SPONTANEOUS AND NONSPONTANEOUS INTERNAL JUGULAR VEIN THROMBOSIS

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Nonspontaneous internal jugular vein thrombosis (IJVT) is an uncommon condition historically associated with deep neck infections during the pre-antibiotic era. Today, trauma to the internal jugular vein from catheterization and repeated intravenous injections by drug users are the leading causes of thrombosis, with direct extension of tumor being a rare cause. Spontaneous IJVT occurs when there are no apparent predisposing causes, although many of these patients may harbor an occult malignant neoplasm. Therefore, careful investigation and follow-up are imperative in these patients. The diagnosis of IJVT is readily confirmed by contrast-enhanced computed tomography or magnetic resonance imaging. Management of IJVT involves anticoagulation, antibiotics, and with few indications for surgical intervention. **HEAD & NECK 12:168–173, 1990**

Internal jugular vein thrombosis (IJVT) is an uncommon, potentially life-threatening vascular disorder caused by various conditions. The pathophysiology of venous thrombosis is succintly described by Virchow's triad for vascular thrombosis. The pathogenesis of thrombosis requires the presence of one or more of the following factors: vascular endothelial (intimal) injury, alterations of blood flow (stasis), and hypercoagulability of the blood.[1]

Historically, during the pre-antibiotic era, IJVT was well recognized as a complication associated with deep neck infections often secondary to pharyngitis, tonsillitis and peritonsillar abscess, retropharyngeal abscess, molar tooth infection, mastoiditis, and acute necrotizing ulcerative gingivitis.[2–5] Since the introduction of modern antibiotic therapy, the complication of IJVT secondary to fulminant head and neck infections has become relatively rare, although it is still occasionally being reported.[6–8]

Today, the two leading causes for IJVT involve direct trauma to the vein. They include the iatrogenic trauma of jugular vein catheterization,[9,10] and repeated injections into these veins by intravenous drug abusers.[8,11] Associated malignancy is another uncommon and sometimes unrecognized etiology for IJVT.

We describe herein three illustrative cases of IJVT. Two cases demonstrate nonspontaneous IJVT, resulting from different mechanisms, and a case of spontaneously appearing IJVT, followed by a discussion of their implications and related management.

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CASE REPORTS

Case 1. A 61-year-old woman underwent a bone marrow transplant for myelofibrosis and was dis-

charged from the hospital in good condition, with an indwelling left subclavian catheter for long-term venous access. Four months later she presented to the emergency room with a 3-day history of fever and left neck swelling. Notable findings on a complete physical examination were a fever of 39.0°C and a tender, warm left neck mass along the anterior border of the sternocleidomastoid muscle.

Following admission to the hospital, routine investigations, including complete blood cell count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), smooth muscle antibody (SMAC), were normal. Chest radiographs indicated that the left subclavian catheter had remained in position. Initial blood cultures grew gram-positive cocci. Computed tomography with contrast infusion revealed a mass with a contrast-enhanced margin and a low-density central portion lacking enhancement on the left side of the neck (Figure 1). The mass was just beneath the sternomastoid muscle extending from behind the angle of the mandible to the supraclavicular region. Considering the patient's immunosuppressed status, the radiologist's initial impression was that this represented a deep neck abscess.

The patient was started on intravenous antibiotics (clindamycin and tobramycin) and taken to the operating room for incision and drainage of a suspected deep neck abscess. Exploration of the neck revealed no abscess, instead the internal jugular vein was found to be completely thrombosed. A segment of the thrombosed vein was biopsied to confirm the diagnosis prior to wound closure. The left subclavian central line was also removed and the catheter tip was sent for culture and sensitivity.

Postoperatively, a venogram was performed to verify the extent of the thrombosis which was found to extend from the base of the skull and also involve the left subclavian vein with extensive collateral circulation. The catheter tip, as well as the blood cultures grew *Staphylococcus aureus*, sensitive to cloxacillin. Therefore, the patient was continued on intravenous antibiotics and heparin with an uneventful convalescence. She was continued on oral anticoagulant therapy for a further 6-month period.

FIGURE 1. Contrast-enhanced computed tomographic scan of the neck at the level of the cricoid cartilage in case 1. Note the mass under the sternomastoid muscle, with a low-density center (representing thrombus) and contrast-enhanced periphery (uptake by the vasa vasorum). An abcess may share many of these features and produce a similar appearance on a contrast-enhanced scan.

