

Fig 3. Postoperative coronary angiogram showing a patent bypass graft, well-visualized left anterior descending, and left circumflex coronary arteries.

branches, and the pulmonary arteries. Coronary artery involvement occurs in about 10% of cases [1], and the presence of a coronary arterial lesion is potentially lethal in Takayasu's arteritis. The ostia or the proximal parts of the coronary arteries are predominantly involved. The surgical treatment options for coronary ostial stenosis due to Takayasu's arteritis have been reported to be CABG [2, 3] and ostium endarterectomy [4]. When utilizing the saphenous vein for CABG, the proximal anastomotic portion of the ascending aorta should be stenosed or occluded if inflammation is extended. Saphenous vein graft failure can occur due to intimal hyperplasia of the saphenous vein graft itself. Arterial grafts, such as those of the internal mammary artery and the gastroepiploic artery, cannot be used when the inflammation extends to the aortic arch or to the descending aorta.

Marfan syndrome is an autosomal dominant disorder of connective tissue involving the skeletal, ocular, and cardiovascular systems [5]. Aortic aneurysm and dissection are the life-threatening cardiovascular complications of Marfan syndrome. Aortic histology in Marfan syndrome shows separation and fragmentation of elastic fibers, termed cystic medial necrosis. The treatment options for aortic root aneurysm in patients with Marfan syndrome have been reported to be composite replacement of the aortic valve and ascending aorta [6] and aortic valve-sparing operations [7].

In our case, the patient had concomitant Takayasu's arteritis and Marfan syndrome, the former involving the left coronary ostium and causing complete obstruction, the latter causing annuloaortic ectasia with aortic regurgitation. Takayasu's arteritis can also cause aortic aneurysm and aortic regurgitation [8], but the aortic histopathology of the patient was suggestive of Marfan syndrome. We successfully performed simultaneous left coronary ostium endarterectomy, CABG, and Bentall

operation in this very rare case. We used a GoreTex vascular graft for CABG due to concerns of saphenous vein graft failure. To our knowledge, this is the first case in which a patient with concomitant Takayasu's arteritis and Marfan syndrome has undergone combined operation for complications of these two diseases.

References

1. Lupi-Herrera E, Sanchez-Torres G, Marcushamer J, et al. Takayasu's arteritis: clinical study of 107 cases. *Am Heart J* 1977;93:94-102.
2. Kihara M, Kimura K, Yakuwa H, et al. Isolated left coronary ostial stenosis as the sole arterial involvement in Takayasu's disease. *J Intern Med* 1992;232:353-5.
3. Amano J, Suzuki A. Coronary artery involvement in Takayasu's arteritis: collective review and guideline for surgical treatment. *J Thorac Cardiovasc Surg* 1991;102:554-60.
4. Kuwahara K, Ohteki H, Itoh T, Naitoh K, Furukawa K, Natsuaki M. Successful combined operation for Takayasu's arteritis. *Ann Thorac Surg* 1991;52:549-51.
5. Pyeritz RE, McKusick VA. The Marfan syndrome: diagnosis and management. *N Engl J Med* 1979;300:772-7.
6. Gott VL, Green PS, Alejo DE, et al. Replacement of the aortic root in patients with Marfan's syndrome. *N Engl J Med* 1999;340:1307-13.
7. Tambeur L, David TE, Unger M, Armstrong S, Ivanov J, Webb G. Results of surgery for aortic root aneurysm in patients with the Marfan syndrome. *Eur J Cardiothorac Surg* 2000;17:415-9.
8. Kalangos A, Baldovinos A, Beghetti M, Vala D, Faidutti B. Ascending aortic aneurysm associated with aortic insufficiency due to Takayasu's arteritis. *Ann Thorac Surg* 1999;68:248-50.

Recombinant Factor VIIa After Aortic Valve Replacement in a Patient With Osteogenesis Imperfecta

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A 26-year-old man with osteogenesis imperfecta and severe aortic regurgitation was scheduled for aortic valve replacement. As previously described by other authors the operation was difficult owing to the friability and weakness of the tissues. Mean blood losses of 153 mL per hour during the first 7 postoperative hours were observed. Despite normal coagulation indicators the bleeding did not stop and recombinant factor VIIa was applied at 40 $\mu\text{g}/\text{kg}$. Bleeding was successfully stopped after this single application.

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Osteogenesis imperfecta (OI) is a group of hereditary generalized connective tissue disorders [1]. Aortic regurgitation is a rare valvular dysfunction present in this patient group: as reported by Hortop and associates [1] 2 of 109 persons with OI have aortic regurgitation visible by echocardiography. Several successful mitral and aortic valve operations for these patients have been reported in the literature [2]. Wong and colleagues [2] summarized 23 cases of open heart surgery in patients with osteogenesis imperfecta and 30% (7 of 23) of the patients had severe postoperative bleeding, resulting in 6 postoperative deaths. One major problem associated with surgery in OI patients is the fragility of the connective tissues due to the underlying disease. Suture lines and a secure seating of the valve prosthesis in the myxomatous annulus were described as a technical challenge for the surgeon [2]. As also noted by Wong and colleagues [2] a second problem is the risk of perioperative bleeding despite normal preoperative and postoperative coagulation profiles.

