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CASE REPORT
Cardiac imaging

Primary thyroid leiomyosarcoma with transvenous extension to the right atrium: a case report

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Background Primary thyroid leiomyosarcoma (LMS) is a very rare tumour with less than 40 published cases yet. Direct metastatic extension into the great cervical veins and caval veins is extremely uncommon. Extension to the right heart has not yet been reported.

Case summary A 62-year-old man was admitted for sudden onset of left neck pain and dyspnoea. Computed tomography and ultrasonography found an extensive mass of the left great cervical veins, superior vena cava, and a nodule in the left thyroid lobe. Transesophageal echocardiography visualized large protrusion of this mass into the right atrium. Cytology of a thyroid nodule diagnosed a benign hyperplastic nodule. The mass was considered to be likely an extensive thrombus. The patient was started on anticoagulant therapy. The next course was complicated by pulmonary embolism and later by enterorrhagia. Despite clinical stabilization, the patient died suddenly. Autopsy finding differed from the clinical conclusion. Microscopic investigation revealed that the mass seen in the cervical veins down to the right atrium was a spindle cell tumour with a primary site in the left thyroid lobe. Immunohistochemistry was consistent with the final diagnosis of primary thyroid LMS.

Discussion Differential diagnosis of the masses of great cervical veins and right atrium can be challenging. Pure venous thrombus and tumour thrombus must be distinguished. Thyroid LMS should also be considered in patients with masses in the right atrium and thyroid nodules.

Keywords Case report • Thyroid leiomyosarcoma • Right atrial mass • Intracardiac metastasis • Internal jugular vein • Superior vena cava

ESC Curriculum 2.2 Echocardiography • 2.4 Cardiac computed tomography • 6.8 Cardiac tumours

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Learning points

- Direct metastatic extension of the primary thyroid leiomyosarcoma (LMS) into the great cervical veins and right atrium is extremely uncommon, but possible.
- In addition to thrombi, tumours or tumour thrombi, respectively, should be ruled out in patients with masses in the great cervical veins.
- Thyroid LMS should also be considered in patients with masses in the right atrium and thyroid nodules.
- Cytologic diagnosis of the thyroid nodules is challenging, and the limits of fine *needle aspiration* biopsy should be emphasized.
- Immunohistochemistry plays a crucial role in the diagnosis of LMS.

Introduction

Primary leiomyosarcoma (LMS) is an extremely rare thyroid tumour.[1–4] LMS accounts for less than 0.02% of primary thyroid malignancies.[5]

In thyroid sarcomas, the tumour thrombus, i.e. a collective form of intravascular metastases with thrombotic elements may very rarely extend into cervical veins. To the best of the authors' knowledge, a case of thyroid LMS with extension to the right heart has not yet been published.

We present a fatal case of primary thyroid LMS with transvenous extension into the right atrium. The diagnosis of LMS was made only post-mortem based upon the histomorphology and immunohistochemical features of the tumour.

Timeline

Day 0	Sudden onset of left neck pain and dyspnoea. Computed tomography (CT) and ultrasonographic finding of a nodule in the left thyroid lobe and extensive mass of the left internal jugular vein, left brachiocephalic vein, superior vena cava, and right atrium. Start of anticoagulant therapy with nadroparin.
Day 2	Echocardiographic finding of a large mass in superior vena cava and right atrium.
Day 3	Cytologic diagnosis of a benign thyroid nodule.
Day 23	The first readmission for the swelling of the left half of the neck, left upper limb, and dyspnoea. CT finding of pulmonary embolization. Start of warfarin therapy.
Day 45	Second readmission for enterorrhagia due to severe hypocoagulation state with warfarin overdose. Haemostatic therapy and red blood cell transfusions.
Day 49	Sudden death.
Day 50	Histological finding of a spindle cell tumour in the left thyroid lobe. Immunohistochemistry was consistent with the final diagnosis of primary thyroid LMS.

