Complete recovery from an unusual cause of coma

A 51-year-old man was admitted to the emergency room because of progressive lethargy, slurred speech, weakness of the right arm and low-grade fever. Physical examination showed no additional neurological deficits. He had a history of a tick bite 6 months previously which had been treated with antibiotics. Apart from leukocytosis (10.5 × 10⁹/l) and raised C-reactive protein (62 mg/l), additional blood examination was normal. Cerebral contrast-enhanced computed tomography (CT) revealed no abnormalities. Cerebrospinal fluid (CSF) examination showed an elevated cell count of 66 cells/l (of which 97% were lymphocytes), slightly elevated protein concentration of 1.03 g/l, a normal glucose level of 3.7 mmol/l and an elevated pressure of 29 cmH₂O.

The onset of progressive lethargy over a period of days, slurred speech and the weakness indicates a lesion of the central nervous system. Given the progression of lethargy, the fever and the absence of acute onset, an infectious origin seemed more likely. This was suggested by the CSF examination, showing an elevated cell count, especially lymphocytes. The differential diagnosis consisted of (viral) meningo-encephalitis – most likely caused by enteroviruses, arboviruses or herpesviruses – neuroborelliosis and vasculitis. Antibiotics and antiviral drugs were started.

Case

Within 2 days, the patient’s condition deteriorated into a deep coma requiring mechanical ventilation. Initial treatment consisted of acyclovir and ceftriaxone, anticipating a possible neuroborelliosis and herpes simplex encephalitis. However, repeated blood and CSF cultures were normal, making an infective origin less likely. Serological tests for Lyme disease and repeated polymerase chain reaction (PCR) testing for herpes simplex virus (HSV) were negative. Systemic vasculitis was ruled out. The patient remained in an areactive coma without focal signs and abnormal brainstem reflexes. An electro-encephalogram (EEG) after 1 week showed non-specific diffuse slow activity. Three weeks after admission cerebral gadolinium-enhanced magnetic resonance imaging (MRI) was performed, showing numerous hyperintense lesions, on T2-weighted images, of the brainstem, the left cerebellar hemisphere, the basal ganglia on both sides and in periventricular locations (Fig. 1a–c).

Case

On ICU admission the main medical problems were (1) respiratory insufficiency requiring mechanical ventilation, (2) progressive loss of consciousness and (3) the unknown origin of the coma. Maintenance of an adequate airway and concomitant aspiration pneumonia necessitated mechanical ventilation. There are numerous possible causes of progressive loss of consciousness, including cerebrovascular accidents, cerebral infections (viral, bacterial, parasites, tuberculosis, Lyme disease), neoplastic and auto-immune diseases (sarcoidosis, vasculitis, SLE). Despite the elevated white cell count and the presence of protein in the CSF, no infectious origin was determined. Screening for HIV and coagulation disorders was negative. Repeated blood and CSF cultures were negative, and there was no response after 14 days of ceftriaxone and acyclovir. Nevertheless CSF analysis after treatment was interpreted cautiously. Many viruses responsible for meningo-encephalitis cannot be identified using common tests. MRI showed multiple hyperintense brain lesions, especially of the brainstem. Because of the massive involvement of the brainstem and persistence of coma for 2 weeks, the prognosis was considered poor.

Case

Acute disseminated encephalomyelitis (ADEM) could not be ruled out, so treatment was continued. Additionally, treatment with intravenous dexamethasone (4 mg four times a day) was started. Upon treatment with corticosteroids for 4 weeks the patient made a slow but full recovery within 2 months. After 2 months...
cerebral gadolinium-enhanced MRI was repeated, showing substantial amelioration of the intracerebral lesions (Fig. 1d–f). One year after treatment the patient still functions well, without relapse.

Case discussion

Elevated pressure, white cell count and protein level in the CSF in combination with the extensive white matter lesions confirmed the diagnosis of ADEM. ADEM is a rare cause of prolonged coma with complete recovery under specific treatment, and intensivists should be aware of this disease. Withdrawal or withholding of care in patients with prolonged coma can hardly be discussed as long as the cause of the coma remains unknown and the prognosis cannot be accurately established. Treatment with intravenous corticosteroids resulted in a full recovery. The absence of a previous infection is a peculiar aspect of our case.

Comments

This case illustrates the remarkable outcome after a long period of coma. Good recovery from a coma is observed in only 10% of reported cases and depends on the aetiology, the accompanying clinical signs, and the depth and duration of the coma [1]. ADEM is a rare monophasic illness that is thought to develop from antigenic mimicry, with antibodies having cross-reactivity to host epitopes in the nervous system. The disorder typically occurs following vaccination or a viral prodrome and is predominantly seen in children and in Japan, where viral encephalitis is more common [2, 3, 4, 5]. A preceding infection is reported in 50–75% of cases [3, 4, 5]. The estimated incidence is 0.8 per 100,000 population per year [3]. Some 0–33% of children and 35% of adults initially diagnosed with ADEM will eventually develop MS [4, 5, 6]. Therefore this diagnosis should be considered, especially in adults. Follow-up by repeated MRI, at intervals not shorter than 6 months, may anticipate this development [7]. The differential diagnosis consists of meningo-encephalitis, meningitis and cerebral involvement in auto-immune diseases [8]. In severe cases, ADEM may lead to coma. There is no standard treatment for ADEM. It is a rare disease, and no formal clinical trials of any therapeutic agent have been published. Thus the management of the disease rests on strategies that have appropriate effects on the plausible disease mechanisms. Present treatments rely on immunosuppression and immunomodulation.
Intravenous corticosteroids (preferably methylprednisolone) is the first choice of treatment and usually leads to full recovery. Plasma exchange and intravenous immunoglobulin should be considered by deterioration on corticosteroids [9, 10].

In conclusion, treatment of coma should be continued when the cause of the coma is unclear, even if there are numerous lesions in the brain. ADEM should be considered in comatose patients with raised CSF pressure, protein and lymphocytes, negative CSF cultures, and multiple white matter lesions on cerebral MRI. ADEM is predominantly seen in children, but also occurs in adults. Recovery may last weeks.

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