

Case Report

Marfan syndrome affecting a whole Sudanese family

Laila M Elmahdi, Sulafa KM Ali

Department of Pediatric Cardiology, Sudan Heart Centre, Khartoum, Sudan.

ABSTRACT

Marfan syndrome (MS, OMIM 154700) is an autosomal dominant disorder of fibrous connective tissue with striking pleiotropism and clinical variability. The cardinal features occur in skeletal, ocular, and cardiovascular systems. We describe a Sudanese family with the father and all his 4 children manifesting the syndrome. To our knowledge, there were no previously reported MS cases from Sudan.

Key words

Marfan syndrome; Echocardiography; Fibrillin-1 gene.

INTRODUCTION

Marfan syndrome (MS) is an autosomal dominant disorder with high penetrance but variable expressivity. Most reported cases have been caused by a mutation in the fibrillin-1 gene, on chromosome 15. There are over 600 currently identified genetic mutations of which 80% were novel [1]. Clinical diagnosis may be difficult in some patients, so the disease is confirmed in patients who satisfy the Ghent criteria [2], which consist of family history, skeletal, eye, cardiovascular, skin, pulmonary and neurological features.

We report a Sudanese family with five members having

Marfan syndrome; the father and all the four siblings.

METHODS

The patients were seen at the Sudan Heart Centre, Khartoum in May 2008 and followed up since then. Clinical examination, as well as a complete 2 dimensional echocardiography, were performed. The patients were diagnosed according to the Ghent criteria [2]. Annual follow up by clinical and echocardiographic examinations were arranged. Genetic testing was planned.

FAMILY REPORT

The patients' father was said to have been tall and with impaired vision, and had died suddenly at the age of 42 years from presumed ruptured aortic aneurysm. The paternal uncle had a similar body habitus. All the siblings (14-year-old female, 11-year-old male, 9-year-old female and 7-year-old male; designated as Patients 1,2,3 and 4 respectively), share the same clinical features typical of Marfan syndrome. All of them were asymptomatic. Physical examination revealed tall stature (height > 90th centile) with long thin limbs and an arm span that exceeded the height (Figure 1). There was a high arched palate, arachnodactyly, positive thumb

Correspondence to:

Professor Sulafa K M Ali,

Consultant Pediatric Cardiologist,
Department of Paediatrics and Child Health,
Faculty of Medicine, PO BOX 102,
University of Khartoum, Sudan.
Email: sulafaali2000@gmail.com

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and wrist signs (Figure 2) and pectus excavatum. Eye examination revealed severe myopia (all of them wear glasses). In addition, Patient 3 has right amblyopia, and divergent squint was present in Patients 2 and 4. Cardiac examination was unremarkable except in Patient 4 who had a machinery murmur at the infraclavicular area. Echocardiography (Figure 3) revealed mitral valve prolapse in all patients with dilated aortic root and aorta- left ventricle junction z score of +2 , aorta at the sinus of valsalva z score of +4, and at the sino-tubular

junction of +2 (Figure 3). There was neither mitral nor aortic regurgitation. Dimensions of the ascending and descending aorta were normal. Patient 4 has a large patent ductus arteriosus.

All patients were started on propranolol 0.5 mg per kilogram per dose 8 hourly and advised to come for follow up on 12 monthly basis. The patient with ductus arteriosus had successful transcatheter device closure. The aortic root measurements continued to be on the same centiles with no excessive increment.



Figure 1- The 4 patients with glasses, tall stature and long arms.



Figure 2- The hands of the 4 patients demonstrating arachnodactyly and thumb sign.

