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Klippel–Feil syndrome: A very unusual cause of severe aortic regurgitation visualized by multimodality imaging

Monica Ahluwalia MD[1] | Sankalp Sehgal MD[2] | Alan F. Vainrib MD[1] | Robert Applebaum MD[1] | Larry Latson MD[3] | Mathew R. Williams MD[4] | Muhamed Saric MD, PhD[1]

[1]Leon H. Charney Division of Cardiology, NYU Langone Health, New York, New York

[2]Department of Clinical Anesthesiology, Weill Cornell Medicine, New York, New York

[3]Department of Radiology, NYU Langone Health, New York, New York

[4]Department of Cardiothoracic Surgery, NYU Langone Health, New York, New York

Correspondence
Monica Ahluwalia, MD, Leon H. Charney Division of Cardiology, NYU Langone Health, New York, NY.
Email: Monica.Ahluwalia@nyumc.org

Abstract

A 51-year-old man with Klippel–Feil syndrome (KFS) and immunodeficiency syndrome, status postintravenous immunoglobulin therapy, presented with shortness of breath. He was found to have severe aortic regurgitation in the setting of a trileaflet aortic valve with thickened leaflets and mild prolapse of the right coronary cusp with left ventricular dilation and borderline left ventricular ejection fraction. Although various cardiac anomalies have been described in KPS, otherwise unexplained severe aortic regurgitation has not been previously reported to the best of our knowledge. The patient underwent an uncomplicated surgical aortic valve replacement with a 25-mm Medtronic Avalus pericardial tissue valve resulting in symptomatic improvement. Intra-operative management and transesophageal echocardiography can be particularly challenging in KFS patients. We describe the first reported case of severe aortic regurgitation in KPS, review the cardiac anomalies associated with the syndrome, and highlight the clinical challenges in intra-operative management of these patients.

KEYWORDS

aortic regurgitation, cervical vertebral syndrome, Klippel–Feil syndrome

1 | INTRODUCTION

Klippel–Feil syndrome (KFS) or cervical vertebral syndrome is a rare, congenital disease characterized by a spectrum of spinal deformities due to a primary defect in the formation of the cervical vertebrae initially described in 1912 by Maurice Klippel and Andre Feil from France.[1] KFS includes a classic triad of congenital fusion of two or more cervical vertebrae (above or below C3), a short neck and low hairline.[1] Several genetic mutations have been associated with KFS including GDF6, GDF3, and MEOX1 that are involved in transcription regulation and signaling pathways affecting somite development.[2]

Although the exact prevalence is unknown, it is estimated to occur in 1 out of 40 000–42 000 newborns, with approximately equal distribution between men and women.[3] Associated anomalies include scoliosis, spina bifida, cleft palate, scapular deformity, rib defects, other skeletal malformations, neurological, and genitourinary abnormalities.[1] Cardiac anomalies are relatively rare and may occur in up to 4%–5% of these patients.[4] We describe the first report of severe aortic regurgitation in a patient with KFS.

2 | CASE REPORT

A 51-year-old man with KPS presented with shortness of breath and decreased exercise tolerance. His past medical history was notable for C1–C3 fusion (Figure 1), multiple lumbar and spinal deformities complicated by radiculopathy, and immunodeficiency syndrome requiring intravenous immunoglobulin therapy. On physical examination, the patient was 5 ft tall, weighed 139 pounds (body mass index 27.3 kg/m^2), and had a short and wide neck, low hairline, and

