Adult opsoclonus-myoclonus syndrome following Mycoplasma pneumoniae infection with dramatic response to plasmapheresis

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Opsoclonus-myoclonus syndrome (OMS) is a rare distinctive movement disorder characterized by involuntary, irregular, fast, conjugated, chaotic saccadic eye movements either in the horizontal plane or multidirectional, and associated with multifocal myoclonus affecting predominantly extremities, trunk and head (1). Hence it is often described as the “dancing eyes dancing feet” syndrome (2). Some patients may have cerebellar dysfunction with dysarthria, truncal ataxia in addition to encephalopathic features. It is thought that a dysfunction in the interaction between the premotor neurons (“burst”, “omnipause” and “tonic” cells) in the paramedian pontine reticular formation is involved in its pathophysiology. In particular, loss or impairment in the “omnipause” cells which inhibit the “burst” neurons, the latter being the initiators of the saccadic eye movement, are considered to produce opsoclonus (3). Alternatively, disinhibition of the fastigial nucleus in the cerebellum, or damage to afferent projections to the fastigial nucleus may also be implicated, and explaining the associated ataxia (4). In adults, idiopathic, paraneoplastic (lymphoma, neuroblastoma, and tumors of lung, breast, ovary, kidney, uterus) and parainfectious (mostly viral) OMS are the most common etiologies (4). Occasionally, celiac disease, and allogeneic hematopoietic stem cell transplantation have been reported as the etiological factor. There is increasing evidence that autoimmune-mediated mechanisms, based on molecular mimicry, are involved in the pathogenesis of opsoclonus (5). Hence a variety of immunomodulatory treatments have been used such as high dose steroids, intravenous immunoglobulin, plasmapheresis and monoclonal antibodies (rituximab) (4).

We describe a young adult, who developed OMS as a parainfectious process secondary to a Mycoplasma pneumoniae infection. This, in addition to a dramatic response to plasmapheresis makes this case a unique observation.

Case Report

A 25-year-old man with no previous past medical history presented to our Emergency Department with a one-week history of acute-onset dizziness and severe unsteadiness initially associated with nausea, vomiting. Three days prior to the onset of his neurological symptoms he had a four-day lasting episode of cough, high-grade fever and chills associated with profuse night sweating for which he was prescribed paracetamol and an antitussive. Subsequently, his fever abated. He was a heavy smoker (20 cigarettes/day), had no allergies and had not received any recent vaccinations, and resided in Qatar for the last two years. He had not traveled for the last two years and was not on regular therapy. There was no history of trauma, drug or toxin ingestion. Neurological examination revealed a conscious well-oriented man in mental distress and with normal speech. He was unable to sit or stand without support...
because of a severe truncal ataxia. Coordination and sphincter function were preserved. There was no neck rigidity. General examination was unremarkable, in particular he was afebrile, had no glands and chest auscultation was clear. Routine biochemical testing, including full blood count on admission were normal. Erythrocyte sedimentation rate was 36 mm/h. Cerebrospinal fluid (CSF) analysis revealed increased protein 1.23 g/l, glucose 3.4 mmol/l and lymphocytic pleocytosis (95 cells, 95% lymphocytes). CSF PCR for TB and HSV were negative. There was intrathecal synthesis of IgG (14.6 mg/dl) with multiple monoclonal bands on isoelectric focusing unique to the CSF. HIV, syphilis and Brucella serology, tumor marks and extensive autoimmune screen (including ANNA-1, ANNA-2, ANNA-3, AGNA-1, PCA-1, PCA-2, PCA-Tr, amphiphysin, CRMP-5, striational, P/Q-type calcium channel, N-type calcium channel, ACh receptor binding, neuronal (V-G) K channel and AChR ganglionic neuronal antibodies) were negative or showed normal values. However M. pneumoniae antibodies (1/320), IgG and IgM were strongly positive. MRI of the brain did not reveal any supra-or infratentorial lesion on the different sequences except for the increased meningeal enhancement after gadolinium administration, likely secondary to intracranial hypotension following the lumbar puncture. In addition MR angiogram showed an oval-shaped enhancing lesion at the bifurcation of the left common carotid artery which later was confirmed to be a carotid body tumor. Chest x-ray was normal. CT chest, abdomen and pelvis for the detection of occult neoplasm were non-contributory. His clinical condition continued to deteriorate and he was started on intravenous immunoglobulin (0.4 g/kg/day for 5 days). However, one week later his neurological status worsened, he started developing irregular myoclonic jerks, involving the head and face and upper extremities particularly the shoulders, arms and forearms. These abnormal movements increased during upper limbs voluntary activity and while the patient tried to sit or stand. In addition he experienced visual hallucinations. At that time, biochemical parameters and cell blood count remained within normal limits, and CSF analysis showed mild lymphocytic pleocytosis (70 cells, 94% lymphocytes) with normal protein and glucose. His clinical condition prompted the initiation of steroid pulse therapy with methylprednisolone (1 g i.v. for 5 days) and the addition of clonazepam 0.5 g t.i.d., but despite these therapeutic measures his condition did not improve and one week later plasmapheresis (each time 3 L, five sessions on alternate days) was started, resulting in a dramatic improvement. Within 4 days he was able to stand, and walk with support, while the myoclonus and opsoclonus improved substantially. He was discharged 9 days after his last plasmapheresis and continued to improve two months after discharge.

