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Case Report

A Patient with Werner's Syndrome Who Underwent Aortic Valve Replacement through Minimally Invasive Cardiac Surgery

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Werner's syndrome (WS) is a genetic disorder presenting with premature senility. In the present study, we performed minimally invasive cardiac surgery (MICS)-aortic valve replacement (AVR) on a patient with Werner's syndrome who presented with aortic stenosis. The patient, a 49-year-old Japanese man, was brought to the emergency room with dyspnea during exercise. On echocardiography, severe aortic stenosis was found and surgery was planned. He had poorly controlled diabetes mellitus and underwent MICS-AVR to avoid the risk of sternal osteomyelitis, which resulted in a good outcome. The aortic valve had sclerotic changes and a genetic disease was suspected based on the onset of aortic stenosis at a young age, characteristic appearance, and various signs of aging. Genetic testing led to the diagnosis of WS.

Keywords: Werner's syndrome, MICS-AVR

Introduction

Werner's syndrome (WS), an autosomal recessive genetic disease, was initially reported by Otto Werner in 1904. It is a progeroid syndrome because several progeroid signs, such as gray hair and cataracts, become apparent after adolescence. This is review of the pertinent literature and a case report of a patient with WS who experienced aortic valve stenosis and received minimally invasive cardiac surgery (MICS) for aortic valve replacement (AVR).

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Case Report

A 49-year-old man experienced dyspnea during exercise and was transferred to a local clinic. A cardiac murmur was detected, and cardiac ultrasound revealed aortic valve stenosis. The patient was referred to our hospital for further examination and treatment. Surgery was indicated because he was diagnosed with severe aortic valve stenosis (maximum blood flow velocity, 4.99 m/s; pressure gradient [PGAV], 61.9 mmHg; aortic valve area, 0.46 cm^2).

Outpatient examination revealed a high-pitched hoarse voice, a bird-like facies (**Fig. 1**), and generalized skin atrophy. At 40 years of age, the patient presented to an otolaryngologist and was diagnosed with hoarse voice caused by type 2 sulcus vocalis according to the classification of Ford. Transplantation of fascia into the vocal fold and thyroplasty were performed at the ages of 40 and 45, respectively. However, the hoarse voice persisted.

Blood tests showed diabetes mellitus with poor glycemic control (hemoglobin A1c [HbA1c], 12.7%). The patient had a history of bilateral cataracts, dyslipidemia, and a refractory plantar ulcer. Cardiac catheterization did not show any significant coronary artery lesions.

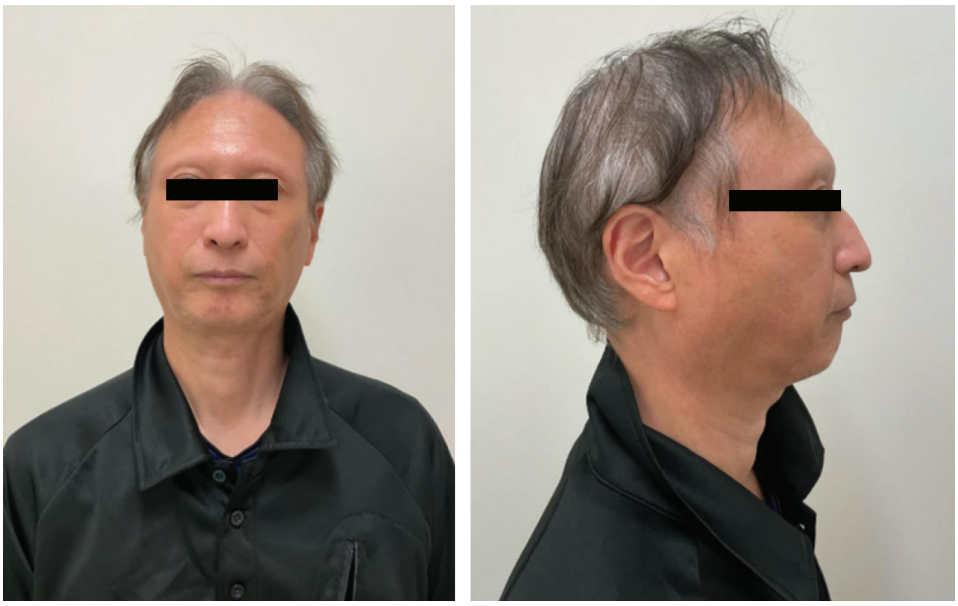

Fig. 1 A bird-like face and gray hair. The Photos are published with the patient's permission.

