Lesson of the Week

Coma and brain stem areflexia in brain stem encephalitis (Fisher's syndrome)

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The assessment of brain stem function in comatose patients is now regular medical practice world wide. When envisaging a diagnosis of brain stem death it is essential, firstly, to establish that the patient is suffering from irremediable structural brain damage of known cause, and, secondly, to exclude the primary or contributory role of reversible causes of apnoeic coma with absent brain stem reflexes. Such causes include drug intoxication, hypothermia, and metabolic and endocrine disturbances.[1-3]

Brain stem encephalitis (Bickerstaff's encephalitis, Miller Fisher syndrome) is characterised by acute ophthalmoplegia, ataxia, and areflexia.[4-7] In unusually severe cases the patient may be comatose and apnoeic and there may be complete paralysis of the motor functions of the cranial nerves.[4-6]

We describe three patients with this condition in whom brain stem areflexia was associated with apnoeic coma. None of them met the first precondition for a diagnosis of brain stem death, emphasising the importance of the necessary preconditions for making such a diagnosis.

Although brain stem encephalitis can cause apnoeic coma and brain stem areflexia, the patients may recover fully. If the criteria and preconditions for diagnosing brain stem death are observed these patients should not be diagnosed as being brain stem dead and they should be given full support while in coma

Case reports

CASE 1

A 56 year old man presented with generalised aches and pains for three weeks, associated with tingling and numbness of the fingertips. By the third week he had become increasingly drowsy and then comatose and had to be ventilated. He was normotensive, had no signs of meningeal irritation, and there was no papilloedema. In the first 12 hours he was comatose and apnoeic with fixed dilated pupils and absent corneal, oculocephalic, oculovestibular, and gag reflexes. The deep tendon reflexes were absent. At 24 hours examination was the same except for the development of shallow respiratory efforts. Five days later he was drowsy but could be roused, with complete internal and external ophthalmoplegia, bilateral facial weakness, tendon areflexia, and normal plantar responses. It was clear later that he had no motor or sensory disturbances in the limbs but had gross limb and truncal ataxia.

Electroencephalography performed on the third day showed bilateral delta activity. The cerebrospinal fluid contained 64 lymphocytes/μl, with normal protein content. Computed tomography of the head showed a low density area in the left occipital lobe, which was thought to be unrelated to his current problem. By the third week he was fully conscious, and further improvement continued so that he had returned to normal four months later.

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CASE 2

A 45 year old man developed chickenpox. Four days after the development of the rash he developed progressive respiratory distress and weakness in the arms and legs, for which he was admitted to hospital and promptly ventilated. On reassessment after ventilation he was found to be conscious but drowsy and febrile with fixed dilated pupils and complete ophthalmoplegia. There was almost complete paralysis of the motor functions of the cranial nerves, grade 3 weakness of arms and legs, tendon areflexia, and normal plantar responses. On the third day, after a short convulsion, he drifted into coma.

He was apnoeic, in spite of a carbon dioxide pressure of over 6·6 kPa (50 mm Hg), and comatose for seven days. His brain stem functions were assessed on the second and fifth day of the coma. He had fixed dilated pupils, absent oculocephalic corneal, oculovestibular, and gag reflexes.

Haematological and biochemical profiles were normal. The cerebrospinal fluid, tested on day 4, showed no pleocytosis but a protein content of 0·69 g/l. Computed tomography performed in the recovery period yielded normal results.

Despite the persistence of the cranial nerve signs, on day 8 he started to respond to painful stimuli by minimal purposeful arm and leg movements and had shallow respiratory efforts. He continued to improve, so that six weeks later he was off the ventilator and was fully conscious, although he had no recollection of the first four weeks in hospital. Three months later he had full range of eye movements, with dilated pupils, fixed to light but briskly reactive to accommodation. Residual profound weakness and wasting of the proximal limb muscles and sensory impairment were present.

CASE 3

A 20 year old man was admitted with a one day history of numbness and heaviness in the extremities and difficulty in keeping his eyes open. He was fully conscious, with bilateral ptosis, complete external ophthalmoplegia, tendon areflexia, and ataxia. A day later he was dysarthric and drowsy but then gradually lost consciousness and had to be ventilated. There were no signs of meningeal irritation or papilloedema. Urgent computed tomography yielded normal results.

Brain stem functions were assessed at 12 and 24 hours after the onset of the coma and he was found to be comatose and apnoeic with absent oculocephalic, corneal, oculovestibular, and gag reflexes. The pupils were dilated but sluggishly reactive to light. The deep tendon reflexes were absent. At 48 hours he was moving his head and arms to painful stimili and had shallow respiratory efforts.

His biochemical and haematological profiles were normal. The cerebrospinal fluid was examined on day 2 and showed no pleocytosis and again on day 15 when it showed an increasing protein content of 0·26 g/l and 5·2 g/l, respectively.

Five sessions of plasmapheresis, exchanging a total of six litres, were performed in the second week with gradual improvement in respiratory effort and consciousness. He needed assisted ventilation for two months.

Four months after the acute illness he had recovered normal function of his cranial nerves but was still disabled with weakness of the arms and legs.

