Short Communication

An Autopsy Case of Fabry’s Disease with Cardiac Manifestations

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We report an autopsy case of Fabry’s disease with cardiac manifestations. Electron microscopic examination of rectal biopsy specimens revealed lamellar bodies and osmiophilic irregular bodies. Biochemical analysis showed low enzymatic activity of \( \alpha \)-galactosidase A in plasma fluid. Microscopic examination on autopsy showed marked hypertrophy and vacuolation of cardiac muscle cells. Intracytoplasmic vacuolation was also found in glomerular epithelial or endothelial cells and smooth muscle cells of renal arteries, Meissner’s plexus in the submucosa of small and large intestines, and smooth muscle cells of arterioles in the cerebrum. The diagnosis of Fabry’s disease was made. The patient died suddenly of cardiomyopathy. ([J Clin Exp Hematopathol 49(2) : 121-123, 2009])

Keywords: Fabry’s disease, cardiomyopathy, autopsy

INTRODUCTION

Fabry’s disease is an X-linked lysosomal storage disease caused by mutations in the gene encoding the lysosomal enzyme, \( \alpha \)-galactosidase A.\(^1\) The resultant deficiency in \( \alpha \)-galactosidase A activity leads to intralysosomal accumulation of neutral glycosphingolipid, ceramide trihexoside, in various organ systems. The disease is characterized by progressive clinical manifestations and premature death from renal failure, stroke and cardiac disease.\(^1\) The incidence of Fabry’s disease has been estimated at 1 in 40,000 to 1 in 117,000 live births for males.\(^1\) The most common clinical features of classical Fabry’s disease are angiokeratoma, hypohidrosis, neuropathic pain, renal dysfunction as proteinuria, gastrointestinal disturbance, cornea verticillata and cardiac failure.\(^2\) The \( \alpha \)-galactosidase A gene consists of seven exons located on the long arm of the X chromosome (Xq22.1) that encode a 101 kd homodimeric glycoprotein. Over 250 mutations have been described spanning all seven exons.\(^3\)

CASE REPORT

The patient was a 62-year-old man who had been suffering from schizophrenia and depression since his twenties. He had angiokeratoma and Fabry’s disease was suspected. Electron microscopic examination of the rectal biopsy specimens revealed the lamellar bodies and osmiophilic irregular bodies. Biochemical analysis showed low \( \alpha \)-galactosidase A activity in plasma fluid (0.48 mmol/hr/mL : normal activity < 6.4), and the diagnosis of Fabry’s disease was made. The patient’s sister was also diagnosed with Fabry’s disease. The patient received enzyme replacement therapy (administration of \( \alpha \)-galactosidase) for four years. Following a cerebral infarction, he was hospitalized due to dysphagia, and died suddenly on the second day of hospitalization. An autopsy was performed.

AUTOPSY FINDINGS

The patient showed marked emaciation. Macroscopic findings showed marked hypertrophy of the anterior, lateral left ventricle wall and septum of the heart and partial thinning of the posterior left ventricle wall (512 g) (Fig. 1). Microscopic examination revealed marked vacuolation of cardiac muscle cells (Fig. 2) with marked replacement fibrosis. Fibrosis was also found in the thinning portion of the posterior wall of the heart (Fig. 3). Electron microscopic examination showed numerous lamellar structures and osmiophilic irregular bodies in the cytoplasm of cardiac muscle cells (Fig. 4). Vacuolation was also found in the endothelial and epithelial cells of glomeruli (Fig. 5) and smooth muscle cells of...
renal arteries, Meissner’s plexus in the submucosa of small and large intestines and smooth muscle cells of arterioles in the cerebrum. In the cerebrum, several small lacunar infarctions were found.

**DISCUSSION**

The patient was diagnosed with Fabry’s disease based on electron microscopic and biochemical findings. The cardiac manifestation of Fabry’s disease is characterized by myocardial hypertrophy with replacement fibrosis. This correlates well with observation of relatively mild diastolic dysfunction in the early stage of the disease, progressing to systolic and severe diastolic ventricular impairment in advanced stages.

The present case showed cardiomegaly (512 g) with marked hypertrophy, replacement fibrosis and vacuolation of cardiac muscle cells, resulting in sudden death due to cardiac dysfunction or failure. In this case, vacuolation of smooth muscle cells in cerebral arteries was found. This finding may be related to an ischemic change which might have resulted in cerebral infarctions. Thus, pathological manifestations were not limited only to the heart, making this case different from cardiac Fabry disease. In recent reports, enzyme replacement therapy has been shown to enhance microvascular endothelial ceramide triheximide clearance in the heart of Fabry’s disease patients, and can decrease left ventricular hypertrophy and improve regional myocardial function. The patient received enzyme replacement therapy, which resulted in no
improvement in symptoms, for reasons which remain unclear. In the future, more detailed analysis is needed to clarify the pathological findings seen in many Fabry’s disease autopsy cases, such as tissue localization or organ specificity of ceramide triheximide storage.

REFERENCES