evoked potentials, long-latency auditory potentials and flash-evoked visual potentials were normal. However, no peripheral and cortical somatosensory evoked potentials could be elicited. Accordingly, nerve conduction studies were indicative of motor and sensory axonal neuropathy. After 5 months, the patient had no apparent cognitive deficit but was still quadriplegic and dependent from the mechanical ventilation. He died on day 158 from nosocomial infection, without motor recovery. Other published cases with a similar admission pattern were reviewed. The prognosis is usually very poor, as most of the patients died or remained severely disabled.

Key words: Fulminant Guillain-Barré syndrome; brain death pattern; mechanical ventilation; motor recovery.

Introduction

Guillain-Barré syndrome (GBS) can present as acute quadriplegia with cranial nerve involvement. We report such a case who presented clinical findings mimicking brain death during 12 consecutive days. This diagnosis could be easily ruled out by electrophysiological investigations. A review of published cases of fulminant GBS outlines the poor functional prognosis of this severe condition.

Case report

A 73-year-old man with a past history of type 2 diabetes mellitus, arterial hypertension, atrial fibrillation and hypercholesterolemia was referred to the hospital for progressive dyspnea, abdominal pain and diarrhea. Bilateral pleural effusion was noted on chest computed tomography (CT) together with enlarged mediastinal lymph nodes. Pleural effusion was related to moderate cardiac left ventricle dysfunction secondary to rheumatic aortic valve disease. The biopsy of the lymph nodes during mediastinoscopy revealed only anthracosilicosis. Four days after mediastinoscopy, he developed acute pulmonary edema due to paroxystic atrial fibrillation and required mechanical-ventilation. When sedation was stopped three days later, the patient opened the eyes but was unable to move his limbs. He presented with flaccid quadriplegia and abolished deep tendon reflexes; consciousness was preserved and there was no oculomotor palsy. Brain CT was unremarkable. A lumbar puncture showed increased protein concentration (99 mg/dl) with 2 cells/mm^3. Nerve conduction studies, performed at day 2, showed absent motor responses in the left peroneal and median nerves and markedly reduced amplitude of motor and sensory action potentials in the left tibial and ulnar nerves. Motor conduction velocities were intact. Sensory conduction velocity in the left ulnar nerve was reduced. As a whole, these findings were indicative of motor and sensory axonal neuropathy, compatible with the diagnosis of GBS (Table 1). Antibodies to GQ1b were positive (1:180). The patient received intravenous immunoglobulins (0.4 g/kg) for 5 days. Three days after the initial neurological examination showing quadriplegia, involvement of the cranial nerves was noted with complete ophthalmoplegia and bilateral palpebral ptosis. Pupils were enlarged and unreactive. No corneal reflex or gag reflex could be elicited. The patient did not trigger the ventilator (apnea testing was however not performed). The oculo-cardiac reflex could not be accurately tested due to atrial fibrillation. There were dysautonomic signs with unstable blood pressure and profuse sweating. The

Table 1

EMG data

Results of nerve conduction studies are presented. Needle electromyography (in the left biceps brachii, tibialis anterior and extensor digitorum brevis muscles) did not reveal any abnormality at rest (data not shown). No voluntary activation could be obtained

Motor Nerve Study		Latency (ms)	Duration (ms)	Amplitude (mV)	Distance (mm)	Conduction velocity (m/s)
Left peroneal nerve	Ankle	NR	NR	NR		
	Head of fibula	NR	NR	NR		
Left tibial nerve	Ankle	6.7	19.6	0.2		
	Popliteal fossa	13.2	11.7	0.3	380	58
Left median nerve	Wrist	NR	NR	NR		
	Elbow	NR	NR	NR		
Left ulnar nerve	Wrist	6.1	10.6	0.6		
	Elbow	10.0	10.7	0.3	225	58
Sensory Nerve Study		Latency (ms)	Duration (ms)	Amplitude (μV)	Distance (mm)	Conduction velocity (m/s)
Left ulnar nerve	Wrist	2.8	3.8	7	110	39

N.R. no response.

Glasgow coma score was 3/15 (E1V1M1). Electrophysiological testing performed at day 7 (electroencephalogram (EEG) and multimodality evoked potentials) did not confirm the clinical suspicion of brain death. EEG showed diffuse slowing (6-7 Hz) of the electrical activity that remained reactive to painful and auditory stimulation. Furthermore, brainstem auditory evoked potentials and flash-evoked visual potentials were normal. Peripheral and cortical somatosensory evoked potentials could not be elicited due to the acute axonopathy. Brain magnetic resonance (MR) imaging at day 3 failed to reveal any lesion. Event-related potentials (ERPs) were investigated at day 9 with a classical oddball paradigm using auditory stimulation. Analysis revealed normal exogenous responses (N100-P200), indicating preserved initial processing of the stimulus in the auditory cortex. We were not able to elicit a reproducible P3 component in the active condition.

The follow-up of the neurological examination is summarised in Table 2. The clinical "brain death" pattern persisted for 12 days. The patient presented during the first two weeks major episodes of cardiac dysautonomia. After 5 months of intensive care therapy, minimal motor recovery was observed only in the upper limbs but the patient was still mechanically ventilated via a tracheostomy. Non verbal communication was possible using eye movements and facial mimicks. He died on day 158 from nosocomial infection.

