Jugular vein thrombosis associated with distant malignancy

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Summary: We describe two patients who developed internal jugular vein thrombosis associated with primary malignant disease arising outside the neck, and in one patient it was the presenting feature. Computed tomography was performed and the findings characteristic of internal jugular vein thrombosis are illustrated. We conclude that malignant disease should be considered in patients presenting with spontaneous internal jugular vein thrombosis with no other predisposing factors and that computed tomography is of value in confirming the diagnosis.

Introduction

There are many predisposing factors in the aetiology of internal jugular vein thrombosis, including head and neck tumours, although to our knowledge there is only one documented association with more distant malignant disease.¹ We report two such cases in which computed tomography (CT) established the diagnosis.

Case reports

Case 1

A 56 year old female presented with a 3-year history of episodic abdominal pain and vomiting, and a 3-month history of diarrhoea and abdominal distension. She had lost 4 stones in weight in the previous year. On examination the only abnormality was ascites. Routine haematological and biochemical blood tests were normal except for an ESR of 70 mm/h. Urinalysis revealed blood and protein and an intravenous urogram suggested a soft tissue pelvic mass or fluid causing bilateral ureteric displacement. An ultrasound of the pelvis confirmed ascites. CT of the abdomen and pelvis demonstrated ascites, extensive para-aortic and mesenteric lymphadenopathy and also a central mesenteric soft tissue mass with radiating soft tissue strands (Figure 1a). The mesentery and small bowel were thickened. The liver was normal and no pelvic abnormality was seen. At exploratory laparotomy there was a mass of para-aortic and mesenteric glands with abnormal tissue compressing one section of small bowel. A small tumour was found

within the left ovary and the patient underwent hysterectomy and bilateral salpingo-oophorectomy. The ovarian tumour was thought to be the primary pathology and therefore lymph node or bowel resection was not attempted. At histology, however, it was shown to be a benign hyalinized fibroma with a margin of argentaffin/argyrophil positive cells, suggesting infiltration by metastatic carcinoid. Urinary 5-hydroxyindoleacetic acid levels were normal. Post-operatively the patient suffered a pulmonary embolus confirmed by isotope ventilation/perfusion studies and was anticoagulated. Anticoagulation was discontinued prior to further laparotomy for small bowel resection and mesenteric node biopsy. However, she developed pain and swelling of the right side of the neck associated with difficulty in swallowing. Coagulation studies were as follows: prothrombin time 16 seconds (control 14 seconds); activated partial thromboplastin time (APTT) 23 seconds (control 33 seconds); fibrinogen 5.1 g/l (normal 2-4); fibrin degradation product monomers 2 µg/ml (normal less than 8); platelet count $617 \times 10^9/l$ (normal 150-400). CT of the neck was performed before and during intravenous contrast and confirmed a right internal jugular vein thrombosis - the dilated vein containing a non-enhancing filling defect (Figure 1b). The right subclavian and brachiocephalic veins and the superior vena cava were patent. The soft tissues of the neck and superior mediastinum were normal. The para-aortic and mesenteric masses persisted unchanged from the original examination.

There was spontaneous resolution of the patient's symptoms without further anticoagulation and at repeat laparotomy a length of tumorous small bowel was resected, together with adjacent lymph nodes. Histology showed small bowel carcinoid

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Figure 1 Case 1. (a) CT scan of abdomen (post oral and intravenous contrast) demonstrating the mesenteric mass with radiating soft tissue strands (arrows) of metastatic carcinoid with ascites (arrowheads); (b) CT scan of neck (post intravenous contrast) demonstrating occlusion of the right internal jugular vein (closed arrow) and patency of the left internal jugular vein (open arrow).

with nodal involvement. At follow-up 8 months later she had had no further thrombotic episodes.

Case 2

A 59 year old man presented with a 2-day history of left sided neck swelling and pain on swallowing. He had no history of local infection, trauma or central venous cannulation. On further questioning he also complained of dyspnoea on exertion and lower costal pain. He had worked as a costing clerk in an asbestos manufacturers for 31 years and his job involved regular trips onto the factory floor.

Figure 2 Case 2. (a) CT scan of neck (post intravenous contrast) demonstrating occlusion of the left internal jugular vein with contrast enhancement of the vessel wall (arrow); (b) CT scan of lower thorax demonstrating encasement of the left lung and aorta by a pleural soft tissue mass (arrow) with early extension into the chest wall (arrowheads).

