The Journal of Laryngology & Otology
July 2004, Vol. **118,** pp. 570–572

Spontaneous bilateral internal jugular vein thrombosis: a sign of metastasis

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Abstract
Head and neck swellings are common referrals to the otolaryngology department, with a wide range of aetiologies. Internal jugular vein thrombosis presenting as swelling in the neck is a rare occurrence. The authors report a case of bilateral internal jugular vein thrombosis secondary to malignant lymphadenopathy of unknown origin. The patient presented with a short history of a diffuse swelling in the neck with neck stiffness. Examination revealed palpable cervical and axillary lymphadenopathy. Causes of spontaneous internal jugular vein thrombosis were discussed.

Key words: Jugular Veins; Thrombosis; Lymphatic Diseases

Introduction

Head and neck swellings are common referrals to the otolaryngologist. These swellings can arise from different tissue planes with different pathologies. Jugular vein thrombosis presented as a neck swelling has been rare ever since the introduction of antibiotics,[1] as such a condition is a well-known complication of acute inflammatory conditions in the head and neck.[2] Common aetiologies of head and neck vascular thromboses nowadays include central venous catheterization and intravenous drug abusers.[3]

Spontaneous bilateral internal jugular vein thrombosis, occurring when there is no apparent pre-disposing regional cause, mechanical or inflammatory, should arouse suspicion of disseminated malignancy.

The authors report here a case of spontaneous, simultaneous internal jugular vein thrombosis, associated with distant metastasis and malignant lymphadenopathy of unknown primary, casting light on causes of venous thrombosis in the head and neck and the possible aetiology in this case.

Case report

A 42-year-old gentleman presented with a four-day history of a right neck swelling. This was acute in onset with some preceding neck stiffness. There was no history of an upper respiratory tract infection. He also had a six-week history of mild epigastric pain with symptoms of reflux, vomiting and weight loss. He is a non-smoker, and there was no relevant past medical history or family history. He had recently been started on a proton pump inhibitor and had commenced a course of oral co-amoxiclav three days previously.

On examination there was a diffuse soft swelling on the right side of his neck with palpable lymph nodes. There was no evidence of concomitant local or systemic infection. The overlying skin was of normal appearance.

The remaining otolaryngological examination including fibre-optic nasoendoscopy was entirely normal. Axillary lymphadenopathy was noted.

Routine blood tests were obtained along with a thrombophilia screen, tumour markers and a monolatex test which was negative. A chest X-ray requested for possibility of primary pulmonary pathology, showed a small pleural effusion at the left base with a raised hemi-diaphragm.

An ultrasound scan of the neck revealed marked bilateral thromboses of the internal jugular veins, (Figures 1 and 2). Several enlarged lymph nodes were seen on the right side from level II to the supraclavicular fossa. These were reported as being of normal morphology with reactive vascular flow. A fine needle aspirate was obtained from one of the nodes. Similar changes were seen on the left but to a lesser degree. The patient was started on heparin.

Contrast-enhanced computerized tomography (CT) scans of the head and neck showed right internal jugular vein thrombosis from just below the jugular foramen to the level of the subclavian vein (Figure 3). The right subclavian vein and the superior vena cava were patent. The left internal jugular vein was thrombosed from the level of the oropharynx to the supraclavicular fossa. There was marked deep cervical lymphadenopathy on both sides, however, each node remained less than 2 cm in diameter.

Histological examination from the aspirated neck lymph node showed non-small cell type malignant cells with prominent nucleoli. Tumour markers revealed raised CA 19-9 (=154), carcino-embryonic antigen (CEA = 32) and alpha-fetoprotein (AFP = 24) with normal human chorionic gonadotrophin (β HCG) and prostate specific antigen (PSA) levels. Gamma-glutamyl transpeptidase (γGT) was also raised.

The patient proceeded to have further CT scans of his thorax and abdomen, USS of his liver, spleen, pancreas and

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Accepted for publication: 10 March 2004.

https://doi.org/10.1258/0022215041615254 Published online by Cambridge University Press

