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Case Report

Left atrial thrombus mimicking myxoma in a patient with hereditary hemorrhagic telangiectasia: Diagnostic and therapeutic dilemmas [☆]

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ABSTRACT

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder characterized by the development of arteriovenous malformations. The arteriovenous shunts may result in high output heart failure, which predisposes to atrial dilatation and atrial fibrillation. Due to recurrent bleeding from epistaxis or the gastrointestinal tract, patients with HHT and atrial fibrillation are at high risk of bleeding if anticoagulated for stroke prevention. In this report, we present a case of a 74-year-old woman with a history of HHT and atrial fibrillation who developed a large left atrial thrombus that initially was thought to represent an atrial myxoma. The diagnosis was confirmed with cardiac magnetic resonance imaging, and the patient underwent surgical resection of the thrombus. This case demonstrates the role of different imaging modalities in the assessment of left atrial masses and presents an opportunity to review the data on safety of anticoagulation in patients with HHT.

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[☆] The patient has consented to publication of the case report and images in this manuscript.

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Introduction

Hereditary hemorrhagic telangiectasia (HHT), or Osler-Weber-Rendu syndrome, is a rare autosomal dominant disorder characterized by the development of malformed blood vessels. The estimated prevalence is at least 1 of 5000 [1]. Clinical manifestations include recurrent epistaxis and gastrointestinal bleeding, pulmonary arteriovenous malformations (AVMs) which predispose patients to hypoxemia and paradoxical embolization, brain AVMs which can cause hemorrhagic stroke, and liver AVMs which can lead to high output heart failure [2]. High cardiac output results from liver AVMs as a compensation to maintain tissue perfusion when a percentage of the cardiac output is ineffective due to the large left to right shunt. High output combined with anemia from recurrent bleeding often results in atrial dilatation and an increased risk of atrial fibrillation [3]. Despite an elevated risk of developing stroke and systemic embolization in the setting of atrial fibrillation, patients with HHT are often not treated with anticoagulants due to concern for increased risk of bleeding. In this report, a patient with HHT and atrial fibrillation was found to have a left atrial mass on transthoracic echocardiogram. Although echocardiographic features were suggestive of a left atrial myxoma, further evaluation with cardiac magnetic resonance imaging revealed a diagnosis of left atrial thrombus.

Case report

A 74-year-old woman with a history of hereditary hemorrhagic telangiectasia complicated by severe bi-atrial enlargement with chronic atrial fibrillation, mild aortic stenosis, recurrent epistaxis, liver arteriovenous malformations, and right iliac artery arteriovenous malformation status post embolization (Fig. 1) presented to clinic. Given her history of severe nosebleeds, the patient had not been anticoagulated, and had been treated with oral tranexamic acid continuously since 2014 to help manage her epistaxis. An echocardiogram was performed to reassess her cardiac function and revealed a 3.1 × 3.2 cm echodense mobile mass in the left atrium attached to the intra-atrial septum on a stalk (Fig. 2, video 1). A cardiac magnetic resonance (CMR) study was obtained to better characterize the mass and revealed an enlarged left atrium with a 2.7 × 2.8 cm mobile, nonenhancing mass with T1 hyperintensity attached to the anterosuperior intra-atrial septum by a thin stalk (Figs. 3 and 4). The CMR also showed a second mass measuring 8 × 5 mm in the left atrial appendage (Fig. 4). Due to the concern for left atrial thrombus with high risk of embolization, the patient was referred to cardiothoracic surgery for resection of the atrial mass, left atrial appendage closure, and Cox-Maze IV procedure. Intraoperative findings were notable for a 3.5 × 3.0 × 1.3 cm mass attached to the intra-atrial septum (Fig. 5) and a smaller mass in the left atrial appendage. Final pathology of both masses was consistent with organizing mural thrombus. The patient's tranexamic acid was discontinued, and postoperatively she was started on low-dose apixaban. She subsequently devel-



Fig. 1 – Iliofemoral angiogram demonstrated embolization coils and ethylene vinyl alcohol copolymer (Onyx, Medtronic, Minneapolis, MN) within the right internal iliac artery and right gonadal vein at the site of the previously embolized pelvic AVM (white arrow).

