clear correlation between early onset and high-dose intravenous glucocorticoids (between 500 and 1000 mg for 3 days), and initial clinical improvement.[7] Furthermore, some recent studies support the use of concomitant therapy with immunosuppressants from onset, as data suggest that this combination therapy is associated with a decrease in the number of late complications.[8] However, this is not implemented in everyday clinical practice.

In the case of our patient, we initially used intravenous monotherapy at 1000 mg for 5 days, (longer than the classical exposure time to high-dose immunosuppression), obtaining very good clinical outcomes with resolution of neurological symptoms and the choroidal inflammation shown by OCT.

We should underscore the recent *C. pneumoniae* infection as a possible trigger of the disease. VKHS is known to be triggered by various (mainly viral) infections, however, we found no cases in the literature that were triggered by *C. pneumoniae* infection, which has been associated with such other autoimmune diseases as Kawasaki disease or multiple sclerosis.[9]

Conflicts of interest

The authors have no conflicts of interest to declare.

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Case report: is there a link between morning glory syndrome and TANGO2 mutation disease, or is this an unusual association?

¿Existe relación entre el síndrome de *morning glory* y la enfermedad por mutación en el gen TANGO2, o es una asociación inusual?

Introduction

Congenital anomalies of the optic nerve are a rare but significant cause of visual deficits.[1] In 1970, Peter Kindler described for the first time a sporadic congenital anomaly of the optic nerve whose cause was not fully understood; involvement was predominantly unilateral, and characterised by an abnormally large optic disc, large excavation, presence of glial tissue remnants, and a radial peripapillary microvascular network. He named the condition morning glory syndrome. Most of these cases manifest during childhood or adolescence, predominantly affecting girls, presenting with symptoms of visual deficit and strabismus.[2]

Case report

Our patient was a 32-year-old woman, born to first-degree consanguineous parents and with history of psychomotor retardation, moderate intellectual disability, non-autoimmune hypothyroidism, and bilateral sensorineural hearing loss. She was being followed up by the neurology department due to episodes of disorientation.

The examination revealed generalised hyperreflexia with increased reflexogenic zone, absence of clonus, and bilateral positive Hoffman sign. The ophthalmological examination revealed exotropia of the right eye. Direct ophthalmoscopy showed right optic disc pallor, and indirect ophthalmoscopy revealed increased size and excavation of the right optic disc. The papilla was surrounded by an abnormally pigmented chorioretinal ring with marked peripapillary atrophy and a radial layout of blood vessels. The centre of the optic disc was covered by whitish glial tissue remnants. The peripheral retina and fovea of the right eye were normal. An A- and B-mode ultrasound study ruled out serous retinal detachment,

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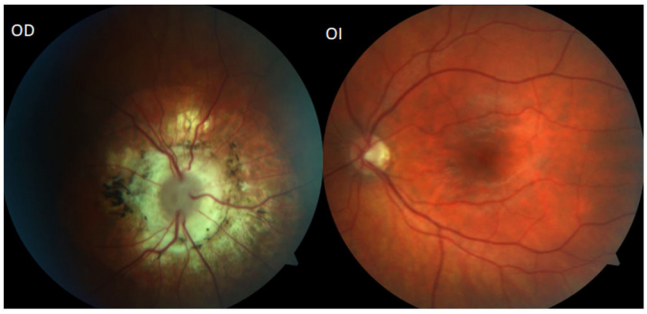

Figure 1 Retinography. Left: eye fundus examination of the right eye with abnormally large optic disc and increased excavation. The papilla is surrounded by an abnormally pigmented chorioretinal ring. Peripapillary atrophy. Right: eye fundus examination of the left eye, with normal findings.

