References

1. Hill A, DeZern AE, Kinoshita T, Brodsky RA. Paroxysmal nocturnal haemoglobinuria. Nat Rev Dis Primer. 2017;3:17028, http://dx.doi.org/10.1038/nrdp.2017.28.
2. Peacock-Young B, Macrae FL, Newton DJ, Hill A, Ariëns RAS. The prothrombotic state in paroxysmal nocturnal hemoglobinuria: a multifaceted source. Haematologica. 2018;103:9—17, http://dx.doi.org/10.3324/haematol.2017.177618.
3. Schrezenmeier H, Muus P, Socié G, Szer J, Urbano-Ispizua A, Maciejewski JP, et al. Baseline characteristics and disease burden in patients in the International Paroxysmal Nocturnal Hemoglobinuria Registry. Haematologica. 2014;99:922—9, http://dx.doi.org/10.3324/haematol.2013.093161.
4. Devalet B, Mullier F, Chatelain B, Dogné JM, Chatelain C. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. Eur J Haematol. 2015;95:190—8, http://dx.doi.org/10.1111/ejh.12543.
5. Ziakas PD, Poulou LS, Pomoni A. Thrombosis in paroxysmal nocturnal hemoglobinuria at a glance: a clinical review. Curr Vasc Pharmacol. 2008;6:347—53, http://dx.doi.org/10.2174/157016108785909742.
6. Poulou LS, Vakrinos G, Pomoni A, Michalakis K, Karianakis G, Voulgarelis M, et al. Stroke in paroxysmal nocturnal haemoglobinuria: patterns of disease and outcome. Thromb Haemost. 2007;98:699—701, http://dx.doi.org/10.1160/TH07-04-0316.
7. Cheng ZJ, Shen YY, Warsame IM, Dai TM, Tu JL. Moyamoya syndrome caused by paroxysmal nocturnal hemoglobinuria. Chin Med J (Engl). 2018;131:2874—6, http://dx.doi.org/10.4103/0366-6999.246065.
8. Arboix A, Jiménez C, Massons J, Parra O, Besses C. Hematological disorders: a commonly unrecognized cause of acute stroke. Expert Rev Hematol. 2016;9, http://dx.doi.org/10.1080/17474086.2016.1208555.
9. Das S, Dubey S, Acharya M, Chatterjee S, Lahiri D, Das G, et al. Thalassemia and Moyamoya syndrome: unfurling an intriguing association. J Neurol. 2019;266:2838—47, http://dx.doi.org/10.1007/s00415-019-09497-5.
10. Capecchi M, Ciavarella A, Artoni A, Abbattista M, Martinelli I. Thrombotic complications in patients with immune-mediated hemolysis. J Clin Med. 2021;10:1764, http://dx.doi.org/10.3390/jcm10081764.

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Facial diplegia in a patient with a brainstem infarction: when the clinical course and ocular symptoms exclude other causes

Diplejía facial en paciente con infarto troncoencefálico: cuando el curso clínico y la clínica ocular excluyen el resto de causas

Dear Editor:

Bilateral facial paralysis is a clinical entity that may be caused by a wide range of processes, including infection, autoimmune diseases, toxic diseases, tumours, and metabolic diseases affecting the peripheral facial nerve.[1,2] Very few cases have been described of WEBINO (wall-eyed bilateral internuclear ophthalmoplegia) syndrome associated with facial diplegia. We present the case of a patient with complete facial diplegia of central origin secondary to brainstem ischaemia, who also presented WEBINO syndrome.

The patient was a 66-year-old man who consulted due to 4 days' progression of instability and oculomotor alterations, of sudden onset. The examination revealed bilateral adduction impairment, contralateral abduction nystagmus, and primary gaze exotropia, with preserved convergence. Due to suspicion of acute bilateral internuclear ophthalmoplegia, the patient was admitted for further study. An MRI study (Fig. 1) revealed a lacunar infarction in the lower paramedian pons; the patient received dual antiplatelet therapy and was discharged.

