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Unusual presentation of more common disease/injury

Fulminant inflammatory neuropathy mimicking cerebral death

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Summary

We report a case of a 44-year-old woman who developed rapidly progressive tetraparesis followed by respiratory failure and abolition of brainstem reflexes. Electrodiagnostic studies excluded the possibility of cerebral death and confirmed the diagnosis of acute motor-sensory axonal neuropathy. The initial fulminant course of the disease was followed by slow recovery to independence in daily activities.

BACKGROUND

Guillain-Barre syndrome (GBS) is an acute postinfectious immune-mediated polyneuropathy.[1 2] In some rare cases, acute neuromuscular paralysis caused by GBS may present as a locked-in syndrome and cerebral death may be erroneously diagnosed. We describe a case of fulminant neuropathy initially mimicking cerebral death.

CASE PRESENTATION

A 44-year-old woman began to complain of headache, nausea and weakness of legs on a day in January 2007. One month before, she had suffered from a cough and subfebrile temperatures. The weakness began to progress rapidly. Next morning she could not get out of bed, due to weakness in legs and hands, and she also noticed obstruction of speech. On the same day she was admitted to the county hospital, with flaccid tetraparesis and dysarthria, while her condition continued to worsen. The same evening she developed dysphagia and respiratory failure, and was therefore intubated and mechanically ventilated, and the next morning she was transferred to the neurointensive care unit. On arrival, the total flaccid tetraplegia with absent tendon reflexes, opthalmoplegia, wide pupils without light reflex and missing oculocephalic reflex were documented. The question emerged of possible cerebral death.

INVESTIGATIONS

Laboratory findings

Initial cerebrospinal fluid (CSF) analysis revealed elevated protein levels that increased dramatically during the first week. At first, minimally elevated leucocyte and erythrocyte counts were detected, raising the possibility of meningoencephalitis (table 1). Repeated analyses revealed the classical albuminocytological dissociation. Elevated leucocyte count and C-reactive protein levels in the peripheral blood analyses were probably related to the pneumonia.

Imaging studies

A brain CT scan was normal, and brain and spinal MRI did not reveal any pathological changes.

Electrodiagnostic studies

As a turning point, an EEG on the third day revealed diffuse continuous slowing down of background activity in the theta range with amplitudes of 30–50 μV, with a preserved posterior rhythm and photic-driving response. Therefore, the possibility of brain death was excluded.

Nerve conduction studies showed no motor or sensory responses on the tenth day. On the twenty-first day, needle electromyography (EMG) showed active denervation potentials (positive sharp waves and fibrillation potentials) in cranial, distal and proximal hand muscles, and no voluntary activation in any of the muscles. The findings were compatible with acute axonal motor and sensory degeneration. On the basis of the EMG results, nerve conduction studies and CSF findings, acute motor-sensory axonal neuropathy (AMSAN), a form of GBS, was diagnosed.

Table 1 Initial and repeated laboratory tests

Analysis	Initial	Day 7
CSF analysis		
CSF protein	1.3 g/l	6.86 g/l (0.3–0.6 g/l)
CSF leucocytes	86×10^6/litre (95% neutrophils)	5×10^6/litre ($<5\times10^6$/litre)
Blood		
Leucocytes	18.41×10^9/litre ($4–10\times10^9$/litre)	7.76×10^9/litre
CRP	12 mg/l (<10 mg/l)	4 mg/l
Electrolytes	Normal	
Liver function tests	Normal	
Kidney function tests	Normal	
Serology		
CMV IgG	Positive	
HSV-1 IgG	Positive	
EBV IgG	Positive	
VZV/HZV IgG	Positive	
Mononucleosis	Negative	
Enterovirus IgG	Positive	
Hepatitis	Negative	
HIV	Negative	

Reference values given in parentheses.
CMV, cytomegalovirus; CRP, C-reactive protein; CSF, cerebrospinal fluid; EBV, Epstein-Barr virus; HSV, herpes simplex virus; VZV/HZV, varicella zoster virus/herpes zoster virus.

DIFFERENTIAL DIAGNOSIS

The first differential diagnostic hypotheses included various central nervous system (CNS) disorders and peripheral causes for fulminant tetraplegia. EEG results excluded the possibility of brain death. Causes for locked-in syndrome needed to be excluded—extreme forms of myasthenia gravis, basilar artery thrombosis, transverse myelitis, high cervical cord compression, botulism and toxic neuropathies.

