

In March 2013, however, diplopia reappeared due to right sixth nerve palsy, with no changes in imaging or CSF analysis results. We added temozolomide, achieving progressive resolution of the neurological symptoms. We switched to cytarabine (3 g/m² intravenously), due to poor methotrexate clearance, and increased intervals between cycles, completing intrathecal treatment with liposomal cytarabine. In June 2015, nearly 3 years after the central nervous system relapse, the patient remained asymptomatic and was receiving no treatment; clinical and laboratory findings showed full resolution of systemic and neurological anomalies. The only remarkable finding was 0.4% clonal lymphocytes in the bone marrow according to flow cytometry. In August 2015, the patient received consolidation chemotherapy and haploidentical stem cell transplantation from one of her children. She is currently in clinical remission.

This case is exceptional due to the patient's long survival time; the fact that she experienced a late, isolated neurological relapse, which is a rather infrequent event⁸ with no predictive factors; and the patient's response to treatment, which was initially good but was subsequently followed by an early relapse and controlled with chemotherapy (this may be explained by the fact that the relapse was initially only meningeal²). Intrathecal rituximab is useful in these cases if combined with systemic and intrathecal chemotherapy.⁹ The literature reports 3 cases of patients with MCL associated with neurological involvement who displayed an exceptionally good response to ibrutinib. However, as these patients were followed up for a short time, reassessment would be necessary to confirm the positive results over time.¹⁰ In any case, these findings represent a huge step forward in the field.

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Migralepsy and migraine in the puerperal period[☆]



Migralepsia y migraña en el puerperio

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Dear Editor:

We present the case of a 34-year old woman with a history of right frontal pulsatile headache between the ages 11 and 20; episodes were preceded by a right faciobrachial tingling sensation and the appearance of a bright zigzag pattern at the centre of the visual field, extending to the periphery for more than 5 minutes. This left a right homonymous scotoma, white or black in colour, which lasted 20 minutes, scoring the maximum of 10 on the Visual Aura Rating Scale (VARS; scores are distributed as follows: 3 points for duration of aura

5-60 min, 2 points for progression of aura ≥ 5 min, 2 points for presence of scotoma, 2 points for zigzag lines, and 1 point for homonymous distribution of visual symptoms). A score of 5 on the scale is diagnostic of aura with a sensitivity of 91% and a specificity of 96%.¹

Eight days after a normal delivery, she experienced a persistent left frontal pulsatile headache for 2 days; she developed right homonymous hemianopia with the described characteristics. She subsequently presented complete vision loss in the form of white scotoma with photopsias; headache was holocranial and intense at that time. The neurological examination conducted at the emergency department revealed bilateral amaurosis with an intact pupillary light reflex. During the examination, the patient presented a generalised tonic-clonic seizure with no other previous manifestations; this lasted 2 minutes and resolved with intravenous diazepam.

The patient was confused following the seizure; she experienced no further seizures after starting treatment with sodium valproate. Headache remitted 6 hours after administration of metamizole and dextketoprofen; amaurosis resolved after 48 hours (VARS, 2 + 2 + 2 = 6). The patient subsequently experienced episodes of hemicranial headache without aura or epileptic seizures.

Brain MRI, cerebral pan-angiography, blood tests (including antinuclear antibodies and anti- $\beta 2$ glycoprotein I levels), and urine and cerebrospinal fluid (CSF) analyses yielded normal results; 2 electroencephalographies (EEG) revealed normal bioelectrical activity, with no epileptiform discharges.

During the postpartum period, the following diagnoses should be considered when an episode of headache with vision loss is accompanied by an epileptic seizure: (1) thrombosis of cerebral veins or arteries and reversible cerebral vasoconstriction syndrome, which may be ruled out by brain angiography; (2) posterior reversible encephalopathy syndrome, which may be ruled out by normal MRI results; (3) postpartum preeclampsia,² which may be ruled out by absence of arterial hypertension and proteinuria; (4) occipital-onset epilepsy with secondary generalisation, which may be ruled out by a normal EEG reading and visual aura not suggesting seizures; (5) meningoencephalitis, which may be ruled out by normal CSF and neuroimaging findings; and (6) migralepsy.

Our patient met the diagnostic criteria for migraine with aura according to the third edition of the International Classification of Headache Disorders, (ICHD-3 beta). An epileptic seizure occurring during migraine aura, or in the hour following the aura, is referred to as migralepsy (epileptic seizure triggered by migraine, according to ICHD-3 beta). Diagnosis requires: (1) presence of an epileptic seizure meeting diagnostic criteria for any type of seizure; (2) presence during migraine aura, or in the hour following aura, and (3) seizure not being attributable to other disorder.^{3,4} Our case matches this definition, as the seizure took place during the migraine aura.