Case presentation

A 62-year-old man with a history of arterial hypertension, type 2 diabetes mellitus was admitted for sudden onset of left neck pain and dyspnoea. Clinical examination revealed mild tachycardia (105 bpm) and tachypnoea (22 rpm), dilatation of the left cervical veins, and swelling of the entire left upper limb. Vesicular breathing without pathological breath sounds was present. Blood pressure and oxygen saturation on ambient air were normal. The left thyroid lobe was painless, slightly enlarged, and stiffer compared with right. Electrocardiogram (ECG) recording was normal except for sinus tachycardia. The chest radiograph was unremarkable.

Laboratory investigations revealed leucocytosis of 30.3 10^9/L (reference range 3.6–11.0 10^9/L), iron deficiency anaemia [haemoglobin 10.3 g/dL (reference range 12.5–15.0 g/dL), and iron 2.4 µmol/l (reference range 6.6–28.0 µmol/L)]. Platelet count was normal. Significant elevations of D-dimer at 8.5 mg/L fibrinogen equivalent unit (FEU) (reference range <0.47 mg/L FEU) and C reactive protein (CRP) at 202 mg/L (reference range <5 mg/L) were noted. Mild elevations of N-terminal pro B-type natriuretic peptide (NT-proBNP) at 486 ng/L (reference range <125 ng/L) and troponin T at 37 ng/L (reference range <14 ng/L) were found. Thyroid stimulating hormone (TSH), free thyroxine, and procalcitonin levels were normal.

Neck ultrasonography revealed a hypoechogenic mass filling the dilated left internal jugular vein (IJV). The left thyroid lobe was inhomogeneous, enlarged (25 × 24 × 44 mm) with a hypoechogenic nodule of 22 × 19 × 20 mm. Several slightly enlarged parajugular lymph nodes were present. Computed tomography (CT)scan revealed a dilated left IJV (20 mm), filled with a hypodense inhomogeneous mass that extended through the superior vena cava (SVC) into the right atrium (*Figure 1* and Supplementary material online, *Figure S1*). The maximum size of the mass was 78 × 42 × 30 mm. This lesion also partially affected the left brachiocephalic and subclavian vein. CT confirmed a nodule with blurred edges measuring 20 × 18 × 20 mm in the enlarged left thyroid lobe.

Two- and three-dimensional transthoracic and transesophageal echocardiography showed the complete obstruction of the visualized SVC by homogeneous hypoechogenic mass. The mass largely protruded into the right atrium and was partially mobile (*Figure 2*, *Video 1* and Supplementary material online, *Video S1*). There was no tricuspid valve obstruction. Inferior vena cava was not affected. The mass displayed on CT and echocardiography was considered as likely to be extensive thrombosis of great cervical veins, SVC, and right atrium.

The patient underwent the ultrasound-guided fine needle aspiration (FNA) biopsy of a nodule in the left thyroid lobe. Cytology revealed a regressively changed benign colloidal hyperplastic nodule, Bethesda II. The patient received therapeutic doses of nadroparin based on anti-Xa levels. As a result, the neck and left upper extremity swelling was reduced, and the patient was discharged.

However, 10 days after discharge, swelling of the left half of the neck, left upper limb, and dyspnoea became more pronounced. The patient was readmitted. CT angiography revealed pulmonary embolization into the right apical segmental artery and subsegmental branches for