Initial moderately elevated CSF leucocyte count raised the possibility of CNS infection. Typically, the increase in CSF leucocyte count should raise doubts about the diagnosis of GBS and indicate the possibility of other disorders such as HIV-related GBS, Lyme disease, West Nile virus infection or poliomyelitis.[1] However, it has been described that moderate pleocytosis may occur in cases of GBS and to our knowledge there is at least one description of a case of fulminant Guillain-Barre syndrome with axonal damage and initial raised CSF leucocyte count (100 leucocytes/mm^3).[3] West Nile virus has been described to cause acute flaccid tetraparesis in some cases.[4] In 2009, 28 West Nile virus cases were reported in Europe, these were in Italy, Hungary, Romania and France.[5] West Nile virus has never been diagnosed in Estonia. The patient had not travelled to endemic regions prior to her illness.

Regarding other possibilities of meningoencephalitis, several common causes of CNS infection were not found in serological tests. As the EEG had only mild slowing, MRI of the brain was normal, and as later discovered the patient was conscious during the illness, it made the possibility of primary CNS infection highly unlikely.

Botulism was considered as potential differential diagnosis for flaccid tetraparesis. Electroneurography and myography indicated the presence of axonal neuropathy and did not demonstrate neuromuscular transmission defect. Later we could specify that the patient could not remember of eating any potentially improperly processed foods. Also her sensory system was involved, both clinically and on neurography, which would be not expected in the case of botulism.

Medicine or substance intoxication could result in axonal polyneuropathy. The patient did not take any medicines or did not have any contact with potential toxins.

Critical illness polyneuropathy (CIP)/myopathy would also appear as axonal polyneuropathy. Usually, it would be expected to appear in intensive care situation after sepsis or multiple organ failure. In our case, rapidly progressing tetraparesis was the initial and leading symptom. She did not have sepsis or multiple organ failure, nor did she have any other critical illness that could have initiated CIP.

TREATMENT

The patient was treated with 25 g/day (0.4 g/kg/day) intravenous immunoglobulin for 5 days.

OUTCOME AND FOLLOW-UP

On the ninth day after the admission, the patient was able to demonstrate the first signs of conscious response by nodding her head. Four days later, she could open her mouth and reported to have tactile sensation. On the sixteenth day, respiratory efforts started to recover and, 1 day later, she was able to open her eyes and raise her shoulders. Thereafter, she recovered gaze movements and minimal hand movements. She required intensive care treatment for 1.5 months, followed by long-term rehabilitation.

The patient remained wheelchair-bound for the first 21 months. After 29 months, she still had a residual flaccid distal tetraparesis, but she was able to walk with assistance. She recalled some of the episodes of the acute illness, but described her memories as somewhat 'foggy'.

DISCUSSION

Few cases of fulminant GBS with total flaccid tetraplegia have been described.[6–10]

The nerve conduction studies and EMG were concordant with AMSAN. Possible CNS affliction was discussed. In particular, the possibility of Bickerstaff brainstem encephalitis (BBE) was raised. BBE, which is characterised by progressive opthalmoplegia, ataxia and disturbance of consciousness, has an overlap with Miller Fisher syndrome and GBS.[11] Since our patient's predominant sign was initially limb weakness, and her consciousness was preserved, we deduced that it was likely to be a case of primary peripheral nervous system involvement. After initial mild clinical improvement in tetraplegia, it was clear that her consciousness was preserved.

The question of the involvement of consciousness in fulminant GBS has been raised before.[12] Our patient described her conscious experiences as altered rather than lost. A hypothesis of severe generalised de-afferentation and de-efferentation has been proposed to explain the incidence of altered consciousness in these cases[12 13] and could explain it in our case.

Although the majority of cases of GBS are demyelinating, there are rare forms with axonal degeneration. Despite the axonal damage in our case the overall outcome, with minimal residual tetraparesis and independence in activities of daily living, was good.

Learning points

- Guillain-Barre syndrome can rarely present as a locked-in syndrome and cerebral death may be erroneously diagnosed.
- EEG can provide irreplaceable evidence for excluding cerebral death and diagnosing locked-in syndrome.
- In some severe cases of acute motor-sensory axonal neuropathy the outcome may be quite favourable.

Competing interests None.

Patient consent Obtained.

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