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Short Communication

Sweat Gland Biopsy: A Possible Early Diagnostic Tool in the Anderson-Fabry Disease

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Abstract: Anderson-Fabry disease is a rare X-linked lysosomal storage disorder caused by deficient or absent activity of the enzyme alfa-galactosidase A. This defect enzyme leads to accumulation of glycolipids, primarily globotriaosylceramide (Gb3), in the vascular endothelium of several organs, including the skin, kidneys, nervous system, and heart. The characteristic early clinical features of Fabry disease include acroparaesthesia, angiokeratoma, heat intolerance, hypohidrosis, cornea verticillata and gastrointestinal symptoms. Later complications occur with the disease progression and include progressive renal failure, hypertrofic cardiomyopathy, cerebrovascular disease and reduced life expectancy. Anderson Fabry disease is therefore a disabling and systemic disease which requires a timely diagnosis. The aim of our article is to propose a biopsy of the sweat glands as a diagnostic method to be used especially in patients who can't be subjected to cardiac or renal biopsy.

Keywords: lysosomal diseases; diagnosis

1. Introduction

Anderson-Fabry disease is an X-linked inherited lysosomal storage disorder caused by a deficient or absent activity of the enzyme α-galactosidase A (α-GAL). This enzyme defect leads to progressive accumulation of glycosphingolipids, primarily globotriaosylceramide (Gb3), within lysosomes in a variety of cell types, including endothelial, smooth muscle cells, epithelial, perithelial, reticuloendothelial, myocardial, ganglion and perineural[1-2]. The characteristic early clinical features of Fabry disease include acroparaesthesia, angiokeratoma, heat intolerance, hypohidrosis, cornea verticillata and gastrointestinal symptoms. Later complications occur with the disease progression and include progressive renal failure, hypertrofic cardiomyopathy, cerebrovascular disease and reduced life expectancy[3]. The diagnosis of Anderson Fabry disease often requires the use of invasive procedures, for this reason it would be desirable to have a non-invasive diagnostic method. Our proposal is to use the biopsy of the sweat glands in order to make a diagnosis with the least discomfort to the patient.

2. Results

Incidence estimations of Fabry disease vary widely from 1:55000 to 1:3000 male births. The true incidence is likely to be higher than originally thought, owing to the existence of milder variants of the disease[4]. Subtle forms are common and may remain undiagnosed until adulthood when irreversible kidney or cardiac damage has occurred[5]. Therefore, making a precise diagnosis is essential in the early stages of the disease. Oligosymptomatic detection of patients with Fabry disease has been hampered by the lack of effective methods for population screening. Endomyocardial and kidney biopsies are performed for evaluation of heart and renal involvment in Fabry disease or for the identification of causative factors in patients with aspecific symptoms, proving the progressive accumulation of glycosphingolipids in various cells, eventually leading to broad spectrum of clinical symptoms[6]. Endomyocardial biopsy findings can demonstrate sarcoplasmic vacuolization of cardiac muscle cells, and presence of lipid storage in all cell types within the heart under light microscopy and lamellated zebra bodies in the cytoplasm under electron microscopy[7]. Kidney biopsy findings by light microscopy and electron microscopy are characteristic and show glycolipid accumulation in glomerular, vascular, interstitial, and distal tubular cells and various degrees of ischemic damage[8]. The level of Gb3 accumulated in tissues and body fluids represent a biomarker reflecting the prognosis, and it has been measured for diagnosis and monitoring of the response to ERT in Fabry

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disease[9]. Sweat gland biopsy can demonstrate the characteristic glycolipid deposits in a simple and relatively non-invasive way and can be used in general and high-risk population. Skin biopsies have shown storage of lamellar intracytoplasmic lipid inclusions in sweat glands, particularly in the myoepithelial cells and the small vessels around the eccrine glands. In the secretory portion of eccrine sweat glands, numerous polymorphic dense inclusions were present in the cytoplasm of clear cells, which consisted of parallel arrays, concentric lamellae, a fingerprint-like pattern, and fine granular or amorphous materials[10] (Fig.1).