Seven days later he consulted due to bilateral peripheral facial paralysis and dysarthria. The physical examination revealed facial diplegia and bilateral Bell's phenomenon (Fig. 2), as well as WEBINO syndrome, without involvement of other cranial nerves or paresis of the limbs; deep tendon reflexes were preserved. Blood tests (autoimmunity, serology, and total protein tests), CSF analysis (no albuminocytologic dissociation), and electroneurography of the limbs yielded normal results. The blink reflex revealed axonal neuropathy of both facial nerves, with involvement of the trigeminofacial reflex arc. A subsequent MRI study (Fig. 1) revealed decreased signal intensity of the paramedian pontine stroke on T2-FLAIR and DWI sequences, linked to the subacute progression of the infarction.

The patient improved during hospitalisation, regaining the ability to partially close both eyes. We hypothesise that nuclear involvement is the most probable cause for our patient's facial diplegia. At 3 months, facial diplegia had improved substantially, but right internuclear ophthalmoplegia and mild right lower facial paresis persisted (Fig. 2).

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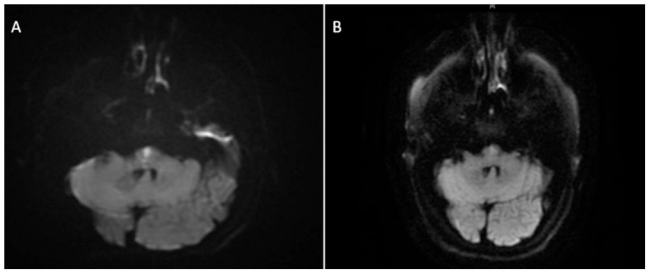

Figure 1 Transverse brain MRI scan, diffusion sequence. A) Restricted diffusion in the lower paramedian pons. B) Decreased signal intensity associated with subacute stroke.

Bilateral facial paralysis is a rare clinical entity, with an approximate incidence of one case per 5 million population. It is usually of peripheral origin; its aetiology is therefore highly heterogeneous, as it is linked to cranial mononeuropathy multiplex. Causes include infections, immune-mediated and metabolic diseases, toxic processes, tumours, and trauma.[1,2] Vascular involvement of central nuclei (pseudoperipheral) has been reported as a cause of unilateral, and more rarely bilateral, paralysis, usually in association with other manifestations of brainstem involvement.[3,4]

The reported cases of pseudoperipheral facial paralysis of vascular origin are caused by ischaemic lesions to the pontine tegmentum.[5] Tegmental infarctions represent only a small percentage of all cases of pontine infarction. They are characterised by the anatomical association between the fascicles of the facial nerve and the structures involved in horizontal gaze, including the abducens nucleus and the medial longitudinal fasciculus.[4,6] This explains the rare cases of facial diplegia of vascular origin associated with one-and-a-half syndrome or gaze palsy manifesting as WEBINO syndrome.[4]

In patients with isolated pontine infarctions, progressive deficits following ischaemic stroke seem to be relatively common, as in the case reported here. Their frequency varies greatly (10%—60%), probably due to the heterogeneity of the criteria applied.[7,8]

In our case, the presence of progressive symptoms and complete facial diplegia made us reconsider the hypothesis of vascular aetiology. In general terms, the diagnostic assessment must include a blood analysis, with complete blood count, glucose concentration, erythrocyte sedimentation rate, serology tests, and autoimmune study. CSF analysis and MRI studies should also be performed.[1]

In our case, complementary studies seeking to detect a possible peripheral cause of cranial mononeuropathy yielded negative results, and the progression of our patient's symptoms also ruled out this hypothesis. Neuroimaging studies did not show an increase in infarct volume that may explain the clinical worsening; this led us to hypothesise that the underlying mechanism may be cytotoxic, which may also explain the rapid improvement of our patient's symptoms.

Our case shows that facial diplegia with upper and lower involvement may occasionally be secondary to an ischaemic lesion involving the facial nerve nucleus in the brainstem, even in the absence of the typical chronology of vascular events. However, this aetiology of bilateral facial nerve involvement is extremely rare, and thorough complementary testing should be performed to rule out other more frequent causes.

