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PROGRESSIVE ENCEPHALOMYELITIS WITH RIGIDITY

A PARANEOPLASTIC PRESENTATION OF OAT CELL CARCINOMA OF THE LUNG

Case report

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ABSTRACT - Progressive encephalomyelitis with rigidity and myoclonus (PEWR) is a rare neurological disorder, characterised by muscular rigidity, painful spasms, myoclonus, and evidence of brain stem and spinal cord involvement. A 73-year-old white man was admitted with a 10-day history of painful muscle spasms and continuous muscle rigidity on his left lower limb. He had involuntary spasms on his legs and developed encephalopathy with cranial nerves signs and long tract spinal cord symptomatology. Brain CT scan and spinal MRI were normal. The CSF showed lymphocytic pleocytosis and no other abnormalities. EMG showed involuntary muscle activity with 2-6 seconds of duration, interval of 30-50 ms and a frequency of 2/second in the left lower limb. Anti-GAD antibodies were detected in the blood. We detected radiological signs of lung cancer during the follow-up, which proved to be an oat cell carcinoma. The patient died two weeks after the diagnosis of the cancer.

KEY WORDS: progressive encephalopathy with rigidity, myoclonus, stiff-person syndrome.

Encefalomielite progressiva com rigidez: uma apresentação paraneoplásica de carcinoma de pequenas células de pulmão. Relato de caso

RESUMO - A encefalomielite progressiva com rigidez e mioclonia (PEWR) é doença neurológica rara, caracterizada por rigidez muscular, espasmos dolorosos, mioclonia e evidência de envolvimento de tronco cerebral e medula espinhal. Um paciente branco de 73 anos foi admitido com história de 10 dias de espasmos musculares dolorosos e rigidez muscular contínua no membro inferior esquerdo. Apresentava espasmos involuntários em membros inferiores e evoluiu com encefalopatia associada a sinais de nervos cranianos e sintomatologia de trato longo de medula espinhal. A tomografia computadorizada de crânio e a ressonância magnética de coluna foram normais. O LCR evidenciou pleocitose linfocítica, sem outras alterações. A EMG mostrou atividade muscular involuntária, de duração de 2-6 segundos, intervalo de 30-50 ms e uma freqüência de 2/segundo no membro inferior esquerdo. Foram detectados anticorpos anti-GAD no sangue. Na evolução, foram observados sinais radiográficos de neoplasia pulmonar, sendo posteriormente diagnosticado carcinoma de pequenas células de pulmão. O paciente faleceu duas semanas após o diagnóstico de câncer.

PALAVRAS-CHAVE: encefalomielite progressiva com rigidez, mioclonia, síndrome do homem rígido.

Progressive encephalomyelitis with rigidity (PEWR) syndrome is a rare neurological disease of unknown aetiology, characterised by muscular rigidity, abnormal postures, painful muscle spasms and myoclonus[1].It is considered as the most severe form of the stiff-man syndrome (SMS), although some suggest it may be a distinct entity. Stiff-man syndrome was originally described in 1956 by Moersch and Woltman[2] as a disorder characterized by progressive fluctuating muscle rigidity and spasms, without other neurological signs. In 1971, Kasperek and Zebrowski[3] described a patient in whom they diagnosed the stiff-man syndrome and encephalomyelitis; at autopsy there was involvement of the lower brainstem and spinal cord. Whiteley and colleagues referred to this illness as PEWR syndrome[4]. Most data available in the literature favour

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the possibility that SMS and PEWR are part of a clinical spectrum with an underlying autoimmune basis, since there are ethiopathogenetic similarities between them[5]. PEWR has been reported as an isolated illness or, more frequently, in association with malignancy (especially oat cell carcinoma of the lung and Hodgkin's disease)[6,7]. The disease follows a relentless course, resulting in death in a few weeks or years.

The aim of this paper is to call attention to the possibility of malignancy in patients presenting with painful muscular spasms of acute presentation.

CASE

A 73-year old white man was admitted with a one-week history of stabbing pain on his left foot, which spread to the entire left lower limb within two days. Three days before admission, he noticed muscular spasms on the left lower limb, which rapidly progressed to the right lower limb. The spasms gradually became very intense and painful, hindering patient's ability to walk. The involuntary movements subsided during sleep and could be triggered by sensory stimuli. The patient had lost 10 kg during the previous 6 months, but had no further symptoms besides the abnormal movements of the legs. There was no sphincter disturbance. He had smoked 20 cigarettes a day during 50 years and had stopped 8 years before.

Upon admission, he was in regular general condition, had a pulse of 92, a temperature of 36.2ºC and his blood pressure was 170 x 100 mmHg. General physical examination revealed no abnormalities. A digital rectal examination showed an enlarged prostate, without nodules. The neurological examination disclosed proximal lower limbs weakness. His knee jerks were brisk and plantar response flexor. Higher mental functions were preserved. He had an increased tonus on the lower limbs with myoclonic jerking. The left foot was constantly held in plantar flexion and he was unable to straighten his legs. He had a mild slurred speech and complained of some difficulty in swallowing. The remainder of the neurological examination was unremarkable.

