References

1. Bergouignan M, Fontan F, Trarieux M, Julien J. Choreiform syndromes in children during cardiosurgical operations under deep hypothermia. Rev Obstet Ginecol Venez. 1961;105:48—60 [article in French].
2. Medlock MD, Cruse RS, Winek SJ, Geiss DM, Horndasch RL, Schultz DL, et al. A 10-year experience with postpump chorea. Ann Neurol. 1993;34:820—6.
3. Przekop A, McClure C, Ashwal S. Postoperative encephalopathy with choreoathetosis. Handb Clin Neurol. 2011;100:295—305.
4. Khan A, Hussain N, Gosalakkal J. Post-pump chorea: choreoathetosis after cardiac surgery with hypothermia and extracorporeal circulation. J Pediatr Neurol. 2012;10:57—61.
5. Levin DA, Seay AR, Fullerton DA, Simoes EA, Sondheimer HM. Profound hypothermia with alpha-stat pH management during open-heart surgery is associated with choreoathetosis. Pediatr Cardiol. 2005;26:34—8.
6. Bisciglia M, London F, Hulin J, Peeters A, Ivanoiu A, Jeanjean A. Choreoathetotic syndrome following cardiac surgery. J Clin Anesth. 2017;36:59—61.
7. Surie S, Tijssen MA, Kloek JJ, Smeding H, Bresser P, de Bie RM, et al. Chorea in adults following pulmonary endarterectomy. Mov Disord. 2010;25:1101—4.
8. Passarin MG, Romito S, Avesani M, Alessandrini F, Petrilli G, Santini F, et al. Late-onset choreoathetotic syndrome following heart surgery. Neurol Sci. 2010;31:95—7.
9. Saft C, Reber D, Streuer M, Andrich J. Post pump chorea in a 77-year-old male. Neurol Sci. 2011;32:699—701.
10. Das P, Shinozaki G, McAlpine D. Post-pump chorea-choreiform movements developing after pulmonary thromboendarterectomy for chronic pulmonary hypertension presenting as ''functional'' movement disorder. Psychosomatics. 2011;52:459—62.
11. Aoyagi K, Higuchi Y, Okahara Y, Yakufujiang M, Matsuda T, Yamanaka Y, et al. Effects of bilateral pallidal deep brain stimulation on chorea after pulmonary thromboendarterectomy with deep hypothermia and circulatory arrest: a case report. Acta Neurochir (Wien). 2018;160:393—5.
12. Kupsy WJ, Drzd MA, Barlow CF. Selective injury of the globus pallidus in children with post-cardiac surge choreic syndrome. Dev Med Child Neurol. 1995;37:135—44.
13. Lefaucheur JP, Bachoud-Levi AC, Bourdet C, Grandmougin T, Hantraye P, Cesaro P, et al. Clinical relevance of electrophysiological tests in the assessment of patients with Huntington's disease. Mov Disord. 2002;17:1294—301.
14. Popkirov S, Schlegel U, Skodda S. Is postoperative encephalopathy with choreoathetosis an acquired form of neuroacanthocytosis? Med Hypotheses. 2016;89:21—3.

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No MELAS syndrome without heteroplasmy levels or multisystem examination☆

No se puede hablar de MELAS sin porcentaje de heteroplasmia ni investigación multisistémica

Dear Editor:

It was with great interest that we read the case reported by Pérez Torre et al.[1] of a 30-year-old man with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome due to variant 3243A>G of the mitochondrial $tRNA^{(Leu)}$ gene. The patient presented unusual global cerebral involvement.[1] We would like to comment on this case.

One limitation of the study is that it does not disclose the percentage of heteroplasmy. The cells of patients with MELAS usually display 2 different populations of mitochondria: some with wild-type mtDNA and others containing mutant mtDNA. If the number of mitochondria with mutant mtDNA exceeds a certain level, the patient will be symptomatic. In the light of the above, it would be interesting to know the percentage of heteroplasmy in hair follicle cells, oral mucosa cells, fibroblasts, muscle cells, and urinary tract epithelial cells of the patient presented by the authors. The percentage of heteroplasmy varies in accordance not only with the tissue analysed but also with the stage of the disease and between first-degree relatives.[2]

Furthermore, the patient received phenytoin (250 mg/day) to treat seizures, but the authors do not indicate whether treatment was started after the first (January 2013) or the second epileptic episode (September 2013). It is also unclear when and why the patient started treatment with levetiracetam, lacosamide, and clonazepam. Phenytoin is known to cause mitochondrial toxicity and is therefore not recommended as the first-line treatment for patients with mitochondrial diseases.[3] Furthermore, the authors do not explain why the patient received 4 different antiepileptic drugs. Were seizures refractory to treatment? May phenytoin have triggered status epilepticus originating in the occipital lobe? It would have been interesting to know how the status epilepticus was resolved. Did the patient start a ketogenic diet?