**Discussion**

The close temporal relationship between the OMS and the flu-like illness, with positive serotesting for recent *M. pneumoniae* along with the reactive CSF, in the absence of evidence of occult malignancy indicates a relation between *M. pneumoniae* infection and OMS. The latency between neurological manifestations and infection and the monophasic pattern with improvement after immunotherapy suggest a parainfectious complication. To our knowledge, cases of *M. pneumoniae*-related parainfectious OMS in adults have not been reported.

Furthermore our case highlights the potential role for plasmapheresis in such cases. It is unlikely and it has not been reported that carotid body tumors can account for OMS. Therefore it was considered a coincidental finding.

Literature data reveal that in young adults the clinical evolution of OMS is generally more benign and the effect of immunomodulatory therapy more effective (6). OMS in young adults is either idiopathic or parainfectious. However literature review on parainfectious OMS reveals that the causative organism can be found in less than 20% of cases (7). Furthermore the pattern in non-paraneoplastic OMS is monophasic and recovery is favorable (6). Unlike our case, most patients respond favorably to IVIG and steroid therapy, even though IVIG therapy seems superior to steroid therapy (8, 9). One week after IVIG therapy, the patient neurological status deteriorated, suggesting probably an antibody rebound effect (10). The significant clinical improvement within five days of initiating plasmapheresis provides evidence of its therapeutic efficacy.

The response to immunotherapy in cases of OMS in addition to the presence of widespread central nervous system lymphocytic infiltrates in autopsies of patients with OMS, suggests an autoimmune pathogenesis (5). It is also suggested that in adults the response to immunotherapy can be used in helping to differentiate between parainfectious/idiopathic, and paraneoplastic OMS (6, 9). Without prior removal of the tumor, paraneoplastic OMS does not respond to immunotherapy including intravenous immunoglobulin, corticosteroids or plasmapheresis (6, 8). In contrast, parainfectious and idiopathic OMS show a beneficial response to immunotherapy (9). However the lack of controlled
clinical trials and the possibility of spontaneous remissions in parainfectious and idiopathic OMS leave us with no evidenced-based therapy. Furthermore none of the immunomodulatory treatments show consistent results. Despite this, IVIG seems to be embraced as the ‘first-line therapy’ in OMS (8). The therapeutic response to IVIG occurs usually within 2-3 days after the initiation of the treatment.

The role of steroid pulse therapy is ambiguous (8, 11). Although delayed corticosteroid effect cannot be ruled out, its beneficial effect remains uncertain in parainfectious OMS. Our case demonstrates that in parainfectious OMS, plasmapheresis should be considered and may be associated with a faster recovery.

REFERENCES


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