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CASE REPORT

Human menopausal gonadotropin-induced bioprosthetic valve thrombosis

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ABSTRACT

Bioprosthetic valve thrombosis (BPVT) is a rare but potentially life-threatening complication. Human menopausal gonadotropin (hMG) is commonly used for ovulation induction and has been associated with arterial and venous thrombosis. We reported a case of BPVT related to *in vitro* fertilization in a 39-year-old female, who underwent redo mitral valve replacement. To the best of our knowledge, this is the first case of hMG-induced BPVT in a young female patient.

Key words: Bioprosthetic valve thrombosis, human menopausal gonadotropin, *in vitro* fertilization

INTRODUCTION

Bioprosthetic valves are the most common artificial valves used in women of childbearing age. It has good hemodynamic properties and obviating the need for long-term anticoagulation.[1] The incidence of bioprosthetic valve thrombosis (BPVT) is low, but it may result in fatal consequences.[1] BPVT has high mortality, and the treatment varies from medical treatment in mild cases to surgical intervention in severely symptomatic patients.[1] Human menopausal gonadotropin (hMG) is commonly used to induce ovulation during *in vitro* fertilization (IVF). In fact, various adverse effects have been reported including venous and arterial thrombosis.[2]

CASE REPORT

A 39-year-old female had a history of mitral bioprosthetic valve replacement (Medtronic Mosaic®) due to rheumatic heart disease 2 years prior to hospitalization. Regular follow-ups with her cardiologists were maintained, and the patient was asymptomatic with a normal prosthetic function on serial echocardiograms. One month prior, the patient sought treatment with *in vitro* fertilization and received 14 injections of (450 IU) hMG. Few days later, she started complaining of progressively worsening shortness of breath until she presented to the emergency department with a blood pressure level of 70/40 mmHg, heart rate of 125 beat/min, and oxygen saturation around 84%. She was hemodynamically unstable needing inotropic and ventilatory support. Ultimately, she was transferred to the Intensive Care Unit for further management.

An emergent echocardiogram was performed. This was followed by a transesophageal echocardiography (TEE) that showed ejection fraction of 55%, two oval-shaped masses on the mitral valve leaflets (arrow) with restricted leaflet motion and a mean gradient of 34 mmHg, a peak gradient of 51 mmHg, and velocity time integral (VTI) of 93 cm. The findings with highly suggestive of BPVT are shown in Figure 1.

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The initial complete blood count showed white blood cells of 8.1 × 10^3/μL, hematocrit of 27.9%, and platelet count of 114 × 10^3/μL. Blood urea nitrogen was 36.7 mmol/l, creatinine of 264 μmol/l, alanine transaminase (ALT) of 64 U/l, and international normalized ratio was 1.9.

Cardiac surgery was immediately consulted, and the patient underwent emergent redo mitral valve replacement surgery with a St. Jude mechanical valve. Intraoperative findings of the thrombosed mitral valve are seen in Figure 2. While on cardiopulmonary bypass and after replacing the valve, a freely mobile thrombus was seen in the left atrium [Figure 3a and Video 1] impinging on the leaflets of the mechanical valve [Figure 3b]. After exploring the pulmonary veins and removal of any existing thrombi, the final TEE confirms normally functioning metallic mitral valve [Video 2]. Patient had uneventful postoperative course and discharged 16 days after surgery; the follow-up echocardiography showed normal mechanical valve function [Figure 4].

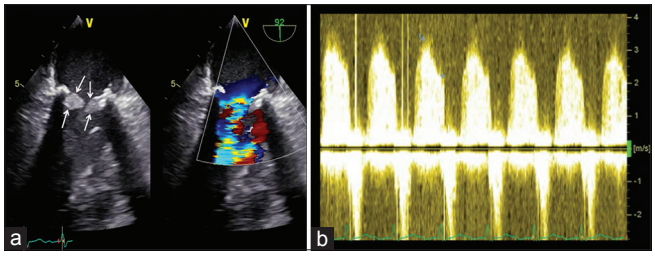

Figure 1: (a) Transesophageal echocardiography: two-dimensional showed thickened mitral valve leaflets (arrow) and color Doppler showed diastolic mitral inflow flow aliasing jet due to blood flow acceleration, and (b) Continuous wave Doppler of mitral valve inflow showed a significant increase in velocity

