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CASE REPORT
Cardiac Imaging

The curious case of a massive right heart thrombosis: a case report

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Background Intraventricular masses are a relatively rare condition ranging from asymptomatic to potentially life-threatening situations.

Case summary Herein, we report a case of a 49-year-old woman under investigation for a massive right ventricular (RV) mass who underwent complete investigation for possible differential diagnosis, in the suspect of RV tumour. Multimodality imaging with cardiac computed tomography and magnetic resonance imaging showed the presence of a massive thrombus partially obliterating the right ventricle. Surgical removal of the mass showed a large area of stratified thrombosis with an underlying area of endocardial fibrosis. The patient has been then discharged in good clinical condition and with lifetime oral anticoagulation.

Discussion Massive RV thrombosis is a rare yet potentially fatal condition. Invasive management is preferable and lifetime anticoagulation is required to reduce possible downstream thrombotic complications.

Keywords Intraventricular masses • Right ventricular thrombus • Anticoagulation • Cardiac tumour • Case report

Learning points

- Intraventricular masses are rare. Presentation ranges from asymptomatic to potentially life-threatening situations.
- Potential differential diagnosis between cardiac tumours, endomyocardial fibrosis, and thrombi are essential.
- Multimodality imaging complemented with clinical information and genetic data is crucial for driving effective treatment.

Introduction

Intraventricular masses are a challenging clinical scenario of either benign or severe origin.[1,2] Intraventricular masses may be due to several aetiologies: from potentially benign conditions, such as thrombi or benign neoplasm, to malignant neoplasm, metastatic tumours, or endomyocardial fibrosis (EMF). These aetiologies carry different prognostic burden.[1,2]

The diagnostic pathway and management rely on clinical aspects and multimodality imaging for a proper diagnosis. Here, we report a case of a right ventricular (RV) mass in a patient with an important thrombophilic state.

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Timeline

Timeline	Event
1 year before	Pulmonary embolism
Day 0	Hospitalization for worsening dyspnoea
Day 1	Echocardiogram and computed tomography scan
Day 2–5	Tumour markers and positron emission tomography scan
Day 7	Cardiac magnetic resonance imaging showed the presence of a massive thrombus partially obliterating the right ventricle
Day 10	Surgery with implantation of mechanical tricuspid valve
Day 11–17	Rehabilitation
Day 18	Discharge

Case presentation

A 49-year-old woman was admitted to the emergency room because of worsening dyspnoea. Past medical history revealed hypertension, diabetes, severe obesity (body mass index 39.7 kg/m^2), and asthma. She had no history of miscarriages or pre-eclampsia. Approximately 1 year earlier, the patient was treated with warfarin for 6 months for an episode of pulmonary embolism and worsening heart failure, with a normal echocardiogram and no RV thrombus. She has a significant family history for thromboembolism: a cousin, carrier of MethyleneTetraHydroFolate Reductase (MTHFR) heterozygous mutation 677 C>T and prothrombin heterozygous mutation 20210 G>A, suffered a pulmonary embolism and has an inferior vena cava filter. A detailed pedigree is shown in *Figure 1*. Her 7-year-old daughter and her sister, both with no history of thromboembolic disease, are carriers of the same mutation.

At admission, the patient was severely symptomatic for exertional dyspnoea. Physical examination showed no signs of overt RV failure and muffled heart sounds. Her blood tests revealed normal full blood count, blood group 0+, and elevated BNP (1543 pg/mL, normal values <100 pg/mL), and the electrocardiogram showed signs of RV overload (tall R wave in V1 and V2). The patient was haemodynamically stable; her blood pressure was 100/60 mmHg, and her heart rate 89 b.p.m.