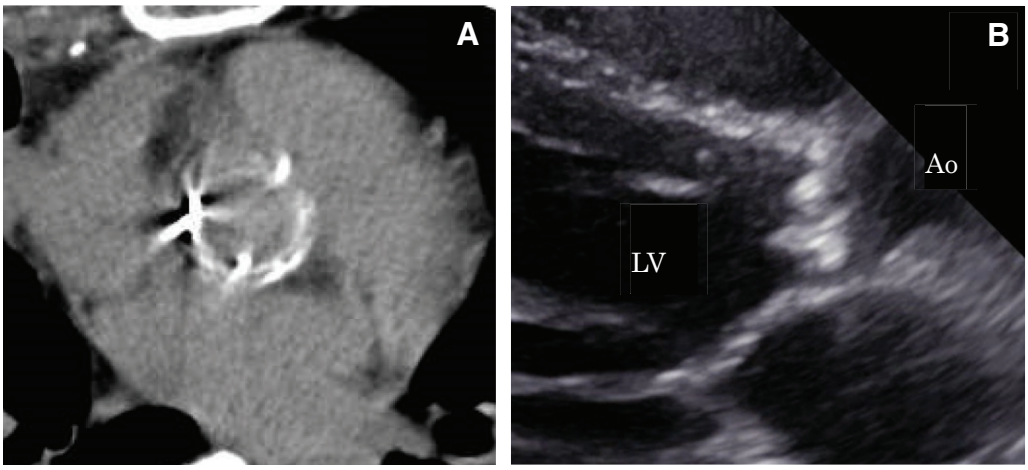

Fig. 2 (**A**) CT scan showing calcification of the STJ. (**B**) High degree of calcification of the aortic valve leaflets and cusps on echocardiography. CT: computed tomography; STJ: sinotubular junction; LV: left ventricle

Computed tomography and cardiac ultrasound showed severe calcification in the sinotubular junction, aortic annulus, and valve leaflets, despite the patient's young age (**Figs. 2A** and **2B**). The patient had no noteworthy family history.

To maintain blood glucose levels between 150 mg/dL and 200 mg/dL, the patient was hospitalized to receive intensive insulin therapy for 1 week prior to surgery.

AVR was performed by MICS through a right mini-thoracotomy. With the patient in the left lateral decubitus position, extracorporeal circulation was initiated with a venous cannula inserted into the right femoral artery and an arterial cannula inserted into the femoral vein. Thoracotomy was performed via an approach from the third intercostal space of the right anterior chest. Aortotomy was performed using cardioplegia. The aortic valve was tricuspid with senile changes including sclerotic changes associated with significant calcification in the valve cups and annulus (**Fig. 3**). The aortic valve was resected, and the calcification in the annulus was removed by using ultrasonic sonopet with a knife. A prosthetic valve (23 mm Mosaic; Medtronic, Dublin, Ireland) was sutured with 12 stitches using a braided suture accompanying a 5-mm spaghetti-type accessory (2-0 in diameter; Wayolax; Matsuda Ika Kogyo Company, Tokyo, Japan) via everting mattress. The postoperative course was uneventful, and the patient was discharged on postoperative day 18.

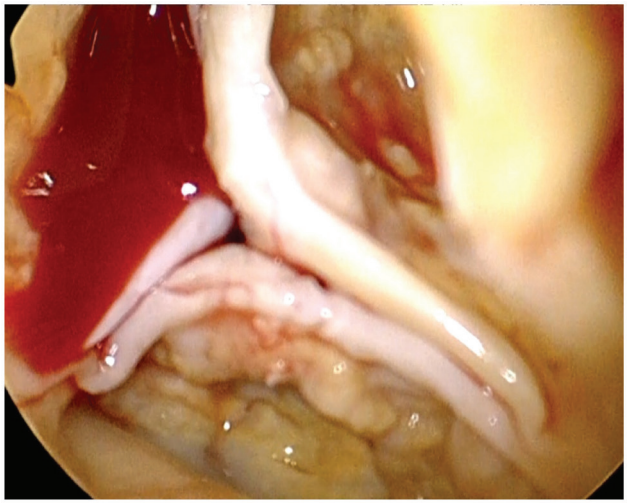

Fig. 3 Sclerotic changes in the aortic valve.

