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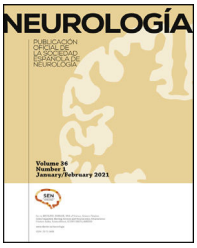

LETTER TO THE EDITOR

Opsoclonus-myoclonus syndrome and prostate cancer. An entity to be aware of

Síndrome de opsoclono-mioclono y cáncer de próstata. Una entidad a tener en cuenta

Dear Editor,

Paraneoplastic syndromes (PNS) are not usually observed in association with prostate cancer.[1] Very few descriptions have been found of opsoclonus-myoclonus syndrome (OMS) associated with prostate cancer, with all cases presenting unfavourable outcomes. We present the case of a patient with ocular flutter and ataxia appearing 2 years prior to diagnosis of prostate adenocarcinoma and urothelial carcinoma. Strictly speaking, our patient does not present opsoclonus but shows ocular flutter and ataxia, which are included in the syndrome.

Clinical case: Our patient is a 68-year-old man with history of hypertension and diabetes, a smoker (12 cigarettes per day), who had been under follow-up for 2 years by our department due to OMS, after being referred by the ophthalmology department. Despite screening for another tumour, and treatment on several occasions of the previously identified urothelial carcinoma with no relapse, he showed no improvement after several cycles of treatment with corticosteroids and intravenous immunoglobulins.

The neurological examination revealed rapid, involuntary, conjugate saccades in both eyes on the horizontal plane only, predominantly in the left eye, compatible with ocular flutter, as well as mildly ataxic gait, which progressed. Results from a complete blood count, biochemical testing, serology study, and immune profile were normal. Tests for tumour markers, onconeuronal antibodies, and surface antigen antibodies (against Hu, Yo, Ri, Zic4, CRMP5, Tr, NMDA, GAD, Ma1/Ma2, and amphiphysin) yielded negative results. A chest, abdomen, and pelvis CT scan revealed no abnormalities. A PET-CT study ruled out underlying neoplasm. Infectious and parainfectious causes were reasonably ruled out, and the CSF analysis yielded normal results; results for onconeuronal antibodies were negative.

At 2 years of follow-up, and due to an increase in prostate-specific antigen (PSA) to 6.9 (22%), a prostate MRI study was performed, revealing a 15 mm lesion in the mid-apical region; a biopsy confirmed acinar adenocarcinoma of the prostate, Gleason score 6 (3 + 3), with no lymphovascular or perineural invasion. A robotic-assisted radical prostatectomy was performed without incident, with the patient showing favourable progression and with a definitive diagnosis of acinar adenocarcinoma of the prostate, Gleason score 7 (3 + 4). The AJCC/UICC staging system indicated pT2a, Pnx, and pMx; we observed foci of high-grade prostatic intraepithelial neoplasia in the rest of the gland. At 6 months, the patient presented ataxia, with some isolated saccades. After one year, he was asymptomatic. The resolution of symptoms rules out a diagnosis of idiopathic OMS. Previous measurements of PSA were < 0.03.

Since the last case published in *Neurología*, we have not found any other description of OMS associated with prostate cancer.[2] In 2016, Storstein et al.[3] reported the largest series of cases of PNS associated with prostate cancer (n = 37), observing that the 3 most frequent syndromes were paraneoplastic cerebellar degeneration, limbic encephalitis/encephalomyelitis, and subacute sensory neuronopathy. In a literature search, we identified only 5 cases of OMS associated with prostate cancer. In four of these cases, the alteration in ocular motility consisted of saccadic oscillations on the horizontal plane only, as in our patient. In 2 cases (reported by Baloh et al.[4]), the patients developed alterations in ocular motility and gait, as well as muscle spasms after diagnosis of prostate cancer. The post mortem examination revealed chronic perivascular inflammation cells and microglial infiltration in the pons and medulla oblongata. As in our case, no antineuronal antibodies were detected. The identification of such new antibodies as anti-glycine receptor antibodies, which are membrane surface antigens,[5] together with their association with OMS and the presence of this antibody in oat cells, suggest an association of both processes. The third patient described was a man with prostate cancer who presented a brainstem paraneoplastic syndrome and altered ocular motility on the horizontal plane; an antibody targeting intraneuronal antigens was detected, although the antigenic target could not be identified.[5] The fourth patient was a man with metastatic prostate cancer who, 18 months later, developed OMS with onconeuronal antibodies (anti-Hu and anti-Yo) and small-cell lung carcinoma,[6] which improved with corticosteroids and chemotherapy. In this case, small-cell lung carcinoma was probably the cause of OMS.

The fifth case, published in *Neurología*, was a classical PNS associated with prostate cancer, and showed favourable progression at one year.[2]

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Our patient was diagnosed with PNS due to the symptom improvement observed after one year of follow-up. Unlike the other 5 patients, in our patient the diagnosis of prostate cancer was established 2 years after onset of OMS and, as in the case reported by Nasri,[6] he presented 2 tumours.

We would like to highlight that OMS is considered a classical PNS, although it is rarely associated with prostate cancer; however, it should be considered in cancer screening studies, even years later. Furthermore, even in the case of periodic treatment with immunoglobulins, only treatment of the underlying tumour may help improve symptoms.

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Mutations in the type IV collagen gen (*COL4A1*) as an unusual etiology of cerebrovascular disease in young adults

Mutaciones en el gen del colágeno tipo IV (*COL4A1*) como etiología infrecuente de enfermedad cerebrovascular en el adulto joven

Dear Editor,

Mutations in type IV collagen genes (*COL4A1* and *COL4A2*) constitute an extremely rare cause of cerebrovascular disease. The first descriptions of the clinical spectrum of this association report the frequent presence of porencephalic lesions with neurological symptoms of highly variable severity, including intellectual disability, ischaemic and haemorrhagic stroke, and epilepsy. In 2005, Plaisier et al.[1] reported a subgroup of patients with well-defined clinical characteristics, showing a frequent combination of both large- and small-vessel disease, especially intracranial aneurysms, as well as ophthalmological defects and non-neurological systemic symptoms. The authors called this constellation of symptoms hereditary angiopathy with nephropathy, aneurysms, and muscle cramps (HANAC) syndrome.

We present the case of a 23-year-old woman who attended the emergency department due to a 3-day history of intense holocranial headache that did not improve with usual analgesia. She did not report phono- or photophobia, focal neurological symptoms, or intracranial hypertension. Results from the neurological examination, including evaluation of meningeal signs, were completely normal. A head contrast CT scan showed a carotid aneurysm with no signs of intracranial haemorrhage; a lumbar puncture revealed absence of xanthochromia or elevated protein levels. A brain MRI study confirmed the presence of an aneurysm and showed extensive leukoencephalopathy mainly affecting the deep white matter. A porencephalic cystic cavity was observed at the level of the anterior horn of the lateral ventricle (Fig. 1). A diagnostic cerebral angiography study was also performed (Fig. 2).

The patient was born in Argentina, and her medical history is not available. The patient's mother reported history of mild psychomotor retardation attributed to prolonged childbirth, and cataract surgery at an early age. She has no known family history, although she has no contact with her father's family. A comprehensive blood analysis including kidney function and creatine kinase (CK) delivered normal results. An ophthalmological examination revealed bilateral

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