CASE REPORT

Tumour thrombus of the inferior vena cava extending into the right atrium in the setting of colon cancer

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SUMMARY

Tumour thrombus is seen in renal cell and hepatocellular carcinoma, but is rarely reported in colorectal cancer.

A woman aged 46 years, with metastatic colonic adenocarcinoma, was found to have a large mass in the inferior vena cava (IVC) extending into the right atrium. Although this lesion was initially thought to be bland thrombus, imaging with contrast-enhanced CT scan and contrast-enhanced ultrasound supported the diagnosis of tumour thrombus. Despite the large size of the lesion, the patient was asymptomatic. Her lack of symptoms, and poor overall prognosis from her cancer led to the decision to avoid aggressive surgical or radiological interventions. Several months later, the patient passed away. At autopsy, there was no evidence of fatal embolisation from the pre-existing thrombus. Diagnosis of tumour thrombus in the IVC is difficult and management can be challenging due to the significant risks associated with treatment options.

BACKGROUND

The occurrence of tumour thrombus is well linked to renal cell carcinoma (RCC) and hepatocellular carcinoma (HCC), and has also been described in adrenocortical carcinoma and pancreatic neuroendocrine tumour. In the context of colorectal cancer (CRC), however, the occurrence of this phenomenon is not commonly reported. A recently published case series of 43 discrete cases provides some insight, but heterogeneity in patient demographics, performance status and tumour histopathology render it difficult to draw any strong conclusions.¹ As a result of the limited occurrence of tumour thrombus in the setting of CRC, there are no guidelines for the diagnosis and management of this complication. In this case, the thrombus was particularly unique in that radiographically, it extended up the inferior vena cava (IVC) directly into the right atrium. With all of these considerations, the risks associated with aggressive treatment or conservative management were both potentially devastating.

Bland thrombus can be usually managed successfully with anticoagulation alone, but in the case of tumour thrombus, this approach does not effectively prevent potentially fatal embolus. Other specialists, such as cardiac surgeons and interventional radiologists, may need to be consulted to consider a surgical or radical interventional approach to remove the tumour thrombus. Despite the presumptive diagnosis of tumour thrombus in our

patient, she was treated with anticoagulation and further palliative chemotherapy. Although cardiac surgery and interventional radiology were consulted, ultimately no aggressive surgical interventions were undertaken. This decision reflected a need to carefully balance our patient's goals, and responsibility to attenuate any immediate risk to her life.

CASE PRESENTATION

A woman aged 46 years presented to her family doctor with a 3-month history of abdominal bloating, fatigue, intermittent nausea and vomiting, anorexia and weight loss of ~10 pounds. Ultrasound (US) imaging of the abdomen demonstrated multiple hepatic lesions, as well as a mass-like lesion at the hepatic flexure of the large colon. Biopsy of a presumed hepatic metastasis indicated a well-differentiated adenocarcinoma of colonic origin (figure 1). Mutational analysis revealed that her cancer was BRAF, KRAS and NRAS wild-type.

Since complete surgical resection of her cancer was not possible due to the extensive nature of her liver metastases, the patient received palliative-intent therapy over the following 18 months. She initially completed 12 cycles of 5-fluorouracil (5-FU) plus oxaliplatin (FOLFOX), to which she had an excellent clinical response. She was then switched to fluorouracil alone due to progressive oxaliplatin-induced neuropathy. Ten cycles of 5-FU monotherapy were administered prior to an observed increase in carcinoembryonic antigen level and a CT scan showing progressive disease. On disease progression, irinotecan was added to her 5-FU regimen (FOLFIRI) for a further 12 cycles. Initially, there was a response to treatment followed by a

Figure 1 Biopsy of liver metastases at diagnosis showing colonic adenocarcinoma with the H&E stain (left) and immunohistochemical staining with CDX2 (right).

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period of stable disease. Shortly after this, she presented to the emergency department with a severe headache. A CT scan of the head demonstrated cerebellar metastases. Neurosurgery was consulted for resection of the cerebellar lesion and the patient recovered well.

Three weeks after the resection of the cerebellar metastases, she presented to the emergency department with an acute history of fever and chills. Blood cultures were drawn and were positive for *Streptococcus mitis*. The origin of the infection was initially unclear, but the differential included cranial abscess in the context of her recent neurosurgery, and infectious endocarditis. To identify the source of infection, a CT scan of the head was performed and there was no evidence of abscess. A transthoracic echocardiogram demonstrated a right atrial lesion. Further imaging with CT confirmed a lesion in the right atrium, and unexpectedly demonstrated that it originated from the distal IVC. She had no signs or symptoms of pulmonary embolus or occlusion of the IVC at this time.

INVESTIGATIONS

Staging enhanced CT of the chest, abdomen and pelvis confirmed an annular constricting colonic mass near the hepatic flexure and multiple liver metastases (figure 2). A large intraluminal mass distending the suprahepatic and intrahepatic IVC was also identified (figure 3). The intraluminal IVC mass was suspicious for tumour thrombus based on its CT attenuation and its similar appearance and density to the liver metastases. However, further imaging characterisation was required to definitively distinguish between tumour versus bland thrombus.