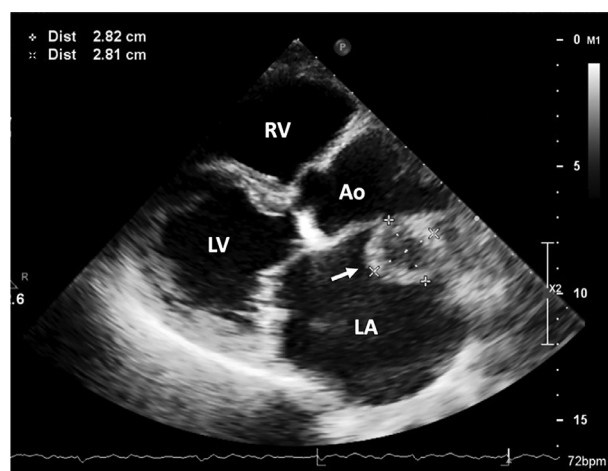


Fig. 2 – Transthoracic echocardiogram depicting left atrial mass (white arrow) in the parasternal long axis view. LA, left atrium; LV, left ventricle; RV, right ventricle; Ao, aorta.

oped severe epistaxis with anemia (hemoglobin 7 g/dL). The apixaban was stopped and she was treated with an infusion course of bevacizumab.

Evaluation of left atrial masses

Transthoracic echocardiogram (TTE) and transesophageal echocardiogram are the initial imaging modalities of choice for the evaluation of cardiac masses. Two-dimensional TTE can provide information about the size and location of the

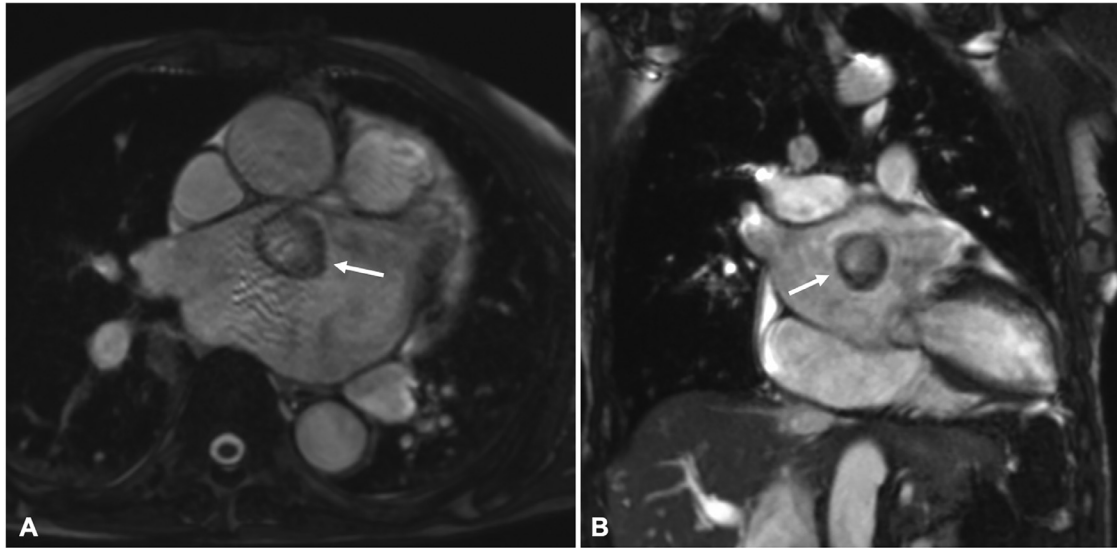


Fig. 3 – Precontrast steady state free precession images were obtained on a Siemens 1.5 Tesla Avanto MRI scanner (Siemens Healthineers, Erlangen, Germany), with axial (A) and coronal (B) imaging demonstrating a 2.7 × 2.8 cm mass (white arrows) in the dilated left atrium, with a thin stalk to the anterosuperior intra-atrial septum.