Recombinant factor VIIa (rFVIIa) has been developed for the treatment of hemophilic patients with inhibitors and has proven its clinical effectiveness in patients with thrombocytopenia and congenital platelet defects [3].

Recombinant FVIIa has also been shown to be an effective treatment for severe, uncontrolled bleeding in patients undergoing heart valve replacement [4]. The mechanism of action is not fully understood. This is the first report of an OI patient with severe postoperative bleeding after aortic valve replacement that was successfully treated with rFVIIa.

A 26-year-old man with osteogenesis imperfecta, hyperlipemia, and arterial hypertension was seen for follow-up. Aortic regurgitation had been diagnosed 3 years earlier. The patient's condition was clinically stable on a regimen of diuretic, angiotensin-converting enzyme inhibitor, and statin therapy. The preoperative cardiac catheterization findings showed severe aortic valve regurgitation with dilation of the left ventricle and a normal ejection fraction of 50%. There were no pathologic findings in the coronary arteries. Because the dilation of the left ventricle had increased over the 3-year follow-up period, the patient was scheduled for aortic valve replacement. The preoperative laboratory findings including the coagulation studies were within normal range. Aspirin and other platelet-inhibiting drugs were not administered before surgery.

A 23-mm aortic valve (On-X) was implanted under normothermic cardiopulmonary bypass. Because of the friability of the aortic tissue 3.0 mL of fibrin sealant (Tissucol Duo S Immuno) was used to stop bleeding from the aortic root. Transfusion of packed red blood cells (RPBC) or fresh frozen plasma (FFP) was not required during surgery. After admission to the intensive care unit an average blood loss of more than 150 mL per hour from the mediastinal chest drain for the first 6 hours required the transfusion of 3 U RPBC, 4 U FFP, and 2 U platelets (Fig 1). A continuous infusion of aprotinin at 100,000 IU/h was started immediately after admission and did not

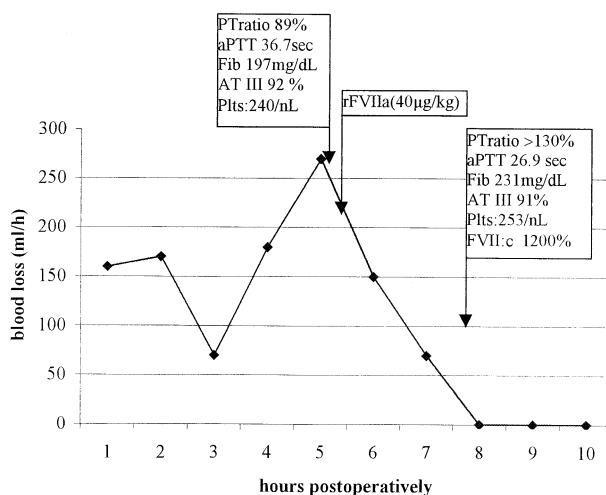


Fig 1. Postoperative blood loss and laboratory findings. (aPTT = activated partial prothrombin time; AT = antithrombin; Fib = fibrinogen; FVII:c = coagulating activity of factor VII in %; Plts = platelet count; PTratio = prothrombin time ratio [method of Quick]; rFVIIa = recombinant factor VIIa.)

reduce the amount of bleeding. The systolic blood pressure was kept between 80 and 100 mm Hg with a continuous infusion of nitroglycerine. The coagulation determinants did not show major abnormalities at this time (see Fig 1). After the blood loss from the mediastinal chest drain exceeded 1,000 mL without any reduction in bleeding rFVIIa was applied at a dose of 40 µg/kg because revision was not considered appropriate owing to the high surgical risk. Bleeding was stopped immediately. No further blood products were needed. The patient was extubated on the morning of the first postoperative day. Myocardial enzymes were raised on the second postoperative day. Creatine kinase (CK) was 5,368 U/L with an MB-fraction of 131.4 U/L and the troponine level was at 67.1 U/L. The ST segments in the lateral leads of the ECG were elevated. The coronary catheterization, which was performed immediately on the same day, showed good aortic prosthesis function. No alterations in the coronary arteries could be identified. The patient was discharged from the intensive care unit on the second day after surgery in stable clinical condition.

