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CASE REPORT

MITRAL MECHANICAL PROSTHETIC VALVE THROMBOSIS FOUR YEARS AFTER DISCONTINUING ANTICOAGULATION: A CASE REPORT

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ABSTRACT: A 40 years lady who underwent a mitral valve replacement with a mechancial prosthesis nine years ago, stopped oral anticoagulants totally. She was asymptomatic and doing her field job with good exercise tolerance for 4 years without any anticoagulation or follow-up and presented now with acute pulmonary edema due to prosthetic valve thrombosis. Echocardiography revealed a large clot on the mitral valve and increased Doppler gradients across the valve. She was given intravenous streptokinase for 28 hours with relief of symptoms, re-appearance of prosthetic valve click and normalisation of flow velocities. She was prescribed oral acenocoumarol and discharged in a stable condition.

CASE: Mrs. N, a 40 years lady was admitted with a two day history of Class IV dyspnea and was diagnosed to have mitral prosthetic valve thrombosis. She had undergone mitral valve replacement with a 27mm Medtronic Hall prosthesis for severe rheumatic mitral regurgitation in 2005; a permanent pacemaker was implanted when she developed complete heart block postoperatively. She was put on acenocoumarol and was on follow-up until 2011with an INR between 2 and 2.5. She discontinued oral anticoagulants and all drugs from August 2011 but reported no complaints – she had fair exercise tolerance and worked as a health worker which entailed field visits. She noticed mild dyspnea, but continued her work for the past 3 weeks, and was admitted now with acute pulmonary edema. The prosthetic valve click was muffled and the ECG showed a paced rhythm. Echocardiogram revealed decreased mobility of the mitral prosthesis with a large clot attached to it. The mitral flow gradients were very much increased with a peak gradient of 60 mm.Hg. And a mean gradient of 40 mm. Hg. She also had moderate aortic regurgitation and pulmonary hypertension with tricuspid regurgitation. The ejection fraction was 61.

A diagnosis of prosthetic valve thrombosis was made and she was given intravenous streptokinase – 2.5 lakh units as an intravenous bolus followed by an infusion of 1 lakh units per hour (for 28 hours). She was administered IV frusemide and sedation on admission in the ICCU. Acenocoumarol was also started at a dose of 2mg daily. By next day morning, she was better, the mitral valve click was well heard and echocardiography revealed a well-functioning mitral prosthesis with acceptable flow gradient – a peak of 8 and a mean of 3. Thrombus was not visible. She was administered enoxaparin 0.6mg bid for 5 days for the oral anticoagulant to take effect. The patient was discharged, in an asymptomatic condiction, and with fair effort tolerance, after 9 days, on acenocoumarol 2mg. daily and aspirin 75 mg.

DISCUSSION: Thrombosis is one of the dreaded complications of prosthetic valve implantation with a reported incidence of 0.3% to 1.3% per patient year.[1] A follow-up study of the first series of patients

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who received a St. Jude prosthesis revealed that 13 of 78 patients who were not on anticoagulants developed valve thrombosis or embolic events.[2] A subsequent meta-analysis found that not using either anticoagulant or antiplatelet led to an incidence of 7.0-10.4 total thrombosis+embolus events per 100 patient years. This risk was reduced to 1.8 by use of anticoagulants.[3] A study of 43 patients with an aortic mechanical prosthesis who had discontinued anticoagulants one year later and were followed up for upto 15 years found that 70% and 59%, were free of thromboembolic events after 5 and 10 years corresponding to a linearised rate of thromboembolic events of 5.2% per patient year respectively.[4] Risk factors for thrombosis include inadequate anticoagulation,[5] mitral position (vs. aortic), caged ball valve (vs. tilting disc and bileaflet).[3] All patients with mechanical valves must be on lifelong anticoagulation targeted to maintain their Prothrombin Time – International Normalised Ratio (PT-INR) at 2 to 3 for an aortic bileaflet valve and 2.5 to 3.5 for a mitral mechanical valve as per all guidelines including the 2014 guidelines.[6]

The duration of symptoms before valve thrombosis is diagnosed varies – a study of 112 patients with obstructed mechanical valves found that 68.2% had symptoms for 1day to 1 week before they were diagnosed and hospitalized.[7] It is not common for recipients of mechanical valves to remain asymptomatic for long periods without any anticoagulation, like our patient.

There have been rare case reports of patients with mechanical valve prostheses surviving several years without anticoagulation.

Besides the series of 43 patients quoted above, there is the report of a 68 year old man with a mechanical aortic prosthesis who had stopped oral anticoagulants 3months after surgery and was seen 23 years later with an audible prosthetic valve click and a mean gradient of 19mm. Hg. He was discharged on dual antiplatelet drugs.[8] Another patient of a stuck aortic valve in a 47 year male presented, with a one-month history of dyspnea and palpitation, 26 years after he had discontinued anticoagulants; he was reoperated and the valve was found to be covered with pannus and some fresh thrombi.[9]

All the cases referred to above were aortic prostheses which are known to carry a lesser risk of thrombosis compared to their mitral counterparts. Mechanical mitral valves functioning without anticoagulation are much rarer. There is a report of two patients with mitral valve replacement are reported to have achieved their target INR after 16 months and 53 months, but surprisingly, had no thromboembolism.[10]

A 46 year patient who had a mechanical mitral valve implanted 27 years ago and had stopped anticoagulants after just one month was seen to have a normally functioning prosthesis with a Prothrombin Time INR of 1.79. He was found to have a warfarin polymorphism with a homozygous mutation in the vitamin K epoxide reducatase complex 1 thus explaining the higher INR level and long-term survival of the valve.[11] These patients were not on some dose of drug, though suboptimal.

