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Case Report

Fabry´S Disease in The Hemodialysis Unit: A Case Report Fabry´S Disease on Hemodialysis

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Abstract

Fabry´s disease is an X-linked inherited disorder that affects the metabolismo f glycosphingolipids, leading to a deficiency or absence of the lisosomal enzyme Alpha- galactosidase A. This deficiency has systemic repercusiones, including renal sclerosis and fibrosis. The patient, a 31-year-old, was referred due to uremic síndrome and required urgent hemodialysis. Additionally, the patient presented symptoms consistent with Fabry´s disease (cardiac, ophthalmologic, dermatologic and neurological), which were subsequently confirmed through genetic testing. Currently, the patient receives agalsidase beta every 15 days during hemodialysis. They are under clinical follow-up with limited improvement in symptoms.

Key words: Fabry´s disease; chronic kidney disease; hemodialysi; agalsidase

Introduction

Fabry disease (FD) is a recessive hereditary pathology linked to the X chromosome that generates a deficit in the synthesis of agalsidase A, causing intravascular deposits of glycosphingolipids in different tissues and organs.

Clinically, it presents two phenotypes, one classic and one late. The first of them begins in childhood while the second manifests in adulthood.

Nephropathy secondary to FD is produced by deposits of glycosphingolipids in the podocytes, mesangium, endothelium of the glomerulus, arteries and arterioles, tubular and interstitial cells, which leads to glomerular sclerosis, vascular lesions and finally interstitial fibrosis.

Case presentation

A 31-year-old male patient, originally from Bolivia, with no known personal pathological history, was referred to the Neuquén Provincial Hospital due to uremic syndrome with criteria for emergency hemodialysis, and pancytopenia. The analysis revealed: urea 399 mg/dl, creatinine 21 mg/dl, hematocrit: 12%, hemoglobin: 3.9 g/dl, white blood cells 3600/uL, platelets 51000/ul, Na 132 mEq/L, K 4.4 mEq/L, urine with proteinuria, hematuria 7-10/cpo and no leukocyturia.

Upon questioning, she reported that since childhood she had tingling/electricity pain in her hands and feet. In the last 2 months prior to the consultation, she began with nausea, vomiting that prevented eating, unquantified weight loss and finally added swelling in her lower limbs and face. Physical examination revealed hypocolored mucous membranes, punctate skin lesions, less than 5 mm, hyperpigmented, palpable, and grouped that did not disappear with digitopressure, distributed in the periumbilical, inguinal, and thigh regions, compatible with angiokeratomas. From the cardiovascular point of view, there was a holosystolic murmur of intensity 3/6 with radiation to the neck and ipsilateral axilla.

Regarding complementary studies, a renal ultrasound was performed, which determined a decrease in both kidneys (RD: 9.61 cm and RI: 8.08 cm). Likewise, an echocardiogram was performed, which showed mild dilation of both atria, and severe concentric hypertrophy of the left atrium with an ejection fraction of 76%. Ophthalmology was consulted and detailed the presence of dry eye, horizontal nystagmus, verticillata cornea, and deep vessel tortuosity.

During the hospitalization period, the patient had an episode of acute disorientation, so a CT scan was requested, which showed sequelae of a vascular event in the anterior portion of the left thalamus with extension to the internal capsule; and angioma in the region of the globus pallidus-right putamen.Given these findings, with the presence of a very florid clinical picture, Fabry disease was suspected, so enzymatic function testing was performed through a fresh drop.At the same time, emergency hemodialysis was started through a temporary catheter with good tolerance; since the stage of CKD was advanced, vascular access was scheduled through an arteriovenous fistula.

The genetics service reported Alpha-Galactosidase A of 0.1 µmol/l/h (VN: ≥ 4.0) and Lyso- Gb3 74.4 nmol/l (VN ≤ 0.9), compatible with EF. Therefore, the Hospital Pharmacy Committee was asked to approve the treatment. She is currently receiving Agalsidase beta (Fabrazyme) 1 mg/kg every 15 days during hemodialysis sessions.Because it is a genetic pathology, the study was extended to the family group, and the presence of the same was determined in her eldest daughter.

Discussion

Fabry disease is a hereditary pathology, triggered by a mutation in the GLA gene, located on the X chromosome, which causes the deficiency or absence of alpha-galactosidase. This causes glycolipid deposits, mainly globotriaosylceramide (Gb3 or GL-3) and globotriaosylsphingosine (lyso-Gb3 or lyso-GL-3) [1] in different tissues and organs such as the kidney, digestive system, nerves, eye, etc.

As for the physiology of the kidney disease, it is not fully studied, at the moment it is known that the deposit of Gb3 in the podocytes increases the expression of the cytokine TGF-beta1 that leads to the synthesis of fibronectin and collagen IV in the extracellular matrix. The proinflammatory state mediated by cytokines, together with the activation of autophagy generated by the alteration of the LC3 protein leads to alterations in podocytes, expressing said lesion with proteinuria, and finally evolving to glomerulosclerosis [2]. Clinically, they are classified into type 1 or classic phenotype and type 2 or adult-onset. Type 1 manifests in childhood with neuropathic pain in hands and feet, abdominal pain and diarrhea, presence of angiokeratomas and hypohidrosis, as well as whorled cornea, hearing loss, and tinnitus [3]. Regarding renal injury, proteinuria has been seen at early ages and after 30 years of age, renal replacement therapy has been required; In this decade, cardiovascular alterations such as arrhythmias, precordalgia, left ventricular hypertrophy, and stroke also appear [3]

The expression of this disease in women should be reconsidered, since it is not always asymptomatic, but depends on the inactivation of healthy or mutated X chromosome, called the “lyonization phenomenon” [3].

Regarding the diagnostic process, the Canadian Fabry Disease Guide [4] proposes the presence of at least 3 of the following 4 criteria: 1) Clinical, with the most specific being the presence of cornea verticillata and angiokeratoma; 2) Biochemical: decreased or absent alpha galactosidase level in whole blood, plasma, or leukocytes, as well as elevated presence of globotriaosylceramide (Gb3) and elevated sphingosine-globotriaosylceramide (Lyso-Gb3) in blood or urine; 3) Molecular: modifications at the DNA level; and 4) Pathological: identify through immunohistochemistry the presence of deposited material (Gb3) in tissues such as kidney, heart, or skin [5].

The treatment of Fabry disease requires a specific therapy through enzyme replacement or pharmacological chaperones. The first of these is given by the administration of agalsidase, in its alpha or beta isoform; while the pharmacological chaperone (migalastat) was recently approved. Likewise, symptomatic support treatment is needed according to each condition

[3] [6].

Conclusions

Fed is a clinically heterogeneous and rare pathology that requires high diagnostic suspicion, with specific studies for its confirmation.

Keeping it in mind will allow to start enzyme replacement earlier as well as to study the family group. Consider its behavior as a chronic, multisystemic and progressive disease that deteriorates the quality of life of the patient and significantly reduces their survival

In the case of our patient, he is on renal replacement therapy under the modality of hemodialysis; after the start of agalsidase, he evolved with improvement of the skin lesions, as well as tolerance to extreme temperatures.

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