Catastrophic cardiovascular consequences of weight lifting in a family with Marfan syndrome

Marfan sendromlu bir ailede ağırlık kaldırmanın yıkıcı kardiyovasküler sonuçları

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Marfan syndrome primarily involves the musculoskeletal, cardiovascular, and ocular systems. Isometric exercises such as weight lifting lead to significant stress along the aortic wall and predispose patients to dissection and rupture. A 30-year-old male patient presented with a complaint of back pain. He had a history of two operations for recurrent inguinal hernia. His father and elder brother died on separate occasions following loss of consciousness after weight lifting. He also had a brother who had undergone an emergency operation for De Bakey type I acute aortic dissection after presentation with acute back pain following weight lifting. The patient was 180 cm tall, had elongated limbs and arachnodactyly. On auscultation, there was a diastolic murmur of 1-2/6 over the aortic area. A chest roentgenogram demonstrated mild cardiomegaly and mediastinal widening. Transthoracic echocardiography showed moderate aortic insufficiency with dilatation of the aortic root and ascending aorta. He was diagnosed as having Marfan syndrome and underwent complete replacement with a composite aortic valve-ascending aortic conduit. Histologic sections of the ascending aortic wall showed medial cystic and myxoid degeneration and loss of nuclei in the media. Von Gieson staining showed elastic fragmentation and loss of elastic lamellae. Screening of other family members showed Marfan syndrome in his sister and in one of his nephews. His other two brothers had Marfanoid habitus without findings of systemic involvement.

Key words: Aneurysm, dissecting/etiology; Marfan syndrome/genetics/complications; weight lifting.

Marfan sendromu esas olarak kas-iskelet, kardiyovasküler ve oküler sistemleri etkilemektedir. Ağırlık kaldırmak gibi izometrik aktiviteler aort duvarı boyunca önemli hemodinamik strese yol açar ve aort diseksiyonu ve yırtılmasına zemin hazırlayabilir. Otuz yaşında bir erkek hasta sırt ağrısı yakınmasıyla başvurdu. Hastanın tekrarlayan inguinal herni nedeniyle iki kez ameliyat geçirdiği; babasının ve bir büyük erkek kardeşinin ağırlık kaldırmaya bağlı gelişen bilinç kaybı sonrasında öldüğü; bir başka erkek kardeşinin de, ağırlık kaldırma sonrası ortaya çıkan sırt ağrısı yakınması nedeniyle yapılan incelemelerde De Bakey tip I akut aort diseksiyonu saptanması üzerine ameliyat edildiği öğrenildi. Boyu 1.80 m olan hastada uzun ekstremiteler ve araknodaktili dikkat çekmekteydi. Oskültasyonda, aort bölgesi üzerinde 1-2/6 şiddetinde üfürüm duyuldu. Göğüs grafisinde hafif kardiyomegali ve mediastinal genişleme izlendi. Transtorasik ekokardiyografide orta derecede aort yetersizliği, aort kökü ve çıkan aortta genişleme saptandı. Marfan sendromu tanısı konan hastaya kompozit aort kapağı-çıkan aort konduiti ile tam replasman uygulandı. Çıkan aort duvarının histolojik kesitlerinde medial kistik ve miksoid dejenerasyon ve media tabakasında çekirdek kaybı; von Gieson boyamasında elastik fragmentasyon ve elastik lamellar kaybı izlendi. Diğer aile bireylerinin taramasında, hastanın kızkardeşinde ve bir erkek yeğeninde de Marfan sendromuna rastlandı; iki erkek kardeşinde ise sistemik tutulum olmaksızın Marfanoid habitus vardı.

Anahtar sözcükler: Anevrizma, diseksiyon/etyoloji; Marfan sendromu/genetik/komplikasyon; ağırlık kaldırma.

Marfan syndrome, originally described in the 19th century, is an autosomal dominant connective tissue disorder associated with the mutation in fibrillin-1 gene located on chromosome 15.[1] It is a multisystemic disorder primarily involving the musculoskeletal, cardiovascular, and ocular systems. Early mortality results primarily from complications associated with aortic dilatation. Isometric exercise such as weight

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lifting causes prominent hemodynamic stress along the aortic wall. This condition may cause aortic dissection in cases with Marfan syndrome.

