

Patient with Behçet Syndrome with Subaortic Pseudoaneurysm Who Underwent the Bentall Operation Showed Improvement after Medical Treatment

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Aortic regurgitation (AR) in children is usually caused by congenital valve anomalies, and Behçet syndrome (BS) can be suspected in cases of isolated AR. Patients with BS undergoing aortic valve surgery due to aortic valve invasion have a high risk of complications, such as leakage around the valve and dehiscence. Cardiovascular involvement occurs in 7%–46% of adult patients with BS and is the main cause of mortality; however, its prevalence is unclear and rare in children. A 12-year-old boy was diagnosed with severe AR associated with BS. A progressive subaortic pseudoaneurysm was observed after aortic valve replacement. The periaortic intracardiac pouch was at risk of rupture; therefore, the patient underwent a Bentall operation. After the Bentall procedure, a newly developed subaortic pseudoaneurysm was detected below the prosthetic valve. However, the risk of rupture reduced as the subaortic pseudoaneurysm regressed with anti-inflammatory drugs alone without reoperation. Repeated surgery is inevitable in patients with BS undergoing aortic valve surgery due to the progressive chronic inflammatory reactions that present with a pseudoaneurysm. Here, we report an 8-year follow-up of a pediatric case of BS with subaortic pseudoaneurysm, highlighting the importance of close follow-up, medical management, and early diagnosis in treating this condition.

Key Words: Behçet syndrome, pediatric, aortic valve insufficiency, pseudoaneurysm

INTRODUCTION

Aortic regurgitation (AR) rarely occurs as an isolated lesion in children and is usually associated with congenital heart diseases, such as bicuspid aortic valve disease, aortic stenosis, or ventricular septal defect.^{1,2} Behçet syndrome (BS) can be suspected

in cases of isolated AR accompanied by symptoms such as oral ulcers. Several criteria have been proposed for diagnosing and classifying BS. Generally, these include mucous, skin, ocular, and vascular manifestations and positive pathergy test.^{3,4} Cardiovascular involvement occurs in 30% of adult patients with BS, and aortic root disease is a major cause of death.^{5,6} Patients with BS undergoing aortic valve surgery due to aortic valve involvement have a high risk of complications, including perivalvular leakage and valve dehiscence. Furthermore, these patients often require repeated surgeries due to progressive chronic inflammatory responses.^{5,7} We encountered a pediatric patient with BS, who had a pouch-like formation under the prosthetic valve after the first valve operation. We present a rare case that showed a good prognosis during an 8-year follow-up, including spontaneous regression of a subaortic pseudoaneurysm, on performing the Bentall operation in parallel with anti-inflammatory therapy. The patient provided informed

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consent to publish relevant data in this manuscript.

CASE REPORT

A 12-year-old boy [height 149 cm, body weight 36 kg, body surface area (BSA) 1.22 m²] was referred to our hospital for severe AR. He had a history of repeated oral ulcers for the last 3–4 years, leading to a diagnosis of BS based on recurrent symptoms at two or more sites. Echocardiography revealed severe AR due to sinus of valsalva aneurysm and perforation of the non-coronary cusp (NCC) (Fig. 1A and B). After treatment with prednisolone 5 mg thrice daily, mesalazine 500 mg once daily, and colchicine 0.6 mg twice daily for approximately 3 months, his aortic valve was replaced with a St. Jude Epic 21 mm prosthesis (Fig. 1C and D). After 6 months, two large outpouching lesions below the aortic annulus (right coronary cusp and NCC side), suggestive of pseudoaneurysm, were found and attributed to the progression of aortitis (Fig. 2A, B, D, and E). Even when preoperative normalization of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were confirmed after medical treatment, pseudoaneurysm developed again after surgery and CRP was elevated up to 14–110 mg/L on postoperative days 1–25. Due to the risk of rupture, the patient was

hospitalized. After confirming that the elevation of the inflammatory marker CRP was stabilized with 2 weeks of intensive drug treatment (including steroids), a Bentall operation with a cryopreserved homograft (20 mm) was performed due to myxomatous changes of aortic wall and subaortic pseudoaneurysm closure (Fig. 2C). The patient continued treatment with anti-inflammatory drugs, including prednisolone (5 mg thrice daily), mesalazine (500 mg once daily), colchicine (0.6 mg twice daily), and methotrexate (7.5 mg once weekly). The postoperative follow-up at 1–2 month intervals revealed no unusual findings. However, at 9 months postoperatively, a new pseudoaneurysm formed below the prosthetic valve. Perivascular dehiscence and pouches were also observed. Medical treatment was changed to prednisolone (10 mg twice daily), cyclophosphamide (50 mg twice daily), azathioprine (50 mg twice daily), and methotrexate (7.5 mg once weekly) (The patient's height is 156 cm, body weight is 50.6 kg, and BSA is 1.48 m²).