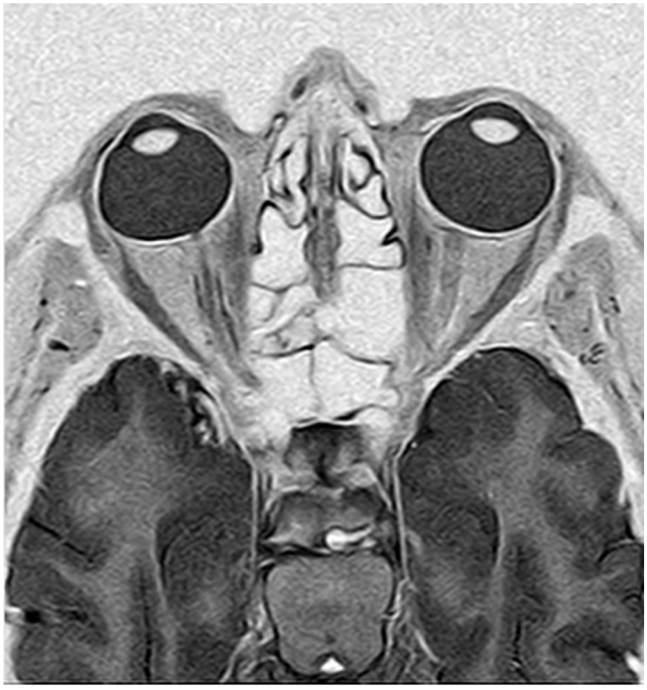

Figure 2 Magnetic resonance imaging study revealing discontinuity of the uveoscleral coat at the most posterior margin of the right eye, at the entry point of the optic nerve.

which is described in up to 30% of cases of morning glory syndrome (Fig. 1).[3,4]

An MRI study revealed a discontinuity of the uveoscleral coat at the most posterior margin of the right eye, at the entry point of the optic nerve (Fig. 2).

Microarray-based comparative genomic hybridisation of the patient and her parents found that both parents were heterozygous for a pathogenic copy number variation of the *TANGO2* gene (heterozygous deletion of exons 3—9), located on chromosome 22q11.21; the patient inherited the mutation in homozygosis.

Discussion

Morning glory syndrome is a congenital anomaly of the optic nerve, with a very low incidence rate. It is more frequent among women and in white populations, and usually manifests unilaterally.[5,6] Its pathophysiology is believed to be due to failed closure of the terminal optic stalk.[1] It may be suspected when the physical examination reveals strabismus, nystagmus, amblyopia, or leukocoria. Ophthalmological alterations are consistent with those described by other authors: abnormally large optic disc, with deep conical excavation, peripapillary pigmentation, and radial microvascular network. Diagnosis is based on fundus examination, with the most outstanding pathognomonic signs being the funnel-shaped morphology of the optic nerve and abnormal discontinuity of the uveoscleral coat at the level of optic nerve insertion.[1]

Up to 45% of patients present associated cerebrovascular anomalies. Endocrine, respiratory, and renal alterations may also appear. It is associated with a mutation of the *PAX6* gene and such other syndromes as the XYY syndrome, neurofibromatosis type 2, and CHARGE syndrome.

A surprising finding in our patient is her moderate psychomotor delay, as the initial genetic study (karyotyping, metabolic and mitochondrial disease study) yielded normal results.

However, the complementary molecular study showed a mutation of the *TANGO2* gene in homozygosis (both parents presented the mutation in heterozygosis). A review of the literature identified different clinical findings associated with this mutation, including recurrent acute metabolic crises, ataxia, disorientation, coma, dysphagia, cardiac arrhythmia, developmental delay, intellectual disability, dysarthria, and seizures, as well as laboratory findings including hypoglycaemia, hyperlactacidaemia, hyperammonaemia, hypertransaminasaemia, and hypothyroidism.

From an ophthalmological perspective, the literature includes reports of exotropia, and some patients have been diagnosed with optic atrophy; otorhinolaryngological findings include sensorineural hearing loss in association with this mutation.[7] These findings are compatible with the phenotype and clinical symptoms of our patient.

The literature does not report any association between morning glory syndrome and the *TANGO2* mutation disease; therefore, we do not know whether this is a coincidental finding or a real association that has not previously been described.

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Typhoid fever presenting with central and peripheral nervous system involvement

Fiebre tifoidea cursando con afectación del sistema nervioso central y periférico

Dear Editor,

Typhoid fever, commonly known as enteric fever, is a significant, resilient community-acquired systemic bacterial infection caused by Salmonella typhi.[1] It is most prevalent in tropical countries like India, due to limited resources, overcrowding, poor sanitation, and major hygienic unawareness, resulting in remarkable morbidity and continues to be a public health challenge even in this era of antimicrobials.[1] Neurological manifestation of typhoid fever is relatively rare,[2] especially nowadays, when almost no case gets complicated thanks to the early institution of effective antibiotics therapy. Landry-Guillain-Barre syndrome and its variant, Miller Fisher syndrome, have been rarely reported.[2–4]

The authors herein report a case of typhoid fever with concurrent central and peripheral nervous system involvement manifesting as splenial lesions on neuroimaging (i.e., the boomerang sign) and Miller Fisher syndrome, respectively.

