Case Report

To Repair or Replace the Mitral Valve in Ehlers-Danlos Syndrome? A Case Report

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Abstract

Cardiac valvular Ehlers–Danlos syndrome (EDS) (type IV) is a rare subtype of the syndrome. The progressive and severe involvement of the heart valves is the principal characteristic of cardiovascular EDS, hence the necessity of the screening of patients with EDS for possible cardiovascular complications.

We herein describe a 17-year-old male patient, with a known case of Ehlers–Danlos syndrome, who was referred to our center due to symptomatic severe mitral regurgitation. Echocardiography showed the flailing of the A3 scallop of the mitral valve (MV) and severe enlargement of the left ventricle and the left atrium with mild systolic dysfunction. A physical examination revealed joint hyperlaxity, skin hyperelasticity, and abdominal hernias. He was, therefore, scheduled for surgery. MV repair was performed via commissuroplasty and ring annuloplasty, with an acceptable saline test. After being weaned from cardiopulmonary bypass, the patient had mild mitral regurgitation, which escalated to moderate-to-severe mitral within minutes. Consequently, the MV was replaced with a bioprosthetic valve. The postoperative course was uneventful.

Due to the high fragility of the MV, any resection and sewing of its fragile leaflets may produce residual regurgitation and necessitate valve replacement. MV replacement may be more logical in such patients. Our patient's postoperative course was uneventful, and he was discharged without symptoms. Over 1 and 3 months of follow-up, he remained asymptomatic, and transthoracic echocardiography showed a normal bioprosthetic MV without paravalvular leakage.

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Introduction

Ehlers–Danlos syndrome (EDS) comprises a group of inherited connective tissue diseases estimated to affect about 1 in 5000 people worldwide. The basic genetic defects are in collagen biosynthesis or structure. There are 13 clinical subtypes of EDS according to the 2017 International Classification of EDS. The phenotypic hallmarks are tissue fragility, joint hypermobility, and skin hyperextensibility.[1,2] Other prominent features of EDS include thin skin, atrophic

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scars, and easy bruising, with inguinal hernia, pectus deformity (especially excavatum), joint dislocations, and foot deformities (eg, pes planus, pes plano valgus, and hallux valgus) constituting minor criteria.[3,4]

Cardiac valvular EDS (type IV) is a rare subtype of the syndrome. It is caused by specific recessive variants in the gene encoding the pro-α2-chain of type I collagen (COL1A2). The major criterion of this subtype is severe progressive cardiac-valvular problems mostly in the aortic valve and the mitral valve (MV). Herein, we report the result of MV surgery on a 17-year-old male patient with severe mitral regurgitation.

Case Report

A 17-year-old male patient, with a known case of EDS, was referred to our center due to severe mitral regurgitation. The patient's presentations were palpitation and exertional dyspnea; nonetheless, his functional status gradually worsened to New York Heart Association functional class III. He had a history of hypothyroidism and 2 surgeries: herniorrhaphy and lipoma resection. On physical examination, he exhibited moderate jugular venous distention with large C-V waves. No right ventricular or left ventricular (LV) heave was found, and cardiac auscultation confirmed a grade IV/XI holosystolic apical murmur. Additionally, fine crackles at the base of both lungs were audible. The extracardiac findings of the physical examination were joint hyperlaxity, skin hyperelasticity, skin translucence, and scar from previous surgeries (Figure 1).

Electrocardiography revealed a normal sinus rhythm, without significant changes (Figure 2). Transthoracic echocardiography demonstrated severe LV enlargement