Approximately 3 years later, the perivalvular dehiscence improved and closed spontaneously, the residual pseudoaneurysm under the artificial valve regressed, and the risk of rupture was reduced (Fig. 3). Thereafter, the patient has been receiving medical treatment (methotrexate 10 mg once weekly, clopidogrel 75 mg once daily, and losartan 50 mg once daily) without any specific symptoms for the last 8 years.

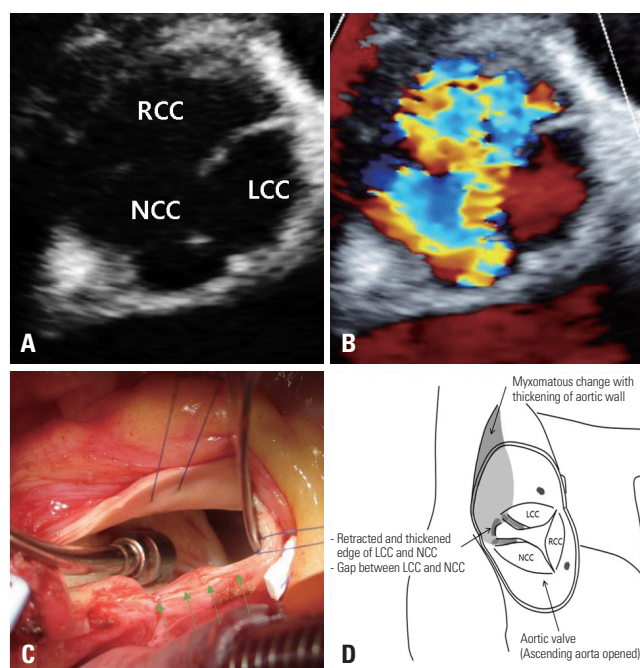


Fig. 1. Initial findings of aortic lesion. (A and B) Initial pre-operative TTE images. Findings from the parasternal short-axis view showed severe AR, suspected to be due to a sinus of Valsalva aneurysm and cusp perforation of the NCC. (C) Operative findings during AVR. Myxomatous change with thickening at the posterior wall above the sinotubular junction was observed (arrows). The other parts looked grossly normal. (D) Mechanism of AR identified during AVR. AR, aortic regurgitation; AVR, aortic valve replacement; TTE, transthoracic echocardiogram; LCC, left coronary cusp; NCC, non-coronary cusp; RCC, right coronary cusp.

DISCUSSION

BS, first described by Behçet in 1937, is a chronic inflammatory disease with a relapsing course.⁸ The diagnostic criteria for Behçet's disease include those established by the International Study Group for Behçet's disease (ISG), published in 1990, and the International Criteria for Behçet's disease (ICBD), published in 2014. According to the ISG criteria, patients with recurrent oral ulcers are diagnosed with BS if they also present with at least two of the following: genital ulcers, eye lesions, skin lesions, or a positive pathergy test. The ICBD criteria use a scoring system that assigns two points for oral ulcers, genital ulcers, and ocular lesions, and one point for a positive pathergy test and neurologic and vascular involvement; a score of 4 or higher confirms the diagnosis.^{3,4,9,10} The disease course is characterized by frequent relapses and spontaneous remission.¹⁰ Although arterial involvement accounts for only 3%–5% of cases,¹¹ vascular signs are a major predictor of mortality and morbidity in BS.^{7,8,10} BS identifies a specific group of patients who experience recurrent inflammatory thrombosis involving the venous and, more rarely, the arterial vascular tree, promoted by an inflammatory response.¹¹ Vascular invasion predominantly includes perivascular neutrophilic and lymphocytic infiltrates without granulomatous inflammatory lesions. Biopsies of patients with vascular malformations often reveal full-thickness fibrotic thickening of the vessel wall and aneurysm formation.¹¹ Disease activity related to vascular involvement should be

comprehensively evaluated based on clinical symptoms and laboratory findings (including CRP, coagulation, fibrinolysis) and imaging findings.¹² In particular, inflammatory markers, such as CRP and ESR, are closely linked to postoperative pro-

gression. Lower levels of these markers correlate with a reduced likelihood of major postsurgical complications, decreased cardiac reoperation rates, and lower mortality rates. Consequently, it is advisable to closely monitor these inflam-