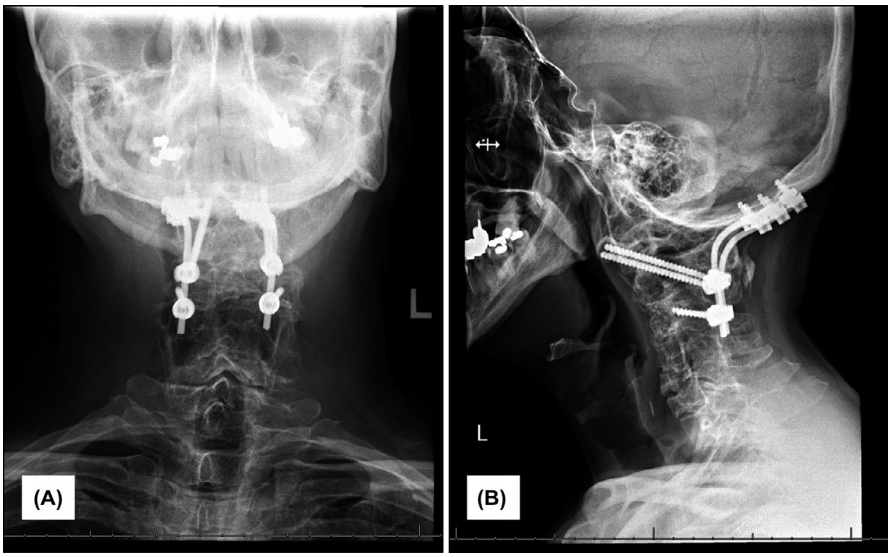

FIGURE 1 Anteroposterior (A) and lateral (B) cervical X-ray images show prior posterior fusion with hardware from the occiput to C3 level. There are multiple cervical vertebral body deformity and fusions consistent with known Klippel–Feil syndrome

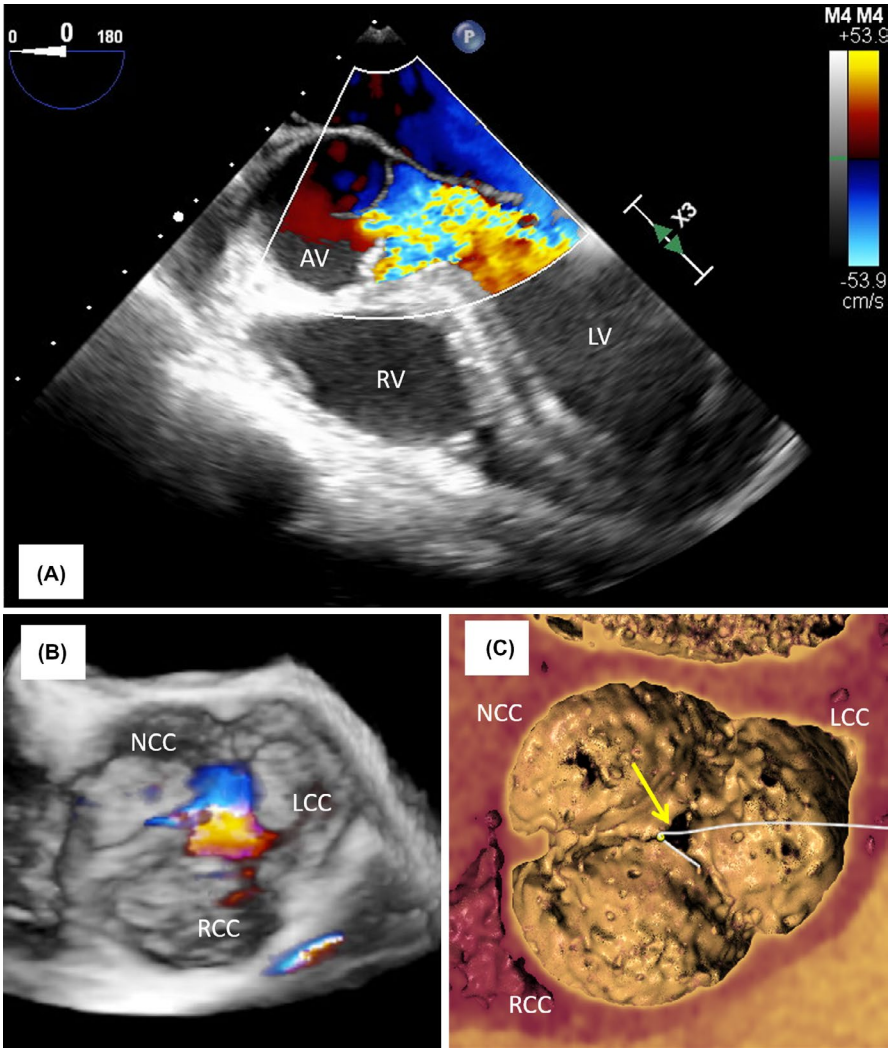

FIGURE 2 Panel A shows severe aortic regurgitation on intra-operative transesophageal mid-esophageal view. Movie S1 corresponds to Panel A. Panel B shows 3D color image revealing thickened aortic valve leaflets and leaflet malcoaptation resulting in severe aortic regurgitation, which has a central regurgitant orifice. Movie S2 corresponds to Panel B. Panel C shows contrast-enhanced 3D computed tomography imaging of trileaflet aortic valve and malcoaptation of leaflets. Movie S3 corresponds to Panel C. AV = aortic valve; LCC = left coronary cusp; LV = left ventricle; NCC = noncoronary cusp; RCC = right coronary cusp; RV = right ventricle