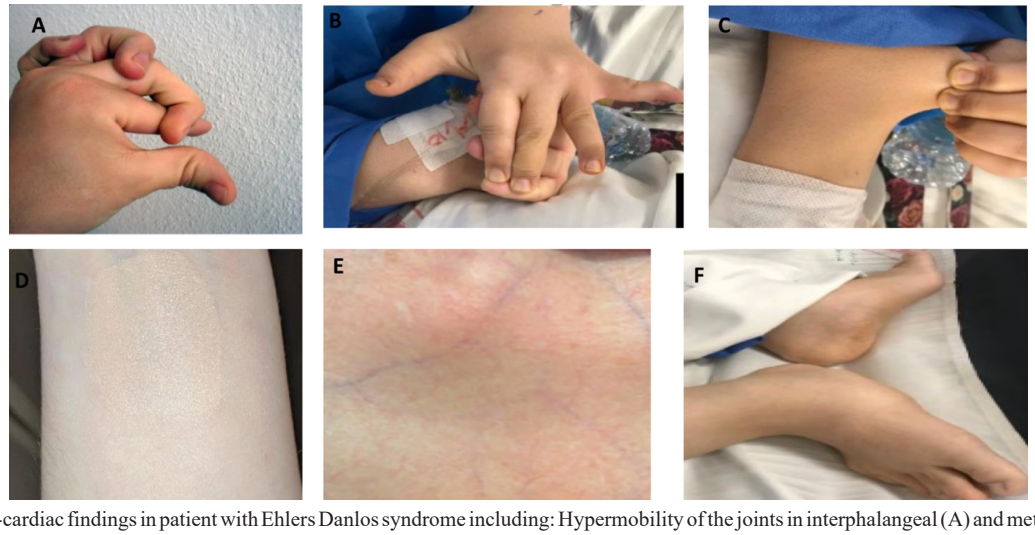

Figure 1. Extra-cardiac findings in patient with Ehlers Danlos syndrome including: Hypermobility of the joints in interphalangeal (A) and metacarpophalenghial (B). Skin hyperextensibility (C): This refers to the ability to stretch the skin beyond its normal range.
Cutaneous features of vascular Ehlers-Danlos syndrome include: thin translucent skin with visible veins (D, E) due to decrease of collagen. Foot deformity: low-arched and flat feet (F)

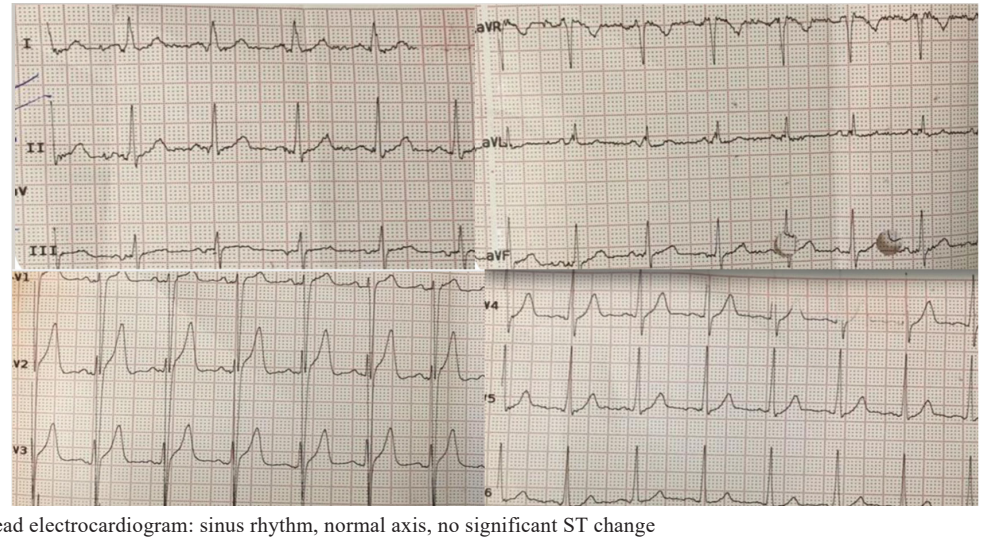

Figure 2. Twelve-lead electrocardiogram: sinus rhythm, normal axis, no significant ST change

(LV ejection fraction ≈55%), LV hyper trabeculation, normal right ventricular size and function, and severe left atrial enlargement. In addition, the MV was thickened and myxomatous, and there was A3 scallop prolapsing (Figure 3), with a linear echodensity at the tip of this scallop, in favor of ruptured chordae (Videos 1–3).

A computed tomography angiography of the thoracic aorta ruled out associated aortopathy and vasculopathy.

Via a median sternotomy with cardiopulmonary bypass and cardioplegic arrest, MV repair was attempted. Notably, the tissue of the MV was fragile. The MV was repaired through commissuroplasty and ring annuloplasty (CG Future, size 26, Medtronic Co), with an acceptable saline test.

Having just been weaned from cardiopulmonary bypass, the patient exhibited mild mitral regurgitation, which worsened to moderate-to-severe within minutes. As a result, the MV was replaced with a bioprosthetic valve. The postoperative course was uneventful, and the patient was discharged without symptoms. Over 1 and 3 months of follow-up, he remained asymptomatic, and transthoracic echocardiography showed a normal bioprosthetic MV without paravalvular leakage.