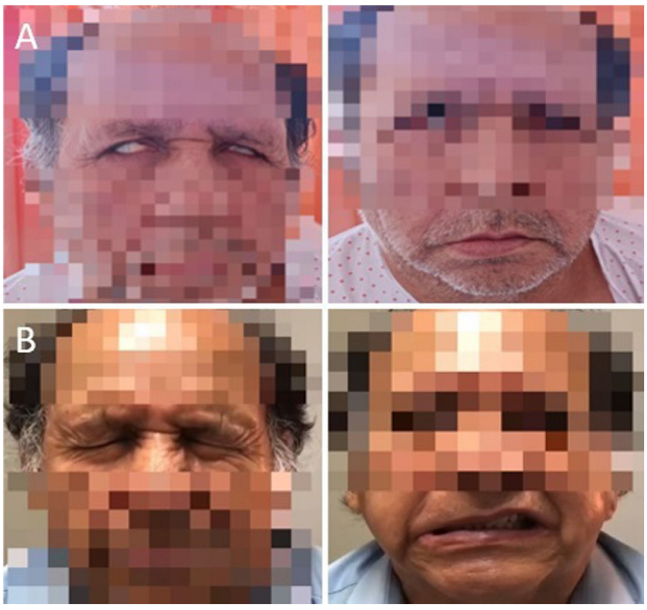

Figure 2 Physical examination. A) Physical examination performed during the patient's second hospitalisation, showing bilateral facial paralysis affecting both the upper and lower face. B) Physical examination performed by the rehabilitation department one month after discharge, showing persistent right lower facial paresis.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Gaudin RA, Jowett N, Banks CA, Knox CJ, Hadlock TA. Bilateral facial paralysis: a 13-year experience. Plast Reconstr Surg. 2016;138:879—87, http://dx.doi.org/10.1097/PRS.0000000000002599.
2. Jung J, Park DC, Jung SY, Park MJ, Kim SH, Yeo SG. Bilateral facial palsy. Acta Otolaryngol. 2019;139:934—8, http://dx.doi.org/10.1080/00016489.2019.1651134.
3. Agarwal R, Manandhar L, Saluja P, Grandhi B. Pontine stroke presenting as isolated facial nerve palsy mimicking Bell's palsy: a case report. J Med Case Rep. 2011;5:287, http://dx.doi.org/10.1186/1752-1947-5-287.
4. Im K, Ju H, Lee M, Roh H. A case report of wall-eyed bilateral internuclear ophthalmoplegia with bilateral facial palsy. J Stroke Cerebrovasc Dis. 2020;29:105139, http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2020.105139.
5. Felicio AC, Bichuetti DB, Marin LF, dos Santos WA, Godeiro-Junior C. Bilateral horizontal gaze palsy with unilateral peripheral facial paralysis caused by pontine tegmentum infarction. J Stroke Cerebrovasc Dis. 2009;18:244—6, http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2008.10.008.
6. Connors R, Ngan V, Howard J. A case of complete lateral gaze paralysis and facial diplegia: the

16 syndrome. J Neuroophthalmol. 2013;33:69—70, http://dx.doi.org/10.1097/WNO.0b013e3182737855.
7. Saia V, Pantoni L. Progressive stroke in pontine infarction. Acta Neurol Scand. 2009;120:213—5, http://dx.doi.org/10.1111/j.1600-0404.2009.01161.x.
8. Gökçal E, Niftaliyev E, Baran G, Deniz Ç, Asil T. Progressive deficit in isolated pontine infarction: the association with etiological subtype, lesion topography and outcome. Acta Neurol Belg. 2017;117:649—54, http://dx.doi.org/10.1007/s13760-017-0827-2.

