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CASE REPORT
Cardiovascular imaging

Thrombosis of Chiari's network in the setting of non-bacterial thrombotic endocarditis occurring under non-vitamin K antagonist oral anticoagulation: a case report

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Background Non-bacterial thrombotic endocarditis (NBTE) is a rare condition characterized by sterile thrombi on undamaged valves. We herein report a case of NBTE involving the Chiari's network and the mitral valve, related to a metastatic cancer, and occurring under non-vitamin K antagonist oral anticoagulant (NOAC).

Case summary A 74-year-old patient with metastatic pulmonary cancer was diagnosed with a right atrium mass during pre-treatment cardiovascular check-up. Transoesophageal echocardiography and cardiac magnetic resonance concluded that the mass was a Chiari's network. Two months later, the patient was admitted for a pulmonary embolism and started rivaroxaban. At 1-month follow-up, the patient underwent a new echocardiography, which showed an increased size of the right atrium mass and the presence of two new masses on the mitral valve. She suffered an ischaemic stroke. Infectious work-up was negative. Coagulation factor VIII was 419%. A NBTE with Chiari's network thrombosis and mitral valve involvement was suspected in the setting of a hypercoagulable state related to the active cancer, and intravenous heparin was started, bridged to vitamin K antagonist (VKA) after 3 weeks. All the lesions were fully resolved on follow-up echocardiography at 6 weeks.

Discussion This case highlights an atypical association of thrombosis on right and left heart chamber with systemic and pulmonary embolism, related to a hypercoagulable state. Chiari's network is an embryonic remnant with no clinical significance and is exceptionally thrombosed. Failure of treatment by NOAC highlights the complexity of cancer-related thrombosis, particularly in NBTE, and the necessity of heparin and VKA in our case.

Keywords Marantic endocarditis • Non-bacterial thrombotic endocarditis • Chiari's network • thrombosis • cancer • Non-vitamin K antagonist oral anticoagulant • Case report

ESC Curriculum 2.2 Echocardiography • 4.11 Endocarditis

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Learning points

- Chiari's network is a benign embryonic remnant in the right atrium, usually of no clinical significance but exceptionally could be thrombosed.
- Non-bacterial thrombotic endocarditis is commonly associated with cancer and manifests mostly by pulmonary and systemic thromboembolic events.
- Treatment of non-bacterial thrombotic endocarditis involves anticoagulation by heparin. Although the evidence for oral anticoagulation is low, it suggests that non-vitamin K antagonist oral anticoagulants are inefficient and should be avoided.

Introduction

Marantic endocarditis, also known as non-bacterial thrombotic endocarditis (NBTE), is a rare condition characterized by thrombi forming sterile vegetations on undamaged valves. It mostly involves the left heart valves and is often associated with hypercoagulable state as in active cancer condition but also in other systemic conditions such as antiphospholipid syndrome and systemic lupus erythematosus.[1] Chiari's network is an embryonic remnant of valve of the sinus venosus, appearing as a thin membrane originating from the Eustache valve and has no clinical significance.[2] We herein report a case of both-sided NBTE involving the Chiari's network and the mitral valve, related to a pulmonary cancer, and occurring under non-vitamin K antagonist oral anticoagulant (NOAC) treatment.

Timeline

Time	Events
3 months prior admission	Diagnosis of metastatic pulmonary cancer. Cardiovascular assessment by transthoracic echocardiography (TTE) shows a right atrium mass. Investigation by transoesophageal echocardiography (TEE) and cardiac magnetic resonance concluded that the mass was in reality a Chiari's network.
1 month prior admission	Bilateral pulmonary embolism. TTE shows the same right atrium mass. Rivaroxaban treatment is initiated.
1 day prior admission	Follow-up TTE: increased size of the right atrium mass and new occurrence of two masses on the mitral valve.
At admission	Febrile, amaurosis fugax, diplopia. Infectious work-up negative. Factor VIII three-time the normal range. Ischaemic stroke at the cerebral magnetic resonance. Non-bacterial thrombotic endocarditis is suspected, involving the mitral valve with thrombosis of Chiari's network. Intravenous heparin is initiated.
2 weeks after admission	Follow-up TTE and TEE: decreased size of the right atrium mass and disappearance of mitral lesions.
3 weeks after admission	Bridge therapy to vitamin K antagonist.
6 weeks after admission	Follow-up TTE: resolution of lesion on the mitral valve as well as the thrombosis of the Chiari's network.