Our patient was totally off anticoagulants for three years, without any effort intolerance or features of valve thrombosis. She had no history suggestive of any bleeding diathesis or coagulation disorder. The case is remarkable in that a mitral Medtronic Hall prosthesis was functioning for 3 years without any thrombosis.

The current admission was due to thrombosis of the mitral prosthesis and a large clot was visible on echocardiography; further, it had totally cleared with streptokinase and a repeat echo revealed no clot with normal Doppler gradients across the prosthesis. It is difficult to answer why the mitral prosthetic valve was apparently clot-free for three years and developed a thrombus now and

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we can only surmise the possible reason thereof. Endothelial, hemodynamic and hemostatic factors contribute to prosthetic valve thrombosis. Endothelialisation takes some weeks to complete; hemodynamic factors lead to localized regions of turbulent flow causing stasis and thrombus formation.[12]

Three basic mechanisms have been defined – firstly, adsorption of plasma proteins, including fibrinogen, onto the surface of the valve prosthesis leads to platelet adhesion and induction of the coagulation cascade. [13] The second factor is the effect of transprosthetic blood flow – 'turbulent' flow due to unphysiological flow that is rapidly changing directions, increases the blood borne shear stress to more than 10 dynes/sq.cm. causing metabolic and structural damage to the endocardium which is prone to further thrombosis. Similarly, blood stasis in recirculation areas downstream of the prosthesis also favors thrombosis. (ibid). In fact, most valves are designed to allow for a mild leak/ regurgitation, to prevent clot in these stasis areas downstream to the prosthesis. The third major reason for thrombosis comprises clot promoting factors including inadequate coagulation, atrial fibrillation, incomplete endothelialisation of the valve sewing ring, and inflammation, often with a raised fibrinogen level.[13] Our patient denied any recent infection or disease causing any systemic inflammation and she was in sinus rhythm. She had not consumed any drug.

Type of valve and location also affect the risk of thrombosis. Thrombosis is 20 times more likely in the tricuspid position; mitral prosthetic valve thrombosis is 2-3 times more common than aortic prosthetic thrombosis (ibid). The introduction of the bileaflet mechanical valve and use of pyrolytic carbon as a valve material have reduced the risk of thrombosis; pyrolytic carbon is more biocompatible and thrombo-resistant and wear resistant.[14]

Non physiological blood flow patterns in the vicinity of prosthetic valves are believed to lead to thrombosis; abnormal flow patterns lead to shear stress on blood cells and platelet activation, while, recirculation and flow stagnation increase contact time between blood cells and activated platelets leading to thrombosis (ibid).

The chief cause of thrombosis in our patient was discontinuing anticoagulants totally. A 20 year study in a single centre revealed 39 cases of prosthetic valve thrombosis with 54% having an INR below 2.5; poor patient compliance with regard to anticoagulant usage in 26%, alteration of the anticoagulant intake due to some other surgery in 26% and multifactorial etiology in 23% were the main causes of thrombosis.[15] 53% of the patients had old and fresh thrombi while 34% had fresh thrombi and 13% had old thrombi (ibid).

Treatment for thrombosis of a mechanical valve prosthesis includes thrombolysis with Streptokinase or surgery with proponents for both. Lengyel and group advocate thrombolysis as the first line of treatment if there are no contraindications[16] while Roudaut and group, with their experience of over 250 cases, prefer surgery.[17] The 2014 AHA guidelines on Valvular Heart Disease have issued the following recommendations.[6]

1. Right side valve thrombosis – IV heparin; if thrombosis is still persisting, fibrinolysis.
2. Left side valve thrombus that is mobile or > 0.8 sq.cm. On Transesophageal Echocardiography (TEE) or any thrombus with the patient in NYHA Class III or IV - emergency surgery.
3. Left side valve thrombus that is small (<0.8 sq.cm.) and recent (<2 weeks) and the patient is in NYHA Class I or II – fibrinolysis if thrombus persisting despite IV heparin.

Though our patient would have thus qualified for emergency surgery, lack of immediate cardiac surgery services, and our prior experience with similar patients, prompted us to opt for IV

thrombolysis, with a successful outcome. In the Indian scenario, Aditya Singh nd group have published data on intravenous thrombolysis in 86 patients, with more than 75% in Class III or IV. Full success with normalization of gradients was noted in over half the cases, and partial success in a quarter; 8% died.[18] Tenecteplase too has been used for prosthetic valve thrombosis.[19]

Thus, our case, adds another question to the enigma of prosthetic valve thrombosis we are still to learn why some patients do not develop a thrombus even when not on oral anticoagulants for long periods. Fortunately, bioprosthetic valves which do not carry this risk and do not require lifelong anticoagulants are being designed with increased longevity and more surgeons are favoring them even in younger patients. Further improvements in bioprosthesis design may soon overcome their disadvantage of valve degeneration/failure and they may soon replace mechanical valves, leaving several questions on valve thrombosis unanswered.

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