Regular chest X-rays had been unremarkable. On examination he had a left supraclavicular fossa swelling with erythema extending over the anterior chest wall. There were coarse crepitations at both lung bases. Investigations revealed an ESR of 51 mm/h. Haematological tests, including platelet count and prothrombin time, were normal. His chest X-ray showed inflammatory changes and increased pleural shadowing bilaterally with a soft tissue nodule at the left lung base. CT showed a left internal jugular vein thrombosis extending from the hyoid to the junction of the left subclavian vein.

There was contrast enhancement of the vein wall and soft tissue swelling around the vein (Figure 2a). The left subclavian and brachiocephalic veins and the superior vena cava were patent. CT of the chest demonstrated encasement of the descending aorta, posterior paravertebral region and left lung base by a pleural soft tissue mass, with early extension into the chest wall (Figure 2b). A soft tissue nodule was seen at the left lung base. The features were those of mesothelioma, and pleural biopsy was reported as showing very pleomorphic mesothelial cells.

The patient suffered a clinical extension of his thrombosis to involve the left subclavian vein and responded to anticoagulation with heparin and nicoumalone. He died 3 months later. Post-mortem examination confirmed the mesothelioma encasing the base of the left hemithorax and invading the mediastinum. The lymph nodes were normal.

Discussion

Both of the patients that we describe had internal jugular vein thrombosis in association with malignancy and in one it was the presenting feature. The commonest cause of internal jugular vein thrombosis is indwelling central venous catheter placement or misplacement.² There is no safe period of catheterization and jugular vein thrombosis has been recorded up to 6 months after catheter removal.³ The side of thrombosis does not always correspond to the side of catheterization.⁴ Other recognized causes include local surgery, infection and intravenous drug abuse. More rarely the jugular vein may be compressed by intrinsic or extrinsic tumour, or by an abscess.⁵ The two patients in this study had none of the above risk factors but did have distant malignant disease. Their thrombosis was a symptomatic manifestation of the coagulopathy due to malignancy. In Case 1 it was preceded by a pulmonary embolism. In Case 2 it was the presenting feature and the patient suffered clinical extension of the thrombosis prior to anticoagulation.

The association of malignancy and coagulation disorders is well known; 50% of patients with tumours and over 90% of patients with metastatic disease will have some detectable coagulation abnormality and up to 15% of patients are symptomatic.^{6,7} The mechanism of tumour-induced coagu-

lopathy remains ill-understood. It may involve the production of coagulation activators, such as tissue thromboplastins and platelet activating factors, or the direct increase of circulating levels of clotting factors, inhibitors of fibrinolysis or platelet numbers.^{8,9} This has been extensively reviewed.^{8,10} Anticoagulation is usually required for symptomatic patients. In Case 1 there was evidence of a hypercoagulable state with a shortened APTT and raised platelet count. The patient had no clinical recurrence of thrombosis after incomplete tumour resection. It is interesting to speculate whether removal of tumour bulk may have contributed to control of the coagulopathy. In Case 2 there was no documented coagulation abnormality.

CT findings in venous thrombosis are characteristic and consist of increased size of the vein, in which the thrombus is seen as a low attenuation non-enhancing filling defect (Figure 1b). The vessel wall enhances due to blood flow through the vasa vasorum¹¹ and secondary reactive soft tissue swelling may occasionally be visible (Figure 2a).³ In acute thrombosis freshly clotted blood will show as an area of increased attenuation due to the unorganized protein fraction of haemoglobin and may be missed on post-contrast scans alone since its density is equal to contrast-enhanced blood.¹²

In both cases CT was of value in the diagnosis of the primary malignancy. Metastatic carcinoid tumour may give CT features strongly suggestive of the diagnosis.^{13,14} These consist of hepatic and/or mesenteric masses, small bowel thickening, and punctate or radiating soft tissue structures in the mesentery due to a serotonin-induced desmoplastic reaction around metastases (Figure 1a). In the second patient CT demonstrated the nature and extent of the mesothelioma.

The cases illustrate the value of CT in confirming the diagnosis of internal jugular vein thrombosis and suggest that patients presenting with spontaneous jugular vein thrombosis, without any other precipitating cause, may have distant malignant disease.

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