REPORTE DE CASO

BILATERAL PALLIDOTOMY IN REFRACTORY DYSTONIC STATUS SECONDARY TO NEURODEGENERATIVE DISEASE ASSOCIATED WITH PANTOTHENATE KINASE: A CASE REPORT

PALIDOTOMÍA BILATERAL EN ESTADO DISTÓNICO REFRACTARIO SECUNDARIO A ENFERMEDAD NEURODEGENERATIVA ASOCIADA A PANTOTENATO QUINASA: REPORTE DE UN CASO

PALIDOTOMIA BILATERAL EM ESTADO DISTÔNICO REFRATÁRIO SECUNDÁRIO A DOENÇA NEURODEGENERATIVA ASSOCIADA À PANTOTENATO QUINASE: RELATO DE CASO

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Abstract

Introduction: Dystonic status is characterized by sustained and continuously dystonic movements that significantly impact the quality of life of the patients.
Clinical Case: We present a 6-year-old child with four days of inability to walk, diaphoresis, and generalized dystonic movements predominantly in the lower limbs. The clinical, laboratory, and radiological findings were consistent with the diagnosis of pantothenate kinase enzyme deficiency associated neurodegeneration with refractory dystonic status. Conservative management with benzodiazepines, baclofen, and antidopaminergic drugs as well as intrathecal baclofen infusion pump were offered, but neither of them achieved a satisfactory response, finally requiring a bilateral pallidotomy. After two years, the patient did not developed any new episodes of dystonic status, without systemic or neurological adverse effects.
Conclusion: Refractory dystonic status is a devastating but infrequent clinical condition, in which surgery can be considered as a therapeutic alternative, capable of safely resolving the status**.**

Keywords: Pallidotomy, Dystonia, Neuronavigation, Basal ganglia, Movement disorders, Baclofen.

Resumen

Introducción: El estado distónico se caracteriza por movimientos distónicos sostenidos y continuos que impactan significativamente la calidad de vida de los pacientes.

Caso Clínico: Presentamos un niño de 6 años de edad con cuatro días de incapacidad para caminar, diaforesis y movimientos distónicos generalizados de predominio en miembros inferiores. Los hallazgos clínicos, de laboratorio y radiológicos fueron consistentes con el diagnóstico de deficiencia de la enzima pantotenato quinasa asociada a neurodegeneración con estado distónico refractario. Se ofreció manejo conservador con benzodiazepinas, baclofeno y fármacos antidopaminérgicos, así como bomba de infusión intratecal de baclofeno, pero ninguno de ellos logró respuesta satisfactoria, requiriendo finalmente palidotomía bilateral. Después de dos años, el paciente no desarrolló nuevos episodios de estado distónico ni efectos adversos sistémicos o neurológicos.

Conclusión: El estado distónico refractario es una condición clínica devastadora pero infrecuente, en la que la cirugía puede ser considerada como una alternativa terapéutica, capaz de resolver el estado de forma segura.

Keywords: Palidotomía, Distonía, Neuronavegación, Ganglios basales, Trastornos del movimiento, Baclofeno.

Resumo

Introdução: O estado distônico é caracterizado por movimentos distônicos sustentados e contínuos que impactam significativamente a qualidade de vida dos pacientes.

Caso Clínico: Apresentamos um menino de 6 anos com quatro dias de incapacidade de deambulação, sudorese e movimentos distônicos generalizados predominantemente em membros inferiores. Os achados clínicos, laboratoriais e radiológicos foram consistentes com o diagnóstico de deficiência da enzima pantotenato quinase associada à neurodegeneração com estado distônico refratário.
O manejo conservador foi oferecido com benzodiazepínicos, baclofeno e antidopaminérgicos, além de bomba de infusão intratecal de baclofeno, mas nenhum deles obteve resposta satisfatória, necessitando, em última instância, de palidotomia bilateral. Após dois anos, o paciente não desenvolveu novos episódios de estado distônico ou efeitos adversos sistêmicos ou neurológicos.

