Conflict of interest

The authors have no conflicts of interest to declare.

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Parkinsonism hyperpyrexia syndrome☆

Síndrome de parkinsonismo-hiperpirexia

Parkinsonism hyperpyrexia syndrome (PHS), otherwise known as neuroleptic malignant-like syndrome, akinetic crisis, or dopaminergic malignant syndrome, is a rare, potentially fatal complication of Parkinson's disease. It is characterised clinically by hyperthermia, autonomic dysfunction, altered level of consciousness, muscle rigidity, and increased serum creatine phosphokinase (CPK) levels. The syndrome is most frequently triggered by the withdrawal or sudden dose reduction of antiparkinsonian drugs. Favourable outcomes require timely diagnosis and appropriate treatment (with levodopa and dopamine agonists).

Clinical case

The patient was a 60-year-old man with an 8-year history of Parkinson's disease, and associated dyslipidaemia; he was receiving pramipexole at 2.1 mg/day, levodopa at 800 mg/day, rasagiline at 1 mg/day, and simvastatin at 20 mg/day. Family members brought the patient to the emergency department due to a 6-day history of fever (reaching 39 °C), sleepiness, disorientation in time and space, visual hallucinations, increased limb rigidity, and increased tremor and bradykinesia, which caused gait instability and frequent falls. Because of these symptoms, the patient was considerably limited in many activities of daily living. One week prior to admission, the patient decided to stop taking all medication, including antiparkinsonian drugs, following symptoms of depression. Physical examination showed a fever of 38.5 °C; pronounced rigidity in all 4 limbs, scoring 3/4 on the Unified Parkinson's Disease Rating Scale (UPDRS); resting and postural tremor in both hands; and generalised bradykinesia (finger taps, foot taps, pronation-supination, leg agility), scoring 3/4 on the UPDRS. Examination of the abdomen and thorax yielded normal results. The patient was admitted to the emergency department, where studies were performed to analyse the fever of unknown origin, and empirical treatment was administered. A complete blood count revealed mild leukocytosis (11 300 leukocytes/mm^3) and high levels of CPK (5000 IU/L); urine analysis, thoracic radiography, and urine and blood cultures all returned normal results. Transoesophageal echocardiography was performed due to suspicion of endocarditis, with no findings. Despite treatment, all initial symptoms persisted. At this point, the neurology department was asked to assess the patient. Upon observing that infection had been ruled out, and suspecting PHS, neurologists decided to restart dopaminergic medication at the original, pre-admission dose. Two days thereafter, rigidity, bradykinesia, and the patient's level

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of consciousness improved significantly, and fever resolved. The diagnostic suspicion of PHS was confirmed by the positive response to treatment; the patient was discharged several days later.

Discussion

PHS occurs in patients with Parkinson's disease who suddenly withdraw or reduce doses of antiparkinsonian drugs, particularly levodopa. The condition was first described in 1981.[1] The syndrome has also been reported in patients with Lewy body dementia following withdrawal of cholinesterase inhibitors,[2] amantadine,[3] and subthalamic deep brain stimulation.[4] Other precipitating factors include co-prescription of neuroleptics, dehydration, very hot climates,[5] and the wearing-off phenomenon.

The syndrome typically manifests with rigidity, fever, altered level of consciousness, and autonomic dysfunction, with onset usually occurring between 18 hours and 7 days after the withdrawal of dopaminergic drugs. After 72 to 96 hours, patients usually develop fever (the most frequent symptom) due to impaired dopaminergic transmission in the lateral hypothalamus, which is essential in controlling heat dissipation. Rhabdomyolysis increases CPK levels, which also contributes to fever due to the release of pyrogens from skeletal muscle; these substances stimulate the hypothalamic region responsible for thermoregulation.[6]

Rigidity, the main cause of disability, is caused by central dopaminergic hypofunction in the nigrostriatal pathway due to the increased release of calcium from the sarcoplasmic reticulum of the skeletal muscle. Patients may also experience altered levels of consciousness due to dopaminergic hypofunction in the mesocortical pathway.[6]

Autonomic dysfunction may manifest as tachycardia, labile blood pressure, and diaphoresis. These symptoms result from suppressed central dopaminergic activity, changes in central/peripheral sympathetic discharge, and alterations in central serotonin metabolism.[7]

Blood analysis may reveal mild leukocytosis, high CPK levels (although this is not a necessary condition for diagnosis), and abnormal levels of liver enzymes. The literature also includes reports of reduced levels of homovanillic acid (a dopamine metabolite) in the cerebrospinal fluid of patients undergoing sudden withdrawal of dopaminergic drugs.[8]

The main condition to be considered in the differential diagnosis of PHS is neuroleptic malignant syndrome; the main difference is that the latter is induced by exposure to dopamine receptor blockers. Other conditions to be considered are serotonin syndrome,[9] malignant hyperthermia,[10] malignant catatonia,[11] and dyskinesia-hyperpyrexia syndrome.[12]

