

Recurrent acute coronary syndrome caused by a primary aortic valve sarcoma: grand rounds and literature review

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Background

Malignant tumours of the aortic valve apparatus are extremely rare and difficult to diagnose. Their proximity to the coronary ostium may cause an acute coronary syndrome (ACS) either by infiltration or by embolization.

Case summary

We report a case of primary aortic valve undifferentiated sarcoma causing recurrent episodes of ACS, and we provide a literature review for primary cardiac valve tumours. This case also highlights the need for further evaluation of other causes of ACS in patients with minimal coronary artery disease risk factors and recurrent ACS.

Conclusions

The majority of valve tumours are fibroelastomas. Sarcomas are rare and lead to poor outcomes.

Keywords

Aortic valve • Cardiac tumors • Sarcomas • Cardiac surgery

ESC curriculum

3.1 Coronary artery disease • 3.2 Acute coronary syndrome • 6.8 Cardiac tumours • 7.5 Cardiac surgery • 9.1 Aortic disease

Learning points

- To recognize cardiac tumours as a rare cause of acute coronary syndrome.
- To understand the different consequences of primary and secondary cardiac tumours on the cardiovascular system.

Primary specialties involved other than cardiology

Cardiac Surgery Medical imaging Pathology Oncology Palliative care.

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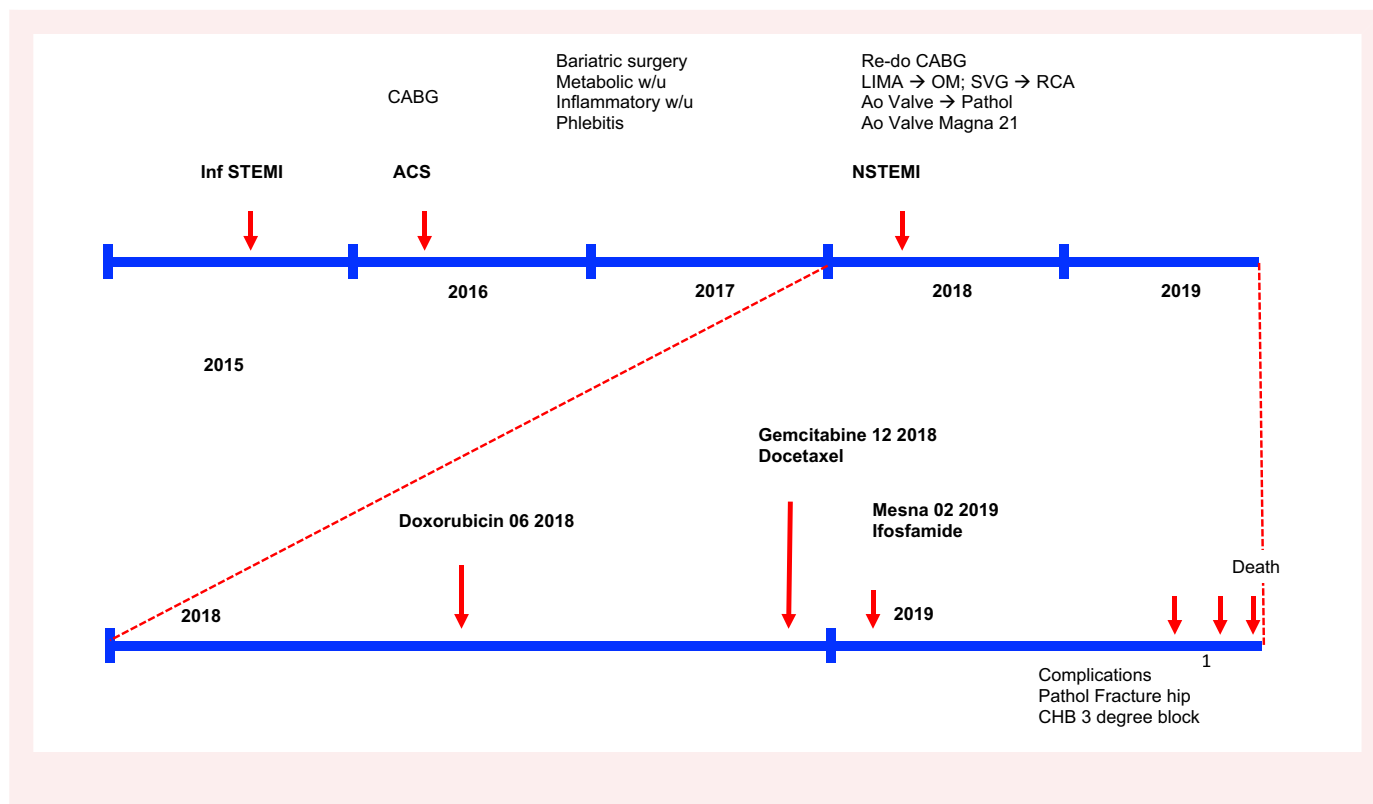
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Timeline

