Warfarin and Herbal Products Interaction Causing Prosthetic Aortic Valve Thrombosis Presenting as Acute Myocardial Infarction

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Myocardial infarction (MI) due to coronary artery embolization is a rare and potentially lethal complication of prosthetic heart valve thrombosis. A 58-year-old man in whom the aortic valve was replaced with a bileaflet mechanical valve presented with an acute anterior MI. Valvular dysfunction was detected by physical examination, and confirmed by two-dimensional echocardiography and cinefluoroscopy. Coronary angiography disclosed embolization of the left anterior descending artery. Thrombotic encroachment of one of the prosthetic valve leaflets was found at reoperation. Failure to achieve adequate anticoagulation was likely due to an interaction between warfarin and herbal products. These findings have significant implications regarding the diagnosis and treatment of acute MI in patients with left-sided prosthetic heart valves, and emphasizes the importance of appropriate anticoagulation in this setting.

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Valve thrombosis is one of the most serious complications following mechanical prosthetic valve implantation. Prosthetic heart valve thrombosis (PHVT) has a reported incidence of between 0.1 and 5.7% per patient-year (pt-yr) (1,2). The clinical presentation may vary, from minimal or absent symptoms to abrupt circulatory collapse or sudden death (3). In patients with mechanical heart valves, the incidence of major embolization is approximately 1% per pt-yr with warfarin therapy (4), and the majority of embolizations manifest as cerebrovascular events (2). The case is reported of prosthetic aortic valve thrombosis which initially presented as an acute myocardial infarction (AMI). This uncommon presentation has significant implications regarding the diagnosis and treatment of AMI in patients with left-sided prosthetic heart valves.

Case report

A 58-year-old Hispanic man had a past history, in 1966, of aortic valve replacement (23 mm St. Jude Medical mechanical valve prosthesis) due to severe aortic regurgitation. The patient was admitted to an outside institution one day after developing a crushing, substernal chest pain which radiated to his jaw, and was associated with sweating, nausea and dyspnea. An electrocardiogram (ECG) (Fig. 1) recorded on admission revealed marked anteroseptal Q-waves, and the patient's cardiac enzymes were remarkably elevated (peak troponin I serum level 254 ng/ml).Conventional treatment for AMI with intravenous metoprolol, nitrates and unfractionated heparin was initiated; however, thrombolysis was not administered because of late presentation. The patient was transferred to the authors' institution for evaluation of progressive congestive heart failure and cardiac

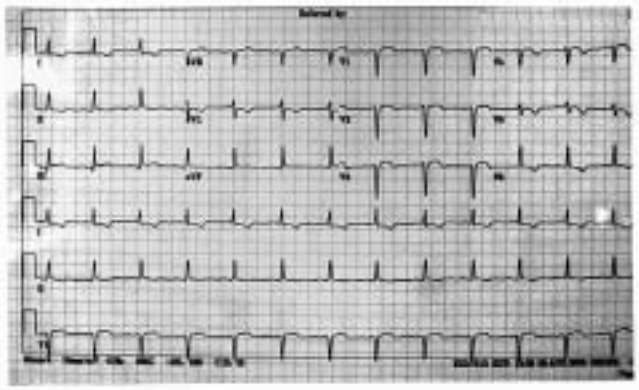

Figure 1: Twelve-lead electrocardiogram showing changes consistent with an anterior myocardial infarction.

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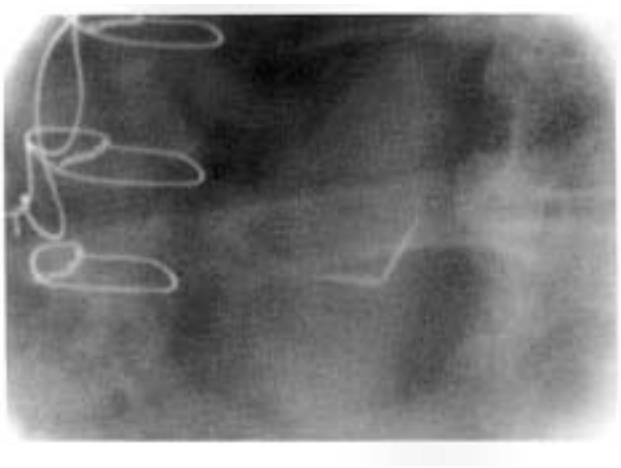

Figure 2: Cinefluoroscopy showing the two mechanical heart valve leaflets in the fully closed position.

