Case report of a ‘snake thrombus’ in the right heart: a rare finding on echocardiography

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Background
A right heart thrombus originating from an inferior vena cava thrombosis (IVCT) is a rare entity. In accordance with venous thromboembolism (VTE), IVCT can be categorized as primary or secondary. Secondary IVCT can be the result of a predisposing hypercoagulable state and/or from external compression on the inferior vena cava (IVC) such as in case of malignancies. Renal cell carcinoma (RCC), amongst others, has been described in the context of secondary IVCT.

Case summary
An 80-year-old man was presented in our emergency department with complaints of dyspnoea and oedema. Echocardiography revealed a large snake-like thrombus in the IVC extending into the right atrium. Subsequent computed tomography resulted in a diagnosis of an RCC. The patient was considered to be in too poor clinical condition for surgical removal. In the next days, his condition deteriorated, after which palliative care was initiated and the patient deceased at day 12 of admission.

Conclusion
A right heart thrombus is a rare finding during echocardiography. This case demonstrates an incidental finding of a ‘snake thrombus’ in the IVC and right heart secondary to RCC. This case illustrates the importance and additional value of echocardiography in the setting of suspected right-sided heart failure.

Keywords
Right heart thrombus • Inferior vena cava thrombus • Renal cell carcinoma • Echocardiography • Case report

Introduction
Venous thromboembolism (VTE) is an important cause of mortality and morbidity and includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). On their way to the lungs, however, DVT may also be observed as a ‘snake thrombus’ in the inferior vena cava (IVC) and even within the right heart. Such thrombi are a rare extracardiac finding (up to 0.1%) in echocardiography.1

Inferior vena cava thrombus (IVCT) is, with a population-based incidence of less than 2/100 000 in 5 years, rare and accounts for about

Learning points
• Echocardiography can differentiate between a cardiac and non-cardiac origin of symptoms suspect for right-sided heart failure, such as a rare inferior vena cava thrombosis (IVCT).
• The finding of IVCT should raise immediate suspicion of underlying pathology, such as malignancy.
• The cornerstone of the treatment of IVCT consists of anticoagulation therapy, preferably with low-molecular-weight heparin (LMWH).
• Tinzapanin could be argued as the LMWH of first choice, due to its large molecular mass and no need for dose reduction at a glomerular filtration rate above 20 mL/min.
1.5% in hospitalized patients with confirmed DVT. The true incidence of IVCT, however, is unknown due to frequent absence of symptoms and lack of standardized methods for its detection and reporting. IVCT most often presents in isolation (78%), but can also result from propagation of thrombus from the iliac veins. Patients with untreated IVCT have high rates of morbidity, ranging from post-thrombotic syndrome (PTS) in about 90%, venous claudication in 45%, to PE in 12–30% of patients. The mortality rate of patients with IVCT is twice as high as those with DVT confined to the lower extremities. The detection of IVCT typically gives rise to a second diagnosis requiring further management and investigation. The clinical outcome is typically determined by the underlying condition that initially caused the thrombosis.

Right heart thrombi, likewise, are a rare entity. Unlike left heart thrombi, they might originate from two sources: (i) transferred or autochthonous or type B clots, which develop within the heart, mainly in the context of right heart failure. Type A thrombi are long, thin, extremely mobile, and have a worm-like appearance, while type B thrombi are less mobile, non-specific clots, resembling left heart thrombi. Compared with patients with type B thrombi, patients with type A thrombi represent a high-risk group, who usually develop severe PE and have a very high mortality, depending on surgical (27% mortality) or conservative treatment (5%).

The current paper describes a rare case of a high-risk type A—thus snake like—thrombus that was observed in the right atrium during echocardiography and which originated directly from the IVC. Its finding led to the diagnosis of renal cell carcinoma (RCC).