ACS: acute coronary syndrome; AVR: aortic valve replacement; CABG: coronary artery bypass graft; PCI: percutaneous coronary angioplasty; STEMI: ST-segment elevation myocardial infarction; w/u: work-up.

of the distal left main coronary artery (LMCA) (Figure 1A, B). An attempt was made to restore the flow in the LMCA, but unfortunately the patient went into cardiac arrest during the procedure. After successful resuscitation, an attempt was made to insert an intra-aortic balloon pump which failed due to the patient's body habitus. The decision was made to send the patient for an urgent coronary artery bypass sur-



Case presentation

A 39-year-old morbidly obese (weight 128 kg, height 170 cm, body mass index 44.3) diabetic female presented to the emergency room with acute onset chest pain. She was not known to have significant past medical history, including hypertension or smoking, but developed type 2 diabetes, associated with her obesity. Other than morbid obesity, the physical examination was not contributory the blood pressure was 110/80 mmHg.

She was diagnosed with an inferior ST-elevation myocardial infarction (STEMI) and was sent for an urgent angiogram. The angiogram revealed a total occlusion of the proximal right coronary artery (RCA) that was successfully stented. No other significant atherosclerotic lesions were noted at that time. Given her favourable evolution, the patient was sent home after initiation of optimal medical therapy and was referred for evaluation of metabolic and genetic causes of premature coronary artery disease (CAD).

A work-up to identify possible rare causes of premature coronary atherosclerosis, such as genetic dyslipidaemia, was performed and came back negative. She was referred for bariatric surgery which resulted in a weight loss of over 100 pounds and subsequent discontinuation of her anti-diabetic medications (metformin 500 mg PO [per os (orally)] bid). However, despite the significant weight loss and the compliance to her antiplatelet therapy, she consulted again for angina less than one year after the first event.

Upon presentation to the emergency room, the patient had diffuse ST depression and refractory chest pain. A repeat angiogram performed via a right radial approach demonstrated a subtotal occlusion

gery (CABG). Both the left anterior descending (LAD) and the first obtuse marginal (OM) were successfully bypassed with saphenous vein grafts because of the urgent nature of the surgery, and the patient's obesity the internal thoracic arteries were not used. The surgery was uneventful except for the ascending aorta that appeared mildly inflamed (Figure 1C). In that context, a biopsy was taken and sent for further analysis. The pathology examination did not reveal any evidence of neoplasia or vasculitis and the patient had a favourable post-operative course. The patient was given guideline recommended treatment for secondary prevention with aspirin, high-doses statin, ticagrelor, and metoprolol.

One year later, the patient presented with recurrence of her typical chest pain and was diagnosed again with a non-STEMI. A repeat angiogram demonstrated an occlusion of the first OM bypass at the site of the aortic anastomosis and a reocclusion of the ostial RCA. The saphenous bypass to the LAD was patent (Figure 1D). Moreover, a transthoracic echocardiogram revealed a decreased ejection fraction of 40–45% and at least moderate aortic insufficiency that was not visualized on previous examination. Given the complexity of the lesions for angioplasty, the patient's young age, and the concomitant aortic regurgitation, decision was made to send the patient for a redo surgery.

During the second surgery, the intra-operative echocardiogram demonstrated severe aortic regurgitation. The striking feature was what appeared to be a whitish, thick inflammatory lesion around both coronary ostia, along the aorto mitral curtain. The valve was also involved in this process with retracted curled edges. An arterial bypass to the OM and a venous bypass to the RCA was successfully performed in addition to the aortic valve replacement with a bioprosthesis.

