When Should We Start Enzyme Replacement Therapy for Infantile Pompe Disease With Severe Cardiomyopathy?

¿Cuándo deberíamos iniciar el tratamiento enzimático sustitutivo de la enfermedad de Pompe infantil con miocardiopatía severa?

To the Editor,

Pompe disease, also known as glycogen storage disease type II, is caused by glycogen accumulation due to a deficiency of the lysosomal acid alpha-glucosidase enzyme by which it is degraded. A total or partial deficiency of this enzyme causes lysosomal glycogen storage leading to a systemic disorder characterized by cardiomyopathy, muscle weakness, hypotonia, and respiratory disorders. Three forms of presentation have been described according to the age at which clinical signs appear: in adulthood, adolescence, or infancy. The latter, characterized by very severe or even total enzyme deficiency, usually manifests in the first months of life and if left untreated causes death within 1 year. This form is specifically characterized by severe cardiomyopathy as a result of glycogen accumulation and manifests as hypertrophic cardiomyopathy on echocardiography and echocardiography. The analysis of enzymatic activity in cultured skin fibroblasts is the diagnostic procedure with the greatest sensitivity and specificity, although it is complex and can delay diagnosis between 4 weeks and 6 weeks. Treatment with recombinant human alpha-glucosidase (rhGAA) is effective regardless of patient age at onset. This approach has been tried even in infants younger than 3 months, obtaining good results in terms of reducing the severity of cardiomyopathy and prolonging survival. Regarding cardiomyopathy, various studies have shown that rhGAA treatment leads to improvements in electrocardiographic abnormalities, reductions in ventricular mass, and improvements in ventricular function. Further, the first effects can be detected within the first weeks of treatment.

If prognosis, procedural delays in assessing enzymatic activity, and the advantages of early treatment are taken into account, it is pertinent to ask whether enzyme replacement therapy could be initiated in neonates with a high suspicion of Pompe disease prior to diagnostic confirmation.

We present the case of a neonate (3 months) who was admitted with symptoms of respiratory failure and presenting feeding intolerance and tachypnea. Hypotonia and generalized areflexia were observed during examination. Blood analysis showed elevated creatine kinase levels. Chest x-ray showed massive cardiomegaly (Fig. 1A) and echocardiogram showed a pattern of left ventricular hypertrophy and a short PR interval (Fig. 1B). Echocardiography showed very severe generalized left ventricular hypertrophy (interventricular septum, 56 mm/m²) that also affected the right ventricle (Fig. 2A) and caused the disappearance of the ventricular cavity in systole (Fig. 2B). Based on this, Pompe...
disease was suspected and a skin sample was taken to analyze enzyme deficiency in cultured skin fibroblasts.

While waiting for the test results, which confirmed a residual enzymatic activity of less than 1%, the patient died of cardiorespiratory failure.

Would high clinical suspicion of the disease have been sufficient to initiate enzyme replacement therapy? In cases such as the one presented in which the clinical manifestations and complementary tests strengthen the suspicion of Pompe disease, and the clinical course suggests an imminent fatal outcome, we suggest that the empirical administration of rhGAA treatment could be of value while awaiting diagnostic confirmation. This approach should be considered if we also take into account that, in its infantile form, the low incidence of this disease confers high specificity and positive predictive value when clinical suspicion is high. Based on these premises, the possible adverse effects that can occur after rhGAA administration become an acceptable risk. Although some of these effects are severe they have low incidence, which is of particular interest especially in cases where the suspected diagnosis is not confirmed by the test results.


*Unidad de Cardiología, Hospital San Juan de la Cruz, Úbeda, Jaén, Spain
bArea Pediátrica del Corazón, Servicio de Pediatría, Hospital Universitario Reina Sofía, Córdoba, Spain
cUnidad de Gestión Clínica de Cardiología, Hospital Universitario Reina Sofía, Córdoba, Spain

* Corresponding author:
E-mail address: jnlsbnll@hotmail.com (J.L. Bonilla-Palomas).
Available online 28 June 2011

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Management and Endovascular Treatment of Traumatic Aortic Rupture

Manejo y tratamiento endovascular de rotura traumática de aorta

To the Editor,

Traumatic rupture of the thoracic aorta (TAR) is associated with high mortality. It is considered the second cause of death in patients with multiple trauma, only exceeded by intracranial hemorrhage. Above all, TAR is caused by deceleration in traffic accidents. It is estimated that less than 25% of patients with intracranial hemorrhage reach hospital alive and that 50% of those who do will die within 24 h. In 90%, rupture occurs at the aortic isthmus; in the remaining 10%, rupture is located elsewhere, eg, at the aortic root or ascending aorta. Unless treated, mortality is 85% to 90%. Lesions are classified as type I (intimal defect), type II (intramural hematoma), type III (pseudoaneurysm) and type IV (rupture with active bleeding). A “wait-and-see” approach is recommended for type I lesions, whereas the other types require emergent treatment within 24 h.

Conventional open surgery (COS) requires left lateral thoracotomy, single-lung ventilation and extracorporeal circulation; early mortality is 10% to 28% and paraplegia ≤16%. In recent years, developments in thoracic endovascular repair (TEVR) have been spectacular and it now offers long-lasting aortic repair through a minimally invasive technique, mortality has fallen by half and paraplegia is down to 2%, making TEVR the treatment of choice for this pathology.

We present the case of a 28-year-old patient with multiple trauma who was admitted to our center following a traffic accident. The patient underwent thoracoabdominal computed tomographic angiography (CTA) and numerous X-rays were taken. Images showed displaced fractures of femora, radii, ulnas, and pelvis; bladder rupture; and aortic pseudoaneurysm (type III lesion, 12 × 8 mm) at the level of the isthmus, 10 mm distal from the left subclavian artery (LSA) outlet (Fig. 1). The patient was stabilized, sedated, and intubated. Once absence of active bleeding had been confirmed, beta blockers were administered to maintain blood pressure at <120/80 mmHg. We decided to undertake emergent TEVR with a 26 × 26 × 150 mm Medtronic Valiant covered stent graft (Medtronic; Santa Monica, California, USA) using left common femoral artery access, occluding 50% of the LSA ostium, under general anesthesia to exclude the pseudoaneurysm from the systemic circulation. Final results were good with no complications. At 1 week, a follow-up CTA demonstrated absence of endoleaks and correct stent deployment with complete exclusion of the pseudoaneurysm (Fig. 2). At 3 months follow-up, the patient was asymptomatic.

Figure 1. Preoperative computed tomographic angiography. Pseudoaneurysm (arrow) with periaortic hematoma (asterisk). A, axial slice; B, sagittal slice; C, 3D reconstruction.