Case presentation

A 74-year-old woman was admitted to our hospital department due to a right atrium mass. Three months earlier, she consulted a haematologist due to persistent fever and lymphadenopathy. A diagnosis of metastatic non-small cell lung carcinoma was made. Cardiovascular assessment before cancer treatment by transthoracic echocardiography (TTE) revealed the presence of a mass in the right atrium. A transoesophageal echocardiography (TEE) and a cardiac magnetic resonance were performed to further evaluate this mass, revealing a filamentous formation of 15 × 15 × 19 mm, originating from the inferior vena cava and extending to the interatrial septum, without gadolinium enhancement (*Figure 1*; see Supplementary material online, Video S1). This mass was interpreted as a Chiari's network, and no specific treatment was proposed at the time. Immunotherapy with pembrolizumab was initiated. One month prior admission, she was hospitalized for fatigue. Physical examination revealed peripheral oedema and elevated jugular venous pressure. Laboratory investigation revealed cholestasis. Due to this right-sided acute heart failure, a computed tomography angiography of the chest was performed and showed a bilateral pulmonary embolism (*Figure 2*). The TTE showed the same previously known mass in the right atrium. Rivaroxaban, a non-vitamin K antagonist oral anticoagulant (NOAC), was started and patient was discharged. One day prior to admission, the follow-up TTE showed an increased size of the right atrium mass, as well as two new masses on the mitral valve (*Figure 3*). The patient was referred to our department.

At presentation, she was still febrile with a body temperature of 38.1°C. She presented persistent dyspnoea for several weeks and reported amaurosis fugax as well as transient diplopia. Except for pulmonary cancer, the patient's medical history was only relevant for arterial hypertension. Her usual treatment included perindopril. Her blood pressure was 120/60 mm Hg, heart rate was 90 beats/min, and oxygen saturation was 96% on room air. The physical examination was irrelevant, and there were no signs of heart failure or neurological deficit. Routine laboratory investigations showed a C-reactive protein at 195 mg/L (normal range < 10.0). Blood cultures were negative multiple times. Immunological assays for anti-phospholipid syndrome were negative. Coagulation factor VIII was 419% (normal range: 60–150%).[3] TEE showed two masses on the mitral valve: the first one on the A2 portion of the anterior leaflet, and the second one on the posterior leaflet (*Figure 4*; see Supplementary material online, *Video S2*). These two masses had the same echogenicity as the one in the right atrium. The valve had neither stenotic nor regurgitant complications. A cerebral magnetic resonance was performed and showed multiple bilateral lesions compatible with ischaemic embolism.

A NBTE involving Chiari's network and mitral valve in the setting of a procoagulant state related to the active cancer was suspected, and intravenous heparin was started. To achieve the target range of activated partial thromboplastin time and anti-Xa level, the patient required a high dose of heparin (50.000 units per day for a weight of 50 kg). TTE and TEE realized 2 weeks after heparin initiation, showed a favourable regression of the right atrium mass, as well as the two lesions on the mitral valve. After multidisciplinary discussion, 3 weeks of intravenous heparin was decided with bridging therapy to vitamin K

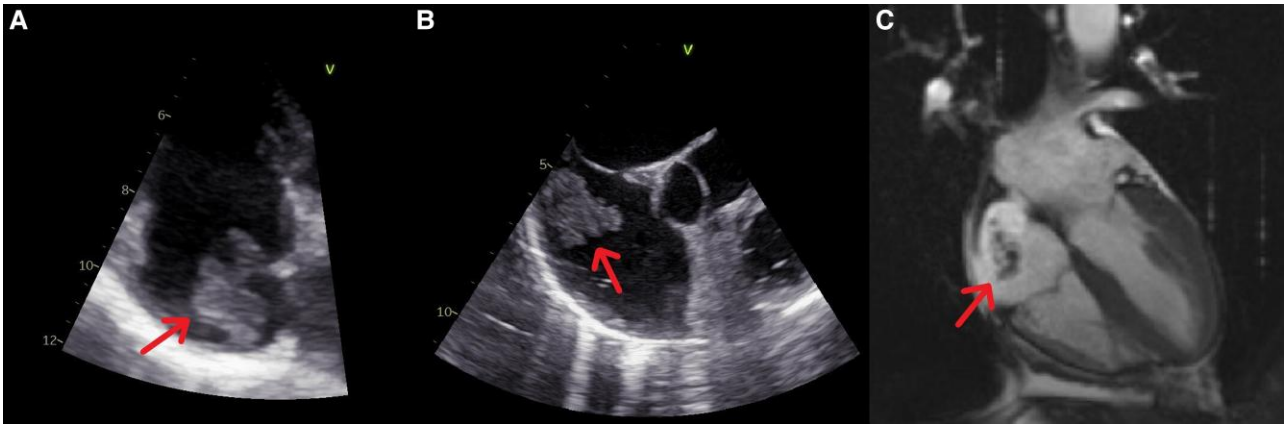

Figure 1 Transthoracic echocardiography (*A*), transoesophageal echocardiography (*B*), and cardiac magnetic resonance (*C*) at first contact. These exams showed the right atrium mass which was attached from inferior vena cava to the interatrial septum (arrow).