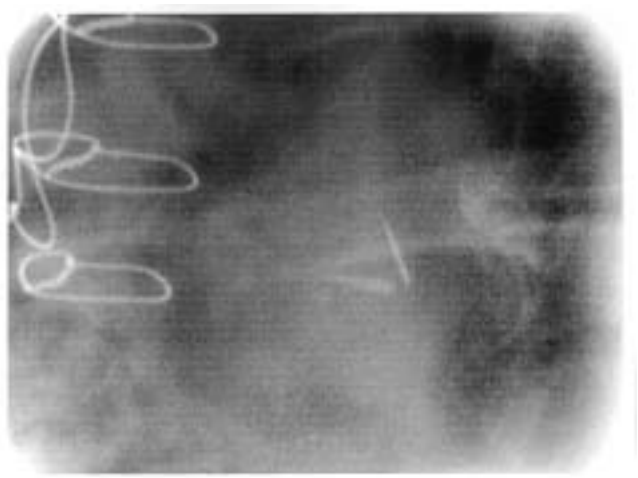

Figure 3: Cinefluoroscopy showing abnormal valve opening due to restricted posterior leaflet movement.

catheterization. On admission to the coronary care unit, a clinical examination showed the patient's pulse to be 102 beats per minute, blood pressure 103/58 mmHg, respiratory rate 24 breaths per minute, and temperature normal. There was no increased jugular venous pressure. He had bibasilar rales, a regular heart rate and rhythm, and a grade 2/6 systolic ejection murmur at the right upper sternal border radiating to the neck. The closing prosthetic valve sound was soft and muffled. There was no peripheral edema, and all peripheral pulses were present. A new ECG showed no further changes, and chest X-radiography revealed a normal-sized heart with evidence of pulmonary edema. Two-dimensional transthoracic echocardiography demonstrated severe valvular aortic stenosis, with a peak systolic gradient of 91 mmHg and a mean gradient of 58 mmHg. The left ventricle was a normal-sized chamber with a calculated ejection fraction of 35%. PHVT was suspected, and further examination with cinefluoroscopy and cardiac catheterization was undertaken. Fluoroscopy revealed a dysfunctional mechanical bileaflet disc prosthesis with the posterior leaflet appearing to barely move with the onset of systole (Figs. 2 and 3). Coronary angiography revealed a small filling defect in the distal left anterior descending artery which was consistent with an embolic event.

At surgery, the posterior leaflet of the prosthesis was found to be stuck in the closed position by thrombus which extended from both hinge points along the posterior orifice of the prosthesis. The prosthesis was excised and replaced with a Carpentier-Edwards porcine bioprosthesis during an uneventful procedure. The patient was discharged home on the sixth postoperative day, and has since remained well and asymptomatic.

The patient's anticoagulation history revealed that he had been optimally maintained with warfarin until three months prior to his present illness, when his International Normalized Ratio (INR) became unsteady, with persistent subtherapeutic levels, requiring progressive increment of his warfarin dosage. On admission to the first hospital, the patient's INR was 1.4. Further investigations showed that the patient had not made any significant dietary changes or had used other medicines that might interfere with the pharmacological action of warfarin; nevertheless, it was discovered that his INR levels became erratic shortly after he began using a combination of herbs to boost his sexual performance.

Discussion

Although there is a lack of sufficient data to calculate the incidence of coronary embolization associated with PHVT, its actual occurrence appears to be uncommon. One possible explanation for this very low incidence may be the perpendicular anatomic disposition of the coronary ostia in relation to the aortic blood flow, decreasing the probability of an embolus entering the arteries.

The clinical presentation of PHVT may vary from insidious onset of mild symptoms to sudden hemodynamic decompensation, yet the condition may lead rapidly to death (3). A prompt diagnosis is therefore crucial. Cinefluoroscopy and transthoracic and transesophageal Doppler echocardiography are reliable diagnostic methods for prosthetic heart valve dysfunction (5,6). For patients in whom the information provided by non-invasive methods is equivocal (3), or who present with additional concomitant features such an acute coronary event, emergency cardiac catheterization is warranted.

The standard therapy for PHVT has been high-risk emergency surgery. Thrombolysis may be used as an

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alternative therapy, but the success rate of this is approximately 70% (3) and the major complication is embolism, with reported rates of 15-25% (7). For these reasons, the present authors believe that thrombolysis is not the treatment of choice for patients who are able to undergo surgery.

It is likely that the patient's prosthetic valve thrombosis was caused by an inability to maintain therapeutic INR levels after he began taking a mixture of herbs. Potential and documented adverse interactions between herbal products and warfarin have been reported (8). To the present authors' knowledge, this is the first report of a life-threatening thromboembolic event presumably linked to an adverse warfarin-herb interaction.

Two important clinical implications can be drawn from these findings. First, when patients with left-sided prosthetic valves present with clinical manifestations of an ongoing acute coronary event, the possibility of PHVT with coronary embolization must be considered in the differential diagnosis. Second, if a patient receiving warfarin presents with a bleeding or thromboembolic complication, or if the INR becomes erratic and difficult to stabilize, then the possibility of a warfarin-herb interaction should also be considered.

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