## Timeline

| Time       | Location                  | Events                                                                 |
|------------|---------------------------|------------------------------------------------------------------------|
| Admission  | Emergency room            | Admission to the hospital with complaints of dyspnoea and oedema with unknown cause. Transthoracic echocardiogram showed IVCT. Start of anticoagulant therapy with tinzaparin 14 000 IE once a day (a 30% dose reduction on the calculated 20 000 IE on his 115 kg body mass). |
| Day 1      | General ward              | Computed tomography scan of the abdomen showed mass in the right kidney suspect for renal cell carcinoma. |
| Day 3      |                           | Computed tomography scan of the thorax showed no metastases. Multidisciplinary consultation: clinical condition too poor for surgery. Plan biopsy to consider for neo-adjuvant chemotherapy. |
| Day 4      |                           | Switch to heparin intravenous due to inadequate anti-Xa level (0.33 U/mL). |
| Day 7      |                           | Progressive kidney failure with congestion. |
| Day 9      |                           | Start of palliative care. |
| Day 12     |                           | The patient deceased. |

## Case presentation

An 80-year-old obese man with a past history of smoking, diabetes mellitus, hypertension, colon, and prostate carcinoma (which were curatively treated with surgery and radiation therapy in 2004 and 2017 successively) was presented in our emergency department (ED) with complaints of progressive dyspnoea and bilateral lower extremity oedema, as well as a weight gain of 10 kg in a few weeks. Medication used by the patient upon admission is listed in Table 1, the dosage of the medication had not been changed recently. Vital signs were normal. Cardiac examination was normal, no additional heart sounds were heard and the jugular veins could not be visualized due to severe obesity. With pulmonary auscultation mildly decreased breath sounds in the lower region bilaterally were heard. Abdominal examination revealed a distended abdomen with tympanic percussion on the left and right side suspect for ascites. In the lower extremities, extensive bilateral oedema was found.

An electrocardiogram showed new-onset atrial fibrillation with normal ventricular response, there were no signs of ischaemia. Laboratory tests revealed normocytic anaemia (haemoglobin level 7.6 mmol/L, normal 8.5–11.0 mmol/L), elevated D-dimer levels (3.17 mg/L, normal -0.50 mg/L), elevated gamma-glutamyl transferase (GGT 89 IU/L, normal -55 IU/L), and decreased renal function (creatinine 233 μmol/L, normal 59–104 μmol/L). For additional laboratory values at the time of presentation, see Table 2. A transthoracic echocardiogram performed at the ED showed a left ventricle with normal dimensions and a preserved left heart function (ejection fraction 60%), a D-shaped left ventricle in both systole and diastole suggesting increased right-sided pressure, mitral annular calcification without valve dysfunction and left atrial dilatation. In the IVC, a ‘snake thrombus’ was seen, visible up to the right atrium (Figure 1A and B, Movies 1 and 2). Patient underwent computed tomography (CT) of the abdomen to screen for possible causes of IVCT which revealed a large mass (9 cm × 10 cm × 8 cm) in the right kidney with growth into the IVC, highly suspect for an RCC (Figure 2A and B). A CT-thorax showed no metastases. The patient was diagnosed with a right-sided T3bN0Mx RCC.

According to current guidelines, anticoagulant therapy was initiated with low-molecular-weight heparin (LMWH). Due to the reduced glomerular filtration rate (GFR) a reduced dose of tinzaparin was administered. After 3 days factor Xa levels were checked and revealed a level of 0.33 U/mL (normal 0.5–1.2 IU/mL), which was

## Table 1 Medication used by the patient upon presentation

| Medication          | Dose            |
|---------------------|-----------------|
| Bumetanide          | 4 mg once a day |
| Darbepoetin alfa    | Every 2 weeks   |
| Insulin degludec/liraglutide 100 E/3.6 mg/mL | 32 E once a day |
| Irbesartan          | 300 mg once a day |
| Nifedipine          | 30 mg once a day |
| Omeprazole          | 20 mg once a day |
| Pregabalin          | 75 mg twice a day |
| Tamsulosin          | 0.4 mg once a day |
considered inadequate and the patient was switched to heparin intravenous. The possibility of neo-adjuvant chemotherapy and surgical therapy were considered in a multidisciplinary team. However, the clinical condition of the patient deteriorated significantly over the next few days with progressive dyspnoea, oedema, and kidney failure. The patient deceased on day 12 of admission, after initiating palliative care.