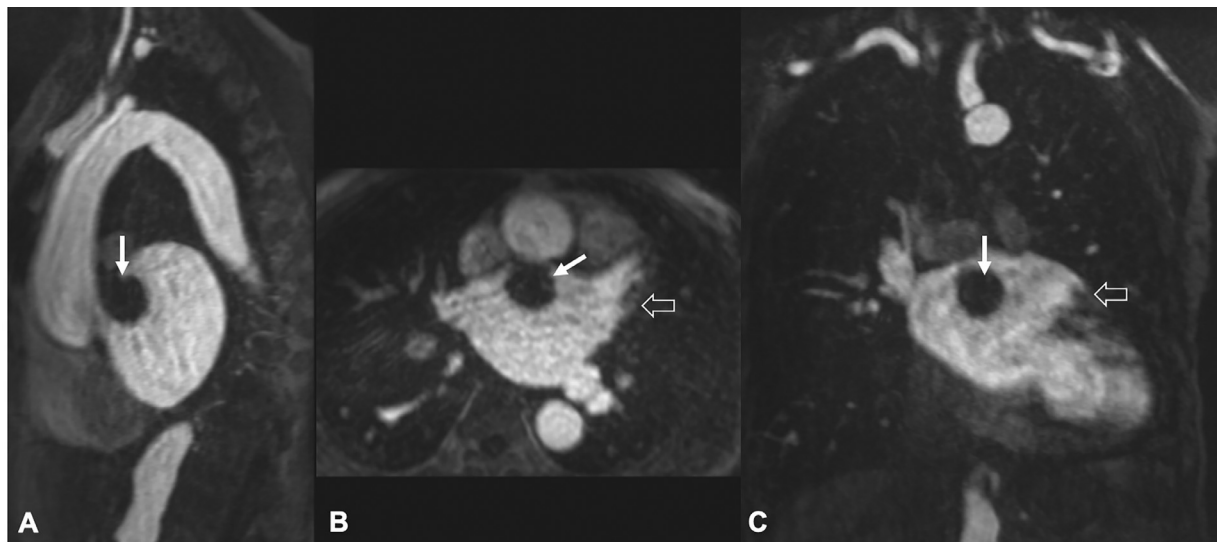


Fig. 4 – High resolution breath-held contrast enhanced MR angiogram in the arterial phase in (A) sagittal, (B) transverse and (C) coronal planes obtained on a Siemens 1.5Tesla Avanto MRI scanner (Siemens Healthineers, Erlangen, Germany), demonstrating the dominant 2.7 × 2.8 cm nonenhancing mass (solid white arrows) in the dilated left atrium, and the smaller lesion in the left atrial appendage (open white arrows).

mass, and Doppler can be used to assess inflow or outflow obstruction of intracardiac flow [4,5]. Three-dimensional and contrast echocardiography, in addition to standard two-dimensional TTE, can provide information about tumor morphology and vascularity [4]. Transesophageal echocardiogram is especially helpful for evaluating atrial masses when there is poor image quality on TTE and when the attachment site of the mass is unclear [4,5]. If the diagnosis remains in question after echocardiography, further imaging studies such as CMR and computed tomography (CT) may be necessary [4].

One of the initial diagnostic steps in the evaluation of a left atrial mass is to distinguish thrombus from tumor. Imaging findings that may suggest a diagnosis of left atrial thrombus include location of the mass within the left atrial appendage, presence of spontaneous echo contrast, enlarged atrial chamber, and presence of stenotic or prosthetic mitral and tricuspid valves [5]. Clinical findings such as low cardiac output state, a diagnosis of atrial fibrillation, and reduction in size of the mass with anticoagulation further raise the suspicion for thrombus [4,5].

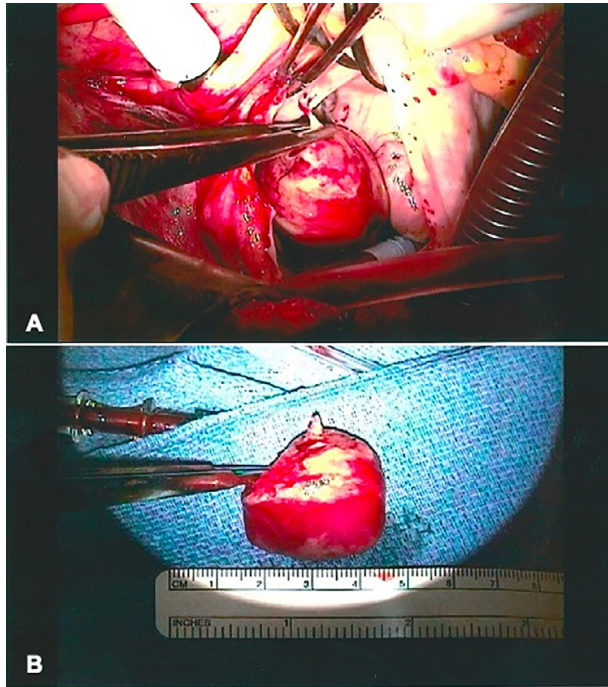


Fig. 5 – Intraoperative images of left atrial mass prior to (A) and after resection (B) revealing the attachment of the mass to the intra-atrial septum by a thin stalk.