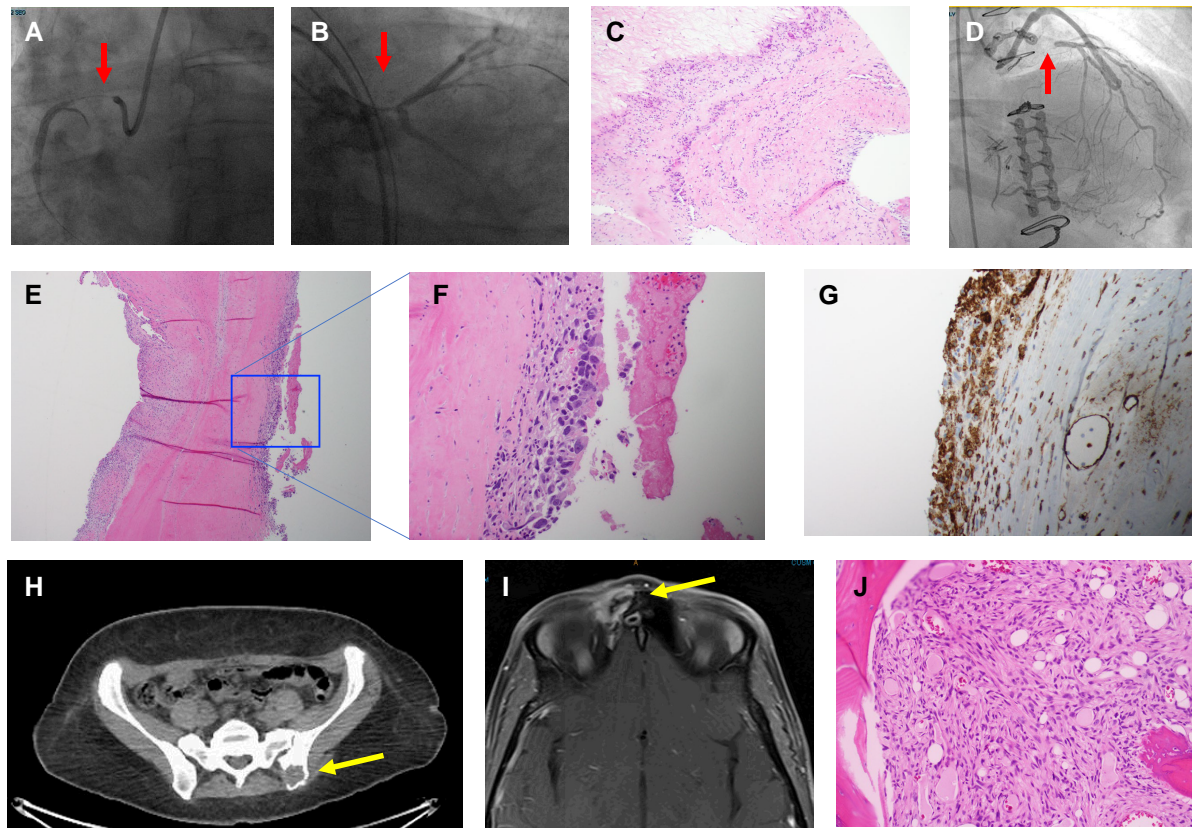


Figure 1 (A) Initial coronary angiogram (2015) showing an occlusion of the right coronary artery; the left main coronary artery, left anterior descending and circumflex arteries were patent. (B) Ostial stenosis of the left circumflex and the left anterior descending arteries were demonstrated after the wire insertion (2016) (C) Biopsy of the ascending aorta showing inflammatory changes and fibrosis. Not diagnostic of a sarcoma. (D) Occlusion of the left main coronary artery and graft to the right coronary artery (2018) (vertical arrows). (E) Aortic valve cusp, magnification 20X, demonstrating a layer of hypercellular neoplastic proliferation coating the entire surface of the valve. (F) Aortic valve cusp, magnification 100X, showing hyperchromatic pleomorphic cells with abnormal mitosis and overlying microthrombus. (G) Immunohistochemical stain for CD31, showing no expression on the malignant cells as expected in undifferentiated sarcomas. (H) PET-computed tomography scan image showing a bone metastasis in the left hemipelvis. (I) Magnetic resonance imaging of the orbits demonstrating an infiltrative bone metastasis invading the right frontal sinus and the superior oblique muscle (arrows). (J) Biopsy of metastatic bone lesion showing undifferentiated sarcoma. PET, position emission tomography.

Pathologic examination of the native aortic valve revealed high-grade undifferentiated (intimal) sarcoma of the aortic valve (Figure 1E, F, G). She was referred to an oncologist.

The initial treatment with doxorubicin failed to show improvement, and the patient was then started on a second line of treatment with gemcitabine and docetaxel and was referred for palliative radiotherapy.