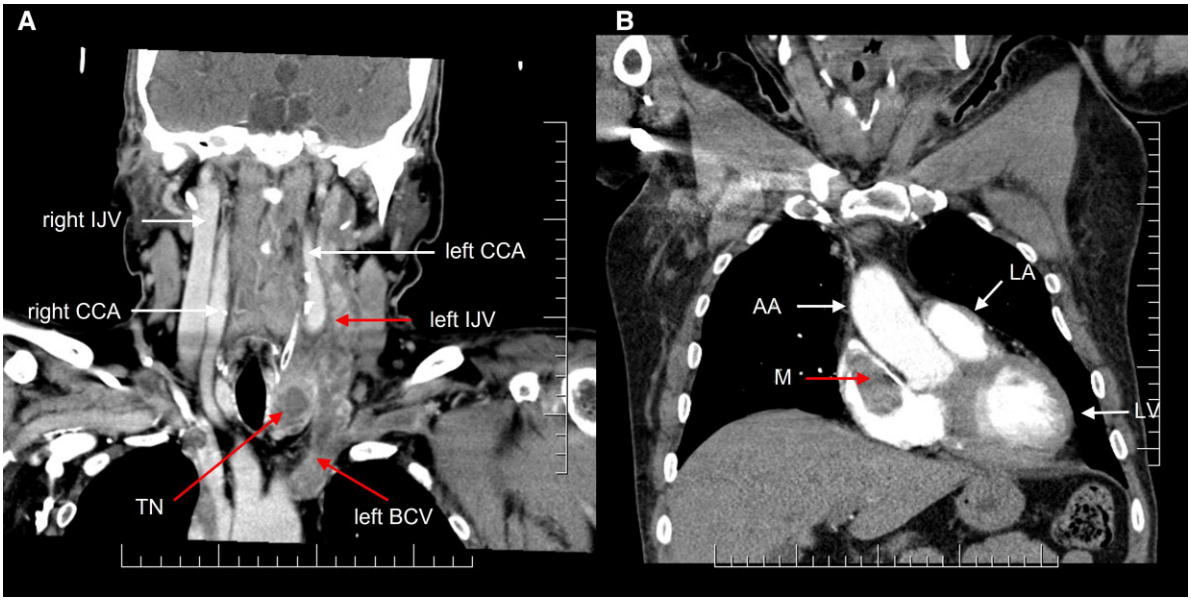


Figure 1 Computed tomography. (*A*) Hypodense mass filling the left internal jugular vein and left brachiocephalic vein. The nodule in the enlarged left thyroid lobe. (*B*) Mass extension into the right atrium. AA, ascending aorta; CCA, common carotid artery; LA, left atrium; LV, left ventricle.

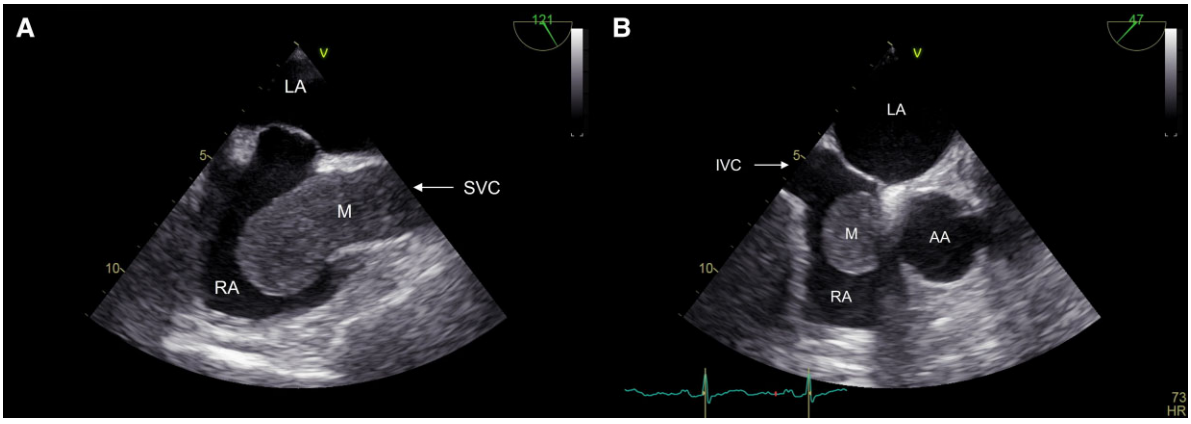


Figure 2 Transesophageal echocardiography. (*A*) Hypoechogenic mass protruding into the right atrium from the completely obstructed superior vena cava. (*B*) The relation of the mass to the inferior vena cava and ascending aorta. LA, left atrium; RA, right atrium.

the right posterior basal segment. The CT finding on the cervical veins, SVC, and right atrium was identical to that at the first hospitalization. The mass was repeatedly diagnosed as an extensive thrombus. CT of the abdomen was without significant abnormalities. The clinical finding was concluded as pulmonary embolism from the right atrial thrombus. The patient's anticoagulation therapy was changed to warfarin and was later discharged. Warfarin was indicated as the second choice due to the failed clinical effect of nadroparin. The international normalized ratio (INR) at discharge was within the therapeutic range.