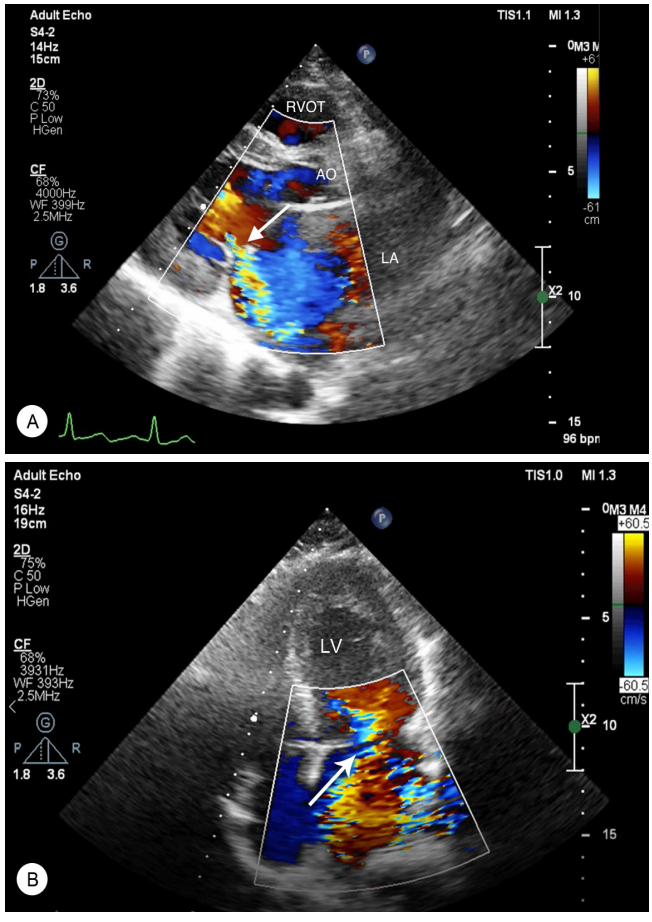

Figure 3. Continuous Doppler analysis of mitral regurgitation, Trans thoracic echocardiography four chamber view (A) and long axis view (B) showed flail of anterior leaflet of mitral valve with severe posterior lateral jet (Arrow)

Discussion

EDS is a complex disease caused by mutations in genes involved in the structure and biosynthesis of collagen, leading to alterations in the structure of many tissues and organs. The cardiac-valvular and vascular involvements of EDS are seen in subtype IV of the disease, with significant cardiovascular characteristics, specifically aortic or MV dysfunction, as well as arterial dilatation and dissection. Specific recessive variants in the gene encoding COL1A2 are known to be responsible for this syndrome. The progressive and severe involvement of the heart valves is the principal characteristic of cardiovascular EDS; consequently, it is necessary to screen patients with EDS for possible cardiovascular complications.[5] We herein presented a case of EDS with severe mitral regurgitation and progressive LV dilatation. The patient's severe mitral regurgitation placed him at risk for LV failure, and he ultimately underwent cardiac surgery at the discretion of the heart team.

The literature contains only a few cases of MV surgeries in patients with EDS, and the standard timing of cardiovascular evaluation for cardiovascular abnormalities has yet to be determined. Furthermore, information is scarce regarding cardiac interventions in this group of patients.

Wiesmann et al[6] reported a case of EDS type I undergoing MV replacement. Unfortunately, the patient expired due to fulminant cardiac failure secondary to a massive paravalvular leak of the prosthetic MV. In contrast, Avlonitis et al[7] reported a successful MV replacement in a patient with EDS type III.

In patients with EDS, who are at high risk for serious bleeding, any intervention may beget complications that occur far less frequently in the general population. Indeed, even orotracheal intubation may cause the dislocation of the temporomandibular joint. The fragility of the internal organs could also prompt spontaneous ruptures.

We described a boy, a known case of EDS, with symptomatic severe mitral regurgitation, severe LV dilation, and reduced LV systolic function. Notably, selecting the best approach to severe mitral regurgitation management is a formidable challenge given the paucity of practical recommendations and the risk of related complications during surgery. What complicates the matter further is the fact that when the healing conditions are seriously affected, cardiac surgery becomes much more controversial. In this patient, the heart team opted for MV surgery due to his symptoms and progressive LV enlargement. Logically, MV repair seems preferable, even in cases similar to ours. Nevertheless, following MV repair and weaning from cardiopulmonary bypass, our patient's mitral regurgitation increased to a moderate-to-severe level, forcing us to finally perform MV replacement with a bioprosthetic valve. It is worthy of note that if mitral regurgitation is caused solely by annular dilation, ring annuloplasty may confer good results.

The selection of the bioprosthetic valve, in this case, was

left to the patient and his family. It was an appropriate choice because of the nature of fragile tissues in patients with EDS, rendering them susceptible to bleeding.

Our patient developed hemarthrosis 20 days after surgery, so we temporarily discontinued his novel oral anticoagulant (NOAC) safely. Subsequently, 4 months after surgery, we discontinued the NOAC. Permanent anticoagulation of mechanical valves is not desirable in patients with EDS because it would add to the risk of bleeding.[8] Still, it is feasible to safely discontinue anticoagulation for bioprosthetic valves after 3 to 6 months.

Conclusion

The cardiac-valvular type of EDS is a rare subtype with a dearth of evidence concerning its management. Challenging complications are expected during therapeutic procedures. In this group of patients with EDS, MV replacement should be preferred to mitral regurgitation repair, with bioprosthetic valves being a more logical option than mechanical valves.

To watch the following videos, please refer to the relevant URLs:

https://jthc.tums.ac.ir/index.php/jthc/article/view/1682/1041
Video 1. Trans thoracic echocardiography, parasternal long axis view showed Flail of anterior leaflet

https://jthc.tums.ac.ir/index.php/jthc/article/view/1682/1042
Video 2. Trans thoracic echocardiography, four chamber view showed severe posterior lateral jet mitral regurgitation.

https://jthc.tums.ac.ir/index.php/jthc/article/view/1682/1043
Video 3. Trans thoracic echocardiography, parasternal long axis view showed severe posterior lateral jet mitral regurgitation.

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