limited neck mobility. Vital signs were normal except for a widened pulse pressure. Cardiovascular examination demonstrated normal heart sounds with a mid-systolic murmur in the left sternal border along with a blowing holodiastolic murmur. He had bounding distal pulses. Laboratory data were unremarkable except for very low immunoglobulin A and M levels. Electrocardiogram showed normal sinus rhythm at a heart rate of 70 beats per minute and left anterior fascicular block.

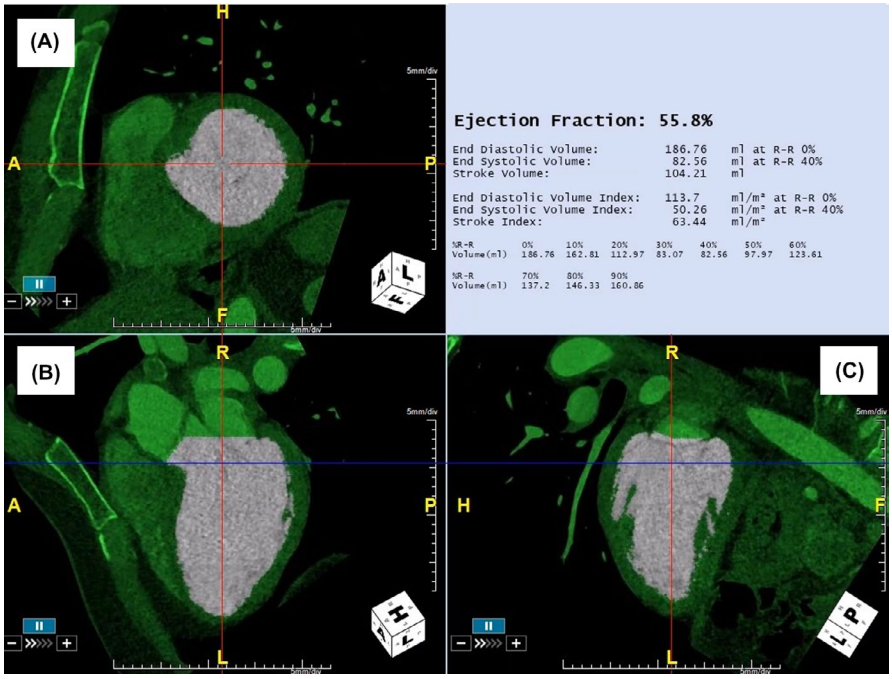

FIGURE 3 Short-axis (Panel A) and long-axis (Panels B & C) 3D contrast-enhanced computed tomography diastolic images demonstrate left ventricular dilation and increased stroke volume in the setting of severe aortic regurgitation. Movie S4 corresponds to Figure 3

A transthoracic echocardiogram revealed severe aortic regurgitation with left ventricular dilation and a borderline normal left ventricular function with an ejection fraction of 50%–55%. Patient was referred for surgical aortic valve replacement given symptomatic severe aortic regurgitation. On intra-operative transesophageal echocardiogram, his aortic valve was trileaflet with thickened leaflets (Figure 2, Panels A and B; and Movies S1 and S2). The right coronary cusp had a mild prolapse. The aortic regurgitation was severe with a central regurgitant orifice and a jet directed anteriorly along the anterior leaflet of the mitral valve. There was no evidence of any mass or vegetation on the valve leaflets to suggest endocarditis. Contrast-enhanced 3D computed tomography (CT) of the chest confirmed the trileaflet anatomy of the aortic valve (Figure 2, Panel C and Movie S3) and demonstrated left ventricular dilation with a large stroke volume (Figure 3 and Movie S4). In addition, aortic dimensions were normal. There was no evidence of coarctation of the aorta or ventricular septal defect.