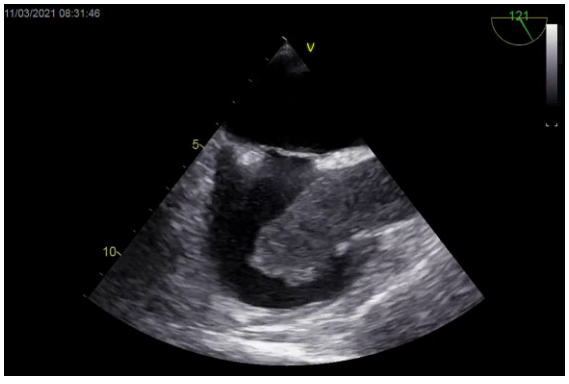
Seventeen days after the discharge from the second hospital stay, he was admitted to hospital due to enterorrhagia. His haemodynamic state was stabilized. Laboratory investigations revealed a decrease in haemoglobin to 9.2 g/dL and a severe hypocoagulation state with warfarin overdose (INR 10.3). The overdose was caused by the erroneous use of an increased warfarin dose. Gastroscopy showed spotted antral gastritis; otherwise the finding was normal. Rectoscopy found no source of bleeding. During the hospitalization, haemoglobin level dropped to 6.6 g/dL. After haemostatic therapy and transfusion of three units of packed red blood cells, the patient showed no signs of active bleeding. The INR value improved to 1.43, and the haemoglobin rose to 11.2 g/dL. Nevertheless, patient suddenly died on the fifth day.

At autopsy, there was a yellowish-white, elastic, nodular mass, 25 mm in diameter, located in the left thyroid lobe, with large areas of central necrosis. The mass propagated through the left IJV, left brachiocephalic vein, and SVC into the right atrium (*Figure 3* and Supplementary material online, *Figure S2*). The microscopic investigation found a spindle cell tumour, likely originating from the venous wall. The tumour was composed of irregular whorled and storiform fascicles of parallelly arranged spindle cells with moderate nuclear pleomorphism and high mitotic rate, including atypical mitotic figures (*Figure 4*). Immunohistochemistry of the tumour demonstrated diffuse reactivity for vimentin, smooth muscle actin, sarcomeric actin, and irregular reactivity for calponin and caldesmon, mainly at the periphery of the tumour (*Figure 5*). Staining for desmin, myogenin, myogenic transcriptional regulatory protein (myoD1), thyroglobulin, cytokeratin coctail (AE1), thyroid transcription factor 1 (TTF1) was negative. The immunohistochemical staining was performed with Flex prediluted antibodies and an immunohistochemical detection system (Agilent Technologies, Santa Clara, CA, USA) in a DAKO Autostainer (DAKO, Glostrup, Denmark). The final diagnosis was primary thyroid LMS, likely arising from the vessel wall. Distant metastases of the tumour have not been found. The autoptic finding was negative in terms of secondary thyroid LMS.

Discussion

Primary thyroid LMS is assumed to arise from smooth muscle cells of the capsular vessels of the gland.[6] It is a strikingly uncommon tumour. So far, less than 40 cases have been published (limited to English).[4,5] This paper adds a new case to the literature. An exceptional feature of this case is the extension of the tumour to the right atrium.

Preoperative diagnosis of thyroid LMS can be very challenging because it has no characteristic imaging features.[1,5] Our case presented here confirms this fact. The dominant imaging finding was an extensive mass in the great cervical veins, SVC, and right atrium. This mass



Video 1 Transesophageal echocardiography demonstrates large hypoechogenic mass extending from the superior vena cava into the right atrium.