Conclusão: O estado distônico refratário é uma condição clínica devastadora, porém rara, na qual a cirurgia pode ser considerada como uma alternativa terapêutica, capaz de resolver o quadro com segurança.

Palavras chave: Palidotomia, Distonia, Neuronavegação, Gânglios da base, Transtornos dos movimentos, Baclofeno.

Introduction

Dystonic status (SD) is an infrequent clinical state characterized by dystonic movements that are sustained continuously and can compromise the life of the patient due to bulbar weakness, respiratory failure, metabolic disorders, exhaustion and pain. (1) It can be associated with infectious diseases, medications, and less frequently with genetic alterations, neoplasms, cerebral hypoxia and autoimmune diseases. (1-3)

We present the case of a pediatric patient with Pantothenate Kinase Associated Neurodegeneration (PKAN), a rare hereditary neurodegenerative disease in which abnormal iron deposits occur in the globus pallidus and in the reticulated portion of the substantia nigra. (4) This pathology can be associated with ED, which can be treated with various non-invasive therapeutic alternatives, but it can also be treated through surgical interventions, which are rarely used to manage refractory ED, such as bilateral pallidotomy under stereotaxy.

Clinical Case:

A 6-year-old female patient with a history of neurodevelopmental delay and generalized dystonia, whose only relevant antecedent was the degree of consanguinity of her parents (first-degree cousins), was admitted to the emergency room due to a clinical course of 4 days with disability for gait, hyporexia, diaphoresis and sustained postural muscle contractions. On physical examination, generalized dystonic movements were found, predominantly in the lower limbs, without respiratory compromise and paraclinical tests that ruled out metabolic alterations.

A brain magnetic resonance imaging (MRI) revealed hyperintensities in the T2 and FLAIR sequences in the internal globus pallidus (iGP) and the posterior arm of the internal capsule bilaterally with the classic "tiger's eye" pattern, being interpreted by neuroradiology as iron deposits (Figure 1A). The sleep electroencephalogram was normal.

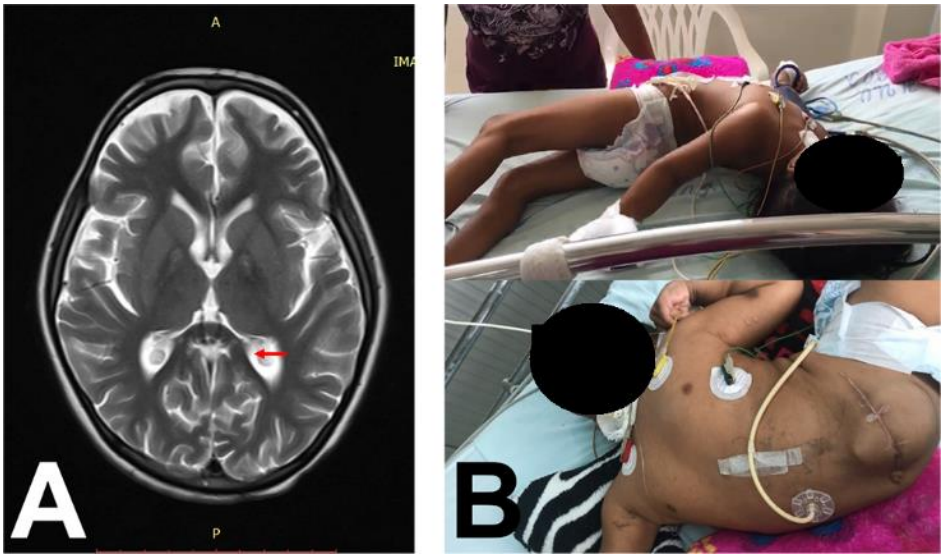

Figure 1. A. Brain MRI of the patient showing the classic “tiger's eye” pattern at the level of the globus pallidus secondary to iron deposits in a PKAN. B. Refractory ED after the patient was taken to surgery for implantation of a pump for intrathecal infusion of baclofen despite having reached a dose of 600 micrograms per day.