Discussion

In diagnosing brain stem death it is mandatory to meet the precondition of irremediable structural brain damage, which in most cases will be due to head injury or intracranial haemorrhage. The report of the Conference of Medical Royal Colleges and their Faculties in the United Kingdom also emphasises the need to exclude the presence of potentially reversible causes of apnoeic coma with brain stem areflexia.[1] We suggest that brain stem encephalitis be included among such causes.

Typically brain stem encephalitis is characterised by acute progressive ophthalmoplegia, dysfunction of other cranial nerves, ataxia, and hyporeflexia and usually results in complete recovery.[4-7] Although some authors believe that it represents a simple variant of the Guillain-Barré syndrome,[7-9] there is now substantial clinical,[6 10 11] radiological,[6 12 13] and pathological[4 6 14] evidence of brain stem disease. Impairment of consciousness and even coma have been reported in the early part of the disease.[4 6] Ventilatory embarrassment has been described in eight patients,[6 15-18] where assisted respiration was very rewarding in all but one patient.[15] Occasionally paralysis of all the motor functions of the cranial nerves develops.[4-6] Sensory functions of the cranial nerves, particularly hearing, are usually preserved.[4-6 16] A fatal outcome is rare, being described in only four cases.[4 6 14 15]

All our patients were comatose and apnoeic (apnoea being strictly tested only in case 2) for a variable period with paralysis of the motor function of the cranial nerves. Repeated testing of brain stem function showed a state of areflexia. The clinical presentation was not predictive of the eventual favourable prognosis, and the diagnosis was made only in the recovery period. Computed tomography of the head was available in the acute phase in cases 1 and 3 but not in 2. Ophthalmoplegia (complete in case 2 and external in case 3) was documented before either patient drifted into coma (no such finding was recorded in case 1), but neither of these findings suggested a favourable prognosis. In the absence of a metabolic or endocrine disturbance, drug intoxication, or hypothermia, any of our patients could have been diagnosed as possibly having encephalitis. Computed tomography would not have excluded such a possibility. Furthermore, the second patient had his illness complicating chickenpox, was febrile, and drifted into coma after a generalised convulsion, and in case 1 the cerebrospinal fluid was abnormal (64 lymphocytes/μl). These features served to strengthen the possibility of encephalitis as a cause for their illness. Pallis recognised encephalitis as a cause of brain stem death.[3] None of the patients were considered brain stem dead, however, because no "irremediable structural brain damage" was shown.

In the presence of coma there are no clinical tests to establish the diagnosis of brain stem encephalitis. As the auditory pathways seem to be immune[4-6 16] auditory evoked responses in the brain stem might be of help. They are absent in brain stem death[19] but, though not necessarily normal, are preserved in brain stem encephalitis.[6 20]

Plum and Posner[21] did not mention brain stem encephalitis (Bickerstaff's encephalitis) as a cause of stupor or coma, nor as a condition needing consideration before diagnosing brain stem death. Pallis, however, recognised the possibility that in the evolution of the condition brain stem areflexia may be found in a drowsy patient.[3] He went on to emphasise the centrality of the history and context in diagnosing brain stem death.

We feel that patients such as those we have described, far from invalidating criteria for diagnosing brain stem death laid down and practiced by physicians world wide,[1-3] in fact reinforce them. When brain stem death is considered in the context of encephalitis, the encephalitis should be well documented as having caused "irremediable structural brain damage." In such a context time is the best way of showing that the lesion is irremediable.

These cases are unusual presentations of an uncommon disease. It is clear, however, that at some stage during the evolution of brain stem encephalitis the association of coma and brain stem areflexia point to a serious illness. Inexperienced physicians may then erroneously consider diagnosing brain stem death, having failed to observe the preconditions for such a diagnosis. This emphasises once again the importance of who makes the diagnosis.

Even if the possibility of brain stem death is correctly discarded, such patients may be denied active therapeutic support. They may be incorrectly denied cardiac resuscitation, for instance, if they develop a cardiac arrest. The serious presentation with an essentially benign outcome was well documented by Bickerstaff and should constantly be borne in mind.[4 5]

In conclusion, our cases illustrate two main points. Firstly, that brain stem encephalitis can cause coma and brain stem areflexia. Secondly, our patients had a favourable outcome, in spite of the serious clinical state during the evolution of their illness.

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Is there any evidence that zinc pyrithione—used in shampoos for eliminating dandruff—is of any value in treating psoriasis?

No. Zinc pyrithione has bacteriostatic and fungicidal properties. When dandruff is due to seborrhoeic eczema, currently regarded as precipitated by pityrosporon ovale, clearly these properties would be beneficial in relieving dandruff.[1] Where dandruff is due to psoriasis, in which epidermal infection appears to play no part, this chemical should have no effect. Sometimes it is difficult in some patients to decide whether their dandruff is due to psoriasis or seborrhoeic eczema, and then products containing zinc pyrithione might be worthy of trial, but there is no rationale for using zinc pyrithione in topical preparations in psoriasis of the scalp. In the 1970s oral zinc was tried in chronic plaque psoriasis because in many patients with psoriasis the serum zinc concentrations were found to be low, but the response was not convincing,[2] and the relevance of low serum zinc concentrations to disease, even in those in which zinc is known to play a part, has largely been discounted.—ALAN B SHRANK, consultant dermatologist, Shrewsbury.

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