In this report, we described a carrier family with Marfan syndrome with severe cardiovascular involvement.

CASE REPORT

A 30-year-old male carrier was admitted to our clinic with back pain. He had a history of two operations for recurrent inguinal hernia. Among his family members, his father and elder brother died on separate occasions during transfer to a hospital following loss of consciousness after weight lifting. He also had a brother who had undergone an emergency operation following a diagnosis of De Bakey type I acute aortic dissection on echocardiography performed after presentation to a medical center with acute back pain following weight lifting.

On physical examination, he had hyperlaxity, pes planus, and a scar tissue in the right inguinal region due to previous operations. He was 180 cm tall, had elongated limbs (arm span 196 cm), and arachnodactyly. On auscultation, there was a diastolic murmur of 1-2/6 over the aortic area. Other findings of physical examination were normal. A chest roentgenogram demonstrated mild cardiomegaly and mediastinal widening. His electrocardiogram was normal. Transthoracic echocardiography showed moderate aortic insufficiency with dilatation of the aortic root and ascending aorta (Fig. 1). The patient was diagnosed as having Marfan syndrome based on the Ghent criteria[2] and underwent complete replacement with a composite aortic valve-ascending aortic conduit (Benthall operation) under elective settings. Following an uneventful postoperative course, he was discharged on warfarin and metoprolol treatment on the fifth day. Histologic

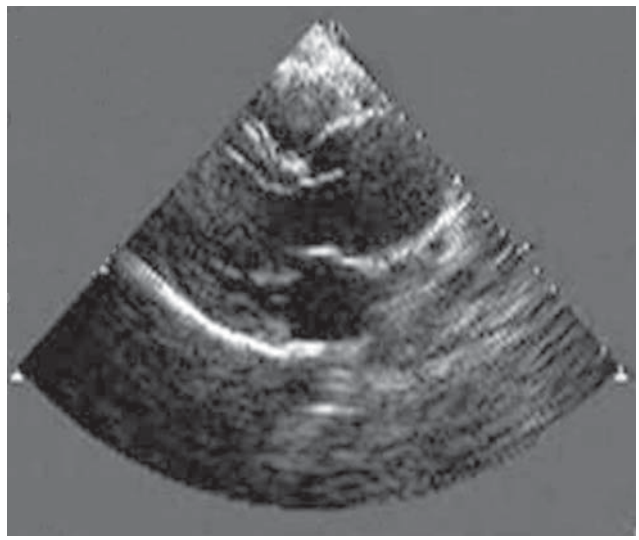

Figure 1. Parasternal long-axis view in systole. Note the dilated aortic root and ascending aorta.

sections of the ascending aortic wall showed no atherosclerotic plaque in the intima. There was medial cystic and myxoid degeneration and loss of nuclei in the media (Fig. 2a). Elastic fragmentation and loss of elastic lamellae were demonstrated with elastic von Gieson stain (Fig. 2b).

Screening of the family members of the patient showed Marfan syndrome in his sister and in one of his nephews, who were then prescribed beta-blocking agents. His other two brothers had Marfanoid habitus without findings of systemic involvement. The presence of a family history (Fig. 3) and the symptoms associated with weight lifting in the deceased father and elder brother were also strongly suggestive of Marfan syndrome.

DISCUSSION

The prevalence of Marfan syndrome is reported between 1/5,000-1/10,000. Although the syndrome is inherited in