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Pure alexia as a presenting manifestation of scrub typhus

Alexia pura como forma de presentación de tifus de los matorrales

Dear Editor,

''Tsutsugamushi triangle'' is an imaginary geographical region (in Asia-Pacific area including, but not exclusively limited to, Korea, Japan, China, India, Taiwan, Thailand, Indonesia, Sri Lanka, and the Philippines) that borrowed its name from the mite-borne rickettsial zoonosis, scrub typhus, an acute undifferentiated febrile illness, caused by *Orientia tsutsugamushi*.[1] Various neurological complications are ever-emerging among the plethora of clinical presentations.[2] This spectrum of neurological manifestations includes aseptic meningitis, meningoencephalitis, cerebellitis, acute disseminated encephalomyelitis, cerebral vasculitis, stroke, myelitis, polyradiculoneuropathy, and cranial nerve palsies.[2—4] However, the involvement of corpus callosum has been rarely reported.[5]

Reversible splenial lesion syndrome (RESLES) or cytotoxic lesion of the corpus callosum (CLOCCs) are usually reversible relatively symmetrical tend-to-be midline lesions, which are observed on brain magnetic resonance imaging (MRI) as unenhanced areas, which show low-diffusion on diffusion-weighted images.[6,7] Amid multitudes of etiologies of RESLES/CLOCCs, acute infective encephalitis is one of the most important.[6,7] RESLES/CLOCCs, particularly when involving the splenium, may sometimes give rise to callosal disconnection syndromes (mostly reversible).[6,7]

We report a novel case of pure alexia (also called alexia without agraphia or word blindness) and RESLES/CLOCCs, in a previously healthy young Indian man following Tsutsugamushi disease who responded well to antibiotic therapy.

A previously healthy right-handed 25-year-old man from West Bengal (India) was admitted to our outpatient clinic with fever, holocranial headache for the last ten days, and inability to read any written document for the last three days; however, he had no problem in seeing objects. His past medical, travel and surgical histories were non-contributory. The patient's oropharyngeal swab test for SARS-CoV-2 was negative by qualitative real-time reverse-transcriptase-polymerase-chain-reaction assay. He was febrile (38.5 °C) and tachycardic (102 min^{-1}). Other vital signs were within physiological ranges. On neurological examination, we found that he could not read a written script, albeit he could normally write when asked. Other language domains were normal, including comprehension, word expression, and repetition. The remaining neurological and neuro-ophthalmological examination was normal. Signs of intracranial hypertension and meningeal irritation were absent.

Complete blood cell count revealed neutrophilic leukocytosis with relative lymphopenia and a raised erythrocyte sedimentation rate (56 mm/h). Liver, kidney, and thyroid function tests were normal, as well as arterial blood gases and serum electrolytes. Serologic tests for malaria parasites, dengue, Japanese encephalitis, and SARS-CoV-2 were negative. Urinalysis and urinary culture ruled out urinary tract infection. Sputum culture failed to show any evidence of infection. Serologic tests for hepatitis B, C, and HIV (1,2) were negative. A chest X-ray and ultrasonographic scan of the abdomen were done and were normal. The brain's MRI revealed non-enhancing low-diffusion signals arising from the splenium of corpus callosum, suggestive of RESLES/CLOCCs (Fig. 1). Cerebrospinal fluid (CSF) analysis was suggestive of infectious etiology (mild increased opening pressure, cell count 30/μl, all lymphocytes; raised protein levels of 80 mg/dL; and low glucose levels 30 mg/dL, corresponding capillary blood glucose level was 118 mg/dL). Gram staining and Ziehl-Neelsen staining were negative. CSF was further tested by PCR method for relevant neuroinfectious agents (e.g., Japanese encephalitis, HSV-1,2, VZV, EBV, CMV, HHV-6,7, enteroviruses, adenoviruses, neurotuberculosis, neuroborreliosis, and neurosyphilis), which came out negative. However, serologic testing for scrub typhus infection (by IgM-ELISA method) was positive. According to the existing institutional management policy, he was put on oral doxycycline (200 mg/day) and azithromycin (500 mg/day) for a week. He became afebrile within 48—72 h of systemic antibiotic therapy. Cognitive dysfunction persisted for another two weeks before complete resolution.

Pure alexia without visual deficits and agraphia is an extremely rare and complex neurological deficit in which the person cannot read, and the ability to write down remains