Subsequent multiphasic CT with precontrast and postcontrast evaluation demonstrated enhancement within the IVC thrombus

Figure 2 Coronal views on contrast-enhanced CT demonstrate the lesion of hepatic flexure (blue arrow), as well as multiple areas of hepatic metastases (red arrows).

Figure 3 Lesion occupying suprahepatic and infrahepatic inferior vena cava (red arrow).

—30 Hounsfield units (HU) precontrast and 56 HU postcontrast—supporting tumour thrombus (figure 4). Radiographically, the thrombus extended all the way from the IVC to the heart.

Contrast-enhanced US (CEUS) performed the same day as multiphasic CT revealed microbubble enhancement of the tumour thrombus component within the intrahepatic IVC (figure 5).

DIFFERENTIAL DIAGNOSIS

- Bland thrombus: Increased risk in the setting of hypercoagulable state of metastatic cancer. Generally non-enhancing on imaging studies.
- Tumour thrombus: Most commonly associated with RCC and HCC, but also seen in testicular, pancreatic and adrenal carcinomas, as well as lymphoma. Generally enhance on imaging studies.

TREATMENT

Cardiac surgery and interventional radiology were consulted to determine the best treatment plan for the tumour thrombus. The patient's case was also discussed at the gastrointestinal multidisciplinary tumour board rounds at our cancer centre. The cardiac surgeons felt that given the patient's poor prognosis from her metastatic disease and significant risks associated with surgery, an open surgical approach was too aggressive. Interventional radiology offered to extract the thrombus with AngioVac, but due to the potential risks of this procedure and the fact that she was asymptomatic from the thrombus, the patient declined. The patient agreed to treat the tumour thrombus conservatively and to restart on palliative chemotherapy with FOLFOX. Systemic anticoagulation with low molecular weight heparin was started due to concern that part of the thrombus may have been bland thrombus.

Figure 4 Sagittal CT images precontrast and postcontrast demonstrating attenuation change in the inferior vena cava lesion in Hounsfield Units (HU).

Figure 5 Grey-scale image (left) and contrast-enhanced image (right). Sagittal plane obtained through the liver along the inferior vena cava (IVC) (asterisks) reveals echogenic material distending the intrahepatic IVC (arrows) on grey-scale imaging that enhances following administration of microbubble contrast.

OUTCOME AND FOLLOW-UP

Over the next 3 months, the patient's clinical condition deteriorated. Her cancer did not respond to further FOLFOX chemotherapy. On progression, she was started on panitumumab, but her cancer continued to progress. When her overall performance status deteriorated as a result of cancer progression, the patient and medical team agreed that supportive care alone at home was in her best interest.

After her passing, an autopsy was conducted. A necrotic mass was found arising from the distal IVC, extending into the right atrium (figure 6). Analysis of the lesion demonstrated that it was consistent with primary colorectal adenocarcinoma (figure 7). Interestingly, the bulk of the IVC was clear, as were the hepatic veins. This supports the notion that the original lesion seen on imaging studies was in fact partially tumour thrombus, and partially bland thrombus. Anticoagulation can be presumed to have reduced the burden of bland thrombus, and at the time of death, all that remained was tumour.

The autopsy did not reveal any embolisation of tumour thrombus, or bland thrombus into the pulmonary arteries. There were, however, extensive metastases in the brain, lung, liver, adrenals and ovaries. Ultimately, the cause of death was not attributed to the tumour thrombus that extended from the IVC into the right atrium, but was felt to be a result of multi-organ failure in the setting of metastatic cancer.

DISCUSSION

CRC is the second leading cause of cancer death in Canada and third leading cause of cancer death in the USA, with ~150 000 new diagnoses made annually.^{2 3} Despite its prevalence, there are few described cases of tumour thrombus in the literature. Risks of treating and not treating a tumour thrombus are potentially life-threatening, and therefore, accurate diagnosis is important. Tumour thrombus is known to occur in as many as 10% of cases of RCC and 10–40% of HCC, so extrapolation of diagnostic and management guidelines may alleviate some of the clinical challenges.^{4 5}

In this case, the first challenge was to characterise the incidentally found mass. Before any further diagnostic imaging was obtained, the presumed diagnosis was bland thrombus.

Figure 6 Posterior aspect of the liver with opened inferior vena cava (arrow head) that enters into the right atrium of the heart. A necrotic tumour mass (star), measuring 6.0×3.5×3.0 cm, is adherent to the right atrial wall. The heart is reflected with the apex present at the top of the image and the aorta can also be seen (double-arrow). Metastatic tumour deposits are also noted within the liver (circle).

This was reasonable, given the well-established link between malignancy and venous thromboembolism (VTE), especially in conjunction with chemotherapy.^{6 7} Additionally, the presence of an indwelling central venous catheter, as well as the patient's recent surgery strengthened the pretest probability of a bland thrombus. However, it was important to rule out the possibility of tumour thrombus since this affects the treatment plan.