Although these diagnostic criteria are clear, cases have been described of migralepsy preceded by migraine without aura,⁵ its diagnosis in some published cases has been questioned,⁶ and the existence of migralepsy as an entity remains a topic of debate.⁴

In migralepsy, migraine aura should be differentiated from epileptic visual hallucinations, which mainly consist of coloured, unstable circular images which consistently follow the same onset and progression patterns, lasting a few seconds and progressing faster than migraine.⁷

The patient displays some unusual clinical manifestations: (1) recurrence of migraine during the postpartum period after 14 years without headache; (2) initial absence of migraine aura and a different location than that of headache; (3) non-habitual aura, consisting in right homonymous hemianopia followed by bilateral amaurosis with photopsias, suggestive of basilar migraine,^{3,8} and described in a case of migralepsy⁶; the duration of amaurosis was also surprising, exceeding that of headache. However, variability of aura characteristics and duration and headache location is a proven fact in migraine.⁹

The mechanism associating migraine and epilepsy remains unknown.⁵ It has been suggested that the occipital cortex has a low excitation threshold during migraine aura; probably, as a consequence of this, the cortical spreading depression wave may facilitate the occurrence of epileptic seizures.^{5,6,10} In support of this hypothesis, mutations of *SCN1A* (which codes for the Na_v1.1 ion channel) have been reported to cause both migraine and epilepsy.¹¹

Ovarian hormones affect the excitability of the cerebral cortex (oestrogens increase excitability and progesterone decreases it).¹² Fluctuations in plasma levels of these hormones condition the occurrence of migraine and epilepsy,¹³ since migraine is more frequent in the catamenial period and less frequent during pregnancy and menopause.^{9,14,15} Ours is the first case of migralepsy during the postpartum period and such a prolonged duration of visual aura.

This case illustrates the variability of migraine manifestations during the postpartum period, since aura may be different than normal, with longer duration, and migraine may manifest without aura^{4,5,8} or cause a first episode of migralepsy.

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Acute Pisa syndrome secondary to betahistine treatment in a patient with mild cognitive impairment ☆☆☆



Síndrome de Pisa agudo tras tratamiento con betahistina en un paciente con deterioro cognitivo leve

Dear Editor:

Betahistine is an oral histamine analogue which, due to its vasodilatory properties, is used habitually to treat episodic vertigo and other inner ear disorders.¹ Adverse effects include headache, confusion, nausea, dyspepsia, and hypotension. The literature describes only one case of acute dystonia² and one of delayed-onset dystonia³ associated with the drug; no paper published to date describes Pisa syndrome (PS).

PS is characterised by an abnormal, dystonic posture of the trunk, causing a lateral inclination with some degree of axial rotation. The condition was originally described in 1972 by Ekbohm et al.,⁴ in patients receiving antipsychotic drugs. Since then, researchers have pointed to other drugs, including antiemetics, antidepressants, benzodiazepines, cholinesterase inhibitors, and almost all dopaminergic drugs, as potential causes of PS.^{5,6} The condition has been described in patients with various neurodegenerative

diseases and with normal pressure hydrocephalus (NPH); other cases are idiopathic.^{5,7,8}

We present the case of a 76-year-old woman, with a history of episodes of vertigo and a one-year history of mild cognitive impairment, for which she was under follow-up at another hospital. Neuroimaging findings were suggestive of NPH. The patient attended the emergency department due to acute-onset lateral deviation of the trunk following a single 16 mg dose of betahistine to treat a vertigo episode similar to those she had previously experienced. She had no further symptoms and was taking no other drugs. The general physical examination revealed no other abnormalities. In the neurological examination, we observed a leftward inclination of the trunk and normal vestibular manoeuvres. A cranial CT scan displayed mild cortical atrophy and increased ventricular volume, with no signs of transudate. Within 24 hours of betahistine withdrawal, the patient's posture returned to normal and she remained completely asymptomatic. The patient was lost to follow-up following discharge.

Past drug exposure is a highly valuable criterion for demonstrating the cause of potential adverse drug reactions; however, we must also consider biological plausibility, consistency, and the statistical strength of the association.⁹ The reproduction of symptoms supports a proposed association; however, given the paramount importance of ethics in the field of medicine, this was not considered in the present case. Clinical suspicion and communication are therefore crucial in these cases, despite the evidential limitations of reporting isolated clinical cases. It is also necessary to verify causality.

This is the first published case of PS occurring subsequently to a single 16 mg dose of betahistine, in a patient with several noteworthy characteristics. Firstly, the patient was under follow-up for mild cognitive impairment at another centre; this may be related to Alzheimer disease or to NPH, given the clinical and neuroimaging findings. Both Alzheimer disease and NPH have been described as potential causes of PS; there is also a possibility of patients being

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