The patient underwent an uncomplicated surgical aortic valve replacement with 25-mm Medtronic Avalus pericardial tissue (Medtronic) with normal prosthetic gradients and no evidence of paravalvular or transvalvular aortic regurgitation. The patient was intubated successfully after second attempt using a video laryngoscope. Although moderately difficult, the intubation was atraumatic. The TEE probe was inserted after a jaw thrust, and there was no resistance upon probe advancement. The patient was extubated post-operative day 0 without any complications.

3 | DISCUSSION

Cardiac anomalies in KFS are relatively rare and can occur in up to 4%–5% of these patients.[4] Ventricular septal defects[4] and coarctation of the aorta[5] have been most commonly described. Less commonly described anomalies include congenital complete heart block,[6] atrial septal defect,[7] aortic and vertebral artery anomalies,[8] ruptured aneurysm of sinus of Valsalva,[9] total anomalous pulmonary venous connection,[10] and levotransposition of great arteries.[11] To the best of our knowledge, this is the first report of KFS-associated severe aortic regurgitation in the setting of trileaflet valve and normal aortic dimensions, thickened leaflets, leaflet malcoaptation, and mild prolapse of right coronary cusp (Figure 2).

In this patient, it appears that KFS per se may have led to severe aortic regurgitation. An alternative explanation could have been his immunodeficiency. However, he did not have immunoglobulin G4-related disease[12] or DiGeorges,[13] the immunodeficiency syndromes previously reported to be associated with aortic valve disease. This patient underwent successful aortic valve replacement with a bioprosthesis with subsequent symptomatic improvement.

Although this patient had an uneventful course under general anesthesia, it is important to recognize that intra-operative management with securing an airway and positioning a KFS patient can be challenging in the setting of cervical fusion.[14] These patients are at high risk for cervical spinal cord and neurological injury. Associated atlantoaxial instability, torticollis, and a short webbed neck can cause limited cervical range of motion. Other spinal and skeletal deformities in KFS may include congenital thoracolumbar kyphoscoliosis, Sprengel's deformity (congenital high scapula), and spina bifida[1] that can make regional anesthesia and catheter placement technically challenging.

Additionally, jaw anomalies in KFS such as mandibular hypoplasia and cleft palate can be associated with upper airway obstruction and obstructive sleep apnea. Furthermore, unstable spine may lead to neurological injury upon head manipulation and positioning, and general anesthesia can be complicated by both difficult ventilation

and difficult intubation.[14] Using awake oral or nasal fiberoptic intubation while maintaining spontaneous ventilation would be ideal and the safest way to secure the airway.[14,15] Similarly, extubation should be performed when the patient is fully awake and protective airway reflexes are established. Overall, recognizing these challenges is imperative and an awake intubation should be planned. If transesophageal echocardiogram cannot be obtained, epicardial echocardiography can be used to help guide the surgeon.

4 | CONCLUSION

In summary, KFS can be rarely associated with cardiac anomalies. Atrial and ventricular septal defect, coarctation of aorta, aortic and vertebral artery anomalies, transposition of the great arteritis, sinus of Valsalva aneurysm, and anomalous pulmonary venous return have been previously described. This case highlights a patient with severe aortic regurgitation who underwent successful aortic valve replacement and uneventful course. Intra-operative management and transesophageal echocardiography can be particularly challenging in these patients.

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ORCID

Monica Ahluwalia https://orcid.org/0000-0002-4487-731X
Sankalp Sehgal https://orcid.org/0000-0002-4204-7929
Alan F. Vainrib https://orcid.org/0000-0002-0832-8452

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Movie S1. On transesophageal echocardiogram, mid-esophageal view, there is severe aortic regurgitation and mild prolapse of the right coronary cusp. AV = aortic valve; LV = left ventricle; RV = right ventricle.

Movie S2. 3D color image of aortic valve reveals thickened aortic valve leaflets and leaflet malcoaptation resulting in severe aortic regurgitation, which has a central regurgitant orifice. LCC = left coronary cusp; NCC = non-coronary cusp; RCC = right coronary cusp.

Movie S3. Contrast-enhanced 3D computed tomography imaging demonstrates trileaflet aortic valve and malcoaptation of leaflets. LCC = left coronary cusp; NCC = non-coronary cusp; RCC = right coronary cusp.

Movie S4. Contrast-enhanced 3D computed tomography short-axis and long-axis views show left ventricular dilation and left ventricular ejection fraction of 55%.

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