Based on guidelines for RCC, there is no strong consensus for the best imaging modality to diagnose and characterise malignant thrombi,⁴ but CEUS and CT scan have been shown to be

Figure 7 Histological images of the tumour involving the myocardium of the right atrium, including H&E staining (left) and immunohistochemistry staining with CDX2 (right).

sensitive and specific for such a diagnosis.⁸ In the case of our patient, CEUS and CT scan were utilised and the reported findings, as discussed above, were convincingly positive for a malignant thrombus. Although not supported by current guidelines, there have been a number of case-studies reporting the utility of fluorine-18 fluorodeoxyglucose (18F-FDG) positron emission tomography (PET)/CT in the diagnosis of tumour thrombus in a number of cancer types.^{9–10} However, in addition to tumour thrombus, 18F-FDG PET/CT scans can also yield positive results in catheter-related thrombus,¹¹ as well as septic thrombophlebitis,¹² which may minimise its diagnostic value.

A working diagnosis of tumour thrombus was established through consultation with a radiologist who reviewed all the diagnostic imaging. However, a partial component of bland thrombus could not be ruled out. The next significant challenge was to determine appropriate treatment.

In HCC patients with tumour thrombus in the portal vein, supportive care leads to an overall survival of 2–4 months, compared with 10–24 months in patients without this complication.^{13–14} Thus, appropriate treatment modalities must be carefully considered. There are no clear guidelines for the optimal management of tumour thrombus in the setting of HCC. The Barcelona Clinic Liver Cancer Staging (BCLC) system classifies HCC with portal vein invasion as advanced disease, for which systemic therapy is the recommended treatment.¹⁵ Guidelines from the American and European associations are agreeable with those from the BCLC.^{16–17} Guidelines currently discourage transarterial chemoembolisation in patients with tumour thrombus, and suggest radioembolisation might become the new standard therapy pending the collection of more solidifying data. Data from two retrospective cohort studies suggest surgical resection of tumour thrombus in HCC patients is often not technically feasible, and also associated with poor patient outcomes.^{18–19}

Venous tumour thrombus formation in RCC patients is a significant adverse prognostic factor. Typically, patients with this complication undergo surgery to remove the kidney and the tumour thrombus, and aggressive surgical resection is the widely accepted therapeutic approach. However, guidelines for RCC state that only patients with non-metastatic disease and an acceptable performance status should be considered for surgical intervention, irrespective of the level of the thrombus.⁴ Thus, extrapolating from RCC, surgical resection would have been inappropriate in our patient case. Additionally, RCC guidelines support treatment with systemic chemotherapeutics, or immunotherapy in patients who are not surgical candidates.

The conclusion drawn by Otani *et al*¹ is to favour surgical resection and subsequent adjuvant chemotherapy in patients with tumour thrombus in the setting of CRC. However, this recommendation is largely based on the results of two cases in which patients achieved a long survival.^{20–21} Applying guidelines

from RCC and HCC, in which tumour thrombus is much more common, to our patient would yield the conclusion that surgical resection would not be the most appropriate option. Ultimately, following multidisciplinary discussion, surgical resection was not recommended due to the associated risks. The patient also declined the treatment offered by interventional radiology, as she was uncomfortable accepting the high risk of potential embolisation. Medical treatment was offered to try to control the size of the tumour thrombus. She received further palliative FOLFOX chemotherapy and subsequently panitumumab. The patient was also anticoagulated with subcutaneous low-molecular-weight heparin to account for the possibility of bland thrombus. Ultimately, she remained asymptomatic from the tumour thrombus in her IVC/RA and autopsy did not demonstrate her cause-of-death being related to that particular lesion. In fact, the lesion was actually less extensive than originally reported by radiology. This was likely due to the anticoagulation which treated a component of bland thrombus. The autopsy results support the treatment decisions that were made with respect to this patient's rare tumour thrombus.

Learning points

- ▶ Tumour thrombus is a rare, but can be a serious complication in patients with colorectal cancer (CRC).
- ▶ Contrast-enhanced imaging can provide diagnostic value to differentiate between tumour thrombus and bland thrombus.
- ▶ Based on extrapolation from similar cases in renal cell carcinoma and hepatocellular carcinoma and limited information in CRC, resection can be considered in certain circumstances.
- ▶ In terminal illness, great care should be taken to balance a patient's quality of life and attempts to reduce disease burden.

Contributors There are five contributing authors to this paper. Each author has signed the attached form as instructed by the BMJ. DM is primarily responsible for drafting the article and doing the appropriate literature review. NAN Worked with DM in drafting the article and was responsible for identifying the case and conception of the article. AF is a pathologist who collected appropriate pathology images and helped explain postmortem findings as relevant to the article. Danny Ng is a radiologist assigned to the case, provided images and captions as well as discussion around diagnostic uncertainty. VCT is a primary physician responsible for patient care, overseeing article and final editing.

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