Chorea following extracorporeal circulation in adults: A case report and brief literature review*

Corea tras circulación extracorpórea en adultos: breve revisión a propósito de un caso

Dear Editor:

Chorea as a complication of cardiopulmonary surgery associated with extracorporeal circulation (ECC) and hypothermia has classically been reported in children,[1] with few cases reported in adults.

We present the case of a 75-year-old man who developed encephalopathy with generalised chorea after aortic valve replacement surgery and coronary revascularisation. Surgery was performed under mild hypothermia (30—32 °c), with an ECC time of 193 min and aortic clamping lasting 140 min. During the postoperative period, the patient did not recover consciousness. A brain CT scan performed at 24 hours showed no focal ischaemic or haemorrhagic lesions, and an electroencephalography showed a delta pattern compatible with hypoxic encephalopathy. One week after surgery, he began to present choreoathetosis affecting the face, tongue, neck, trunk, and limbs during episodes of disorientation (). A brain MRI performed 5 days after onset of chorea revealed hyperintense punctiform lesions to the basal ganglia in T2-weighted images, with no restriction detected on diffusion sequences. No significant results were observed in the laboratory analysis, which included copper metabolism, blood smear, erythrocyte sedimentation rate, kidney function, thyroid hormones, and anti-streptolysin O antibodies. We ruled out previous use of neuroleptics or other dopamine receptor-blocking agents. Encephalopathy resolved, but chorea persisted. Symptomatic treatment included haloperidol dosed at 5 mg/8 h, and amantadine at 200 mg/day was added after 4 days. No improvement was observed and treatment was replaced by progressive doses of tetrabenazine of up to 62.5 mg/day, with complete remission at 48 hours. Doses were gradually decreased, and fully suspended at 2 weeks. Six weeks after surgery, the patient remained asymptomatic without treatment ().

Chorea after ECC is a rare complication of open-heart surgery, and is classically described in children with congenital heart disease. Incidence ranges from 1% to 18%,[2,3] and has decreased thanks to surgical and anaesthetic advances that have improved brain perfusion during these procedures. Symptoms may include generalised chorea, dysphagia, dysarthria, and hypotonia, which typically start 3 to 12 days after the procedure; symptoms are transient in half of cases.[4] According to the experience with children, duration of circulatory arrest (aortic clamping),[2] ECC time,[3] prolonged periods of deep hypothermia (< 20 °C),[2,3] alpha-stat pH strategy,[5] and history of cyanosis or developmental delay[3,5] have been proposed as risk factors. Medlock et al.[2] proposed a significant association between circulatory arrest time, deep hypothermia, and chorea after ECC; however, cases have been reported in both children[4] and adults[6] without this association. In adults, the literature mainly includes isolated clinical case reports (Table 1).[6—11] The study by Surie et al.[7] reported a series of 5 cases of chorea after ECC out of a total of 106 patients undergoing pulmonary endarterectomy; chorea was associated with the duration of the circulatory arrest and the rate of rewarming after hypothermia. Adults generally recover after a period of weeks or months. However, in some cases,[7,11] symptoms persist and cases have even been described in which patients required deep brain stimulation of the internal globus pallidus (GPi). The presence of new ischaemic lesions in the basal nuclei on MRI sequences may be associated with poorer prognosis, which is more related to vascular chorea. The pathophysiological mechanisms causing chorea after ECC remain unknown. Hypoxia/ischaemia associated with decreased brain circulation during surgery has been suggested as a possible mechanism[2,3]; this would favour reversible damage to the basal ganglia, with the GPi being especially vulnerable.[12] Decreased inhibition of the thalamo-cortical radiations by the GPi would favour a hyperkinetic disorder. This transient dysfunction of the basal nuclei has been demonstrated by alterations in brain FDG-PET scans and somatosensory evoked potential studies.[9] The association between chorea and abnormal somatosensory evoked potential study findings have previously been described in Huntington disease.[13] In addition to the hypoxia/ischaemia theory, another hypothesis has been proposed that considers chorea after ECC as a form of acquired neuroacanthocytosis secondary to the mechanical trauma to erythrocytes during ECC.[14]

In short, chorea after ECC is an infrequent complication of cardiopulmonary surgery caused by unknown mechanisms. Neuroleptics and tetrabenazine improve symptoms, and prognosis is generally favourable in the absence of new ischaemic lesions.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.nrleng.2018.08.002.

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Table 1 Summary of published clinical cases of chorea after extracorporeal circulation.

Patient	Sex	Age (mean ± SD)	Hypothermia	ECC duration (min)	Circulatory arrest duration (min)	Intervention	Brain MRI	Treatment	Duration
Freeman et al.[8]	Woman	52	Deep (< 20 °C)	NR	NR	Dissection of aortic aneurysm	Normal	Haloperidol	4 months
Surie et al.[7]	3 women 2 men	45 ± 12.3	Deep (< 20 °C)	137 ± 26	63 ± 26	Pulmonary endarterectomy	Normal Motion artefact NR Ischaemia in the basal ganglia	Haloperidol	4 weeks Persistent 1 week Persistent
Saft et al.[9]	Man	77	Moderate (32 °C)	144	74	Aortic valve replacement and coronary bypass	Normal Normal	Tetrabenazine	3 weeks Persistent, mild
Das et al.[10]	Woman	24	NR	NR	NR	Pulmonary endarterectomy	Ischaemia in the basal ganglia	Risperidone	9 months
Bisciglia et al.[6]	Woman	73	No hypothermia	68	34	Aortic valve replacement	Normal	Tiapride	Mild at 7 months
Aoyagi et al.[11]	Man	35	Deep (< 20 °C)	85	85	Pulmonary endarterectomy	Severe ischaemia in the basal ganglia	Refractory DBS of GPi	Persistent, severe
Our case	Man	75	Moderate (32 °C)	193	140	Aortic valve replacement and coronary bypass	Previous ischaemia in the basal ganglia	Tetrabenazine	6 weeks

DBS: deep brain stimulation; ECC: extracorporeal circulation; GPi: internal globus pallidus; MRI: magnetic resonance imaging; NR: not reported; SD: standard deviation.

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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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