Brain CT scan and MRI of the head and spine were all normal. Complete blood count, serum PSA and chest and spine radiographs were all normal. A lumbar puncture disclosed a CSF with 25 lymphocytes and no red cell; protein was 0.046 g/l and no neoplastic cells, bacteria and fungi were found. The patient's serum level for anti-GAD antibodies was 64 UI/l (normal values are below 1 UI/l), Electromyogram revealed involuntary muscle activity with 2-6 seconds of duration, interval of 30-50 ms and a frequency of 2/second on the left lower limb.

The patient initially received diazepam up to 80 mg per day and phenytoin 300 mg per day. He also received high-dose intravenous immune globulin (0.4 g/kd/day) for 5 days. There was partial relief of the abnormal painful movements.

Diazepam had to be discontinued due to drowsiness and respiratory discomfort on the 8th day of admission. As the respiratory discomfort worsened, another chest radiography was performed and showed an area of consolidation in the left lower lobe (Fig 1). Cephtriaxone was then prescribed. His swallowing became impaired, and a feeding tube was inserted. Non-invasive ventilation was tried. Clindamycin was added to the antibiotic scheme. Cephepime was substituted for cephtriaxone, as the patient still had the pulmonary image on X-ray and the pneumonia was hospital-acquired. Despite the antibiotic scheme, on the 11th day a tracheal tube had to be inserted and he was transferred to the ICU. He remained there for 10 days and went back to the room with a Venturi mask.

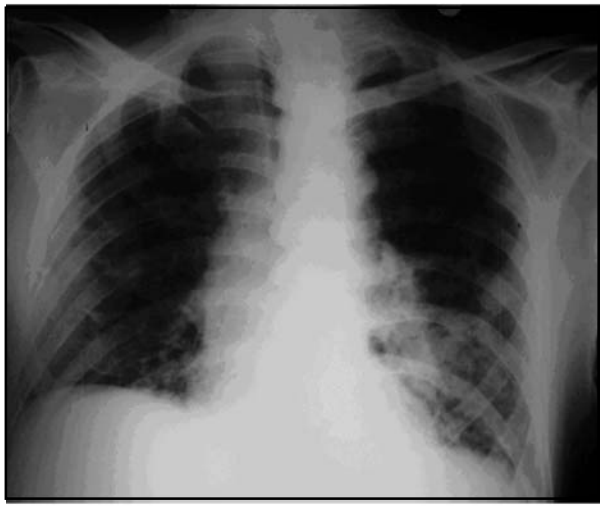

Fig 1. Chest radiograph, showing an area of consolidation on the left lower lobe.

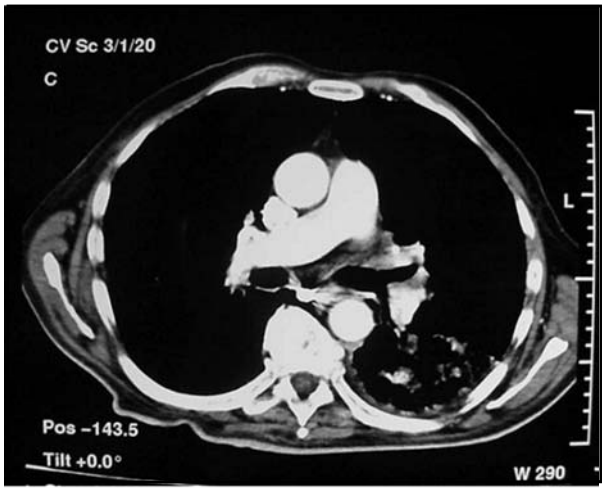

Fig 2. high resolution chest CT scan, with pulmonary mass on the left lower lobe and mediastinal lymphadenopathy.

A new chest radiography still showed the left lower lobe consolidation. There was no fever, cough or leucocytosis. A chest CT scan revealed a pulmonary mass on the left lower lobe and mediastinal lymphadenopathy (Fig 2). Bronchoscopy showed a mass in the left main bronchus. Biopsy revealed an oat cell carcinoma of the lung.

The neurological manifestations were attributed to a paraneoplastic disorder, as there was temporal association with the discovery of the oat cell carcinoma. The patient was started on chemotherapy, but he died two weeks afterwards.

DISCUSSION

Malignancy is frequently associated to PEWR syndrome. The diagnosis of our patient was particularly difficult since the initial chest radiography was normal. Although the aetiology of PEWR is not clear, most studies point to an important role of humoral immunity. Recent reports showed high prevalence of anti-GAD (glutamic acid decarboxylase) antibodies in patients with SPS[8]. The finding of these antibodies is associated with autoimmune disease, particularly diabetes-mellitus, hypothiroidism, Graves' disease and vitiligo[1].

Neurophysiological findings of PEWR consist of continuous motor unit activity. At neuropathology, PEWR is characterized by an inflammatory process with perivascular lymphocyte infiltration, increased microglial activity, astrocytic gliosis and neuronal loss, affecting mainly the brain stem and spinal cord, especially in the cervical region[9].PEWR is a rare disorder presenting with the cardinal symptoms of stiff-person syndrome, associated with brain stem and spinal cord involvement[10]. It is a severe illness that must be considered in the differential diagnosis of every patient with acute encephalomyelopathy with muscular spasms and myoclonus. We think that patients with this combination of symptoms should be screened to neoplasm, especially oat cell carcinoma of the lung.

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