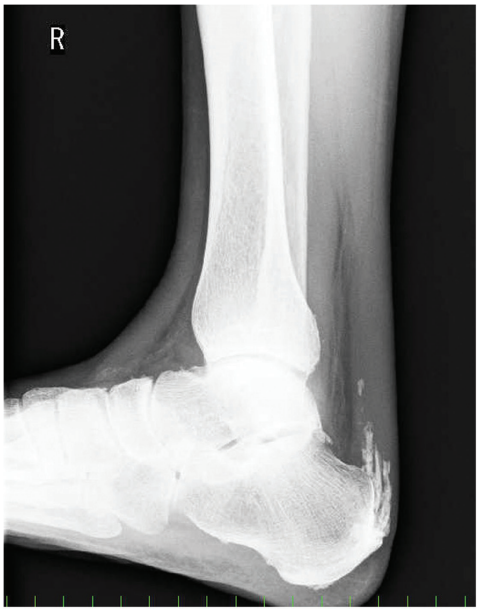

Fig. 4 Calcification of the Achilles tendon.

Genetic disease was suspected based on the patient's medical history and severe aortic valve stenosis due to sclerotic changes, although he was young. Ankle radiography showed calcification of the Achilles tendon (**Fig. 4**), and the patient's radiographic findings correlated with the major signs of the diagnostic criteria for WS. Subsequently, genetic testing was performed; the results showed a homozygous mutation 4, and the patient was diagnosed with WS.

Discussion

Werner's syndrome, a type of progeria and a rare genetic disease, was initially reported by Otto Werner in 1904. In Japan, there are approximately 2000 patients with WS, which accounts for two-thirds of all cases globally. No therapeutic methods are currently available. In patients with WS, arteriosclerotic disease and malignant tumors are the two main causes of death, and the patients' mean life expectancy is 54 years.[1)]

The main signs of Werner's syndrome are (1) progeroid hair changes (gray hair and baldness), (2) bilateral cataracts, (3) skin atrophy/skin sclerosis (corns and callus), (4) refractory ulceration, (5) calcification of soft tissues (e.g., the Achilles tendon), and (6) a bird-like facies. Other signs of WS include (a) high-pitched hoarse voice, (b) abnormal glucose and lipid metabolism, (c) bone disorders such as osteoporosis, (d) nonepithelial tumors and thyroid cancer, (e) consanguineous marriage, (f) early-onset arteriosclerosis, (g) primary hypogonadism, and (h) short stature and low weight. Patients who have all main signs or who meet ≥3 main signs and have the gene mutation are definitively diagnosed with Werner's syndrome.[2)] Since our patient met all main signs and genetic testing revealed changes specific to the syndrome, he was diagnosed with WS.

A literature search was performed on articles published between 1994 and 2019 regarding patients with WS who underwent aortic valve stenosis repair, which identified only 6 patients.[3–8)] Ages ranged from 18 to 66 years. The types of valves were a homograft (1 patient), bioprosthesis (1 patient), transcatheter aortic-valve implantation (TAVI) (1 patient), and mechanical aortic valve (3 patients). Median sternotomy was performed on all patients except for the patient receiving a TAVI. No patient underwent MICS.

Severe diabetes mellitus develops in some patients with WS. To prevent this complication, our patient received treatment; however, he experienced diabetes mellitus with poor glycemic control (HbA1c, 12.7%). Although, glycemic control was accomplished in the hospital preoperatively, there was concern over the risk of sternal osteomyelitis following median sternotomy.[9)] Thus, MICS was performed through a right mini-thoracotomy, which prevented the risk of sternal osteomyelitis.

Mechanical valves are generally preferred at the patient's age. Considering that this patient presented with severe diabetes mellitus, severe systemic arteriosclerosis, and various comorbidities that had developed from a young age, these conditions were considered likely to cause diseases such as embolism and hemorrhage in the future. At that time, we predicted that it would be difficult to continue anticoagulant therapy for

the mechanical valve or that anticoagulant therapy would interfere with the treatment. Therefore, a bioprosthetic valve was selected with the patient's consent. The patient was diagnosed with WS after surgery; however, it was our understanding that selecting a bioprosthetic valve was appropriate, owing to the prognosis of this disease.

A bioprosthesis was used as a prosthetic valve in accordance with the patient's request. If the valve deteriorates in the future, TAVI treatment is considered to be the first choice. Since the patient has no history of median sternotomy, there are no concerns about sternal adhesion, thus preventing secondary damage and reducing the risk if valve implantation is required in the future.

AVR through MICS may be an extremely effective treatment method for Werner's syndrome.

Conclusion

In this study, AVR was performed through MICS on a patient with WS who experienced aortic valve stenosis, which resulted in a favorable outcome.

Disclosure Statement

There are no competing or conflicts of interest in relation to the submitted manuscript.

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