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BRIEF REPORT

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Fulminant Guillain-Barré syndrome mimicking cerebral death: case report and literature review

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Abstract A 45-year-old woman was admitted to the intensive care unit (ICU) for respiratory arrest. One day prior to admission, she had been nauseated and in a state of total exhaustion. On the night of admission she was unresponsive and developed gasping respiration. The patient was comatose with absent brainstem reflexes and appeared brain dead. Blood chemistry findings and brain magnetic resonance imaging were normal. Electroencephalogram revealed an alpha rhythmical activity unresponsive to painful or visual stimuli. The cerebrospinal fluid showed an albuminocytological dissociation. Guillain-Barré syndrome (GBS) was suspected. The electrophysiological evaluation revealed an inexcitability of all nerves. The pathological findings of the sural nerve biopsy indicated an axonal degeneration secondary to severe demyelination. GBS can very rarely present with coma and absent brainstem reflexes. This case illustrates the importance of electrophysiological tests and laboratory and imaging studies in patients with suspected brain death where a cause is not clearly determined.

Key words Guillain-Barré syndrome · Autonomic neuropathy · Axonopathy · Demyelination · Brain death · Inexcitable nerves

Introduction

The diagnosis of Guillain-Barré syndrome (GBS) is based on a combination of clinical and laboratory features. It is typically a monophasic, subacute, symmetrical, predominantly motor neuropathy. The clinical, pathological and electrophysiological features of GBS indicate pathological and aetiological heterogeneity [1, 2, 3]. In rare cases GBS can present acute quadriparesis and cranial nerve involvement. We report the observation of a patient who presented a state mimicking cerebral death. In fact, the patient's efferent nerves were completely dysfunctional and she suffered from fulminant GBS with inexcitable peripheral nerves.

Case report

A 45-year-old woman was admitted to the intensive care unit (ICU) following respiratory arrest. She had complained of backache for 2 weeks. One day prior to admission she was nauseated and in a state of total exhaustion. On the night of admission she was unresponsive and developed gasping respiration. She required immediate intubation and mechanical ventilation due to respiratory arrest. No sedative drugs had been administered. On examination, she was apyrexial, her heart rate was 85 beats/min and arterial blood pressure was 140/80 mmHg. Her pupils were 5 mm and did not react to light. There was no voluntary ocular, facial, tongue or pharyngeal movement. The limbs were flaccid and immobile. Motor power was grade 0 (Medical Research Council grade) in all four limbs and deep tendon reflexes were absent. She had no cephalic or peripheral response to pain and no response to a suction catheter inserted into the trachea. Vestibulo-ocular reflexes after the injection of 20 ml of iced water into each external auditory meatus were absent. Vertical eye movements could not be elicited. Gag and corneal reflexes were absent.

Table 1 Initials and complementary laboratory tests. Results were all normal or negative

Initials laboratory tests		Complementary laboratory tests	
Full Blood Count	Normal	HIV	Negative
Urea	Normal	HIV p24	Negative
Electrolytes	Normal	Hepatitis B antibodies	Negative
Liver function tests	Normal	Viral Titers	Negative
Toxicology screen	Negative	VDRL/TPHA	Negative
Heavy metals	Negative	IgG anti GM1	Negative
Urine porphobilinogen	Negative	Anti-nuclear factors	Negative
Botulinum toxin	Negative	Campylobacter jejuny	Negative
Muscles enzymes	Négative		
Calcium/phosphate levels	Normal		

Table 2 Repeated neurological examinations during the first month

	Day 3	One week	Three week	One month
Patient's condition	No change	No change	Change[a]	Change[b]
Response to pain	No	No	Yes	Yes
Ophthalmoplegia	Yes	Yes	Yes	No
Autonomic dysfunction	No	Yes	Yes	No
Pupillary involvement	Yes	Yes	Yes[c]	No
Lumbar puncture	–	Dissociation	–	–
EEG	–	Change[d]	–	–
Sural Nerve biopsy	–	–	Axonal[e]	–