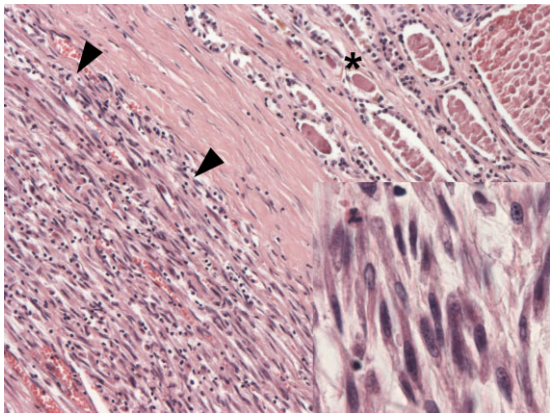


Figure 4 Thyroid gland tissue (*) infiltrated by a spindle cell sarcoma (arrow). Haematoxylin and eosin, original magnification 100×; insertion 400×.

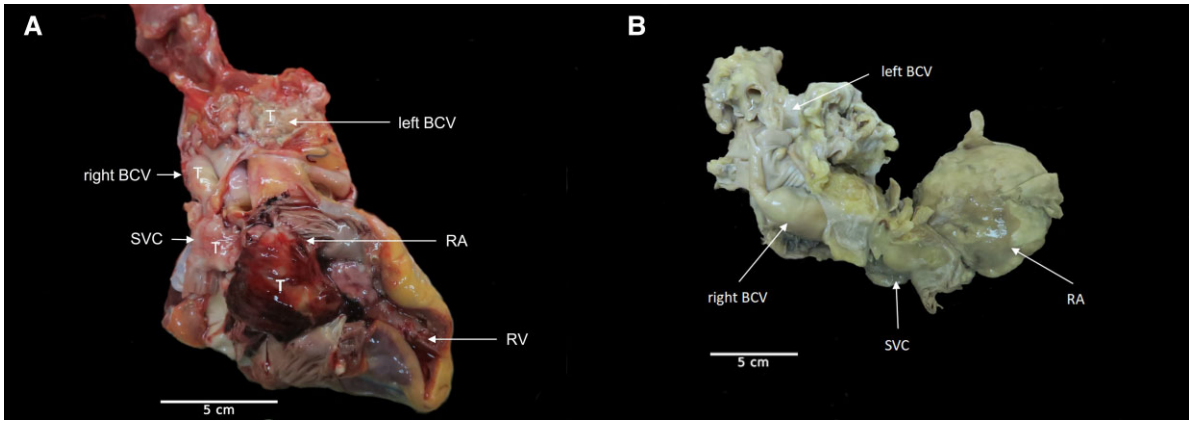


Figure 3 Autopsy macroscopic examination. (*A*) The tumour affecting the left and right brachiocephalic vein, superior vena cava, and right atrium. (*B*) The total tumour specimen. RV, right ventricle.