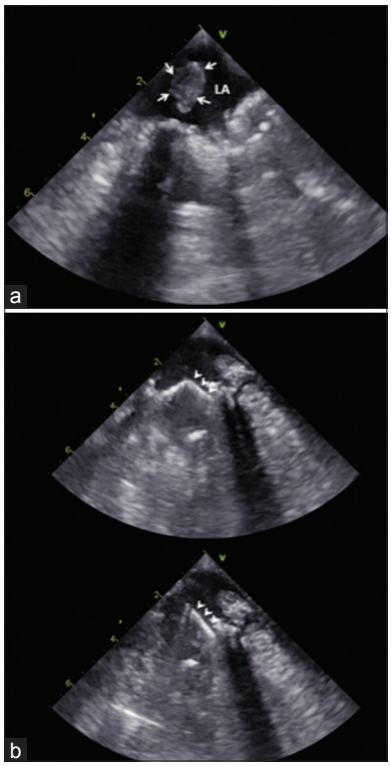

Figure 3: (a) First intraoperative transesophageal echocardiography showed freely mobile large thrombus in the left atrium (arrows) and (b) second intraoperative transesophageal echocardiography revealed immobile mitral valve leaflet (arrowhead)

DISCUSSION

Although the exact mechanisms of BPVT are not well understood, there are various underlying factors related to valve thrombosis such as hemostatic activation which results in hypercoagulable state, leaflets wall shear stress produced by blood flow perturbations, and patient-related factors such as atrial fibrillation, renal insufficiency, obesity, diabetes mellitus, and low cardiac output states.[3] The incidence of valve thrombosis is around (6%) post bioprosthetic mitral valve implantation;[4,5] moreover, BPVT represents 11.6% of totally explanted valves due to bioprosthetic valve dysfunction.[6]

The diagnosis and differentiation of BPV dysfunction as a result of pannus versus thrombus formation is challenging.

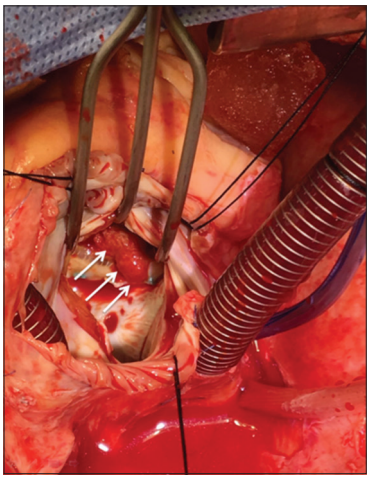

Figure 2: Intraoperative image showed a large thrombus in the bioprosthetic mitral valve (arrows)

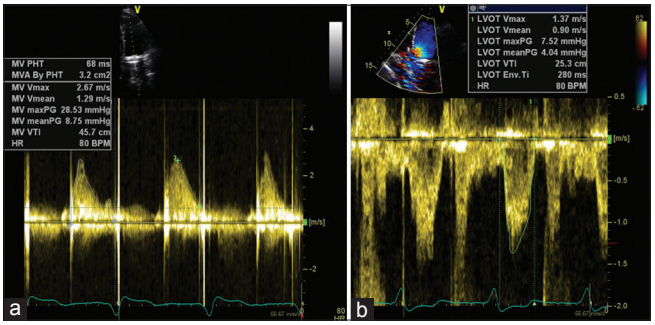

Figure 4: Follow-up echocardiography. (a) The mitral mean gradient 8.7 mmHg peak gradient 25 mmHg, pressure half-time of 68 ms, and (b) the VTImv/VTIlvot = 1.8, indicating a normal prosthetic valve function

However, thrombosed prosthetic valves have more acute onset of symptoms which our patient had.[1] BPVT can be asymptomatic and detected by a routine echocardiography.[7] On the other hand, BPVT can be life-threatening and may result in severe symptoms, hemodynamic instability, and rapid deterioration.[1] Commonly used echocardiographic features to help diagnose BPVT are an increase in the mean transvalvular gradient >50% above baseline values within 5 years, thickened leaflets, and restriction in leaflets mobility.[1,8,9]

The initial treatment of subclinical or mild BPVT in hemodynamically stable individuals is a Vitamin K antagonist if no contraindications to anticoagulation.[1] However, in severely symptomatic and hemodynamically unstable patients, surgical valve replacement might be indicated.[1]

Thromboembolic disease associated with ovarian stimulation syndrome is an uncommon yet potentially fatal complication of IVF. A literature review by Jing and Yanping[2] reported that a total of 112 cases of thromboembolism associated with ovulation induction, 35.7% were arterial in origin, and 64.3% were venous, but no BPVT was reported. Interestingly, Udell *et al*.[10] conducted a population-based cohort of 1,186,753 women, of whom 6979 gave birth after fertility therapy and reported that women who had received fertility treatment had significantly lower death, hospitalization for a major adverse cardiovascular, thromboembolism, and heart failure after 10 years of follow-up. However, a very recent analysis by Sennström *et al*.[11] reported that IVF results in twofold increase in the risk of thromboembolic events when compared to non-IVF pregnancies. Moreover, hospitalized IVF patients due to ovarian hyperstimulation syndrome had 100-fold increased risk of thromboembolic events when compared to non-IVF pregnant population.

CONCLUSION

To the best of our knowledge, this is the first case of BPVT induced by hMG treatment for IVF, successfully treated with surgery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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