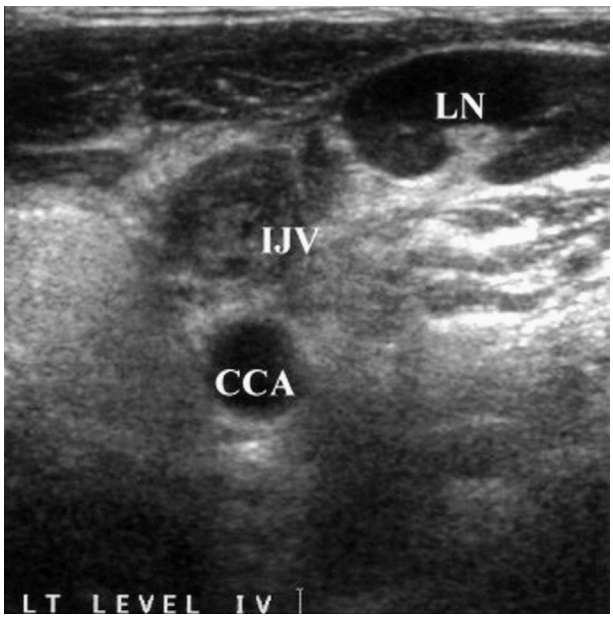

FIG. 1

Transverse ultrasound scan of lower left neck showing thrombosed IJV anterior to CCA. A lower enlarged deep cervical node is present. (IJV = internal jugular vein, CCA = common carotid artery, LN = lymph node).

testes, and an oesophagogastroduodenoscopy (OGD). CT of the thorax showed bilateral pleural effusions, a pericardial effusion and small nodes in the aorto-pulmonary window. Scans of the abdomen showed three lesions in the liver (which on ultrasound looked more suggestive of haemangiomata than metastases). There was a diffuse lymphadenopathy within the mesenteric fat and some free fluid in the pelvis. OGD showed a thickened stomach wall but no mucosal lesion and normal histology. No masses were found in the thorax, abdominal viscera or scrotum.

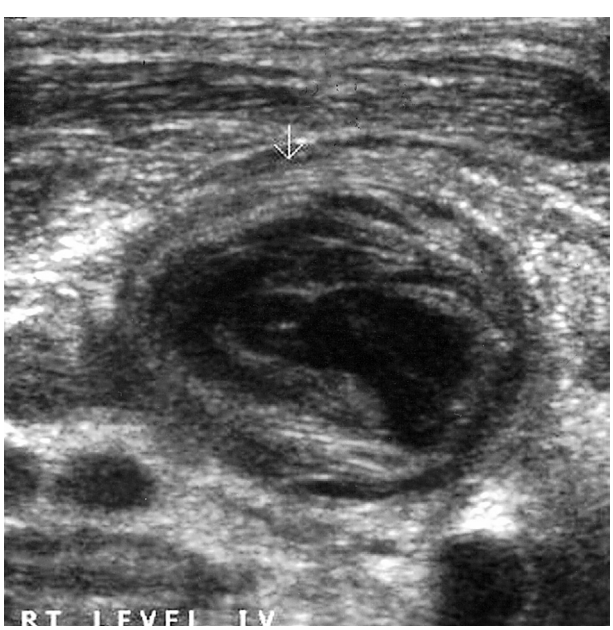

FIG. 2

Transverse scan of right neck showing thrombosis in the right IJV (arrow) and surrounding inflammatory change

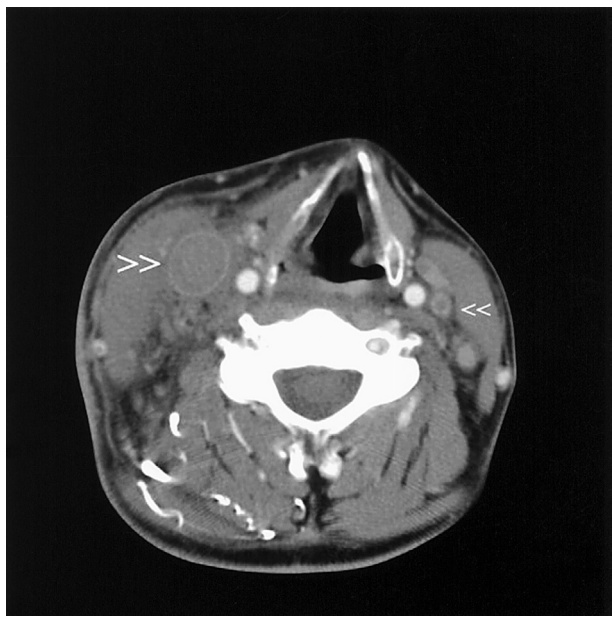

FIG. 3

Axial CT scan at the level of the larynx. Arrows pointing towards a thrombosed, small left IJV and a thrombosed, enlarged right IJV with surrounding small volume lymphadenopathy and inflammatory change

Excision biopsies were obtained from the right axillary and neck nodes. Microscopic analysis of these nodes showed a diffuse infiltration of moderate to poorly differentiated squamous carcinoma. With a diagnosis of malignant lymphadenopathy with an unknown primary site the patient was reviewed in the combined head and neck oncology clinic. At the time of writing the patient had received three cycles of cisplatin and 5-fluorouracil. His lymphadenopathy has clinically regressed and his symptoms have improved.