A diagnosis of exacerbated generalized dystonia with baseline neurological status deterioration was made. Given the clinical, paraclinical, and neuroradiological findings, the pediatric neurology service would expect that it was a PKAN associated with the condition described, which had a favorable recovery prognosis given a multimodal pharmacological management plan. Initial treatment included clonazepam, baclofen, risperidone, and oral levodopa/carbidopa. However, the patient persisted with dystonic movements that subsided with sleep, and then progressed, generating a deterioration in the respiratory pattern, and then a diagnosis of DS was made, requiring management in the ICU with intravenous midazolam infusion and an increase in baclofen dose to 50mg a day. Despite treatment, the condition got worst, generating a permanent opisthotonus posture, requiring administration of anesthetics and relaxants to maintain adequate oxygenation with invasive mechanical ventilation.

Given the refractoriness to management, a neurosurgical assessment was requested to consider other therapeutic alternatives given the severity of the case, with risk of death and a prognosis already reserved at the time of requesting this assessment.

Intrathecal baclofen infusion was considered as the first interventional management alternative, considering the presence of an anatomical alteration of the iPG (iron deposits), a condition that could negatively and significantly alter any type of neurosurgical intervention on the basal ganglia. An intrathecal baclofen infusion pump was implanted, starting with an infusion dose of 300 micrograms per day (positive preoperative test with 150 micrograms), achieving improvement for 7 days, during which the status temporarily resolved.

Subsequently, the patient presented rapidly progressive generalized dystonic movements again, with ventilatory failure and the need for readmission to the ICU. Intrathecal baclofen dose was increased to 600 micrograms per day, however, the patient's status got worst, developing permanent opisthotonus that was only controlled with general anesthesia, requiring mechanical ventilation (Figure 1B).

The medical board with the neuroradiology service, concluded that the iron deposits did not fully compromise the postero-ventral region of the iPG, and discussed the possibility of performing a bilateral pallidotomy or deep brain stimulation (DBS). Considering the deteriorated nutritional status of the patient, the high risk of infection, systemic involvement of the disease, reserved prognosis of her pathology, and a fragile psychosocial environment, it was decided to take the patient to a bilateral pallidotomy.

Four thermal pallidal lesions were made at 80ºC for 60 seconds each in the posterior, lateral and ventral region of the bilateral iPG without complications (Figure 2).

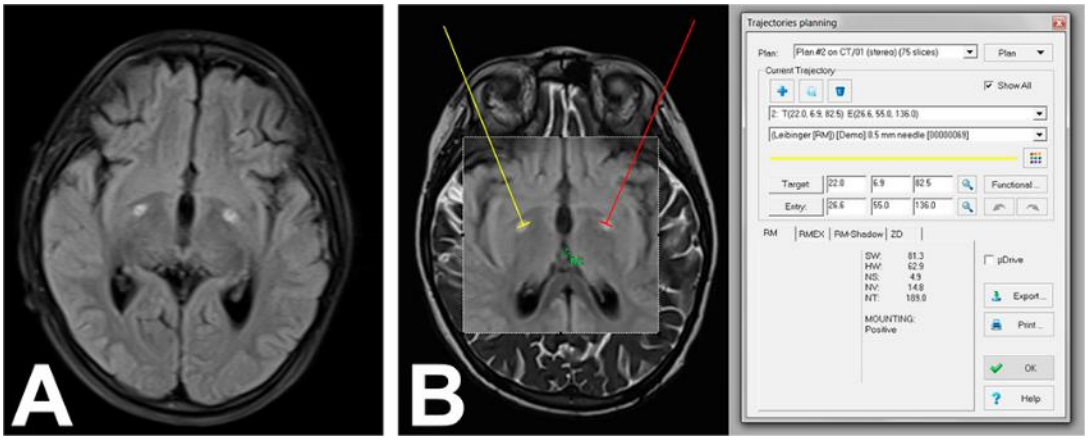

Figure 2. Image fusion between preoperative and post-bilateral pallidotomy brain MRI in a patient with refractory ED secondary to PKAN. The almost exact correspondence between the presurgical planning and the postoperative result is shown.

