Letters to the Editor

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS syndrome)

Inflamación linfocítica crónica con captación perivascular de la protuberancia y respuesta a esteroides (síndrome de CLIPPERS)

Dear Editor,

First described in 2010, chronic lymphocytic inflammation with pontocerebellar perivascular enhancement responsive to steroids is better known by its acronym, “CLIPPERS”. Since then, approximately 50 cases have been published, one of them in a Spanish-language journal and another 2 in the Spanish population. It is frequently mistaken for other diseases, and, since it has a specific treatment, it is especially important to know this entity. We are presenting a patient with CLIPPERS syndrome and reviewing his clinical-radiological condition.

The patient is a 66-year-old female with a history of atrial fibrillation, who progressively developed gait instability, dysphagia, dysarthria, peripheral facial palsy and right internuclear ophthalmoplegia. She was treated with oral anticoagulants, and her symptoms fluctuated in intensity but did not disappear. Laboratory blood test was normal, including tests for autoimmune (antineuclear antibodies, anti-neutrophil cytoplasmic antibodies, sedimentation rate, anti-glutamic acid decarboxylase antibodies and antithyroid antibodies), serologies (HIV, syphilis, herpes simplex and herpes zoster, Epstein–Barr virus), RCT and anti-neuronal antibodies in serum and cerebrospinal fluid, which had 2 cells/mm³ with normal glucose and proteins, and did not contain oligoclonal bands. On thoracic CT scan, no adenopathies were found. A head MRI showed punctiform lesions located in the pons that absorbed contrast (Fig. 1) and an intracranial MR angiography was normal. The patient received 1000 mg of methylprednisolone IV for 5 days only, with a great improvement, although on examination she demonstrated a horizontal nystagmus and an inability to perform tandem gait. Eleven months later, the gait worsened until she was no longer able to walk without help, in addition to trismus with tongue biting, which was treated with botulinum toxin in the masseter muscles and a wired jaw. She improved again with the previous dose of methylprednisolone, and the improvement was maintained with 90 mg of prednisone on alternate days of maintenance. However, every time the dose was decreased, the patient’s condition would worsen. After 5 years of follow-up, she died of unknown causes.

CLIPPERS syndrome is recognised by 2 clinical characteristics and one neuroimaging characteristic: brain stem symptoms and signs (the most frequent are ataxia, diplopia, facial paraesthesia, etc.), which improve with corticosteroids and get worse when they are suspended; and, on MRI in the pons region, punctiform images with “salt and pepper” appearance or curved with contrast absorption. Pontine biopsies have always shown infiltration of the perivascular spaces by T cells, which is why it has been included among the inflammatory diseases of the brain stem. But, the aforementioned triad is sufficiently specific to lead to diagnosis without the need for biopsy if other diseases of the brain stem that require a differential diagnosis have been ruled out, such as multiple sclerosis, neuromyelitis optica, neurosarcoidosis, Behçet’s disease, Bickerstaff’s encephalitis, primary lymphoma and primary vasculitis or infectious vasculitis of the central nervous system and paraneoplastic syndrome. T-cell infiltration and response to corticosteroids demonstrate an immuno-mediated origin of currently unknown cause. It has been postulated that, rather than being a disease, it could be a syndrome with several aetiologies. Only in one case has it evolved to B-cell lymphoma, and it has been postulated that it could be a rare cause of lacunar infarcts. There is agreement, however, and this is part of the syndrome’s definition, that when immunosuppression is interrupted, the condition usually worsens and at least 20 mg of prednisone are recommended per day to prevent it. This entity is probably underdiagnosed and patients may receive an erroneous diagnosis and treatment for a

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period of time, as was the case with the presented patient. For that reason, spreading knowledge about this clinical-radiological syndrome is particularly important, not only for its good response to corticosteroids, but also to limit diagnostic manoeuvres with morbidity, such as brain biopsy, which should only be performed in very select cases.