Unfortunately, the positron emission tomography scan done for the tumour staging demonstrated bone metastases in the ribs and left hemipelvis (Figure 1H), which confirmed a stage IV metastatic cancer. Patient was started on liposomal doxorubicin chemotherapy and radiotherapy (8Gy to affected ribs). The patient underwent a course of gemcitabine and docetaxel. Chemotherapeutic drug choices were limited by the patient's poor left ventricular function due to multiple ischaemic events. Mesna and ifosfamide were then substituted, along with another course of palliative radiotherapy to ribs, hip, and right orbit (8Gy) (Timeline). Despite the treatment, patient complained of progressive bone pain. A computed tomography (CT) scan was done to assess the response to treatment and demonstrated progression of multiple new bone metastases. In addition, the patient developed new right supraorbital pain, which was shown to be another infiltrative bone metastasis on magnetic resonance imaging (MRI) (Figure 1I, J).

Subsequent CT scans demonstrated progression of the metastatic lesions despite treatments. She also developed complete heart block, likely due to the local infiltration of the tumour in the myocardium, for which she had a permanent dual chamber pacemaker implanted in the left sub-clavicular area. Unfortunately, the patient passed away less than 4 years after the initial ischaemic event. No autopsy was performed respecting the patient's and her family wish.

Table 1. Review of cases of primary valvular cardiac tumour by location and malignity			
Location	Benign, n (%)	Malign, n (%)	Total, n (%)
Aortic valve	16 (30)	3 (6)	19 (35)
Mitral valve	15 (28)	7 (13)	22 (41)
Tricuspid valve	6 (11)	1 (2)	7 (13)
Pulmonary valve	4 (7)	2 (4)	6 (11)
Total (%)	41 (76)	13 (24)	54 (100)

Table 2. Review of case reports of a primary aortic valve tumour

Year of publication	References	# of patients	Patient age and gender	Neoplasia found	Benign (B) vs. malign (M)	Presentation
2014	Alves ³	4	—	Papillary fibroelastoma	B	—
2005	Bossert et al. ⁴	1	71 F	Papillary fibroelastoma	B	Syncope
2005	Bossert et al. ⁴	1	63 F	Papillary fibroelastoma	B	Syncope
2005	Bossert et al. ⁴	1	58 M	Papillary fibroelastoma	B	Syncope
2005	Bossert et al. ⁴	1	78 F	Papillary fibroelastoma	B	Routine echography
1991	Edwards et al. ⁵	2	—	Papillary fibroelastoma	B	Sudden death
1991	Edwards et al. ⁵	4	—	Papillary fibroelastoma	B	Chronic heart failure
1991	Edwards et al. ⁵	1	—	Papillary fibroelastoma	B	Stroke
2016	Wang et al. ⁶	1	—	Papillary fibroelastoma	B	—
2017	Okoro et al. ⁷	1	63 M	Synovial sarcoma	M	Transient ischaemic attack
2008	Ramos et al. ⁸	1	41 F	Undifferentiated sarcoma	M	Dyspnoea
2008	Eisenstat et al. ⁹	1	5 F	Myofibroblastic sarcoma	M	Sudden death (coronary embolism)

—, unknown.

Discussion

We report a case of a primary aortic valve poorly differentiated sarcoma in a 39-year-old woman causing coronary obstructions and acute myocardial infarctions. Such malignant tumours are extremely rare and difficult to diagnose. They can cause acute coronary syndromes (ACS) either by infiltration (as in the present case) or by embolization. We reviewed the current literature for primary cardiac valve tumours. This case shows the difficulties in identifying such neoplasms and the complexity of therapeutic interventions; it also highlights the need for further evaluation of other causes of ACS in patients with minimal CAD risk factors and recurrent ACS.

While it is uncommon to see an ACS in a young patient without risk factors, seeing multiple recurrences of ACS is even rarer. This should raise the suspicion for uncommon causes of premature coronary artery disease (CAD) including genetic disorder, congenital abnormality or underlying neoplastic process.¹ Primary cardiac tumours represent a real diagnostic challenge and are often overlooked due to their rarity. These can cause an ACS by several mechanisms depending on their location such as embolization, infiltration, or external compression of the coronary arteries.² In addition, cardiac tumours can cause arrhythmia by myocardial invasion, systemic embolization of tumour fragment or thrombus and can also cause various valvulopathies by compression/destruction of the leaflets. Here, we report a case of primary aortic valve undifferentiated sarcoma causing recurrent episodes of ACS and we provide a literature review for primary cardiac valve tumours. This case also highlights the need for further evaluation of other causes of ACS in patients with minimal CAD risk factors and recurrent ACS. In retrospect, the consideration that multiple cardiac surgeries could have contributed to dissemination of the sarcoma is noteworthy, however unlikely, given the location of the metastases.