The echocardiogram showed normal left ventricular size and function, dilated right atrium (End Systolic Area (ESA): 40 cm^2), enlarged right ventricle with qualitatively reduced function, and an intraventricular mass partially obliterating the ventricular cavity, normal pulmonary valve function, and estimated systolic pulmonary arterial pressure of 26 mmHg. At first, to rule out the hypothesis of cardiac neoplasm, the patient underwent a computed tomography (CT) scan, which revealed large hypodense mass with no enhancement compatible with a massive thrombus involving the right ventricle, the right atrium, and the superior vena cava (*Figure 2*), though with no evidence of pulmonary embolism and no mediastinal lymphadenopathy. Neoplastic

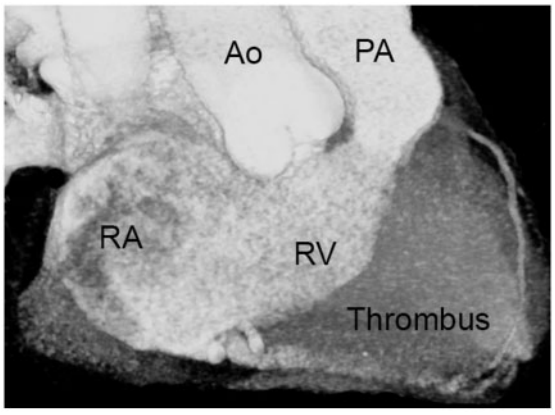


Figure 2 Three-dimensional computed tomography reconstruction of the right ventricular outflow tract partially obliterated by the massive thrombosis originating from the right atrium (*A*). Different reconstruction highlights the subvalvular stenosis of the right ventricular outflow tract with an area of 0.95 cm^2 without the pulmonary artery's involvement (*B*).

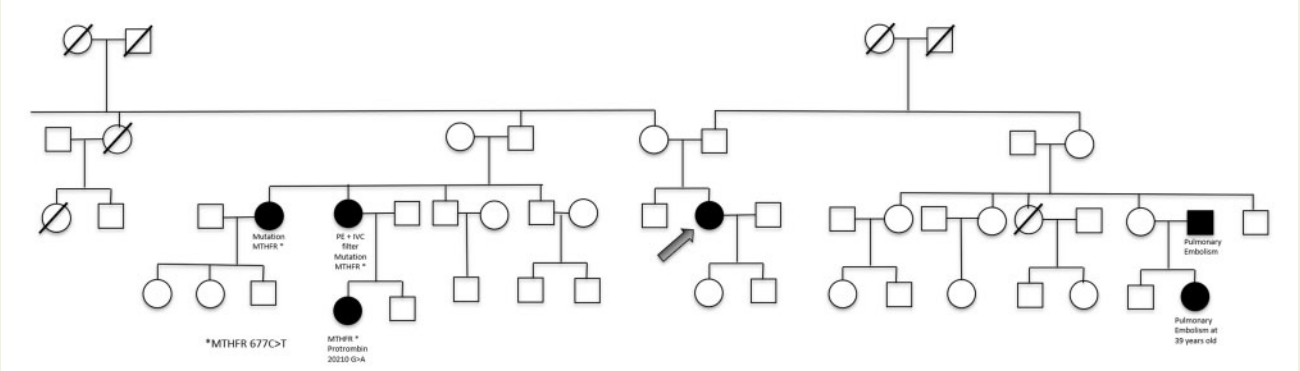


Figure 1 Patient's family pedigree.

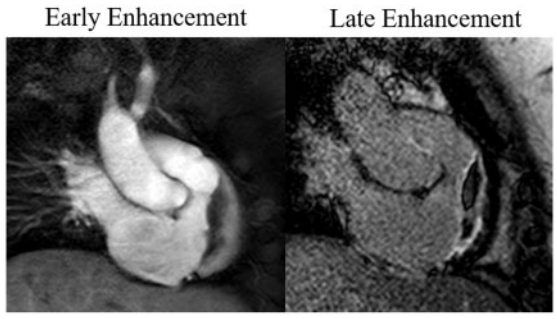


Figure 3 T1-weighted image early after gadolinium administration in four-chamber view shows hypointense masses occupying the right ventricular apex and the right atrium's posterior aspect. The insert shows the T1-weighted image 10 min after gadolinium administration in right ventricular three-chamber view. The hypointensity of the core of the mass persists, whereas there is late gadolinium enhancement along the endocardial border.