Case 2. A 79-year-old man presented to the Otolaryngology—Head and Neck clinic with a large neck mass and dyspnea. On physical examination there was a 10 × 5 cm nontender mass on the left side of the neck extending from the level of the thyroid notch to the supraclavicular region, compressing the trachea and pushing the larynx to the right side. The mass was deep to the sternomastoid, hard, and appeared to be attached to the deep structures. The remainder of the head and neck examination was normal.

Clinically, a thyroid carcinoma was suspected, and fine-needle aspiration cytology revealed malignant cells. The chest radiograph showed multiple lesions which were suggestive of metastases, and bronchial washings revealed malignant cells. An ultrasound of the neck and mediastinum showed the left neck mass with thrombosis of the internal jugular vein. Contrast-enhanced computed tomography delineated the extent of the mass. Although there was no retrosternal extension, there was compression of the larynx and the trachea, as well as thrombosis of the internal juglar vein and a patent carotid. The patient was taken to the operating room for exploration of the neck and debulking of the tumor to safeguard his airway. There was a large thyroid carcinoma infiltrating into the trachea and the great vessels. The jugular vein was thrombosed from the level of the hyoid bone to the clavicle.

Frozen and permanent histopathology confirmed that this was an unresectable anaplastic thyroid carcinoma. Therefore, limited debulking with tracheostomy was performed to protect the

airway. Despite anticoagulation, the patient passed away on the sixth postoperative day from a massive pulmonary embolus.

Case 3. A previously healthy 53-year-old man presented to the emergency department of the hospital with a 5-day history of mildly tender right lower neck swelling, accompanied by mild odynophagia for solids. He had no significant past medical history and was taking no medications. Physical examination revealed a well, afebrile, moderately obese male with a diffuse and doughy right mid-neck and supraclavicular fullness, mostly under the sternomastoid muscle. Direct fiberoptic flexible laryngoscopy and the remainder of the head and neck examination were normal. Examination of his left lower leg revealed evidence of mild and very localized superficial thrombophlebitis with no antecedent history of trauma. Further questioning regarding this revealed that he had noted similar recurrent and spontaneously resolving episodes of such lesions over a 6-week period, suggesting a pattern of migratory superficial thrombophlebitis.

Following admission to the hospital routine investigations, including CBC, PT, PTT, platelet count, SMA-20, and a chest radiograph, were normal. Computed tomography of the neck and mediastinum revealed complete thrombosis of the right internal jugular vein from the level of the hyoid bone down to the the superior vena cava, which remained patent. There was a small amount of thrombus extending into the right subclavian vein.

Extensive investigations performed during this hospitalization included: a ventilation perfusion lung scan suggesting a low probability of pulmonary embolism. A venogram of the right arm revealed nonfilling of the right subclavian vein with extensive collaterals, explaining the lack of swelling in that extremity. Carcinoembryonic antigen (CEA) and acid phosphatase levels were normal. Computed tomography and ultrasonogram of the abdomen and pelvis, endoscopic retrograde cholangiopancreatography, barium enema, barium swallow with an upper GI series, gastroscopy, colonoscopy, and platelet studies were all normal. Biopsy of a thrombosed superficial leg vein revealed an intravascular-organizing thrombus. Therefore, no clear etiology for thrombosis of his right internal jugular vein could be elucidated, despite the very extensive investigation. The patient was treated with intravenous heparinization and clindamycin. His neck swelling decreased markedly, and he was discharged on oral coumadin therapy.

Eight days after discharge, he was again readmitted with recurrent swelling of his right neck, despite adequate anticoagulation with a therapeutic prothrombin time. Repeat contrast-enhanced computed tomography revealed thrombosis of the internal jugular vein from the skull base to the superior vena cava. Intravenous heparinization was restarted with rapid subsiding of the neck swelling. He was subsequently discharged on twice daily subcutaneous injections of 15,000 U heparin to maintain his PTT at approximately twice the normal levels. He continued to be followed, and 8 months after his diagnosis of IJVT he developed a compression fracture of a thoracic vertebra that was suggestive of osteolytic metestases. Once again, extensive investigations failed to reveal a primary malignancy, and he is currently being considered for treatment with chemotherapy and external beam radiation.

DISCUSSION

The clinical presentation of IJVT can be misleading, rather vague, and easily overlooked. The most consistent clinical manifestations are neck pain with a tender swelling or mass in the neck, usually along the sternomastoid muscle. Leukocytosis and fever are inconstant. In the pre-antibiotic era, acute septic thrombophlebitis of the internal jugular vein would result in the dramatic appearance of facial and eyelid swelling, pitting edema of the mastoid skin, accompanying the other findings.[4,7,8] This type of presentation is unlikely to occur today. Without a previous recent history of some head and neck infection, central venous catheterization, or intravenous drug abuse, a high index of suspicion is necessary to reach the diagnosis of IJVT. However, this diagnosis should be included in the differential diagnosis of any painful neck swelling.