Discussion

Swellings in the head and neck region are a common referral to the otolaryngology department; however, jugular vein thrombosis presenting as a neck swelling is a rare primary presentation.[4] Mechanisms that increase the occurrence of thrombosis are explained by the Virchow's triad: venous stasis, vessel wall damage and state of hypercoagulation. Venous drainage in the head and neck differs from that of the extremities and viscera in that they are less susceptible to thrombosis. The head and neck veins are valveless, their drainage being aided by gravity in the upright position, and have distensible walls which expand or collapse with respiration and pumping of the heart.

Aetiology

The internal jugular vein is an uncommon site of spontaneous thrombosis. The aetiology can be divided into local (factors affecting the vessel wall and venous flow), and systemic (factors affecting the constitution of the flow).

Local factors. Most otolaryngologists would be well aware of localized disease in the head and neck causing thrombophlebitis in that region – infections of the paranasal sinuses, otological, facial or orodental infections. These have been on the decrease since the use of antibiotics. Iatrogenic factors such as central venous catheterization or pacemaker wiring remain the main

https://doi.org/10.1258/0022215041615254 Published online by Cambridge University Press

TABLE I
ASSOCIATED TUMOUR TYPES IN TROUSSEAU'S SYNDROME

Primary tumour	Percentages in 541 cases of Trousseau's syndrome
Lung	25.6
Pancreas	17.4
Stomach	16.8
Colon	15.2
Prostate	6.5
Head and neck	<2

causes of such a condition,[5,6] as well as neck vein injection. In a retrospective study of patients with internal jugular vein thrombosis, intravenous drug abuse was found to be the cause of 57 per cent of cases.[2]

- **Internal jugular vein thrombosis can present as a swelling in the neck**
- **Causes of spontaneous internal jugular vein thrombosis are classified into local and systemic**
- **Local causes are mainly head and neck infections or iatrogenic**
- **Systemic causes include hypercoagulable status and its aetiology**
- **Disseminated malignancy is an important factor in increasing thrombogenicity**

Systemic factors. Systemic factors leading to head and neck venous thrombosis are mainly related to conditions that predispose to the hypercoagulable state. These include thrombogenic disorders, myeloproliferative disorders, oestrogen use, pregnancy and postpartum state, and malignancies.

The association between malignancy and thrombophlebitic events were first described by Armond Trousseau, where migratory thorombophlebitis was associated with gastric carcinoma.[7] Since then, Trousseau's syndrome has been expanded to include a broad spectrum of coagulation disorders with a wide variety of malignant tumours.[8]

Sack *et al.* (1977)[7] reviewed 541 cases of Trousseau's syndrome, and listed the associated tumour types in order of decreasing frequency, as shown in Table I. However, it must be noted that most of these thromboses occur in the vascular system of the extremities and occasionally the viscera. Vascular thrombosis secondary to this syndrome presenting in the head and neck has been reported rarely, and all of those reported occurred intracranially.[9]

It is thought that tumour cells activate the blood coagulation system either by directly stimulating thrombin formation[10] or by inducing mononuclear cells to synthesize procoagulants, such as tissue factors, prothrombin activators and factor V activators.[11] Cancer cells may also mediate increasing aggregation and adherence of platelets, or activate endothelial cells by certain cytokines (eg. TNF, IL-1) to generate substances that stimulate the production of coagulation tissue factors.[12] All these result in hypercoagulability in patients with malignancies.

Primary presentation of spontaneous jugular vein thrombosis has been reported in the past, with different pathologies including anti-phospholipid syndrome, and lymphoma.[4] However, in cases where there is no history of any obvious head and neck infection, spontaneous internal jugular vein thrombosis needs to be treated with suspicion.

In this case, the reason for bilateral simultaneous internal jugular vein thrombosis could be due to the hypercoagulable state of the patient secondary to his malignant lymphadenopathy, and possibly an increased resistance in venous flow as a result of his pleural and pericardial effusion.

Conclusion

Bilateral spontaneous internal jugular vein thrombosis is a rare presentation. In the absence of obvious head and neck pathology or haematological disorder, disseminated malignancy should be suspected.

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Mr V. Singh takes responsibility for the integrity of the content of the paper.
Competing interests : None declared

https://doi.org/10.1258/0022215041615254 Published online by Cambridge University Press