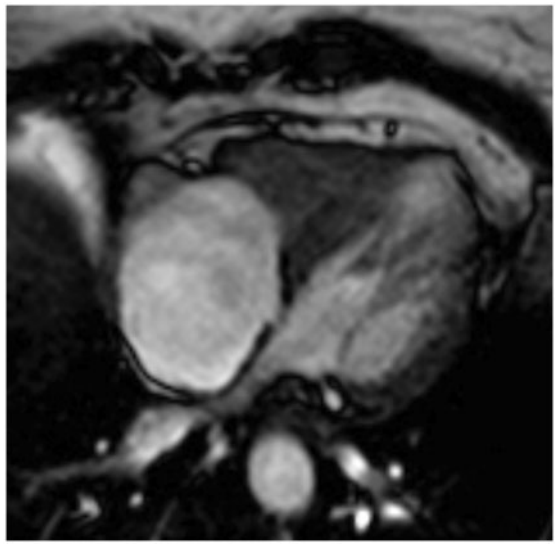
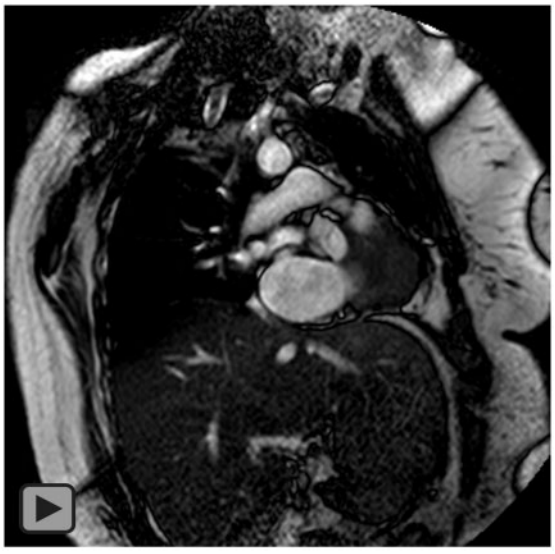


Figure 4 Four-chamber view showing that the right ventricle is partially obliterated.

markers were negative besides elevated Ca 125 (113.3 U/mL—normal values 0–35 U/mL). Positron emission tomography (PET) did not detect any lesion with increased metabolism. Thus, the initial suspicion of neoplasm was excluded.

Lower limbs and abdomen ultrasounds showed no deep vein thrombosis and normal cave-portal system. However, at that stage, the diagnosis of EMF could not have been excluded.

The cardiac magnetic resonance imaging (MRI) showed normal left ventricle and confirmed the presence of a large hypointense mass in T1 with no gadolinium enhancement compatible with a massive thrombus partially obliterating the right heart and involving the RV apex on top of possible endocardial fibrosis (*Figures 3* and *4* and



Video 1 Steady-state free precession cine-imaging in right ventricular three-chamber stack showing an isointense mass occupying the right ventricular free wall and extending partially into the right ventricular outflow tract.

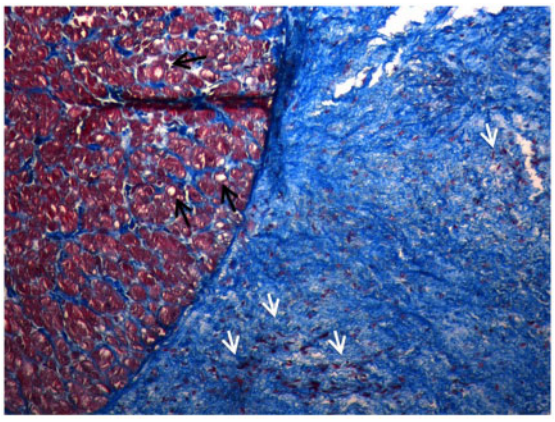


Figure 5 Azan–Mallory staining of the surgical specimen. A large thrombus is tightly attached to the ventricular myocardium, which appears severely permeated by fibrotic tissue branches. Several blood cells (white arrows) are trapped within the thrombus. The black arrows show numerous apoptotic/necrotic myocytes with loss of the contractile apparatus.

Video 1) suggesting underlying obliterative cardiomyopathy or spontaneous massive thrombosis of the right ventricle. The RV function was qualitatively reduced as well.