Comment

In the case presented here postoperative bleeding in a patient with osteogenesis imperfecta after aortic valve replacement was successfully treated with a single dose of rFVIIa. This patient initially had severe postoperative blood losses. As described in the literature, this a common problem with OI patients undergoing cardiac surgery [2]. Owing to the high risk associated with rethoracotomy in this patient the application of rFVIIa was the safest and most efficacious treatment course in our opinion.

As a possible explanation for the mechanism of rFVIIa action we hypothesize that the formation of a tissue factor-FVIIa complex locally at the site of vessel injury initiated a local plug formation. Vessel injury exposes tissue factor to the blood stream where it complexes with rFVIIa, resulting in a local thrombin formation. Thrombin itself activates platelets and factors V and VIII, resulting in a further generation of thrombin [5]. Conversely, a tissue-factor independent effect on hemostasis has been described with high doses of rFVIIa [5]. High levels of rFVIIa can activate enough FX and FIX on platelets resulting in the further generation of thrombin, which in turn activates other platelets. That leads to a massive generation of thrombin ("thrombin burst") that promotes the formation of a stable clot at the site of bleeding [5].

Although we do not know the exact mechanism of action in our patient we have to assume some systemic activation due to the decrease in prothrombin time (international normalized ratio) and the increase of factor VIIc activity after the administration of low-dose rFVIIa. FVIIc activity has been proposed as a reliable monitoring marker for high-dose rFVIIa treatment [6].

In the patient in this case report, signs of myocardial ischemia developed postoperatively. To rule out any thromboembolic complication in the coronary system after the application of rFVIIa, a coronary catheterization was performed on the first postoperative day. All findings were normal.

This is a report of successful treatment with rFVIIa of postoperative bleeding in a patient with osteogenesis imperfecta and aortic valve replacement. Considering the high rate of bleeding complications after cardiac surgery and the high risk associated with surgical reexploration in these patients, rFVIIa treatment may represent a novel and effective therapeutic option.

References

1. Hortop JH, Tsipuras P, Hanley JA, Maron BJ, Shapiro JR. Cardiovascular involvement in osteogenesis imperfecta. *Circulation* 1986;73:54-61.
2. Wong RS, Follis FM, Shively BK, Wernly JA. Osteogenesis imperfecta and cardiovascular diseases. *Ann Thorac Surg* 1995;60:1439-43.
3. Monroe DM, Hoffmann M, Allen GA, Roberts HR. The factor VII-platelet interplay: effectiveness of recombinant factor VIIa in the treatment of bleeding in severe thrombocytopenia. *Semin Thromb Hemost* 2000;26:373-7.
4. Hendriks HGD, van der Maaten JMAA, de Wolf J, Waterbolk TW, Slooff MJH, van der Mer J. An effective treatment of severe intractable bleeding after valve repair by one single dose of activated recombinant factor VII. *Anesth Analg* 2001;93:287-9.
5. Hoffmann M, Monroe DM, Roberts HR. Activated factor VII activates factors IX and X on the surface of activated platelets: thoughts on the mechanism of action of high-dose activated factor VII. *Blood Coag Fibrinolysis* 1998;9(Suppl 1):61-5.
6. Johannessen M, Nielsen G, Nordfang O. Comparison of the factor VII:C clot analysis and a modified activated factor VII analysis for monitoring factor VII activity in patients treated with recombinant activated factor VII. *Blood Coag Fibrinolysis* 2000;11(Suppl 1):159-64.

Left Ventricular Assist Device for Right Side Assistance in Patients With Transposition

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Right (systemic) ventricular dysfunction is well described after Senning operations for transposition of the great arteries, and patients with congenitally corrected transposition of the great arteries. Transplantation remains the only definitive therapy for refractory heart failure, however patients may deteriorate clinically prior to the availability of a donor heart. This report details the implantation of a TCI Heartmate (Thoratec Corp., Pleasanton, CA) as a morphologic right ventricular assist device to bridge these patients to transplantation.

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Right (systemic) ventricular dysfunction is well described after Senning operations for transposition of the great arteries (TGA), [1] and patients with congenitally corrected transposition of the great arteries (ccTGA). Patients initially do well, but often deteriorate with right (systemic) ventricular failure after the second decade of life [2]. Transplantation remains the only definitive therapy for refractory heart failure. The number of patients suffering from irreversible heart failure after atrial switch operations, and also after Fontan-like interventions will likely increase during the next several years. In the absence of a donor organ, these patients may expire secondary to end-stage heart failure. This report describes 2 patients, one with TGA post-Senning procedure, and the second with ccTGA postvalve replacement, who were each successfully bridged to transplantation with a TCI Heartmate left ventricular assist device (LVAD) placed in the morphologic right ventricle.

Case Reports

Patient 1

D.M. is a girl, who at 4 months of age underwent a Senning procedure for D transposition of the great vessels. She did well until age 15, when she presented with cyanosis, secondary to an intraatrial baffle leak. She

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