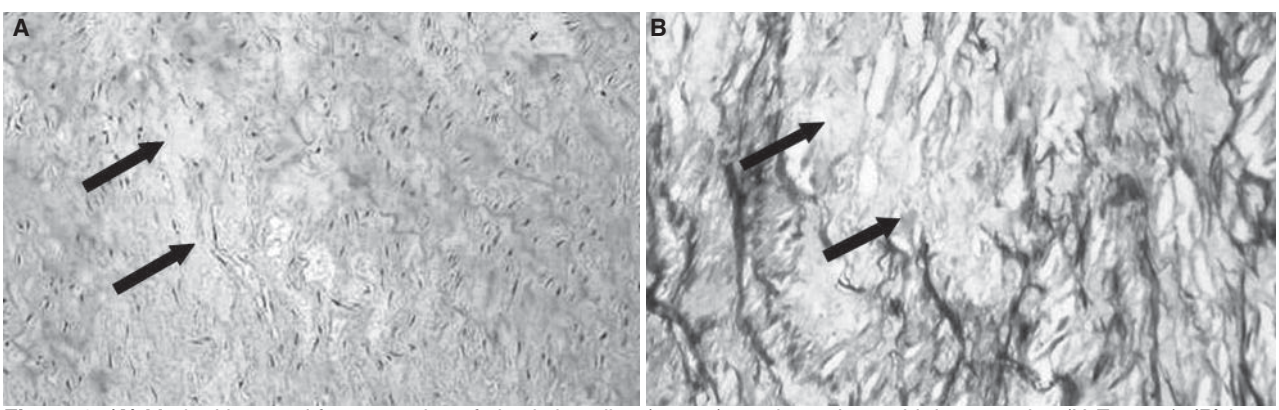

Figure 2. (A) Marked loss and fragmentation of elastic lamellae (arrows), cystic, and myxoid degeneration (H-E x 200). **(B)** Loss (arrows) and fragmentation of elastic lamellae (elastic von Gieson stain x 200).

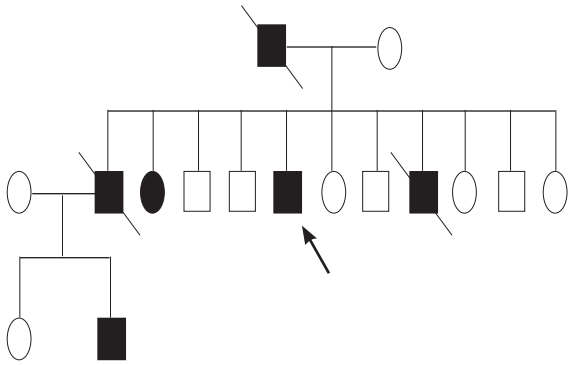

Figure 3. Pedigree of the family. Circle: female family member; rectangle: male family member; cross line: deceased family member; bold symbol: documented Marfan syndrome; arrow: the index case.

an autosomal dominant manner, it may develop due to sporadic mutations in one-fourth of the cases. There is no gender or racial predilection, but affected males show a shorter survival than females.[3]

This multisystemic disorder primarily involves the musculoskeletal, cardiovascular, and ocular systems. Cardiovascular features typically include mitral valve prolapse, progressive dilatation of the proximal aorta leading to aortic regurgitation, aortic dissection, or rupture. Aortic dilatation is progressive throughout life and beta-blockers reduce the rate of dilatation, aortic dissection, and congestive heart failure.[3] Fibrillin-1 is the major candidate protein responsible for Marfan syndrome and its synthesis, secretion or matrix incorporation are affected in the majority of the patients. Fibrillin-1 is a main component of extracellular microfibrils that are important for elastogenesis, elasticity, and homeostasis of elastic fibers. Failure of fibrillin-1 to incorporate into the extracellular matrix leads to fragmentation of elastic fibers, resulting in cystic medial necrosis. These changes in the media of the aortic wall predispose patients to aortic dissection, which is the most common cause of death in Marfan syndrome.[4] Weight lifting is one of the most common type of isometric exercise we perform in our daily life. Isometric exercises lead to rapid increases in systolic and diastolic blood pressure without decrease in total peripheral vascular resistance.[5] These hemodynamic changes lead to significant stress along the aortic wall and predispose to dissection and rupture in cases with cystic changes in the media layer of the aorta as occurs in Marfan syndrome.[6] There are several case reports demonstrating the relationship between aortic dissection and weight lifting in cases with or without Marfan syndrome.[7]

In conclusion, sudden death associated with weight lifting may occur in Marfan syndrome. Individuals with Marfan syndrome or a positive family history should be warned about catastrophic consequences of weight lifting and to avoid isometric activities.

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