[a] She could nod and shake her head in response to question
[b] She started to move her eyes and open her mouth
[c] The right and left pupils were 4 and 3 mm respectively
[d] A posterior rhythmical activity at 7–8 hz
[e] Axonal degeneration secondary to acute inflammatory demyelination

Tests indicated the absence of all brainstem reflexes. Initial laboratory tests performed, as showed in Table 1, were all normal or negative. An electroencephalogram (EEG) carried out on the 1st day of hospitalization revealed symmetrical generalized low voltage rhythmical alpha activity of 7–11 Hz. No response was seen to painful or visual stimuli. Brain magnetic resonance imaging, brain stem auditory and goggle flash visual evoked potentials were normal. An examination of cerebral fluid showed it to have normal pressure, be clear and colourless and have a protein concentration of 0.9 g/l (normal < 0.45 g/l). It contained 1 mononuclear cell/mm^3 and 3.6 mmol/l of glucose (blood glucose was 5.9 mmol/l). Due to this "albuminocytological dissociation" a diagnosis of GBS was suspected. Electrophysiological studies were performed on the 3rd hospital day. All the motor nerves were inexcitable to high voltage, long duration electrical stimulation at conventional distal stimulation points. Compound muscle action potentials over the median were absent, as were ulnar, posterior tibial and peroneal nerves bilaterally. The sensory nerves were also inexcitable. Needle electromyography (EMG) revealed fibrillation potentials and positive waves in deltoid. No voluntary motor units could be obtained. In addition, as showed in Table 1, complementary laboratory studies were performed. They were all normal or negative.

The patient had no previous or concurrent illnesses that could have caused the neuropathy. She was treated with four plasma exchanges. The repeated neurological examinations during the 1st month are shown in Table2. A tracheotomy was performed 6 days after admission and weaning from mechanical ventilation was started 2 months later. Eight months later spontaneous ventilation was possible without oxygen. She was able to communicate with staff and relatives. Nevertheless, she recovered only grade 3 power in the upper limbs, grade 2 power in the lower limbs and only limited movement of the fingers.

Discussion

The striking feature of this case was the initial clinical impression. On admission to hospital the patient was unresponsive with absent brainstem reflexes and appeared brain dead. She was in respiratory arrest (there was total paralysis of the respiratory muscle) and we did not perform an apnoea testing, one of the prerequisites for the diagnosis of brain death. Brain death is the current medical definition of death when the other body organs continue to function and is defined as an irreversible cessation of all functions of the entire brain, including the brainstem. Before the declaration of brain death, an aetiology must be identified that could explain the clinical picture and all reversible causes must be excluded. GBS mimicking brain death is very rare. [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15]. Table 3 shows the cases reported in the literature. Our patient was a 45-year-old woman. The disease occurs at all ages but with peak frequency in the fifth decade of life. The occurrence rate is higher for men than for women. We find the same epidemiology in typical GBS [3].

Table 3 Clinical characteristics, treatment and outcome of patients with Guillain Barre syndrome mimicking cerebral death

Case	Age/sex	Suspicion of GBS	Suspicion of brain death	Treatment	Outcome[a]
Carroll et al. 1979 [4]	45/M	Progressive flaccid tetraparesis	Day 2	Not specified	Walk with help
Kotsoris et al. 1984 [5]	44/M	Ascending paralysis	Day 2	Not specified	Recovered progressively[b]
Drury et al. 1987 [7]	63/M	Muscle weakness	Day 2	Not specified	Not specified
Coad et al. 1990 [6]	43/M	Muscle weakness Diplopia	Day 4	Not specified	Recovered progressively
Hassan et al. 1991 [8]	45/M	Muscle weakness Diplopia	24 hours	Not specified	Weelchair bound
Fuller et al. 1992 [9]	63/M	Muscle weakness	Day 2	Plasma exchange + corticosteroids	Died on day 18
Marti-Masso et al. 1993 [10]	58/F	Dysphonia Difficulty swallowing	24 hours	Plasma exchange	Walk alone, mild weakness in limbs
Tan et al. 1995 [11]	50/F	Muscle weakness	Day 4	Gamma Globulin	Died on day 97
Bohlega et al. 1995 [12]	45/M	Muscle weakness	Day 3	Plasma exchange + Gamma Globulin	Severely disabled
Hughes et al. 1997 [13]	27/M	Muscle weakness Difficulty swallowing	Day 2	Gamma Globulin	Fingers weakness
Berciano et al. 1997 [14]	67/M	Dyspnea Muscle weakness	Day 2	Plasma exchange + corticosteroids	Died on day 18
Bakshi et al. 1997 [15]	6/M	No	On admission	Gamma Globulin	Walk with help
Reported case	45/F	No	On admission	Plasma exchange	Severely disabled