Discussion

Fulminant GBS mimicking brain death is a rare occurrence, with about 20 cases reported in the literature, either as an isolated syndrome or as a complication of traumatic brain injury (Feasby *et al.*, 1986; Coad & Byrne, 1990; Palace & Hughes, 1994; Berciano *et al.*, 1997; Vargas *et al.*, 2000; Stojkovic *et al.*, 2001; Friedman *et al.*, 2003; Moussouttas *et al.*, 2004; Ortiz-Corredor *et al.*, 2007; Rivas *et al.*, 2008). The neurological assessment is particularly difficult in this latter condition.

As with milder forms, there is a slight male predominance, peak presentation in the fifth decade of life, and often a history of a recent minor respiratory or gastrointestinal illness.

The diagnosis of fulminant GBS is based on clinical features (presence of areflexia and quadriparesis), presence of albuminocytologic dissociation upon lumbar puncture and finally electrophysiological findings. The cerebral imaging studies by CT or MR are typically normal.

In our patient, the presence of antibodies to GQ1b ganglioside was correlated to the opthalmoplegia documented clinically. Indeed, anti-GQ1b antibody positivity has been described in the spectrum of disease ranging from Miller Fisher Syndrome, GBS with ophthalmoplegia and Bickerstaff's brainstem encephalitis (BBE) (Paparounas, 2004). A lack of antibodies does not however exclude these diagnoses.

Table 2

Evolution of the neurological findings from the onset of quadriplegia

Delay	Neurological findings
Day 1	Diagnosis of GBS, conscious, flaccid quadriplegia, no ophthalmoplegia
Day 3 – Day 14	GCS 3/15 (E1V1M1), complete ophthalmoplegia, absence of brainstem reflexes, no spontaneous breathing
Day 15	Some lateral movements of the head to verbal command
Day 16	Some movements of the jaw
Day 18	Intermittent eye opening to verbal command
Day 19	Spontaneous eye opening, persisting unreactive mydriasis, persisting ophthalmoplegia
Day 26	Recovery of horizontal eyes movements and pupillary light reflex
Day 27	Triggering during mechanical ventilation
Day 31	Minimal upper limb motor activity (scapular movements grade 1 according to Medical Research Council grading)
Day 158	Dependent from mechanical ventilation, death from nosocomial infection

Antibodies to GM1 are associated with the axonal form of GBS, but were absent in the present case.

Several features argument against the diagnosis of BBE: initial absence of opthalmoplegia, early preservation of consciousness, signs of dysautonomic failure and finally absence of brainstem lesion upon brain MRI (Odaka *et al.*, 2003).

In the review of 13 similar cases by Vargas *et al.*, the suspicion of brain death diagnosis occurred on day 2 in most of the cases (Vargas *et al.*, 2000). The duration of this particular clinical pattern is variable, but as illustrated by our case, can exceed one week (Martì-Massò *et al.*, 1993).

Various EEG patterns can be recorded in these patients, clearly allowing to rule out brain death. The most common pattern was the presence of an alpha rhythm, unresponsive to painful and auditory stimulation (Carroll & Mastaglia, 1979; Drury *et al.*, 1987; Hassan & Mumford, 1991). In other cases, the EEG showed preserved sleep patterns or reactivity to sound. A few cases were investigated concomitantly by evoked potentials, showing normal visual or brain stem auditory evoked potentials, as in our patient (Fuller *et al.*, 1992; Ragazzoni *et al.*, 2000; Vargas *et al.*, 2000).

The preservation of partial consciousness is possible at the early phase and the presence of ERPs could be expected in some cases. Ragazzoni *et al.* reported the presence of a mismatch negativity in one of the two cases of fulminant GBS at the acute stage of the disease and only the presence of an exogenous auditory response in the second case (Ragazzoni *et al.*, 2000). In our patient, the absence of recordable ERPs does not definitely exclude the persistence of a partial conscious state. As the patient could not communicate verbally, his recollection of events during the acute phase could not be assessed.

The fulminant clinical course in GBS together with the electrical inexcitability of the motor nerves usually indicates a poor functional prognosis. In the series collected by Vargas *et al.*, among the 13 patients, only 2 recovered with minor deficits (weakness in fingers or limbs) (Vargas *et al.*, 2000). Three patients died and remaining cases were severely disabled. Complete recovery seems exceptional (Moussouttas *et al.*, 2004). No significant long-term cognitive deficits have been noted in the survivors. This confirms that residual weakness is mainly observed among the patients who had nerve inexcitability on EMG, with a severe rapidly progressive disease and a need for respiratory support for more than 1 month.

This observation illustrates the value of multimodality evoked potentials investigations in documenting the preservation of brain processes in patients with fulminant forms of GBS mimicking the clinical pattern of brain death. The final prognosis is usually very poor.

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P. Hantson,
Department of Intensive Care,
Cliniques St-Luc,
Avenue Hippocrate, 10,
1200 Brussels (Belgium).
E-mail: philippe.hantson@uclouvain.be