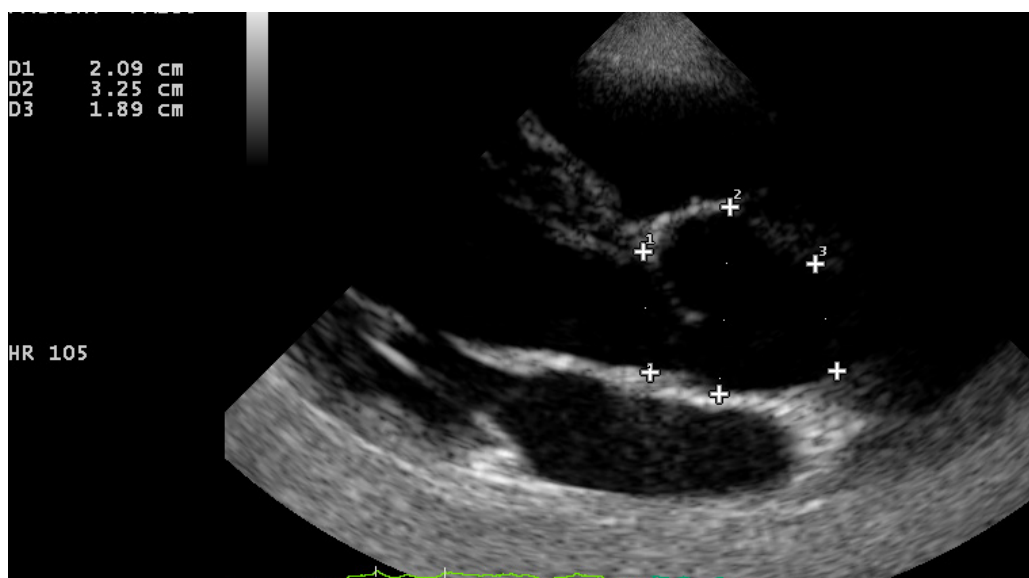


Figure 3-Echocardiographic parasternal view of patient 4 showing dilated aortic root: 1.aorta: Left ventricle junction of 20 mm; 2.sinuses of valsalva 32,5mm; 3.sinotubular junction 18,9 mm.

DISCUSSION

This family represents an autosomal dominant disease affecting all the siblings, and to our knowledge no such family has been described from Sudan before. The type and degree of cardiac lesions were similar in all the patients. In addition, the youngest boy has a patent ductus arteriosus closed by transcatheter route with an occluding device. Similar cases were reported where a ductus arteriosus was closed by device in patients with Marfan syndrome indicating the safety of this less invasive catheter approach [3].

Cardiovascular manifestations of MS are mainly aortic root dilatation and mitral valve prolapse. Aortic root dilatation which is found in 50 % of children with MS is the major cause of death, typically progresses with time leading to dissecting aneurysms [4]. Echocardiographic measurement of the left ventricle – aorta junction, sinus of valsalva, sinotubular junction, ascending and descending aorta dimensions should be carefully made and compared with standard values. Management depends on the Z scores of these measurements. If the z score is increasing and approaching 4 the patient should be started on beta blockers which have a proven effect on slowing aortic root growth and improving survival [5].

The optimal timing of elective aortic repair in children is uncertain. It has been suggested that the aortic root dimensions be plotted serially against body surface area and operation be considered if the diameter begins to increase rapidly from a previously stable percentile even if the absolute measurement is less than 50 mm which is the reference figure used to refer adults for surgery [6]. An increase of >10 mm/year is regarded as rapid enlargement in children [7]. In the present family with history of sudden death, it is mandatory to plan the surgery early enough because familial aortic dissection has been frequently reported [8,9]. However, the presence of 4 affected individuals implies important psychological and financial stresses.

There is a need to improve early detection of MS. It is well documented that patients with MS who remain undiagnosed until adulthood have well-established cardiovascular pathology frequently requiring surgical intervention [10]. On the other hand, the use of beta blocker, restriction of vigorous physical exercise, monitoring of aortic size and elective surgical repair of the aorta, all lead to improving prognosis of patients with MS in the recent years. Also genetic testing and counseling are cardinal for the proper management and prevention of such familial cases.

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