Due to ineffective treatment with heparin and anticoagulants for 10 days, the patient required surgical debulking of the right cavities and a mechanical tricuspid valve replacement (ON-X 27–33). Histology revealed a large area of stratified thrombosis, with an underlying area of endocardial fibrosis, caused either by primary

Table 1 Thrombophilic essays and most relevant laboratory findings performed during the index hospitalization

Essay	Value	Normal range
Haemoglobin (g/dL)	14.8	13–16
Platelets ($\times 10^3$/mm^3)	318	200–400
Eosinophil ($\times 10^3$/mm^3)	0.02	0.1–0.4
Creatinin (mg/dL)	1.3	0.9–1.1
ANA, Extractable nuclear antigen (ENA), anti-DsDNA, anti-mitochondria, Antineutrophil Cytoplasmic Antibodies (ANCA), anti-smooth muscle (anti-SM), Anti-Liver-Kidney Microsomal (anti-LKM), anti-TG, reumathoid factor		Negative
C3 (mg/dL)	141	90–180
C4 (mg/dL)	40	10–40
IgM (mg/dL)	59	40–230
IgG (mg/dL)	1071	700–1600
IgA (mg/dL)	185	70–400
IgE (mg/dL)	55	0–55
Omocystein (μmol/L)	11	<15
Lp(a) (mg/dL)	**82**	<30
hsPCR (mg/L)	**10.6**	1–3
Protein C (%)	89	70–140
Protein S (%)	91	55–124
LAC Dilute Russell's viper venom time (dRVVT) (ratio)	1.15	<1.2
LAC SCT (ratio)	0.87	<1.2
Factor VIII (%)	**187**	50–150
Factor IX (%)	98	65–150
Factor XI (%)	122	65–150
Factor XII (%)	89	50–150
Prothrombin 20210 mutation		Absent
Factor V Leiden mutation		Absent
MTHFR 677 C > T mutation		**Present (heterozygous)**
MTHFR 1298 A > C mutation		**Present (heterozygous)**

Bold values are those above reference range.

fibrosis or direct compression on the ventricular wall by the thrombus, although not meeting the criteria for EMF (*Figure 5*).

Despite multimodality imaging raised the suspicion for cardiac thrombus, definite diagnosis have been reached only after histology.

Immediately after surgery, the patient rapidly recovered and progressively normalized the RV systolic function.

A complete thrombophilia screening showed MTHFR heterozygous mutation for polymorphism 677 C>T and 1298 A>C and elevated factor VIII activity (187%—normal values 50–150, confirmed 6 months after the acute phase) in the absence of other thrombophilic mutations (*Table 1*).

The patient has been discharged from the hospital in good conditions with lifetime oral anticoagulant therapy with warfarin aiming a target INR between 2.5 and 3.5 due to the high thrombophilic profile and the mechanical tricuspid valve replacement.

Discussion

Though of different origin, intraventricular thrombi and neoplastic lesions may present with downstream thromboembolism (*Table 2*).[6,7] In the case presented above, the clinical and echocardiographic suspicion of intraventricular neoplasm presenting with pulmonary embolism was very high at admittance. However, based on the imaging analysis performed (CT-scan, PET, and MRI), which displayed a massive thrombus with a large fibrotic area underneath, the clinical hypothesis of a massive ventricular thrombosis rose dramatically. However, even after the cardiac MRI, a diagnosis of EMF could not be invariably excluded, requiring histological analysis for a precise diagnosis of a spontaneous massive RV thrombosis.

Massive RV thrombosis is a rare yet potentially fatal condition. Although intraventricular thrombi are usually secondary to severe ventricular dysfunction, a thrombophilic state may lead to their formation regardless of ventricular function. In patients with preserved ventricular function, intraventricular thrombosis may be secondary to acquired hypercoagulability, inherited protein defects, or pathological conditions, leading to augmented clotting formation.[8] Heterozygous MTHFR mutations, present in up to 45% of the population,[9] are *per se* mildly associated with an elevated risk of thrombosis (odds ratio for venous thrombosis 1.27).[7] On the other hand, elevated levels of factor VIII procoagulant activity (FVIII:C), a fundamental cofactor for activated factor IX (FIXa), have not been unquestionably associated with an increased risk for either venous or arterial thromboembolism.[10]

For many years, FVIII deficient patients with haemophilia A had significant bleeding diathesis. Poles apart, novel evidence demonstrated