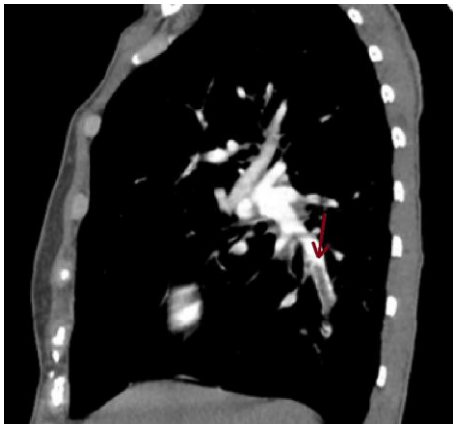

Figure 2 Computed tomography angiography of the chest. Arrow showing pulmonary thrombus.

antagonist (VKA) for life (international normalized ratio target range 2.0–3.0). Follow-up TTE and TEE at 6 weeks showed a persistent filamentous structure coming from the inferior vena cava, which is consistent with the Chiari's network (*Figure 5*). The mitral valve was free from vegetations. On the oncologic level, the patient did not respond to immunotherapy and is undergoing chemotherapy.

Discussion

Chiari's network is an embryonic remnant of valve of the sinus venosus, appearing as a thin membrane originating from the Eustache valve and connecting to another part of the right atrium. The prevalence of Chiari's network is about 2% of the population.[2] Even though it is usually of no clinical significance, it could be confused with vegetation, thrombus, tumoural mass, or tricuspid valve disruption. Thrombosis of Chiari's network is exceptional and is mostly related to catheter like Hickman catheter.[4] On the other hand, some authors report the Chiari's network as a protective filter against pulmonary embolism.[5] In our case, thrombosis of Chiari's network was related to a both-sided NBTE. The pro-coagulant state from paraneoplastic origin due to an active pulmonary cancer led to thrombosis of the network as well as of the mitral valve. The high level of circulant coagulation factor VIII, which was three times normal range, attests to this pro-coagulant state. All the work-up for infectious disease was done in our patient and was negative, excluding an infectious endocarditis. Autoimmune diseases such as anti-phospholipid syndrome were also ruled out. Due to the shape of the lesions and the bilateral distribution, including two lesions on the mitral valve, primary cardiac masses such as papillary fibroelastomas or myxomas were considered unlikely. The diagnosis of NBTE was made after ruling out these diagnoses. Right-sided as well as both-sided NBTE are exceptional and are limited to a few case reports, where diagnosis was often established post-mortem.[6,7,8] To our knowledge, the association of Chiari's network thrombosis and involvement of mitral valve in the setting of a both-sided NBTE have never been described. The patient experienced embolic events in both pulmonary circulation (pulmonary embolism) and systemic circulation (ischaemic stroke) due to thrombosis in both the right and left cardiac chambers.

Expansion of the right atrium mass and the occurrence of the lesions on mitral valve under rivaroxaban treatment revealed the failure of NOACs in NBTE. The pathogenesis of NBTE in cancer is not entirely understood but is probably related to a hypercoagulable state of multifactorial aetiology.[9] Therefore, therapeutic anticoagulation, particularly parenteral during initial management, is necessary, as described in our case. International guidelines support heparin, both unfractionated and low molecular weight, as well as specific treatment of the underlying condition.[10,11] Regarding oral anticoagulation, evidence is limited to case reports and case series.[9] NOACs have not been evaluated and seem inefficient as reported by some case reports in the literature.[12,13,14,15]

At the follow-up TTE of our patient, after 2 weeks of heparin treatment, the mitral valve lesions and the right atrium mass completely disappeared, leaving only a small filamentous structure corresponding to the Chiari's network. Follow-up TTE and TEE, 3 weeks after bridging therapy from heparin to VKA did not show any recurrence of NBTE. Although there is little evidence about VKA in NBTE, it seems to be a more appropriate oral anticoagulant treatment than NOACs, as illustrated by our case. Similarly, in anti-phospholipid syndrome, another cause of NBTE, NOACs are not recommended, especially in patients with triple anti-phospholipid antibody positivity or arterial thrombosis.[16] If recurrence under VKA should occur, lifelong treatment by low-molecular weight heparin would probably be mandated.