A 34-year-old previously healthy female from lower socio-economic strata of rural West Bengal (India) was brought to the emergency department with high-grade fever for the last seven days, unsteady gait, and recurrent falls in the last three days. It was associated with a history of recent onset progressive paresthesia involving bilateral lower extremities, ascending gradually from toes in a stocking pattern for the last five days. Initially, along with low-grade fever, she also had developed a diarrheal episode for two days, followed by generalized abdominal discomfort and headache, for which she has been prescribed some medicines from local quacks without any relief of symptoms. Clinical examination revealed that she was anxious, febrile, and had mild dysarthria, axial and appendicular ataxia, external ophthalmoplegia, gaze-evoked horizontal nystagmus, generalized hypo-to-areflexia, and reduced sensitivity sensation of all modalities below knee level. She also had relative bradycardia and mild soft splenomegaly. Signs of meningeal irritation were absent. Visual acuity, color vision/perception, pupillary reflexes, intraocular pressures, and fundoscopic examinations were non-contributory. Cognitive, motor strength, and autonomic functions revealed no abnormality. She tested negative for SARS-CoV-2 and was admitted with a provisional diagnosis of infection-associated Miller Fisher syndrome.

Complete blood cell count revealed mild anemia (hemoglobin 9.0 g/dL), elevated erythrocyte sedimentation rate (80 mm/h), relative lymphopenia, and thrombocytopenia (platelets count = 60,000/μl (reference range 150,000—450,000). Liver function tests showed an approximately two-fold rise of the transaminases. Renal and thyroid function tests and blood glucose levels were within normal limits. Diagnostic tests were negative for endemic infections like malaria, dengue, Leptospira, Japanese encephalitis, and scrub typhus. However, Typhi Dot IgM (ELISA) was found to be positive. Magnetic resonance imaging (MRI) of the brain demonstrated a non-enhancing hypertense lesion on T2-weighted image and T2-FLAIR, with substantial diffusion restriction on diffusion-weighted imaging sequences, involving the splenium of the corpus callosum, suggestive of boomerang sign (Fig. 1). MR angiography of the brain was normal. Cerebrospinal fluid (CSF) studies revealed lymphocytic pleocytosis (10 cells/μl, all lymphocytes), slightly low glucose levels (48 mg/dL, normal range 50—80 mg/dL), and normal protein levels (46 mg/dL, normal range 15—50 mg/dL) without any albuminocytologic dissociation. Oligoclonal bands, anti-aquaporin 4, and anti-myelin oligodendrocyte glycoprotein antibodies were not detected in the CSF and serum. However, serum GQ-1b-IgG antibodies were positive. CSF polymerase chain reaction for relevant neuroviruses and tuberculosis and tests for neurosarcoidosis and neuroborreliosis were negative. Tests for Mycoplasma, Campylobacter jejuni, influenza, HIV, and hepatitis viruses were also non-reactive. Sensory and motor nerve conduction studies revealed bilateral sensory-motor polyneuropathy, predominantly axonal; needle electromyography and repetitive nerve stimulation tests were unremarkable. Blood cultures resulted positive for Salmonella typhi.

As per institutional protocol on admission, she was put on empirical intravenous antibiotics (ceftriaxone) and other symptomatic therapies. When the Typhi Dot IgM report came positive (day three of admission), we added oral azithromycin (600 mg/day for one week) to ceftriaxone (4 g/day for two weeks). Symptoms of the immediate infective illness waned rapidly within seven days of the institution of antibiotic therapy. However, symptoms due to Miller Fisher syndrome did not respond until we prescribed intravenous immunoglobulins (0.4 g/kg/day for five days, on day eight of admission). The anti-GQ-1b-IgG report came positive at the same time. Ophthalmoparesis and ataxia improved remarkably within five days of the institution of intravenous immunoglobulins therapy. After three weeks of in-hospital stay, the patient could be discharged with