

Patient with Von Willbrand Disease Undergoing Mitral Valve Repair: A Strategy for the Control of the Coagulopathy

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We report the case of a 60-year old woman with type I von Willebrand disease who underwent mitral valve repair. The patient required special care due to the coagulopathy, and factor VIII (VIII_f) and von Willebrand factor (vWf) concentrate was necessary prior to, during and after surgery. No complications occurred during or after surgery. Nine months later, the patient is asymptomatic. Correction of VIII_f and vWf to adequate levels enabled a safe surgical procedure.

Mitral valve repair is performed with cardiopulmonary bypass using extracorporeal circulation (ECC). Blood contact with the surface of the plastic material of the ECC tubes, as well as the stress caused by the blood pumping circuit, leads to coagulation changes and hemolysis.

Coagulation changes resulting from the surgical procedure associated with the platelet dysfunction caused by the von Willebrand disease require the elaboration of a strategy for the perioperative period with the purpose of preventing excessive bleeding in patients undergoing surgical procedures. Recent studies show that the continuous infusion of VIII_f and vWf (8Y™) concentrate in patients with type I von Willebrand disease is safe and prevents significant bleeding during surgical procedures¹.

The following report refers to a patient with type I von Willebrand disease who required mitral valve repair. VIII_f and vWf concentrate was used as a strategy for the control of the coagulopathy.

Case Report

Sixty-year old woman with type I von Willebrand disease under medical treatment since childhood was admitted in our service on January 14, 2005, with a history of dyspnea on daily exertion for two months. She was taking digoxin 0.25mg/day and furosemide 40mg/day.

The patient was a hepatitis C virus carrier and was under treatment with interferon. She had a past medical history of rheumatic fever in childhood, one episode of bacterial

endocarditis in mitral valve in 1998, and hypothyroidism. She reported previous episodes of gingival bleeding and epistaxis.

Physical examination revealed a patient in good general condition, good color, hydrated, with no cyanosis, jaundice or fever. She had no respiratory distress; her blood pressure was 130x80 mmHg, heart rate 72 bpm, and respiratory rate 20 bpm. Cardiac examination revealed a grade 1/6 systolic murmur in the mitral area and a grade 1/6 diastolic murmur in the mitral area.

An electrocardiogram (ECG) was performed, revealing sinus rhythm with alterations suggestive of left atrial overload, left ventricular overload, and alterations in ventricular repolarization. The preoperative echocardiogram showed mitral valve thickening, posterior leaflet prolapse due to rupture of the chordae tendineae with severe regurgitation, mild increase of left ventricular end-diastolic diameter and normal function. The patient underwent a coronary angiography which did not show any coronary lesions and confirmed the diagnosis of severe mitral regurgitation. Surgical repair of the mitral valve was then indicated.

On account of the coagulation deficiency, the patient required special pre-, intra-, and postoperative care, because the main concern was the risk of a significant bleeding. Decreased vWf levels due to von Willebrand disease also cause a reduction in blood VIII_f level, which makes the adequate replacement of these two factors necessary for the prevention of bleeding and control of the coagulopathy.

A replacement regimen with VIII_f and vWf concentrate was then prescribed. For the preoperative period, one day prior to surgery, 50IU/kg of VIII_f and vWf concentrate were administered intravenously (IV). In the intraoperative period, 3500 IU (180m/h) of VIII_f were given via a syringe pump. Twelve hours after the end of the procedure 20 IU/kg of VIII_f were given intravenously. From the first to the fifth postoperative day 50 IU/kg were given once a day. From the sixth to the seventh postoperative day 30 IU/kg were given once a day. And from the ninth to the fifteenth postoperative

Key words

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Case Report

day 50 IU/kg were given once a day every other day. The total amount of concentrate administered was 50000 IU (100 bottles) as recommended by the UK Haemophilia Centre Doctors' Organization².

Anesthetic induction with routine anesthetic agents was uneventful. A median sternotomy was performed, and with the use of ECC the left atrium was opened and the mitral valve was exposed. The echocardiographic diagnosis was confirmed intraoperatively, and rupture of three chordae tendineae of the posterior leaflet was found. Mitral valve repair was performed using quadrangular resection of the posterior leaflet and annuloplasty with double Teflon with edge-to-edge suture of the leaflets, thus obtaining a favorable final outcome.³ The surgical procedure was uneventful.

ECC time was 55 minutes, aorta clamping time was 44 minutes, and total anesthesia time was 5 hours and 45 minutes. The St. Thomas blood cardioplegia was used. Aprotinin was administered IV at a dose of 1ml per 10 seconds with no hypersensitivity reactions, followed by a 100ml/h dose for one hour and, after surgery, 50ml for one hour, in a total of 1,000,000 IU.