References

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Pulmonary embolism in a patient with familial thrombophilia due to homozygotic genetic mutation in 2020c>T

Tromboembolia pulmonar en un paciente con trombofilia familiar de origen genético debida a homocigosis en mutación 2020c>T

Dear Editor,

Homozygosis in 2020c>T mutation is a rare genetic alteration, previously undescribed in our country, which leads to coagulation disorders and a high tendency to suffer from thromboembolism. We present the case of an 84-year old male patient with a history of HBP, atrial fibrillation, chronic cardiac failure, implanted pacemaker and a biological mitral prosthesis, who was also recently diagnosed with inherited thrombophilia (homozygosis in 2020c>T mutation). He was under treatment with 4 mg acenocoumarol (prior INR of 1.4 a week before admission, and 2.2 20 days before), 80 mg/24 h valsartan, 40 mg/24 h furosamide, 25 mg/48 h spiranolactone, 20 mg/24 h pantoprazole, 160 mg/12 h megestrol, 52.5 mg/kg/h one patch and a half/72 h buprenorphine TTS, 650 mg/8 h paracetamol, 50 mg/8 h diclofenac, 16 mg/12 h betaistine, 50 mg/12 h sulpaprude, 5 mg/24 h finasteride, 1 mg/24 h lorazepam, 10 mg/24 h citalopram, 0.5 mg/24 h risperidone and 25 mg/24 h quetiapine.

The patient was hospitalised due to presenting sudden-onset dyspnoea at rest. Previously, he had been independent for basic every day activities and walking, but over the course of the preceding month he presented pronounced functional decline, to the point of being bedridden. Initial diagnostic tests showed a pacemaker rhythm of 72 bpm on ECG and mild normocytic anaemia as well as leukocytosis with neutrophilia, mild thrombocytopenia (haematocrit: 36.8%, Hb: 12.2 g/dl, mean corpuscular volume: 97.7 fl, leukocytes: 14.5 x 10^9/l, with 83.4% of neutrophils and platelets 92 x 10^9/l), and significant renal failure (creatinine: 7.1 mg/dl), with marked uremia (urea: 420 mg/dl and moderate-serious hyperkalaemia (K 7.1 Eq/ml). The remaining ions were normal (Na 139 Eq/ml, ionic Ca 4.5 mg/dl). Cardiac enzymes were determined, and the result was creatine kinase 63 UI/l and troponin T-HS of 202.6 ng/dl. The coagulation study revealed a prothrombin activity of 4%, Quick’s time 199.2 s, activated partial thromboplastin time 1.53 s and INR 20.12, with an initial D dimer of 119,468 mg/ml (laboratory cut-off: 500). Arterial blood gas analysis detected: pH 7.384, pCO2 13.6 mmHg, pO2 89 mmHg, HCO3 13.3 mmol/l and 94.5% O2 saturation. Brain natriuretic propeptide was 4,702 pg/ml. Thoracic X-ray showed no acute evolution findings. Abdominal ultrasound scan showed decreased kidney size for both kidneys and pronounced parenchymal atrophy. Due to the previous findings, treatment was initiated with intravenous sodium heparin, furosemide perfusion and fluid therapy. Upon suspicion of pulmonary thromboembolism, echocardiogram was requested with the following results: mildly dilated left ventricle with moderate-septal hypertrophy, preserved systolic function, moderately enlarged left atrium, pronounced aortic valve sclerosis with mild stenosis and moderate aortic insufficiency, mild enlargement of the right cavities with preserved right ventricular function, mild tricuspid insufficiency and presence of moderate pulmonary hypertension, with a pulmonary blood pressure of 48 mmHg. Later, a Doppler ultrasound scan of the lower limbs was completed, which showed the left internal saphenous vein with intraluminal echogenic content, which included peripheral linear calcification, compatible with superficial venous thrombosis. In light of these findings, even in renal failure, we decided to order a pulmonary scintigraphy, which detected subsegmental perfusion defects in the apical-posterior segment of the left upper lobe and in the apical segment of the right upper lobe. After withdrawal of sodium heparin and establishment of new oral anticoagulation, the platelet count normalised. Gait rehabilitation was initiated with good initial tolerance to standing position, proceeding to recovery of ambulation. The polypharmacy was reduced, with suspension of buprenorphine, betaistine, sulpiride, diclofenac, citalopram, megestrol, quetiapine and risperidone.