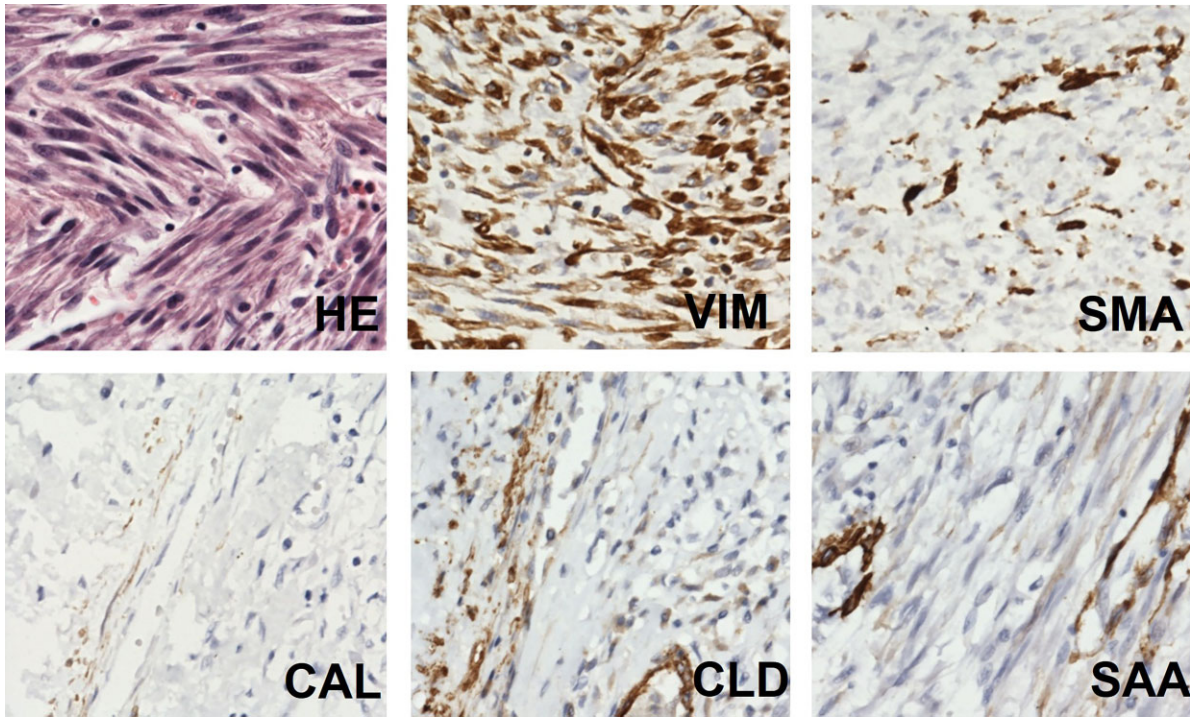


Figure 5 Immunophenotype of the spindle cell tumour was diffusely positive for vimentin, smooth muscle actin, sarcomeric actin. Positivity for calponin and caldesmon is more pronounced at the periphery of the tumour. Haematoxylin and eosin, 200×.

was considered intra vitam to be a thrombus, and the patient was started on anticoagulant therapy. Negative cytology from the thyroid nodule reduced the likelihood that the mass was a tumour. This finding predominantly led to diagnostic confusion. False-negative FNA results for thyroid nodules have been reported as 0–14%.[7] Rebiopsy after an initially benign or inadequate FNA yielded the correct diagnosis in approximately half of cases. Although FNA is a useful test, clinical findings should overrule cytologic data in order for timely treatment to occur.[7] Furthermore, the diagnostic yield of FNA in primary thyroid LMS is not sufficiently known. Core needle biopsy has the potential to overcome the limitations of FNA by obtaining a large tissue sample.[8] In our case, the final diagnosis was made only post-mortem, based on the immunohistochemical features.

In the case of venous masses, a thrombus, tumour, or tumour thrombus, respectively, must be distinguished. The typical contrast-enhanced CT findings for purely venous thrombus include distended veins with enhancing walls, low-attenuating intraluminal filling defects, and adjacent soft-tissue swelling. On the other hand, tumour thrombus show enhancing heterogeneous intraluminal tumour thrombi and low-density thrombi surrounded by a rim of contrast,[9] called a ring sign. This sign indicates the possibility of surgical removal by thrombectomy.[10] However, it is not always easy to distinguish tumour thrombus and venous thrombus as both may occur simultaneously. Therefore, early initiation of anticoagulants to prevent and dissolve the existing thromus is essential.[11]

It is debatable whether the early diagnosis of the thyroid LMS would significantly improve the patient's prognosis. We assume that the prognosis would be unfavourable even in the case of early intensive therapy. Vujosevic et al. presented the course of primary thyroid LMS in 29 published cases. Of the 26 patients with known outcomes, 17 passed away. Of these, 15 died within one year from their initial diagnosis.[4] The prognosis is poor, with an estimated 1-year survival rate of 5–10%.[12] Aggressive surgery, adjuvant radiotherapy, and chemotherapy have shown no beneficial effect on survival.[2] An efficacious multidisciplinary treatment protocol is lacking.[1]

Lead author biography

Dr. Juraj Dubrava graduated from Comenius University in Bratislava as Summa Cum Laude. He received his PhD degree in Internal Medicine from Comenius University. He serves as a senior cardiologist at the Department of Cardiology, University Hospital in Bratislava, Slovakia (Clinical Head). He is especially interested in clinical cardiology and echocardiography. In addition, his research interests are focused on heart failure, cardio-neurology, and cardio-oncology. Since 2015, he has been a Fellow of the ESC (FESC).

Supplementary material

Supplementary material is available at *European Heart Journal – Quality of Care and Clinical Outcomes* 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's next-of-kin in line with COPE guidance.

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