Discussion

Our case showed an incidental finding of an IVCT secondary to RCC presenting as a right heart, snake-like (type A) thrombus during echocardiography.

In accordance with VTE, IVCT can be categorized as primary/idiopathic or secondary/provoked. Primary IVCT develops without an identifiable cause. Secondary IVCT is the result of a predisposing hypercoagulable state such as thrombophilia, malignancy, inflammation, previous surgery, smoking, obesity, congenital IVC abnormalities, nephrotic syndrome, or oral contraceptives. Secondary IVCT can be further categorized into (type 1) IVCT with outflow obstruction in which IVCT is caused by the presence of caval stenosis/occlusion resulting from extrinsic compression or from a lesion within the IVC, and (type 2) IVCT without outflow obstruction in which IVCT develops in the absence of caval stenosis/occlusion and is induced by a disease or risk factor.

Malignant tumours such as renal cell, hepatocellular, adrenocortical, and pancreatic carcinoma as well as Wilms’ tumour and retroperitoneal metastases have been described earlier in the context of IVC compression and IVCT. In fact, in a large observational study, IVCT was associated with cancer in 37.5% of cases, although in <0.1% of patients hospitalized with cancer IVCT was diagnosed.

RCC is the most common form of kidney cancer, with a peak incidence in the 6th and 7th decade of life. It is more common in men than women with a 1.5:1 male predominance. Risk factors among other things include smoking, obesity and hypertension. Textbook presentation of the classical triad of flank pain, haematuria, and palpable abdominal mass is rare. It is reported that more than 70% of RCCs are detected incidentally by non-invasive imaging used to investigate various non-specific symptoms. Venous migration and tumour thrombus formation are unique aspects of RCC, and it is reported up to 10% of all patients with RCC. The process of

| Laboratory values | Reference range | Level at admission |
|-------------------|----------------|-------------------|
| Haemoglobin       | 8.5–11.0 mmol/L | 7.6               |
| Sodium            | 135–147 mmol/L  | 134               |
| Potassium         | 3.5–5.0 mmol/L  | 4.4               |
| Creatinine        | 59–104 μmol/L   | 233               |
| Blood urea nitrogen | 2.1–7.1 mmol/L | 30.4              |
| eGFR (MDRD)       | ≥90 mL/min/1.73 m² | 24             |
| C-reactive protein | -10 mg/L      | 12                |
| Alkaline phosphatase | -115 IU/L   | 90                |
| Gamma-GT          | -55 IU/L       | 89                |
| ALAT              | -35 IU/L       | 30                |
| ASAT              | -35 IU/L       | 32                |
| NT-proBNP         | -12 pmol/L     | 210               |
| D-dimer           | -0.50 mg/L     | 3.17              |

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; Gamma-GT, gamma-glutamyltransferase; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

Figure 1 (A) Two-dimensional transthoracic echocardiography image obtained upon admission in subcostal view shows a large snake-like thrombus in the inferior vena cava (asterisk). (B) Two-dimensional transthoracic echocardiography image obtained upon admission in subcostal view shows a large snake-like thrombus in the inferior vena cava extending into the right atrium (asterisk).
Thrombus formation is thought to be due to endothelial damage and subsequent thrombosis incurred from tumour invasion into the IVC wall as well as the prothrombotic state of malignancy. In addition, if the tumour gives compression on the IVC it causes turbulent flow and venous stasis, facilitating formation of thrombus.

IVC-T is an entity difficult to diagnose at clinical presentation. There is a variety of symptoms which can occur according to the extentiveness of the thrombosis. Common complaints are related to lower extremity DVT such as leg pain and swelling. Clot migration might result in embolization to the lungs and to renal and hepatic veins. In case of PE, dyspnoea and pain may be accompanying symptoms. When the renal veins are involved, flank pain, oliguria, anuria and haematuria may be observed. When obstruction of the hepatic veins occurs and liver venous outflow is compromised, hepatic congestion and failure may result in lower extremity oedema, ascites, caput medusa (dilated superficial abdominal veins), liver dysfunction, and jaundice.