Table 2 **Main differential characteristics for cardiac masses**

	Thrombus	Sarcoma	Myxoma	Rhabdomyoma	Fibroelastoma	Fibroma	Lipoma
Age at presentation	Adulthood	Young adults	Young adults	Childhood	Elderly	Childhood	All ages
Most common location	Apex (RV or LV)	Any chamber (angiosarcoma originates in the right atrium)	Interatrial septum	Ventricular walls, AV valves, outflow tract	Valves	Ventricles	Any chamber + pericardium
Number	Single or multiples	Multiples	Solitary	Multiples	Solitary	Solitary	Single or multiples
Morphology	Exuberant size, jagged edges	Heterogeneous with epicardial, endocardial and intracavitary extension	Cauliflower-like, attached to the septum	Pedunculated	Small (<1 cm), rare calcifications	Large size, calcified	Very large, broad base
Echocardiogram	Associated with regional wall motion abnormalities, useful contrast images	Multilobate masses with ill-defined margins	Mobile, narrow stalk	Hyperechogenic masses	Sparkling edged mass	Small, mobile, pedunculated valvular mass + calcifications	Hypoechogenic mass
Cardiac MRI	Acute: intermediate T1 and T2; chronic: low T1 and high T2	Heterogeneous T1 and T2	Heterogeneous, high T2	Isointense on T1; high T2	N/A	Isointense T1, low T2	Homogeneous increased T1
CT	Absence of enhancement	Low attenuation	Heterogeneous	Hypodense	N/A	Low attenuation + calcification	Homogeneous fat attenuation

Adapted from Refs.[1–5]
AV, atrioventricular; CT, computed tomography; LV, left ventricle; MRI, magnetic resonance imaging; RV, right ventricle.

the flipside; indeed elevated levels of FVIII might facilitate a pro-thrombotic state.[10] Individuals with factor VIII levels >150 IU/dL had a three-fold increased risk of thrombosis than those with levels <100 IU/dL and each 10 IU/dL increment lead to a 10% risk increase for venous thromboembolism (VTE),[11] and recurrent VTE.[12]

Furthermore, AB0 blood group significantly influences plasma levels of the complex FVIII-von Willebrand factor (VWF). Individuals with blood group 0 have ~25–30% reduction of procoagulant activity of the factor VIII:C.[10] Therefore, in our patient, 0+ serogroup, factor VIII activity was consistent with an even higher activation compared to the non-0 individuals.

Many cases of VTE or PE due to FVIII:C hyperactivity have been reported,[11,12] however, to the best of our knowledge, massive thrombosis of the right ventricle and atrium has never been described so far. Elevated factor VIII levels are associated with decreased Protein S and Protein C activity and enhance thrombin formation. Synergic effects of MTHFR mutations and elevated factor VIII activity may explain the severe pro-thrombotic state, which led to massive RV thrombosis. Therefore, routine screening of thrombophilic mutation also might include factor VIII hyperactivity in selected cases.

Interestingly, no pregnancy disorders or other embolic events have been reported, besides the pulmonary embolic event, suggesting a relatively recent onset, or worsening, of the hypercoagulable state, apparently without significant triggers. Conversely, right atrial enlargement and endocardial fibrosis were compatible with a long-standing thrombotic process. Lifelong oral anticoagulants with VKAs (due to the mechanical prosthetic valve) are required and, in those cases, international normalised ratio (INR) should be maintained among 3–4 to avoid any possible thrombotic recurrence or prosthetic valve blockade. No data are available for novel oral anticoagulants in patients with elevated factor VIII activity and MTHFR mutations. However, whenever feasible, anticoagulation with VKAs may be preferable.

Conclusions

Intraventricular masses are rare conditions ranging from EMF, cardiac tumours, or thrombi, with different prognostic burden. Multimodality imaging is crucial for the diagnosis. Thrombophilic screening might reveal important findings driving effective management of these patients.

Lead author biography

Dr Jessica Artico received her MD degree at the University of Udine, Italy. After that, she moved to the University of Trieste for her Cardiology training and attended the Policlinico San Donato Milanese, Milan, Italy, and the St Bartholomew's Hospital in London for more training in advanced cardiac imaging. Her main focus is on advanced imaging and cardiomyopathies.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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 written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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