Coagulation tests and blood count were performed periodically to assess the patient's coagulation status. The Activated Partial Thromboplastin Time (APTT) prior to surgery was 37 seconds, and the patient had a mild thrombocytopenia (129,000 platelets). The strategy adopted to establish the balance in the patient's coagulation system was adequate and achieved the goal of decreasing APTT down to close the normal value, which is 28 seconds, during the perioperative period. The postoperative echocardiogram showed a competent mitral valve and normal ventricular dimensions and function. Postoperative cardiac auscultation was normal.

No complications occurred in the postoperative period. The patient was discharged on the ninth postoperative day, using vWf and VIIIIF concentrate according to the regimen previously presented, in addition to Ypsilon™ and furosemide. After nine months of follow-up, the patient remains asymptomatic from the cardiovascular point of view; she has not suffered any bleeding episodes in the follow-up period.

Discussion

Von Willebrand disease is the most common hereditary bleeding disorder among the general population, occurring in one out of 100 to 500 individuals⁴. Von Willebrand factor (vWf) is a multimeric plasma glycoprotein whose main functions are to facilitate platelet adhesion to the damaged vascular endothelium by binding to the platelet membrane, and also to function as a factor VIII carrier and stabilizer in plasma. Reduced vWf levels or inadequate functioning of this protein result in impaired coagulation.

Von Willebrand disease is classified as quantitative, type 1 and 3, when a decrease or absence of vWf occurs, respectively, and as qualitative, when inadequate functioning of vWf occurs, characterizing the type 2 disease⁵. Type 1 is the mild form of the disease in which the individual may present usually mild clinical symptoms. However, the degree and magnitude of hemorrhagic manifestations may vary among individuals and the assessment of the need for prophylaxis aiming at

preventing bleeding in patients undergoing surgical procedures depends on the assessment of the patient's coagulation status by the hematologist. Type 3 is the severe form of the disease, in which there is usually no production of vWf, and patients with this form of the disease undergoing surgical procedures always require prophylaxis aiming at preventing hemorrhagic complications in the intra- and postoperative periods².

Physicians should suspect von Willebrand disease in the presence of the following signs: symptoms of bleeding such as epistaxis; gingival bleeding; menorrhagia; bleeding following tooth extraction; low activity of ristocetin cofactor (vWF:RCO); and the presence of family history of bleeding, since this is an hereditary disease⁶.

Reports of surgical treatment of heart valve diseases in patients with von Willebrand disease are rare in the literature. It is important, however, that general practitioners and cardiovascular surgeons be on the alert when evaluating patients and screening coagulation disorders, so as to prevent possible surgical complications; they should also be familiar with the most frequent coagulation disorders. Komp et al⁷ and Aris et al⁸ demonstrated that cardiac surgery may be performed in patients with von Willebrand disease provided that VIIIIF levels are corrected.

Patients with other coagulation disorders, such as hemophilia, have also been undergoing cardiac surgery with favorable results. Tarasoutchi et al⁹ reported the successful operation of a hemophilic patient with mitral and aortic valve disease of rheumatic etiology undergoing aortic valve replacement and mitral commissurotomy; in this case a VIIIIF replacement regimen was used to control the coagulation disorder in the intra- and postoperative period.

There are reports in the literature of patients with aortic stenosis who developed von Willebrand disease due to the stress caused in the endothelium and the inflammatory reaction with reduction of plasma vWf levels. This disorder proved to be reversible with valve replacement¹⁰.

Knowledge on the pathophysiology of von Willebrand disease is of great medical importance, since hemorrhagic complications may occur in pregnant women and major surgeries. Patients with von Willebrand disease undergoing major surgeries usually require prophylactic therapy aiming at preventing hemorrhagic complications². Treatment, when indicated, may be performed with the administration of desmopressin, factor VIII concentrate and platelets. The need for each of the interventions previously mentioned depends on the type of disease, on the coagulation status, and on the assessment by the hematologist, who can determine which treatment is the best to be adopted according to each patient's needs. Prophylactic therapy with VIIIIF and vWf concentrate replacement was chosen because of the favorable outcomes found in the literature with the use of this therapeutic modality.

Conclusion

Mitral valve repair in the patient with von Willebrand disease undergoing VIIIIF and vWf replacement regimen in the perioperative period was successful and no hemorrhagic complications occurred. In conclusion, the strategy used was effective in the control of the coagulation disorder, and

enabled the performance of the surgery with no complications; it may be used in other patients with the same disease who require surgical procedures.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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