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Mental Deficiency and Unstable Bladder in a Case of Marfan's Syndrome

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Key Words

Marfan's syndrome
Mental deficiency
Unstable bladder

Abstract

We report a case of Marfan's syndrome in a 23-year-old Arab man presenting with unstable bladder, and who was also found to have a mental deficiency. Familial occurrence of marfanoid habitus and heart abnormalities were detected. This is the first report of Marfan's syndrome in a patient from Kuwait and the Gulf region.

Introduction

Marfan's syndrome is an autosomal dominantly inherited connective tissue disorder characterized by cardiac, vascular, ocular and skeletal manifestations. Mutations in the gene coding for fibrillin are now known to cause variable and pleiotropic manifestations of this condition [1, 2]. Premature death in Marfan's syndrome is most often due to cardiac complications which can be prevented by early diagnosis and management [3].

Here we report a case of Marfan's syndrome in a 23-year-old Kuwaiti man present-

ing with recent urinary incontinence, and mental deficiency diagnosed when he was 16 years old. A younger brother had the same skeletal and cardiac manifestations. Isolated heart abnormalities were also found in several members of the family.

Case Report

B.N., a 23-year-old Kuwaiti man was admitted to the hospital for investigation of urinary incontinence of 2 months' duration which was both diurnal and nocturnal. He also complained of occasional chest pain and easy fatigability during the previous 2 years.

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1011-7571/98/0071-0074\$15.00/0

This article is also accessible online at:
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Family history showed that both parents were healthy and nonsanguineous; his mother was from Saudi Arabia and the father was from Kuwait. The maternal father died suddenly at 55 years of age from a heart attack. The patient had 2 brothers, 17 and 16 years of age, and 3 sisters 22, 18 and 12 years of age. The 16-year-old brother had a similar habitus as the patient at that age.

The pregnancy was uneventful with birth at term. No major problems were reported until the patient was 16 years old when he grew tall and thin with stooping posture. He left school because of poor performance. The diagnosis of moderate mental retardation (IQ 70) was then made by a psychiatrist. The patient worked as a clerk with minor responsibilities for the past 3 years.

Physical examination revealed marfanoid features: a slender habitus, with a height of 1.83 m, arm span of 1.94 m (arm span-to-height ratio was 1.06), and a weight of 54 kg. The head circumference was 52 cm. He had a high arched palate, scoliosis of 25° C, hyperkyphosis, and moderate pectus excavatum. Hands and feet were long (21 cm and 27 cm) with unusually long metacarpals and phalanges. Metacarpal index was greater than 8.4. Hallux was short and the second toe was longer on the right foot and without flexion contractures (fig. 1). Cardiac auscultation demonstrated a systolic murmur heard best at the apex.

Testicular size and body hair distribution were normal. The IQ was 77 (Wechsler Adult Intelligence Scale). Ophthalmological examination was normal. Neurological examination detected no abnormalities on cranial nerves and in the limbs; tone, muscle bulk, power and gait were normal, and abnormalities of tendon or skin reflexes were not found.

Laboratory findings included normal results on routine hematological and biochemical tests. Blood aminoacids were normal and no aminoaciduria was found. Homocystine was not detected in the blood. Radiology of lumbosacral spine including CT scan and MRI were normal. Ultrasound of the abdomen was also normal.

MRI of the brain and the EMG and nerve conduction studies were found to be regular. Cardiac ultrasound showed aortic regurgitation and mitral valve prolapse. The diameter of the aortic root was 30 mm. Urodynamic study showed a residual volume of 70 ml, an uninhibited contraction after 26 ml, and a low compliance after 200 ml. Voiding pressure was 80 cm. Sensation was normal. Dyssynergia of detrusor and sphincter was not found by EMG. Diverticula were not detected by cystoscopy.

Fig. 1. A 23-year-old patient with Marfan's syndrome. Arm span-to-height ratio is greater than 1.05.