[a] Outcome at twelve months
[b] Outcome at twelve weeks

When confronted with "comatose state", the diagnosis of fulminant GBS is difficult. Eleven times out of 12, the presenting history and the rapidly progressive areflexic paralysis could lead to the diagnosis of GBS. The clinical suspicion of brain death occurred on day 2, at least, in nine cases. Nevertheless, in our observation, there were no obvious, initial clinical criteria for the diagnosis of typical GBS. A diagnosis of GBS is based on a large list of arguments, including imagery, biological and electrophysiological examinations. The concentration of protein in cerebrospinal fluid, with fewer than 10 cells/mm^3, is a feature which strongly supports the diagnosis of typical GBS [1, 2]. In our case the albuminocytological dissociation strongly supported the diagnosis of GBS. The results of cerebrospinal fluid in GBS resembling cerebral death are reported in Table 4. The albuminocytological dissociation was found 9 times out of 12. In the other three cases, cerebrospinal fluid was normal or showed pleocytosis.

The results of EEG, EMG and pathological features concerning GBS mimicking cerebral death are reported in Table 4. In some cases [7, 11, 13, 14, 15] the observed EEG pattern (sleep pattern or reactivity to sounds) abolished any concern about brain death. Nevertheless, EEG patterns in the other six reported examples showed a similar unresponsive alpha rhythm in the acute state. The distribution and the lack of responsiveness can suggest a brain stem lesion leading to alpha coma, i.e. a reactive alpha rhythm seen on EEG which was consistent with consciousness, recorded in a paralyzed patient who clinically appeared to be comatose.

In our patient, the initial EEG was unaffected by visual stimuli and showed an alpha rhythm while, at the same time, the visual evoked potentials were normal. Fuller et al. [9] reported the case of a patient with pseudoaxonal GBS who also presented normal visual evoked potentials to flash and brain stem auditory evoked potentials and an elevated EEG unaffected by visual and painful stimuli. In both observations, the EEG evidenced an alpha rhythm. Westmoreland et al. [16] have described an alpha rhythm in five patients who have sustained cardiac or respiratory arrest. Nevertheless, the prognosis of alpha rhythm was far worse in these patients than in our patient. Our patient, and the patient in Fuller's study, had completely dysfunctional efferent nerves and probably were in the so-called alpha-delta stages of sleep during the EEG. In our patient the preservation of cerebral cortical function was supported by a second EEG, which showed a posterior rhythmical activity. The present case illustrates the importance of repeated EEG in this group of brain stem syndromes without obvious cause.

The initial electrophysiological evaluation in our observation and in these fulminant GBS cases showed an inexcitability of all nerves. Inexcitability of motor nerve

Table 4 Cerebrospinal fluid, EEG, EMG, and pathological features characteristics of patients with Guillain Barré Syndrome mimicking cerebral death

Case	Cerebrospinal fluid	EEG	EMG	Pathological feature
Carroll et al. 1979 [4]	Dissociation[a]	Alpha[b]	Missing	Missing
Kotsoris et al. 1984 [5]	Dissociation	Alpha	Inexcitability[c]	Missing
Drury et al. 1987 [7]	Dissociation	Reactive	Inexcitability	Missing
Coad et al. 1990 [6]	Dissociation	Alpha	Missing	Missing
Hassan et al. 1991 [8]	Normal	Alpha	Missing	Missing
Fuller et al. 1992 [9]	Dissociation	Alpha	Inexcitability	Axonal[e]
Marti-Masso et al. 1993 [10]	Dissociation	Alpha	Missing	Missing
Tan et al. 1995 [11]	Normal	Reactive	Inexcitability	Missing
Bohlega et al. 1995 [12]	Dissociation	Missing	Inexcitability	Axonal
Hughes et al. 1997 [13]	Dissociation	Sleep	"compatible"[d]	Axonal
Berciano et al. 1997 [14]	Pleocytosis	Reactive	Inexcitability	Axonal
Bakshi et al. 1997 [15]	Dissociation	Sleep	Inexcitability	Demyelination
Reported case	Dissociation	Alpha	Inexcitability	Axonal