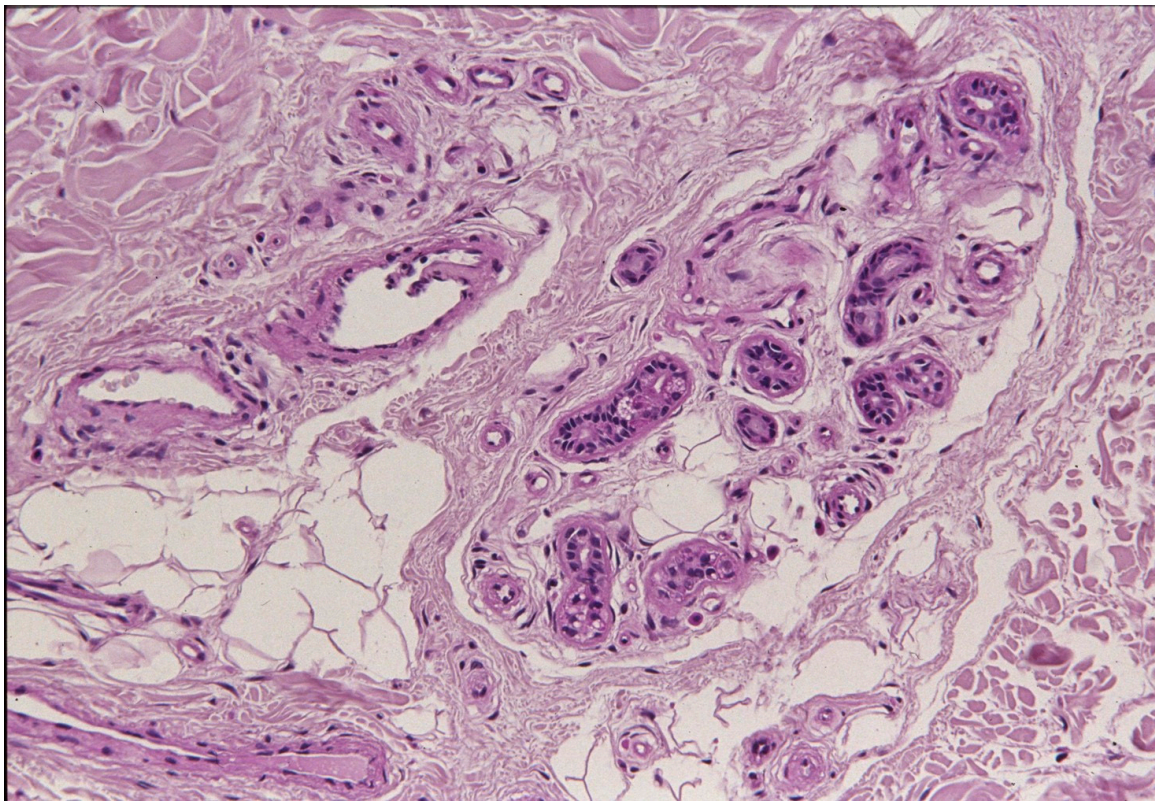

Figure 1. Characteristic glycolipid deposits in the secretory portion of the gland (H&E x 160). Male, 40 years.

3. Discussion

We believe that sweat gland biopsy represents an important alternative to the impediment of conventional biopsy technique, that would requires haemodynamic procedures and is achievable with risk and discomforts for patients. Baseline sweat gland morphological findings may provide important informations supporting treatment decisions and also may have a prognostic impact. The purpose of our study is to define sweat glands morphological abnormalities in children and adolescents with Fabry disease with minimal symptoms and establish a baseline morphological diagnosis of the disease before to undergo to kidney or endomyocardial biopsy or when the classical approach is not possible because of some complications, with minimal discomfort for patients. These patients would benefit form early diagnosis, appropriate treatment, follow-up and surveillance. We emphasizes the difficulties in clinical practice in diagnosing Fabry disease in oligosymptomatic patients and the potential role of histological examination, thus highlighting that a close collaboration between the dermatologist and pathologist is crucial to search for diagnostic lesions. It is obvious that further study and research is needed so as to determine the best procedures with which to make the biopsy, and the criteria for the evaluation of the obtained diagnostic parameters.

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