When imaging and clinical findings are less suggestive of thrombus, primary and secondary (metastatic) cardiac tumors must be considered. Cardiac tumors are rare and only 5% are primary cardiac tumors (autopsy incidence of 0.001%–0.03%) [6,7]. Primary cardiac tumors can be either malignant or, more commonly, benign. Benign cardiac tumors include myxomas, rhabdomyomas, fibromas, papillary fibroelastomas, hemangiomas, teratomas, pericardial cysts, and lipomas [4,7]. A left atrial mass arising from or near the intra-atrial septum, such as in our case, is suspicious for cardiac myxoma, which is the most common benign cardiac tumor [7]. If ambiguity remains despite echocardiography, CMR and CT imaging can provide

additional information such as tissue characterization and, in the case of tumors, assessment of surrounding anatomy for invasion or spread [4]. In our case, the addition of CMR imaging was useful in establishing a diagnosis. The presence of a nonenhancing mass with T1 hyperintensity in the left atrial appendage was indicative of thrombus as opposed to left atrial myxoma. By contrast, myxomas often have T1 hypointense signals and T2 hyperintensity due to high extracellular fluid content, as well as heterogeneous enhancement following administration of gadolinium (Figs. 6 and 7) [4,8]. The clinical history of atrial fibrillation in a patient who was not on anticoagulant therapy and was also on tranexamic acid, a procoagulant, further supported a diagnosis of thrombus.

Anticoagulant and antiplatelet therapy in hereditary hemorrhagic telangiectasia

Patients with HHT are at increased risk for developing venous thromboembolism or may have a comorbid condition (ie, stroke, atrial fibrillation, and myocardial infarction) that carries an indication for anticoagulant or antiplatelet therapy [9]. These patients may be advised to avoid anticoagulants due to concern for exacerbating their risk of hemorrhage. There are no published large-scale studies of safety or clinical outcomes with the use of anticoagulation or antiplatelet therapies in patients with HHT. Current international guidelines based on expert consensus and small observational studies advise that epistaxis from HHT is not an absolute contraindication to anticoagulation or antiplatelet therapy, and that the decision to use these agents should be based on an assessment of risks and benefits for each patient. Furthermore, patients being considered for anticoagulant or antiplatelet therapy should be screened for cerebral and pulmonary AVMs, as these would increase the risk of life-threatening bleeding [1].

In a study using an online survey, 273 of the 973 (28%) respondents with HHT reported using antiplatelet or anticoagulant therapy [10]. Many reported worsening of nosebleeds, however, 40% of the treatment episodes were associated with no reported change in epistaxis. Notably, there was a signifi-

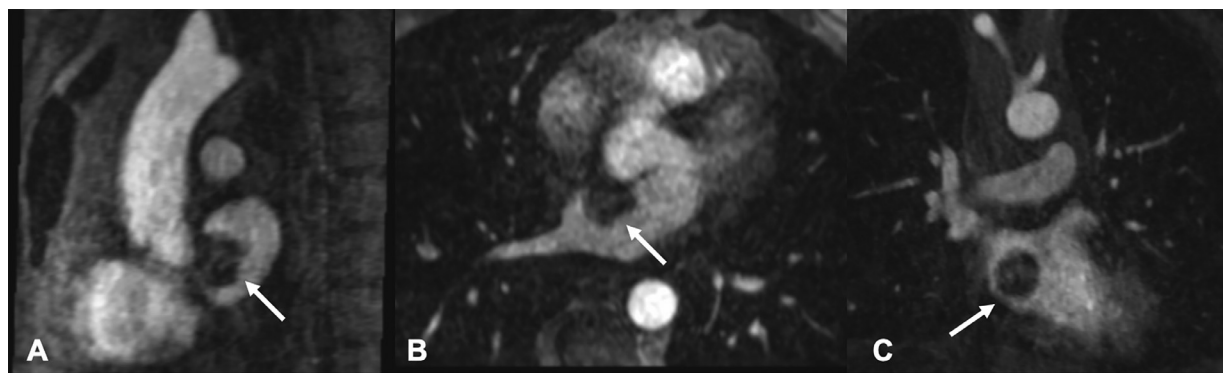


Fig. 6 – High resolution breath-held contrast enhanced MR angiogram in the arterial phase in (A) sagittal, (B) transverse and (C) coronal planes obtained on a Siemens 1.5 Tesla Avanto MRI scanner (Siemens Healthineers, Erlangen, Germany), demonstrating subtle early heterogeneous enhancement of a left atrial myxoma on early post-contrast imaging (white arrows).