In conclusion, we report a NBTE involving the Chiari's network and the mitral valve, related to a hypercoagulable state in the setting of a

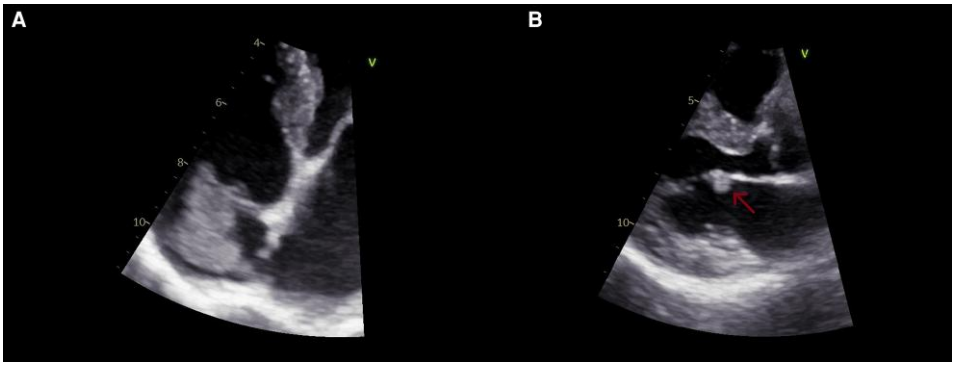

Figure 3 Transthoracic echocardiography at admission, after 1 month of rivaroxaban treatment. (*A*) Showing an increased size of the right atrium mass. (*B*) Showing the new occurrence of mitral lesion (arrow showing the vegetation on the anterior leaflet).

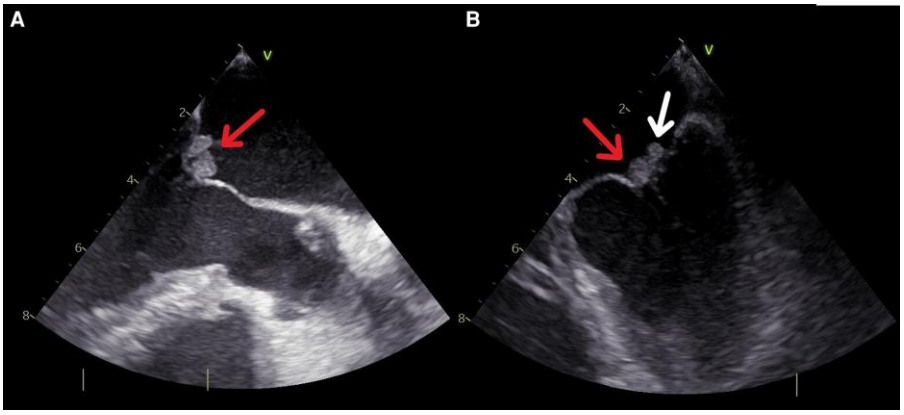

Figure 4 Transoesophageal echocardiography at admission. Transoesophageal echocardiography showed the two vegetations on the mitral valve: the first one on the posterior leaflet (*A*, arrow; *B*, left arrow), the second one on the anterior leaflet (*B*, right arrow).

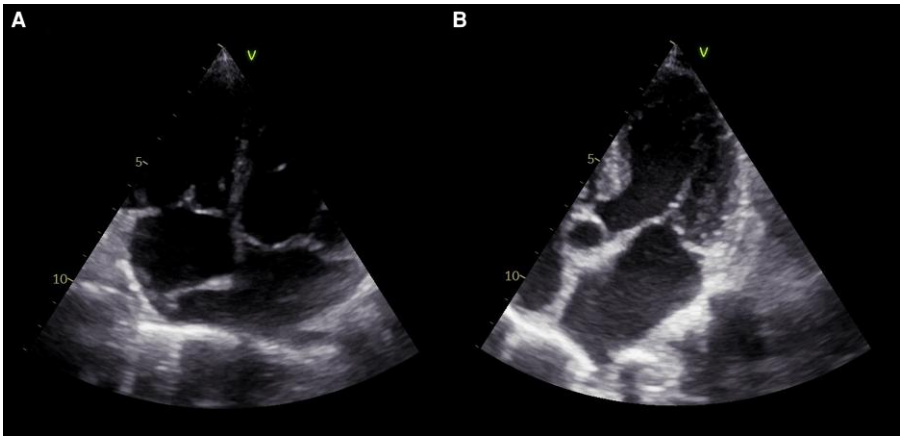

Figure 5 Transthoracic echocardiography after treatment with heparin and vitamin K antagonist. (*A*) Showing a persistent filamentous structure in the right atrium after resolution of thrombosis, consistent with the Chiari's network. (*B*) Showing the resolution of lesions on the mitral valve.

metastatic neoplastic disease, occurring under NOAC and successfully treated by heparin and VKA.

Lead author biography

Wael Zaher graduated from Medical faculty of the Université Libre de Bruxelles in 2018. He is currently completing residency in cardiology in Brussels and is planning to pursue electrophysiology fellowship.

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 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.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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