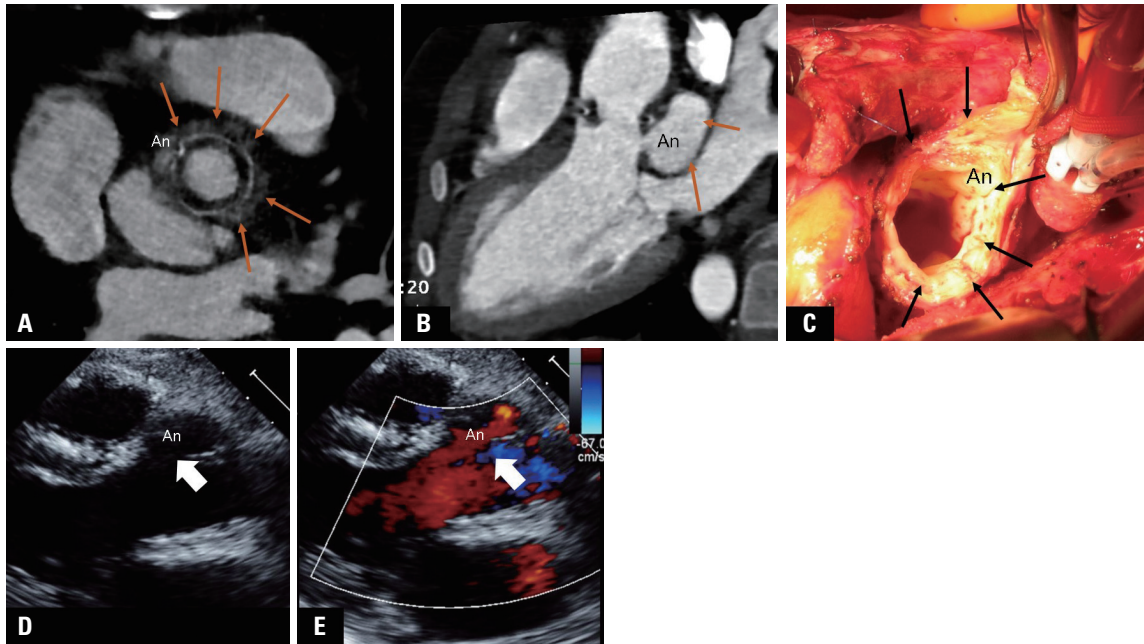


Fig. 2. Newly developed aortitis around the prosthetic valve 6 months after AVR. (A) Cardiac CT image. Soft tissue thickening around the tissue valve ring with aortic valve leaflet thickening (arrows). (B) Cardiac CT image. Two large outpouching lesions below the aortic annulus (RCC and NCC sides), suggestive of pseudoaneurysm, were observed (arrows). (C) Operative findings during Bentall operation. Thickening of whole aortic wall, suggesting chronic inflammation (arrows). (D and E) Post-Bentall operation TTE. Newly developed pseudoaneurysm with communication (white arrow). AVR, aortic valve replacement; CT, computed tomography; LCC, left coronary cusp; RCC, right coronary cusp; TTE, transthoracic echocardiogram.

