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Internal jugular vein thrombosis due to ovarian hyperstimulation syndrome

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Abstract
Internal jugular vein thrombosis from non-otological causes is not well documented in the otolaryngology literature. The authors report a case of left internal jugular vein thrombosis due to severe ovarian hyperstimulation syndrome. Causes, investigations and treatment of internal jugular vein thrombosis from non-otological causes are discussed.

Key words: Jugular Veins; Thrombosis; Ovarian Hyperstimulation Syndrome

Introduction

Internal jugular vein thrombosis is a rare entity with the potential for serious consequences. Internal jugular vein thrombosis from non-otological causes is not well documented in the otolaryngology literature. Chronic ear disease used to be the potential cause of internal jugular vein thrombosis via infection of the lateral sinus, but because of the use of intravenous antibiotics this is nowadays rarely seen.

The most common causes of internal jugular vein thrombosis nowadays are: drug abuse, central venous catheterization and functional neck dissection. Rarer causes include Lemierre's syndrome, severe ovarian hyperstimulation syndrome and disseminated malignancy. Internal jugular vein thrombosis presents as painful and tender neck swelling with limitation of head movement. We present here a case of severe ovarian hyperstimulation syndrome as the cause of internal jugular vein thrombosis.

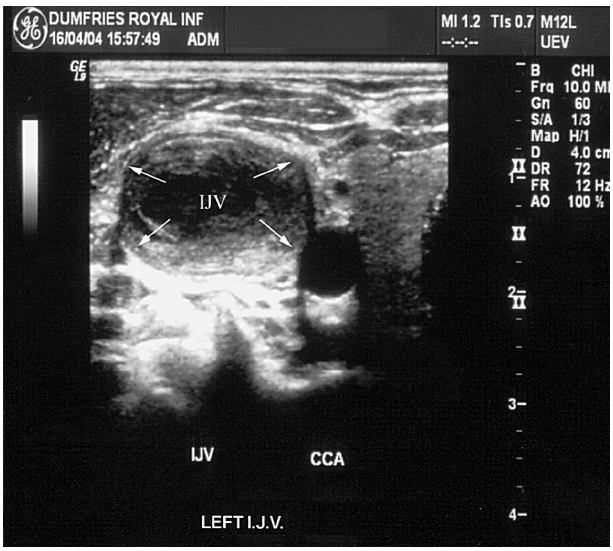

FIG. 1
Ultrasound of left internal jugular vein (IJV) (white arrows indicate the edge of the vein wall full with thrombus).

Case report

A 23-year old woman pregnant with twins of four weeks gestational age presented with painful swelling of the left side of the neck and limitation of neck movement over a period of two days. She was nauseated and had vomited twice in the previous 24 hours, and she had lost weight recently. There was a history of sore throat five days before her neck problem and her general practitioner had prescribed a course of oral penicillin. She had conceived with the aid of *in-vitro* fertilization (IVF) and embryo transfer. She developed severe ovarian hyperstimulation syndrome two weeks before her neck problem, with abdominal pain, ascites and pleural effusion. She was admitted for treatment under her gynaecologist and discharged from the hospital seven days later.

Physical examination showed a raised body temperature of 38.7°C and tender swelling on the left side of her neck. Complete ENT examination including flexible fibre-optic nasopharyngoscopy was normal. Ultrasonography with colour Doppler scanning revealed occlusion of the left internal jugular and left subclavian veins (Figures 1–3). Full blood test showed only leucocytosis of 18.7×10^9 cells/l (normal range 4.0–11.0), and a high level of C protein of 89 mg/l (normal range 0–10). Urea and electrolytes, coagulation screen and liver function tests were normal. Blood cultures were negative for aerobic or anaerobic infection seven days later. Factor V Leiden mutation was negative and prothrombin gene 20210A mutation was absent.