Another limitation of the case report is the lack of information on the patient's family history. Nearly two-thirds of

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mtDNA mutations are inherited by maternal transmission; we may therefore hypothesise that the mother either was affected or was an asymptomatic carrier. If the mother was not a carrier of the mutation, the authors should have determined whether the mutation detected in the patient was sporadic.

The high serum carnitine levels constitute another unusual finding.[1] Most patients with primary mitochondrial diseases display secondary carnitine deficiency in the blood, which explains why some patients benefit from L-carnitine supplementation.[4]

Patients with MELAS syndrome present not only muscle and brain alterations, but also endocrine, cardiac, and gastrointestinal manifestations. Therefore, the study by Pérez Torre et al. should have disclosed whether the patient presented short stature, hypothyroidism, hypoparathyroidism, diabetes, hypoaldosteronism, hypocortisolism, or hypogonadism. Patients with MELAS syndrome should also be screened for such heart conditions as arrhythmia or cardiomyopathy, which have diagnostic and therapeutic implications: the literature reports an increased risk of sudden cardiac death among patients with MELAS syndrome[5]; intractable heart failure requires heart transplantation.[6] There is also evidence that patients with mitochondrial diseases present greater risk of cardiac hypertrabeculation/left ventricular noncompaction cardiomyopathy,[7] which can be complicated by heart failure, ventricular arrhythmia, and cardiopulmonary failure.

In summary, the study would have been more informative if authors had gathered genetic data on the patient and his first-degree relatives and screened for mild or subclinical manifestations of multisystemic disease. Mitochondrial diseases are frequently associated with multisystem manifestations, which may present at disease onset or appear during the course of the disease.

References

1. Pérez Torre P, Acebrón-Herrera F, García Barragán N, Corral Corral Í. Global cerebral involvement and L-arginine use in a patient with MELAS syndrome. Neurologia. 2018, http://dx.doi.org/10.1016/j.nrl.2018.03.022. pii:S0213-4853(18)30151-8.
2. Choi BO, Hwang JH, Cho EM, Jeong EH, Hyun YS, Jeon HJ, et al. Mutational analysis of whole mitochondrial DNA in patients with MELAS and MERRF diseases. Exp Mol Med. 2010;42:446—55.
3. Finsterer J. Toxicity of antiepileptic drugs to mitochondria. Handb Exp Pharmacol. 2017;240:473—88.
4. Vallée L, Fontaine M, Nuyts JP, Ricart G, Krivosic I, Divry P, et al. Stroke, hemiparesis and deficient mitochondrial beta-oxidation. Eur J Pediatr. 1994;153:598—603.
5. Seitun S, Massobrio L, Rubegni A, Nesti C, Castiglione Morelli M, Boccalini S, et al. MELAS syndrome with cardiac involvement: a multimodality imaging approach. Case Rep Cardiol. 2016;2016:1490181.
6. Bhati RS, Sheridan BC, Mill MR, Selzman CH. Heart transplantation for progressive cardiomyopathy as a manifestation of MELAS syndrome. J Heart Lung Transplant. 2005;24:2286—9.
7. Limongelli G, Tome-Esteban M, Dejthevaporn C, Rahman S, Hanna MG, Elliott PM. Prevalence and natural history of heart disease in adults with primary mitochondrial respiratory chain disease. Eur J Heart Fail. 2010;12:114—21.

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Is there scientific evidence for the use of venlafaxine to treat neuropathic pain?☆

¿Existe evidencia científica para el empleo de venlafaxina en dolor neuropático?

Dear Editor:

Venlafaxine was the first serotonin—norepinephrine reuptake inhibitor (SNRI) to be marketed in Spain, in 1995. This antidepressant is indicated for the treatment of major depressive episodes, generalised anxiety disorder, social anxiety disorder, and panic disorder (with and without agoraphobia), as well as for preventing recurrence of major depressive episodes.[1] Although the summary of product characteristics does not list neuropathic pain among the drug's indications, venlafaxine is considered a first-line treatment in the latest clinical management guidelines.[2,3] After venlafaxine, other serotonin—norepinephrine reuptake inhibitors were authorised in Spain, including duloxetine, indicated for the treatment of painful diabetic peripheral neuropathy in adults, and desvenlafaxine, with no indication for neuropathic pain.

The antidepressant effects of venlafaxine result from increased neurotransmitter activity in the central nervous system.[4] Both venlafaxine and its active metabolite O-desmethylvenlafaxine are powerful serotonin-norepinephrine reuptake inhibitors and weak dopamine reuptake inhibitors. Neither drug has shown significant affinity for muscarinic, histamine, or $\alpha 1$ adrenergic receptors in vitro. Their action on these receptors is thought to be similar to the anticholinergic, sedative, and cardiovascular effects of other psychotropic drugs. Venlafaxine and O-desmethylvenlafaxine do not inhibit monoamine oxidase activity.[5]

Our literature review aimed to provide updated information on the use of venlafaxine for the treatment of neuropathic pain.

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