The most common complications of PHS are respiratory insufficiency, sepsis, seizures, disseminated intravascular coagulation, and renal insufficiency; the latter 2 complications indicate poor prognosis. The condition has a mortality rate of 10%-30%, with prognostic markers including advanced age, high Hoehn and Yahr scale score, and the absence of the wearing-off phenomenon prior to onset.[5]

The main approach for treating PHS is promptly resuming the dopaminergic drug, either orally or by nasogastric tube; if these options are not viable, apomorphine may be administered.[5] Dantrolene is another alternative if the patient presents high CPK levels and a risk of renal insufficiency, or if rigidity causes respiratory failure. Some authors have reported treatment with electroconvulsive therapy[13] and steroid pulse therapy.[14]

These patients often require intensive care with respiratory support and central venous pressure monitoring; antipyretics, water replacement, and physical measures are also recommended in patients presenting hyperthermia.

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Cranial mononeuritis multiplex as the initial manifestation of systemic lupus erythematosus: A diagnostic challenge☆

Multineuritis craneal como comienzo de lupus eritematoso sistémico: un reto diagnóstico

Dear Editor:

Mononeuritis multiplex (MM) is an infrequent disorder that may be secondary to a number of diseases, which makes aetiological diagnosis difficult.[1] Infectious and inflammatory aetiologies may be difficult to differentiate. Magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis are useful tools for determining the cause of MM. We present the challenging case of a patient with MM whose symptoms were initially thought to be associated with herpes simplex virus (HSV) infection but who later developed the typical symptoms of systemic lupus erythematosus (SLE). Very few cases of MM secondary to SLE have been described in the literature[2]; cases of MM as an initial manifestation of SLE are even rarer. Our patient was a 42-year-old man with a history of hemifacial spasm due to left-sided facial paralysis in adolescence and recurrent symptoms of oral herpes virus infection.

The patient came to our department due to left-sided facial dysaesthesia, which was interpreted as neuralgia of the second branch of the left trigeminal nerve. Symptomatic treatment achieved little improvement. A brain MRI scan revealed thickening of the left trigeminal nerve (Fig. 1). Our patient had experienced recurrent symptoms of oral herpes virus infection a month previously; the MRI findings were therefore thought to be due to HSV reactivation. The patient returned to our department 9 months later, reporting worsening of the dysaesthesia; he also presented diplopia, secondary to left sixth cranial nerve palsy. We performed an additional brain MRI scan: thickening of the second branch of the trigeminal nerve persisted, with the sixth cranial nerve showing no alterations. A CSF analysis disclosed no relevant findings, viral serology results were negative, and the results of an immunological study were negative for antiphospholipid antibodies and positive for antinuclear antibodies (1:320). The patient was not receiving any drugs that may have induced lupus erythematosus. Due to suspicion of MM of inflammatory origin, we started treatment with megadose methylprednisolone therapy, achieving symptom improvement after 3 weeks of treatment. The patient was examined by the rheumatology department, reporting a 6-month history of arthritis affecting the elbows and lower limbs, which prevented him from exercising, a 2-month history of mouth ulcers, and photosensitivity. These symptoms, together with the presence of positive antinuclear antibodies, pointed to SLE.[3,4] The patient was diagnosed with SLE as the initial manifestation of MM, and started treatment with cyclophosphamide; symptoms disappeared and the MRI findings of nerve thickening and contrast uptake resolved (Fig. 2). Around 50% of patients with SLE display central nervous system (CNS) involvement.[5] This usually occurs 2 years after diagnosis of SLE.[4] Cranial nerve palsy is infrequent, accounting for 0.5%-1% of all neuropsychiatric manifestations.[5] Most of the cases published in the literature report isolated cranial nerve palsies, with cranial MM being extremely rare.[2] Cranial nerve palsy is rarely associated with SLE; palsies are normally secondary to a concomitant central or peripheral nervous system disorder (meningitis, Guillain-Barré syndrome, or cavernous sinus inflammation). In many cases, the pathogenic mechanism of cranial neuropathies in SLE is difficult to determine. Several mechanisms have been proposed; the most widely accepted is antibody-mediated neuronal involvement, which causes vasculopathy, intrathecal production of proinflammatory cytokines, and accelerated atherosclerosis.[6] It is uncertain whether the pathogenic mechanism of SLE is inflammatory, thrombotic, or mixed. The eighth and tenth cranial nerves are the most frequently affected in SLE.[7] The literature describes 2 cases of isolated twelfth cranial nerve involvement secondary to SLE[8,9] and 3 cases of isolated fifth cranial nerve involvement.[10] Optic neuropathy is the most frequent neuro-ophthalmological manifestation of SLE.[7] Ocular involvement secondary to cranial nerve palsy is rare, with the sixth cranial nerve being the most frequently involved.[7] Regarding MM, Keane[2] examined the causes of multiple cranial neuropathy in 979 patients and found only one case secondary to SLE. The literature includes 2 cases of MM associated with SLE: one patient with SLE and sarcoidosis who displayed third and sixth cranial nerve involvement combined with peripheral neuropathy,[5] and another patient with SLE with neuro-ophthalmological

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