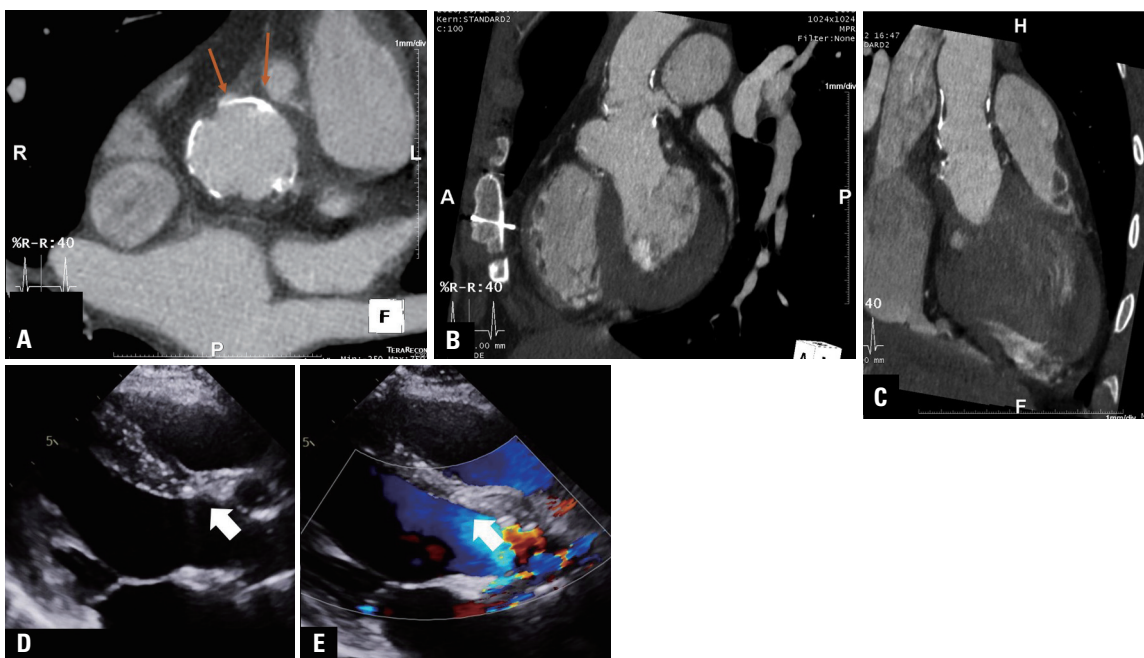


Fig. 3. Regression of the residual pseudoaneurysm and improved perivalvular dehiscence. Three years after anti-inflammation, immunosuppressant medical treatment. (A, B, and C) Cardiac CT images. The perivalvular dehiscence improved and closed spontaneously, and the residual pseudoaneurysm under the artificial valve regressed (arrows). (D and E) TTE. The lesions of chronic inflammation observed in Fig. 2D and 2E have regressed and shown improvement (white arrow). CT, computed tomography; TTE, transthoracic echocardiogram.

matory markers and consider administering anti-inflammatory and immunosuppressive treatments as needed.^{6,12-15} Understanding the role of inflammatory and coagulation components in BS vascular events is critical to define the most effective treatment strategies.¹⁰ However, high-quality studies with strong evidence, such as multicenter large-scale controlled trials, on anti-inflammatory and immunosuppressive agents are lacking. Prescription protocols for appropriate medications and their durations have not been firmly established.

Aortic valve replacement (AVR) and the Bentall operation, also known as aortic root replacement (ARR), are considered standard treatments for aortic root involvement in adults with BS.¹⁶ Although surgical intervention for AR in BS is relatively rare, recurrent inflammation can cause complications, such as paravalvular leakage, valve detachment, hemorrhage, and pseudoaneurysm formation after valve replacement, often requiring reoperation.^{5,8,12,17} The risk of valve dehiscence tends to be higher with AVR alone. To relieve these complications, consideration of the Bentall operation from the outset may be advisable.^{18,19} However, in the Bentall operation, suture detachment can occur at the anastomotic site of the aortic root. Untreated pseudoaneurysms can be fatal if they rupture, necessitating aggressive treatment, including surgery, for all adult patients with aortic pseudoaneurysms to prevent life-threatening complications.^{12,20} This pediatric patient presented with a subaortic pseudoaneurysm due to chronic recurrent inflammation after the first AVR. Immediately after the second surgery of ARR for whole myxomatous changes in the aortic wall, aortitis aggravated again. Despite medical treatment stabilizing the inflammatory markers, a pseudoaneurysm recurred, and CRP levels increased after surgery. At that point, reoperation was deemed not the optimal treatment option. Therefore, instead of urgent reoperation, the inflammatory markers were stabilized using anti-inflammatory drugs, such as steroids and azathioprine, for 36 months. Compared to previous surgical procedures, active medical regimens have improved the results. Eight years later, there were no complaints of specific symptoms and no evidence of progression in CT or echocardiography. Furthermore, pseudoaneurysm formation and perivalvular dehiscence improved without repeated surgery. In addition to surgery, medical treatment and pediatric age are considered important factors.

In summary, we reported a pediatric case of BS with severe AR in a patient who underwent valvular surgery due to the disease's characteristic progressive inflammatory reaction. Later, a pseudoaneurysm and perivascular dislocation developed; however, immunosuppressive and anti-inflammatory treatments resulted in aneurysm regression without requiring further surgery.

AUTHOR CONTRIBUTIONS

Conceptualization: Jo Won Jung. **Data curation:** Chang Sin Kim. **Formal analysis:** Jo Won Jung. **Investigation:** Hanbyul Lee. **Methodology:**

Jo Won Jung. **Project administration:** Jo Won Jung. **Resources:** Jo Won Jung. **Software:** Hanbyul Lee. **Supervision:** Jo Won Jung, Jong Gyun Ahn, and Han Ki Park. **Validation:** Jo Won Jung. **Visualization:** Han Ki Park. **Writing—original draft:** Hanbyul Lee. **Writing—review & editing:** Hanbyul Lee. **Approval of final manuscript:** all authors.

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