Subsequently, she was transferred to the ICU, where one week later, anesthesia and intravenous relaxants were progressively withdrawn, being finally extubated and the DS resolved. She was transferred to hospitalization and later discharged. Figure 3 shows the patient during her follow-up appointment three months after successful surgery.

Figure 3. Patient with PKAN and refractory DS in the postoperative period of bilateral pallidotomy with resolution of DS and successful withdrawal of anesthetics, muscle relaxants and mechanical ventilation.

During the two-year follow-up, the patient has not developed new episodes of DS, currently with multifocal dystonia, with good adherence to pharmacological treatment, and she attends the neurodevelopmental rehabilitation program and the follow-ups by the treating specialties. A brain MRI was performed as a control, in which iron deposits and bilateral pallidotomy are evident without new associated findings. The patient tolerated the surgery adequately and there were no adverse effects, also, there was no baseline state deterioration of her disease. For the publication of this report, the endorsement of the ethics

committee of Hospital Universitario del Valle and the informed consent of the patient's mother were obtained.

Discussion:

Refractory DS is a rare clinical entity, (5) which can occur in association with rare genetic disorders such as PKAN, (6) and requires early surgical management to avoid complications such as clinical deterioration or death. To avoid fatal or highly morbid outcomes, there are three neurosurgical options that can allow the patient to resolve the status: intrathecal baclofen infusion, pallidotomy or DBS, the latter being the surgical option with the greatest experience and acceptance. (7) This procedure has low morbidity and mortality, is reversible and has good results in terms of status control. (3) However, it is the most expensive procedure, and requires fundamental biopsychosocial conditions (optimal nutritional status, low risk of infection, and a robust support network). In addition, they need adequate access to the provision of highly complex health services for the post-operative management and control of a device with these characteristics, all in the context of a disease with an adequate prognosis for recovery.

The clinical conditions and risk of complications of the patient reported here, as well as the compromised neurological prognosis, impossibility of adequate postoperative controls, poor support network and limited socio-cultural conditions, lead to the decision of performing a bilateral pallidotomy (8). This is an ablative procedure that involved radiofrequency lesioning of the bilateral iPG, with resolution of the status and appropriate for her clinical context, as well for her family, social, and cultural situation.

Regarding neurosurgical management alternatives, the implantation of an intrathecal baclofen infusion pump has shown interesting results in favor of this therapy in the management of generalized dystonias. (3) However, of the three alternatives, it is the one with the least experience; it is considered that less than 10% of patients with DS have been managed with it, with successful reports, but also failures.(1-3) Moreover, iPB DBS is emerging as the best option to combat refractory DS, with the greatest experience worldwide and has achieved great outcomes, with a significant number of patients in whom the sedatives and mechanical ventilation can be removed, with reports of cases with improvement in their preoperative state, with a very low rate of postoperative morbidity and mortality.(1-3,9) By 2018, 42 cases treated with this device had been documented, with resolution of the status in most patients and a single death

secondary to this condition.(9) Regarding pallidotomy as management of refractory DS, there are few case reports, finding only 10 in our literature review,(1,10) including two of them with PKAN, in which one of them was a 9 year old boy also treated with the combination of intrathecal baclofen infusions and bilateral pallidotomy, presenting satisfactory evolution. Although, as the authors of this similar case report point out, only palliative measures are generally recommended in these cases, this more aggressive approach is justified given the relief of the intense pain associated with the spasms, which allow the patients to be discharged home without the prolonged stay in intensive care, with the morbidity and mortality that characterize DS. (11)

Conclusions:

Refractory DS is a devastating but infrequent clinical condition, in which a neurosurgical option can be considered, being bilateral DBS of the iPG the most accepted one, with the greatest evidence. However, when clinical and biopsychosocial contexts are not suitable for performing it, the treating team is suggested to consider a bilateral pallidotomy as a therapeutic alternative, with the ability to resolve the status in a safely way

Statements

Statement of Ethics

Study approval statement: The procedures carried out respected ethical standards in accordance with the Declaration of Helsinki. For the publication of this report, the endorsement of the ethics committee of Hospital Universitario del Valle.

Consent to participate statement: The informed consent of the patient's mother was obtained.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

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