Because of her previous history of sore throat, high body temperature and marked leucocytosis, Lemierre's syndrome was considered as a differential diagnosis. Initially treatment consisted of intravenous fluid, intravenous antibiotics and low-molecular-weight heparin for seven days. After negative blood culture the antibiotics

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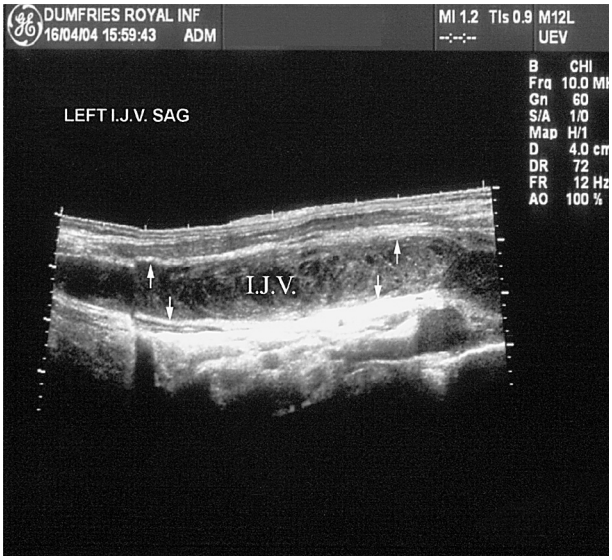

FIG. 2

Ultrasound of left internal jugular vein (IJV) (white arrows indicate the edge of the vein wall full with thrombus).

were discontinued. Ten days after her admission, she was discharged from hospital. During the hospital admission, the obstetrician, haematologist, bacteriologist and physician were involved in the management of the patient. Three weeks later, she went back to work. Six months later ultrasonography of her neck showed partial resolution of the left internal jugular vein thrombosis.

Discussion

Internal jugular vein thrombosis is a rare entity with the potential for serious consequences. Internal jugular vein thrombosis normally presents as painful and tender neck swelling. Chronic ear disease has the potential to cause internal jugular vein thrombus through infection of the lateral sinus, but since the introduction of antibiotics this is nowadays rarely seen.[1]

The internal jugular vein begins in the cranium at the conclusion of the sigmoid sinus. It exits the cranium via the jugular foramen and then courses through the anterior neck lateral to the carotid artery in the carotid sheath. It is covered by the sterncleidomastoid for most of its length. It joins the subclavian vein to form the brachiocephalic vein.

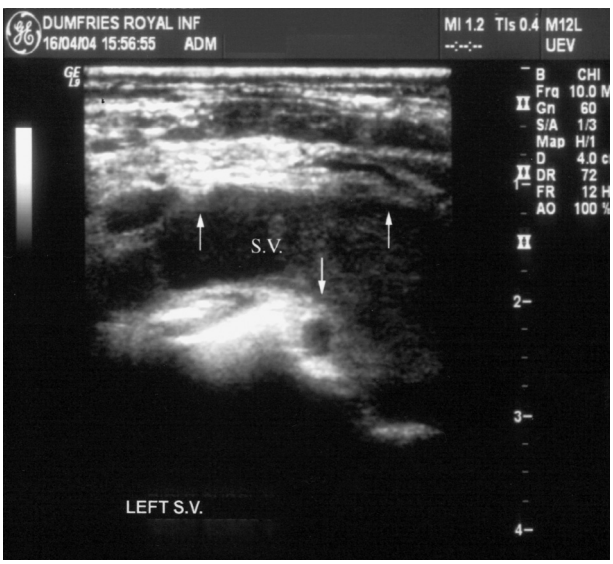

FIG. 3

Ultrasound of left subclavian vein (SV) (white arrows indicate the edge of the vein wall full with thrombus).

Nowadays drug abusers comprise 57 per cent of all cases of internal jugular vein thrombosis.[1,2] This is usually seen in those who have been injecting for a long time and have exhausted all peripheral access sites. Here, there is high risk of septic thrombophlebitis caused by methicillin-resistant strains of *staphylococcus aureus*.[2] The second most common cause of internal jugular vein thrombosis is central venous catheterization.[1] The catheter itself acts as the nidus for clot formation, even with catheters which are bonded and flushed with heparin.[2] Polyethylene catheters are the most thrombogenic (70 per cent), followed by silicone (20 per cent) catheters, and polyurethane (17 per cent) catheters which are significantly less thrombogenic.[3] Secondary subclavian vein thrombosis due to catheterization is more common and less innocuous than once thought. Another common cause of internal jugular vein thrombosis is functional neck dissection.[4] Rarer causes for internal jugular vein thrombosis are: disseminated malignancy,[5] ovarian hyperstimulation syndrome[6–9] and Lemierre's syndrome.[10–12]