Hence, in the presence of IVC-T, it is important to evaluate renal and liver functions. IVC-T is normally diagnosed with lower extremity ultrasonography, CT, magnetic resonance imaging, or trans-catheter venography, but can accidentally, such as in our case, be found during echocardiography while visualizing the right atrium and/or the IVC.

The goals of treatment of IVC-T are the treatment of acute symptoms, minimizing the risk of PE and reducing the risk of residual symptoms such as lower limb swelling and pain, and chronic episodes such as PTS. Aetiology directs treatment, in which pharmacotherapeutic, endovascular, and surgical options are available.

The primary treatment is anticoagulation therapy for reducing thrombus propagation and to attenuate symptoms. Anticoagulation therapy should always be targeted to the patient, taking into account the concurrent risk of bleeding. Although there are no specific guidelines for anticoagulation management in patients with IVC-T, the 2017 European Society of Cardiology guidelines for the diagnosis and management of DVT recommend the use of anticoagulation with LMWH in both the acute and chronic phase in the setting of malignancy, since the superiority of LMWH over short-term heparin followed by vitamin K antagonists is well documented. The present ESC guideline lacks a recommendation on a specific LMWH or on dose reduction in patients with cancer and/or reduced GFRs. However, several studies have meanwhile addressed this issue. Tinzaparin has the highest molecular weight among LMWH (see Table 3) and is therefore less dependent on renal clearance as it is mainly metabolized through the reticulo-endothelial system. Tinzaparin stands out as no dose reduction (of the therapeutic dose of 175 IU/kg) or factor Xa measurement is needed if the GFR is above 20 mL/min (as opposed to >30 mL/min for e.g. daltepa-, enoxa-, and nadroparin). In retrospect, the dose reduction that was applied in our case thus seems unjustified and the observed inadequate factor Xa levels are in line with the studies previously described.

For patients with primary and secondary IVC-T, the use of catheter-directed thrombolysis (CDT) can result in a lower risk of developing PTS. The benefits should outweigh the increased risk of bleeding. There are limited data on the use of pharmacomechanical thrombolysis (PMT), but it can be considered in primary IVC-T over CDT alone because it can improve the efficiency of thrombolysis. However, Vedantham et al. showed no significant differences in the occurrence of PTS between patients who underwent PMT in addition to anticoagulation therapy and patients treated with anticoagulation therapy alone. There was a difference in the severity of PTS for the intervention group, but the improvement in quality of life from baseline to 24 months did not differ significantly. Finally, for secondary IVC-T, the main strategy is to take away the associated risk factors, thus treating the underlying disease.

Movie 1 Two-dimensional transthoracic echocardiography image obtained upon admission in subcostal view shows a large, highly mobile, snake-like thrombus in the inferior vena cava up extending into the right atrium.

Movie 2 Two-dimensional transthoracic echocardiography image obtained upon admission in subcostal view shows a large, highly mobile, snake-like thrombus in the inferior vena cava up extending into the right atrium.
Conclusion

In this case, we present a rare finding of an intra-cardiac snake thrombus originating from the IVC on echocardiography which led to the diagnosis of RCC. The case illustrates the importance of echocardiography in the setting of symptoms of right-sided heart failure. The finding of a right heart thrombus or an IVCT mandates further investigation of an underlying cause, while its swift treatment may prevent acute fatal consequences such as massive pulmonary emboli.

Lead author biography

Nienke A.M. Bosman was born in Woerden, the Netherlands in 1991. She received her medical training at the Vrije Universiteit of Amsterdam. Currently, she is following her residency in Cardiology at the OLVG Hospital in Amsterdam.
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’s next of kin in line with COPE guidelines.

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