[a] Albuminocytologic dissociation
[b] Alpha rhythm activity unresponsive to painful and auditory stimulation
[c] Inexcitability of motor and sensory nerves
[d] Compatible with Guillain Barré syndrome
[e] Axonal degeneration secondary to severe demyelination

fibres with distal supramaximal stimulation is an unusual electrophysiological finding. Inexcitable motor nerves in the initial stages of GBS are due to distal pathology of the motor axons, either distal conduction block or axonal degeneration. The nature of these changes cannot be predicted by the results of the initial electrophysiological evaluation, including the presence or absence of active denervation [17]. Severe axonal degeneration in GBS is associated with a poor clinical outcome whether the axonal damage is a primary event or is secondary to inflammatory demyelination. A poor clinical outcome can be suspected on the basis of the fulminant clinical course and the electrical inexcitability of the motor nerves.

A few patients, fulfilling the clinical criteria for acute GBS, have shown extensive axonal degeneration with little or no histological evidence of demyelination. These cases have been labelled axonal GBS and are characterized by an inability to stimulate peripheral nerves, rapidly progressive tetraplegia and poor recovery [18]. In the reported cases concerning GBS mimicking cerebral death and in our patient, the pathological findings of the sural nerve biopsy indicated that the early pathological mechanism was demyelination. The exact physiopathology and whether these patients have distal demyelination and conduction block with secondary axonal loss or axonal degeneration, or both, are still unclear.

To add to the difficulty in the initial diagnosis, our patient presented with non-reactive mydriasis. Pupillary abnormalities have rarely been described [9]. Nevertheless, the preganglionic sympathetic and parasympathetic fibres that supply the pupil are thinly myelinated. Although external ophthalmoplegia was mentioned in the proposed criteria for diagnosis of GBS [2], internal ophthalmolplegia (i. e., pupillary involvement) was not included.

The various treatments used for these fulminant GBS mimicking cerebral death are reported in Table 3. The different therapeutic methods are specified in only seven cases. It is therefore difficult to establish treatment guidelines for these patients. In addition, in a recent study of patients with GBS, including those with inexcitable nerves, the outcomes in response to plasma exchange or infusion of gamma globulin, or a combination of both treatments, did not differ [19].

Our patient showed poor recovery. In GBS, 3–8 % of patients die from complications, such as sepsis, adult respiratory distress syndrome, pulmonary emboli or, in rare cases, unexplained cardiac arrest perhaps related to dysautonomia [1]. Only 15 % of patients have no residual deficit. Five to ten percent have permanent disabling weakness and 65 % have persistent minor problems [1]. The outcome of patients with fulminant GBS who appeared brain dead are reported in Table 4. Three patients died, two from cardiac arrest related to dysautonomia and one from a massive anterior myocardial infarction. Two patients showed poor recovery, with permanent disabling weakness. The others could walk with persistent minor problems. GBS mimicking brain death has a poor recovery rate and a high mortality, particularly in relation to dysautonomia. It is a fact that nerve inexcitability on EMG, the need for ventilatory support for more than 1 month and severe rapidly progressive disease can all lead to residual weakness [20].

Guillian-Barré syndrome can, in rare cases, present signs of coma and absent brainstem reflexes. This is an important variant of GBS to consider, because it is potentially easy to make a misdiagnosis without a good antecedent history and the consequences are disastrous. This case illustrates the importance of electrophysiological tests and laboratory and imaging studies in patients with suspected brain death where the cause is not clearly determined.

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