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COMPLETE RESOLUTION OF FABRY DISEASE RELATED MILD LEFT VENTRICULAR HYPERTROPHY AFTER 8 MONTHS OF FABRAZYME REPLACEMENT THERAPY - CASE REPORT

***[1]Dr. Ibrahim Asi Ali Al Sabawi and [2]Dr. Safana Yaman Wageeh**

[1]Consultant Nephrologist/ Research Hospital in Mosul-Iraq.
[2]M.B.Ch.B- SHO Nephrology/ Research Hospital in Mosul-Iraq.

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***Corresponding Author: Dr. Ibrahim Asi Ali Al Sabawi**
Consultant Nephrologist/ Research Hospital in Mosul-Iraq.

ABSTRACT
Fabry disease is caused by hereditary deficiency of the enzyme α galactosidase A (α-Gal A), resulting in the intracellular accumulation of neutral glycosphingolipids with terminal α-linked galactosyl moieties. Clinically, this leads to progressive CKD, pain crises, sweating abnormalities, vascular cutaneous lesions, and cardiac and eye abnormalities. Enzyme replacement therapy stabilizes and slow progression of Fabry disease, with more benefit when started at an early age. We report a 32y old Asian Iraqi male who came to out-clinic as potential kidney transplant Donor for his 34 y old brother who has end stage kidney disease of unknown etiology. The donor and during routine investigation discovered to have mild left ventricular hypertrophy by echo study which was unexplained, the patient only mentioned intermittent chest pain heavy in nature occur with activity, other investigations was normal, a genetic screening of him and his brother came with fabry disease, genetic screening of other siblings discovered another affected brother and two carriers female, fabrazyme was started to all affected males regardless of the symptoms and a complete resolution of left ventricular hypertrophy after 8 months was achieved, this case report points to the importance of early diagnosis and treatment of Fabry disease related complications.

KEYWORDS: galactosidase, fabrazyme, Fabry disease related complications.

INTRODUCTION

Fabry disease is an X-linked lysosomal disorder caused by hereditary deficiency of the enzyme α galactosidase A (α-Gal A) that leads to excessive deposition of neutral glycosphingolipids in the vascular endothelium of several organs and in epithelial and smooth muscle cells. Progressive endothelial accumulation of glycosphingolipids accounts for the associated clinical abnormalities of skin, eye, kidney, heart, brain, and peripheral nervous system.[1,2] In affected males, the initial features of the disease are seen in childhood and early adolescence and consist of paresthesia and pain in the hands and feet with episodic pain crises.[3] The course of the disease is variable but usually leads to ESKD in the third to sixth decade. There is risk of premature death because of myocardial or cerebral infarctions. Glycosphingolipid accumulation in coronary artery endothelial cells and in the myocardium results in coronary artery narrowing, which may lead to angina, myocardial infarction, or congestive heart failure. Left ventricular hypertrophy (LVH) may be an early finding.[4] Arrhythmias resulting from infiltration of the conduction system and valvular lesions also may occur.[5] Severe Fabry disease in a female reflects extensive inactivation of the X chromosome carrying the normal α-Gal A allele. Prevalence of the classic form is up to 1 in 22,570 males by newborn screening studies and 1 in 1390 males for the males with milder phenotype.[6] The diagnosis and treatment of Fabry disease can be challenging, the signs and symptoms may be nonspecific, and if manifestations in different organs are considered in isolation, the unifying diagnosis may be missed. If the family history suggests a diagnosis of Fabry disease, genetic testing and counseling should be offered to all family members, regardless of their sex. The introduction of enzyme replacement therapy with recombinant humanα-Gal A (α galsidase) has transformed the treatment of Fabry disease.[7,8] RCTs showed that α galsidase administration for 5 to 6 months resulted in reduced plasma and urine Gb3; amelioration

of neuropathic pain; enhanced quality of life; clearing of Gb3 deposits from kidney, heart, and skin; and improved cerebral blood flow. Treatment of classic Fabry disease patients with α galsidase-β with baseline proteinuria of less than 1 g/day had stabilization of GFR over 5 years of follow-up.[9] This case report point to the importance of early initiation of enzyme replacement therapy in the early course of the disease before end organ damage occur.

CASE PRESENTATION

We present a case of 32 years old Asian Iraqi male who has no co-morbidities and came to our hospital as potential kidney transplant Donor to his 34 years old brother who has unknown cause of end stage kidney disease, during workup of the donor, mild left ventricular hypertrophy was discovered by echo study, his brother "the recipient" also discovered to have hypertrophic cardiomyopathy by echo study.

The patient give a history of intermittent palpitation, central, heavy in nature chest pain elected by activity and relieved by rest and easy fatigability, he give family history hypertension and type II diabetes but no family history of ESKD. On examination an average build young man who looks healthy and well, nothing was significant by systemic examination of cardiac, respiratory, abdominal, musculoskeletal and nervous systems.

Vital signs: blood pressure 120/80 mmhg, pulse rate 62 bpm regular with good volume, SPO_2 99% in room area, tem.37.1c.

The patient also was sent for CBC, renal function test, which all was normal and give no explanation for the abnormal results of echo study.

A genetic screening of him and his brother was done and came with diagnoses of Fabry disease, all siblings was screened also showed another asymptomatic brother and two asymptomatic sisters are carriers of the affected allele.

Enzyme replacement therapy was started for affected males regardless of symptoms with only regular follow-up of aymptomatic females carriers, after 8 months of fabrazyme replacement therapy in a dose of 70mg every 2wks, follow-up echo study of our case show complete resolution of mild LVH and normal cardiac function.

DISCUSSION

This case show us the importance of early diagnosis and management of fabry disease patients, and give us a clue about the effectiveness of fabrazyme replacement therapy in the management of these cases especially when they are discovered early in the course of the disease.

CONCLUSION

Early diagnoses and management of fabry disease patients with enzyme replacement therapy can reverse mild cardiac hypertrophy and improve health and overall prognosis.

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