Acute Pulmonary Edema Secondary to Pregnancy in a Patient With the Mitochondrial Disease MELAS

To the Editor,

The MELAS syndrome (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes) is a mitochondrial disease with heart manifestations in which conduction alterations and hypertrophic (more frequent) or dilated cardiomyopathy are the most outstanding.

A pregnant 23-year-old female undergoes, neurology and cardiology consultations for possible mitochondrial disease (short of height, deaf and with asymptomatic Wolff-Parkinson-White syndrome). On ECG concentric ventricular hypertrophy and normal ventricular function were found, with no other cardiovascular history. Her mother had died at 42 years of age diagnosed with MELAS syndrome, with hypertrophic cardiomyopathy, multiple episodes of acute lung oedema, deafness and reticence. Her grandmother had died in the fourth decade of life due to non-specified heart causes.

From the 20th week of gestation on she began to have episodes in which she had difficulty breathing accompanied occasionally by typical chest pain. During week 23 she had a new episode of dyspnoea, with coughing and right hemithorax pain of pleural characteristics, which caused her to come in to maternity emergency and after which she remained hospitalized.

During physical exam paleness, jugular ingurgitation, tachycardial tones without murmurs and bilateral crepitant rale on auscultation were found. The ECG showed a sinus rhythm with 130 beats/min, a PR interval of 0.04 seconds and a delta wave. Analysis showed: creatinine, 1.4mg/dl; troponin I, 4.42 ng/mL; WBC, 14 370/µL (neutrophils, 13 520/µL, without band neutrophils). Basal blood gasses showed pCO₂, 24 mmHg; pO₂, 45 mmHg, and pH, 7.44.

Twenty-four hours after admission the patient worsened and a chest x-ray showed a pattern of acute lung edema requiring orotracheal intubation and invasive mechanical ventilation. A heart US was performed (Figure 1) and concentric hypertrophy of the left ventricle was seen with a severely depressed systolic function (EF, 30%). Treatment with furosemide, nitroglycerine and dopamine at diuretic doses was initiated.

Four days after admission to the intensive care unit (ICU), fetal death was determined and expulsion took place, subsequently the placenta was extracted and curettage performed. On the tenth day the patient was extubated. The follow-up cardiac

Figure 1. Echocardiogram images during an acute event, it is possible to see the significant improvement in systolic function. A: during admittance, in M mode; B: after hospital discharge, in M mode; C: after discharge in 2D mode.
The echocardiogram showed improvement of ventricular function (EF 45%). The ECG showed a sinus rhythm with 90 beats/min, a PR interval of 0.04 seconds and a delta wave (Figure 2).

After discharge, the haematology service continued an ambulatory study of the patient, and found presence of lupic anticoagulant and resistance to activated protein C. At the same time, in the neurology external consulting offices the genetic study was completed and the diagnosis of MELAS syndrome confirmed with the finding of mutation A3243G in the mitochondrial DNA (blood sample). After 5 years of follow-up in cardiology consulting offices, ventricular function has remained normal (EF >55%) with no new signs of heart failure.

The combination of mitochondrial myopathy, encephalopathy, lactic acidosis and ictus type episodes constitute a mitochondrial disease known as MELAS. It is exclusively inherited from the mother and 80% of cases are due to a mutation of the A3243G gene of the tRNA of mitochondrial DNA. Other clinical signs are deafness, diabetes, dystonia, short height, and cardiovascular symptoms including dilated and hypertrophic cardiomyopathy, alterations of conduction and Wolff-Parkinson-White syndrome.

It is well-known that there are metabolic and haemodynamic changes during pregnancy that lead to an increase in mitochondrial function to generate more energy. In patients with mitochondrial dysfunction, this is exacerbated, and there is clinical worsening; in the case of this patient this caused heart failure with ventricular dysfunction that resolved progressively after foetal death and expulsion.

The relation between lupic anticoagulant and abortion in this type of patient is not clear. However, some studies have shown an increase in oxidative stress in the presence of these molecules, which increases the unfavourable conditions when there is coexistence with a mitochondrial disease such as MELAS.

There are very few cases described of worsening of mitochondrial diseases during pregnancy, and pregnancy must be considered a high risk factor in these patients.

Miriam V. Sánchez and Rafael Romero
Servicio de Cardiología, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain

REFERENCES
To the Editor,

Proximal pulmonary artery aneurysm (PAA) is defined as a dilation of the pulmonary artery trunk or its main branches. It is an infrequent disease of difficult diagnosis that is usually silent and is an autopsy finding. Occasionally, it causes severe complications such as airway compression, pulmonary artery (PA) dissection and intravascular thrombosis. Pulmonary hypertension (PH) is considered an important factor involved in its pathogenesis, and has mainly been described in patients with more severe PH such as is seen in the Eisenmenger syndrome. The incidence rate of these aneurysms in the population of patients with PH is low.

Of the 320 patients included in our pulmonary hypertension unit (mean PA pressure 56 mm Hg), we found 4 cases of proximal PAA diagnosed with chest CT after the appearance of complications. These 4 patients had severe PH (mean PA pressure 55 mmHg on catheterisation) of different aetiology (2 cases of idiopathic arterial PH and 2 cases of Eisenmenger syndrome). Before PAA diagnosis, the patients were in functional classes II-III of the WHO and in treatment with acenocoumarol and specific drugs for PH (2 patients with sildenafil and 2 patients with a combined therapy with sildenafil and subcutaneous teprostinil). Two of them came in to the emergency service with a persistent dry cough and one with compressive athelectasia. A chest CT showed an aneurysmatic dilation of the pulmonary trunk and its branches (PAA diameter 47-67mm) with non-occlusive thrombosis in its interior and bronchial compression (Figure 1). Perfusion gamma scintigraphy ruled out perfusion defects indicating lung thromboembolism. Thrombi are relatively frequent in PAA and make it necessary to carry out a differential diagnosis with chronic thromboembolic PH. The hypercoagulability study was normal and other causes associated with PAA were ruled out. In all patients specific treatment for PH was intensified, compressive symptoms disappeared and anticoagulation was maintained due to the risk of thrombosis in the PAA region. The patients have been reviewed every 3 months without recurrence of clinical symptoms seen (follow-up: 2-3 years). In the follow-up CT carried out, the persistence of aneurysms without complications was confirmed.

The fourth patient was admitted with chest pain; a chest X-ray showed dilation of the main PA (Figure 2); chest CT showed an aneurysm of the PA trunk and its main branches of 46.6mm in diameter and a flap of the intima at the origin of the left PA. The lobular arteries arose out of the true artery lumen and were compressed by the false lumen of the aneurysm. No recent factors that could have precipitated dissection were found, except for the PH itself. The possibility of surgical treatment was ruled out due to the high risks of the intervention, as also was the possibility of percutaneous repair due to the risk of occlusion of the lobular arteries. Anticoagulant treatment was suspended and specific PH treatment intensified. In the follow-up CT, it was seen that the dissection had not progressed. The patient has worsened clinically and is currently on the waiting list for cardiopulmonary transplant.

In our experience, intensification of specific PH treatment improves airway compression, which was the most frequently seen complication in our patients. Maintenance of anticoagulation, although controversial, is usually necessary due to the risk of PAA thrombosis, although it may be necessary to suspend it in cases of haemoptysis, progressive