The Family

The mother was of slim habitus. She had arachnodactyly, short hallux and a second toe longer on the right foot. The father was short and stocky. Cardiac ultrasonography of the parents and the 22-year-old sister was normal. A 16-year-old brother was slender, with mild pectus excavatum, scoliosis of 20° and kyphosis. He also had a highly arched palate with crowding of teeth and no microcephaly (the head circumference was 54). Incontinence of urine was not reported and mental retardation was also not found. Echocardiography on the brother showed aortic dilatation. Two sisters and another brother had evidence of mitral valve prolapse. The family refused skin biopsy and further genetic examination.

Discussion

With the advent of molecular testing, the diagnostic approach to Marfan's syndrome has been revised, and a new criteria for clini-

cal and phenotype assessment were proposed [4]. We report on an Arab man from Kuwait who has major clinical manifestation of Marfan's syndrome including skeletal and cardiac abnormalities, and a brother who independently met the diagnostic criteria of Marfan's syndrome. There were no eye manifestations in our patient and in his family; eye abnormalities are not required for the diagnosis of Marfan's syndrome [5]. The patient's major problems were mental retardation and urinary incontinence. Sphincteric disturbances, particularly retention of urine, have been reported in patients with Marfan's syndrome in association with lumbosacral osteomeningeal abnormalities [6] such as sacral meningocele [7]. Such abnormalities were not detected in our patient. There was no bladder outflow obstruction or neuropathic disease. The diagnosis of an idiopathic instability of the bladder was made. It has been estimated that 10% of the population may suffer from detrusor instability [8]. Therefore, it is likely that the association of Marfan's syndrome and unstable bladder in our case is accidental. However it brought to attention the patient's condition and had important implications for further management.

Marfan's syndrome is sometimes confused with homocystinuria. Mental retardation is a characteristic feature of homocystinuria, and not of Marfan's syndrome. Sporadic cases of Marfan's syndrome and various degrees of mental retardation have been reported [9]. Our patient had the diagnosis of mental retardation for years and despite that we found only a borderline value of his IQ. This led us to consider the syndrome of x-linked mental retardation with marfanoid habitus, described by Lujan et al. [10], and more recently by Fryns and Buttiens [11]. We found some of the clinical criteria to qualify for that diagnosis as being: mild mental retardation, marfanoid habitus, short hallux, the second toe rela-

tively long on one foot, normal secondary sexual development and normal testicular size [12]. However, the patient had no characteristic craniofacial appearance, generalized hypotonia and nasal voice, and therefore this entity was unlikely. A number of syndromes with overlapping clinical features of Marfan's syndrome were also considered. Again, the patient did not have some of the almost constant features seen in Marfan-related disorders and Ehler-Danlos syndromes such as hypotonia and muscular hypotrophy [13].

Marfan's syndrome shows a high degree of clinical variability both between and within families. Various clinical phenotypes seen in selected families may be not due to single fibrillin mutations but rather to different genetic alterations [14]. In our case, family screening detected a younger brother with closely related phenotype and cardiac abnormalities by echocardiography. Another brother and 2 younger sisters had equivocal manifestations of the disorder with probable cardiovascular risk [14, 15]. The mother had a similar isolated skeletal manifestation in one foot. We were not able to proceed with the skin biopsy for genetic testing as the family refused the procedure.

The main benefit of family screening is the identification of previously undiagnosed patients at risk of cardiac complications, since a common diagnostic test for Marfan's syndrome is still not available. The usefulness of novel polymorphic and repeat sequences in the presymptomatic diagnosis of the condition has been reported [2, 16]. The importance of diagnosing Marfan's syndrome is to prevent life-threatening complications and afford genetic counseling. Severe aortic regurgitation and acute aortic dissection are the most common complications which usually occur after childhood but may also occur at any age. The value of oral beta-adrenergic blockade in slowing the rate of aortic-root dilatation in

Marfan's syndrome was demonstrated [15]. Following the current recommendation in the management of this condition, we have instituted beta-adrenergic blockade treatment with atenolol in the patient and his affected brother, and undertaken a regular follow-up of the family members with probable cardiovascular risk [17].

Acknowledgment

We would like to thank Mrs. Zahra Karnal and Mrs. Augustilia G. Pinto for their help in preparing the manuscript.

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