A literature review was performed by searching bibliographic database of life sciences and biomedical information and biomedical and pharmacological bibliographic database of published literature databases from inception to December 2019. From a total of 61 articles found, 14 were removed due to duplication and 33 were removed after title and abstract screening. The remaining 14 articles were analyzed and included in this review.

We identified 54 separate cases in which both tumour location and histology were specified (Table 1). Valvular tumours involved more

frequently the mitral (41%) and aortic (35%) valves. In our series, 41 (76%) of the primary valvular tumours were histologically benign vs. 13 (24%) malignant. Of all primary aortic valve tumours, 16 (84%) cases were benign papillary fibroelastomas and 3 (16%) cases were sarcomas. The latter represents 6% of all the valvular tumours in this series (Table 2).

In this literature search, where data on clinical presentation were available, most patients with aortic valve tumours presented symptomatically. Only one was found on routine echocardiography. Symptoms varied between syncope presumably secondary to outflow tract obstruction, dyspnoea and congestive heart failure from valvular dysfunction, and embolic events. When embolic events occurred, they were often neurologic or led to sudden death. There were two cases of sudden cardiac deaths where the patients were found to have coronary ostial obstruction or coronary embolism on autopsy. This case presentation was unique with the recurrent myocardial infarctions and multivessel stenosis due to ostial coronary infiltration by tumour.

Primary cardiac tumours are rare entities that may present with coronary ostial infiltration and recurrent episodes of ACS in the absence of other risk factors for CAD. This case also highlights the need for further evaluation of other causes of ACS in patients with minimal CAD risk factors and recurrent ACS. As shown in this case, the clinician must be mindful of the differential diagnosis in a patient that does not fit the classic picture of a patient with recurrent ACS.

Lead author biography



Martine Parent is a community cardiologist practicing in Montreal, Canada.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal – Case Reports* online.

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None

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that consent for submission and publication of this case report including images, laboratory work and associated text has been obtained from the patient in line with COPE guidance.

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References

1. Gulati R, Behfar A, Narula J, Kanwar A, Lerman A, Cooper L, Singh M. Acute myocardial infarction in young individuals. *Mayo Clin Proc* 2020;**95**:136–156.
2. Maleszewski JJ, Bois MC, Bois JP, Young PM, Stulak JM, Klarich KW. Neoplasia and the heart: pathological review of effects with clinical and radiological correlation. *J Am Coll Cardiol* 2018;**72**:202–227.
3. Chan EY, Ali A, Zubair MM, Nguyen DT, Ibarra-Cortez SH, Graviss EA, Shapira OM, Ravi V, MacGillivray TE, Reardon MJ. Primary cardiac sarcomas: treatment strategies. *J Thorac Cardiovasc Surg*. Published online ahead of print 1 February 2022.
4. Bossert T, Gummert JF, Battellini R, Richter M, Barten M, Walther T, Falk V, Mohr FW. Surgical experience with 77 primary cardiac tumors. *Interact Cardiovasc Thorac Surg* 2005;**4**:311–315.
5. Edwards FH, Hale D, Cohen A, Thompson L, Pezzella AT, Virmani R. Primary cardiac valve tumors. *Ann Thorac Surg* 1991;**52**:1127–1131.
6. Wang Y, Wang X, Xiao Y. Surgical treatment of primary cardiac valve tumor: early and late results in eight patients. *J Cardiothorac Surg* 2016;**11**:31.
7. Okoro KU, Roby MD, Sane DC, Budin RE. Infiltrating cardiac synovial sarcoma presenting as acute cerebrovascular accident. *Case Rep Med* 2017;**2017**:8539606.
8. Ramos RB, Branco LM, Galrinho AI, Cunha J, Oliveira MF, Fragata J, Ferreira RC. Primary undifferentiated sarcoma of the mitral and aortic valves. *J Heart Valve Dis* 2008;**17**:348–351.
9. Eisenstat J, Gilson T, Reinman J, Sampson B. Low-grade myofibroblastic sarcoma of the heart causing sudden death. *Cardiovasc Pathol* 2008;**17**:55–59.