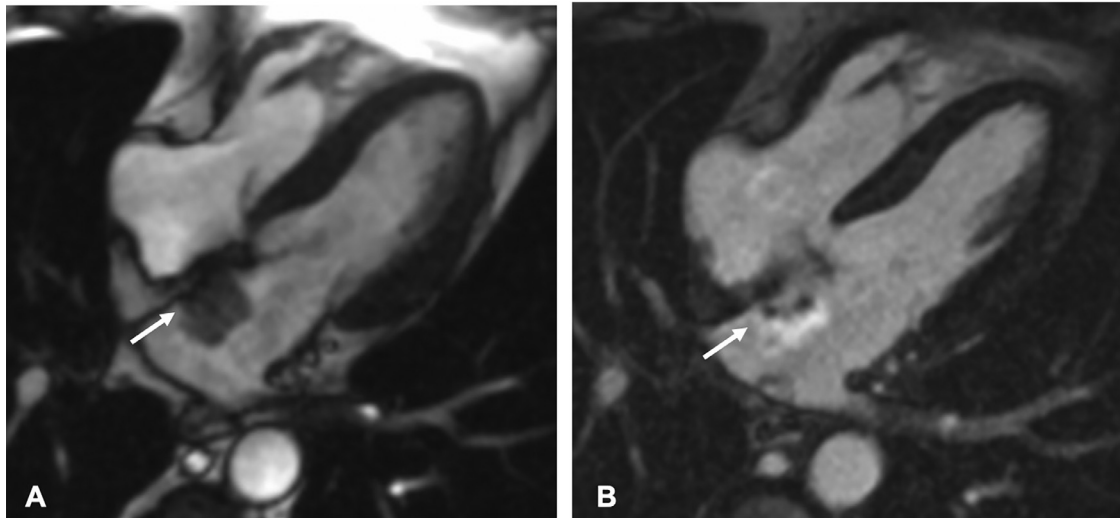


Fig. 7 – Precontrast horizontal long axis balanced SSFP image (A) demonstrates a smoothly marginated mass (white arrow) attached to the intra-atrial septum. 10-15 minute postcontrast magnitude inversion recovery sequence in the horizontal long axis plane at the same level (B) demonstrates heterogeneous enhancement of the left atrial mass, consistent with a myxoma. Both sequences taken on Siemens 1.5 Tesla Avanto MRI scanner (Siemens Healthineers, Erlangen, Germany).

cantly increased rate of hemorrhagic events other than epistaxis reported by patients on anticoagulant therapy as compared to antiplatelet therapy (19.5% vs 8.8%). The authors concluded that these data show a wide variation in the side effect profile and risk for hemorrhage among patients with HHT.

If the benefits of anticoagulant therapy are believed to outweigh the risks, heparin and warfarin are traditionally the first-line choices in patients with HHT. This is predominantly due to the availability of published observational data with regard to the tolerance of these older agents as well as available reversal agents [11]. A retrospective study of 43 patients with HHT receiving anticoagulant or antiplatelet therapy in Canada showed tolerance of 85% to warfarin, 67% to unfractionated heparin, 91% to low-molecular weight heparin, 77% to aspirin, and 67% to clopidogrel [12]. The most common reason for early cessation was an increase in epistaxis. The study reported a 23% incidence of severe complications while on anticoagulant or antiplatelet therapy (defined as emergency room visits, hospital admissions, or blood transfusions) and a calculated rate of 0.1 severe complications per patient-year [12].

More recently, a small retrospective study of 32 treatment episodes among 28 patients at HHT centers in Europe looked at the safety of direct oral anticoagulants (DOACs). This study found that 75% of the treatment episodes were associated with a reported increase in the severity of nosebleeds (73% for apixaban, 85% for rivaroxaban, and 33% for dabigatran). They concluded that, of the DOACs, apixaban appeared to be associated with less bleeding complications than rivaroxaban. Furthermore, 3 of the 11 patients who did not tolerate a DOAC due to exacerbation of nosebleeds were successfully able to use an alternate DOAC [11]. Our patient was initially started on a reduced dose of apixaban (2.5 mg twice daily) due to concern for bleeding, but she subsequently developed severe frequent epistaxis, which resulted in discontinuation of the anticoagulant.

Conclusion

The diagnostic evaluation of left atrial masses requires integrating clinical history with transthoracic and transesophageal echocardiographic findings. If a diagnosis remains uncertain after echocardiography or a cardiac tumor is suspected, CMR and CT imaging can provide additional information about tissue characterization and involvement of extracardiac structures. Patients with HHT and high-flow liver AVMs are at risk of developing atrial enlargement, which can lead to atrial fibrillation and left atrial thrombus. In patients with HHT who develop left atrial thrombus, anticoagulant therapy should be considered after an assessment of the patient's risk of bleeding.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2020.07.050.

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