In 1936, Lemierre[10] described 20 cases of septic thrombophlebitis of the internal jugular vein after oropharyngeal infection; approximately 90 per cent of patients had died within a few weeks of its onset. Most cases of Lemierre's syndrome are caused by infection with *Fusobacterium necrophorum,* which typically occurs in healthy young adults.[11] Classic Lemierre's syndrome is characterized by: (1) primary infection in the oropharynx, (2) septicaemia documented by at least one positive blood culture, (3) clinical or radiological evidence of internal jugular vein thrombus, and (4) at least one metastatic focus in the body, usually in lung.[12] About 60 cases of classic Lemierre's syndrome have been described;[11] it is a potentially fatal condition despite antibiotic treatment. Lemierre's syndrome is treated by a long intensive course of broad-spectrum antibiotics with or without anticoagulants.[2,11]

In 1991, Fournet *et al*.[13] were the first to report a case of internal jugular vein thrombus after IVF complicated by ovarian hyperstimulation syndrome. From 2 to 6 per cent of patients undergoing IVF may develop ovarian hyperstimulation syndrome, and in 1–2 per cent this syndrome may be severe enough to cause thrombus formation in the upper extremities rather than lower extremities.[7] The syndrome is characterized by enlarged, multicystic ovaries. The production of vaso-active substances results in increased capillary permeability, causing a massive shift of fluid out of the intravascular space. This produces the clinical syndrome of ascites, pleural effusion, haemoconcentration, and renal and liver dysfunction.[6] Only 4–12 per cent of patients with internal jugular vein thrombosis associated with ovarian hyperstimulation syndrome may show pulmonary embolism.[6] Intravenous albumin at the time of IVF has been reported to decrease the incidence of severe ovarian hyperstimulation syndrome[8]. The high prevalence (4–7 per cent) of Factor V Leiden mutation in Western populations can contribute to thrombotic complications in this syndrome.[7] A Factor V Leiden mutation screen is usually routinely performed with IVF. In November 1996, a new genetic marker for thrombophilia risk was identified by the same group that identified Factor V Leiden.[14] They found a prothrombin gene mutation at nuclear position 20210 involving a G to

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A transition. This mutation can contribute to a high incidence of venous thrombosis rather than arterial thrombosis formation. The prothrombin gene mutation was found in 2–3 per cent of a healthy normal Caucasian population. It seems that marked leucocytosis and increased levels of fibrinolytic activators may be signs of imminent thromboembolism in those patients with ovarian hyperstimulation syndrome.[7] The treatment of the internal jugular vein thrombosis associated with this syndrome includes antibiotics and long-term anticoagulant.[6,7] Warfarin cannot be administered to pregnant women because of its known teratogenicity.[7] Low-molecular-weight heparin is used to prevent and treat thrombus formation because it does not cross the placenta, it affects bone mineral density less during long-term use than standard heparin, and lastly it does not require routine laboratory monitoring.[9]

- **Internal jugular vein thrombosis is a rare entity with the potential for serious consequences. Most cases arise as a complication of chronic otitis media**
- **This case report documents a rare case of internal jugular vein thrombosis secondary to severe ovarian hyperstimulation syndrome**

Almost all cases of internal jugular vein thrombosis present as painful and tender neck swelling associated with limitation of neck movement, with or without high fever. Blood investigations are important to rule out any infection or complications and they include: full blood count, urea and electrolytes, coagulation screen, blood culture, and liver and kidney function tests. In cases of ovarian hyperstimulation syndrome both the Factor V Leiden mutation and prothrombin gene mutation must be screened. Ultrasound examination of the neck and abdomen is essential to confirm the presence of the internal jugular vein thrombus and to rule out any intra-abdominal complications. Venous duplex ultrasonography is accurate, safe, non-invasive and widely available. It shows a dilated and incompressible vein, and may feature either a lack of venous pulsation or a flow that does not vary during sniffing or the Valsalva manoeuvre.[11] Computed tomography or magnetic resonance imaging may also demonstrate thrombus.

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