Previously, the diagnosis of IJVT was primarily one of clinical presumption, sometimes confirmed by jugular venography. In addition to being invasive, venography carried the risk of further spread through embolization of a potentially septic process. The advent of contrast-enhanced computed tomography and its use to confirm the presence of IJVT has been reported previously.[9–11]

The CT findings in IJVT show a low-density intraluminal thrombus within the vein, encircled by a sharply defined brighter vessel wall.

This is due to uptake of the contrast by the vasa vasorum. By comparison, the jugular vein on the other side is bright and homogeneous because it enhances readily with contrast material. With these characteristic findings the only other major diagnostic consideration would be a deep neck abscess, which may share some of the same features on contrast-enhanced computed tomography. This was illustrated by our first case, although in retrospect, the CT findings were more compatible with IJVT.

Recently, magnetic resonance imaging (MRI) has been suggested as the preferred diagnostic imaging modality for IJVT.[12] The reported advantages of MRI include sensitivity to blood flow rates, greater soft tissue contrast, avoidance of intravenous contrast, and radiation exposure. Ultrasonography has been advocated as well for imaging jugular vein thrombosis, since it is noninvasive without radiation, rapid, and more cost-efficient. But its disadvantages are the lack of its imaging ability beneath the clavicle or under the mandible, and its failure to detect a recent thrombus which has little echogenecity.[12] Therefore, it appears that contrast-enhanced CT remains the preferred imaging modality for confirming the diagnosis of IJVT, having surpassed venography, at least until MRI becomes more widely available.

Catheterization of the jugular veins has become a common procedure for purposes, such as rapid fluid replacement in hypovolemic states and central venous pressure measurements or hyperalimentation. Chastre et al. found radiographic or autopsy evidence of IJVT in 65% of 63 patients following central venous catheterization.[13] Prevention of thrombotic phenomena by the proper use of central venous catheters may help to minimize the risk of thrombus formation. These measures include the use of soft catheters and adherence to aseptic techniques,[14] while changing catheter sites every 12 to 14 days.[15,16] Thrombosis as a complication of internal jugular vein cannulation (including intravenous drug abuse), or indwelling catheters may be considerably more common than is clinically appreciated. Thrombosis may be incomplete without total occlusion of the vessel lumen, or extensive collateral venous circulation results in the IJVT not being clinically apparent.[13–16]

Intravenous drug abuse may be the leading cause for IJVT in certain populations with large numbers of intravenous drug users. This occurs because some of these individuals eventually begin to inject into the internal jugular vein after having exhausted all their peripheral veins.[8,17] IJVT resulting from direct tumor extension and compression, as illustrated by case 2, is very rare.

The most feared complication of IJVT, although uncommon, is pulmonary embolism as demonstrated in case 2. Ahmed and Payne reported a 5% incidence of pulmonary emboli in IJVT.[14] Other complications are septic emboli, generalized septicemia, facial edema, and pseudotumor cerebri.[8,18–21]

Historically, the treatment of IJVT was primarily surgical, namely, ligation and excision of the internal jugular vein. Before the advent of modern antibiotics, IJVT was nearly always the result of deep neck infections or abscess, and often associated with erosion of the carotid artery.[5,6] Rupture or ligation of the carotid artery contributed to the high mortality and morbidity in these patients.

Currently, treatment relies on antibiotics and anticoagulation, with few indications for surgically entering the neck. Intravenous penicillin combined with penicillinase-resistant antibiotics are administered until culture results are obtained. Alternatively, clindamycin or third-generation cephalosporins can be used in the penicillin-allergic patient. The organisms isolated depend on the etiology of the IJVT. If IJVT is secondary to deep head and neck infections, aerobic and anaerobic streptococci are common with *Staphylococcus aureus* more common in intravenous drug abusers.[7,19]

The use of anticoagulant therapy is recommended to reduce the risk of pulmonary embolism. The suggested regimen includes 1 week of intravenous heparin with close monitoring of PTT followed by oral coumadin therapy to achieve a therapeutic PT. Cohen et al. suggested that anticoagulation should be continued for 3 months, except in intravenous drug abusers, due to the high risk of hemorrhagic complications in this population.[8] The use of heparin is especially important in patients having IJVT associated with malignancies, or "spontaneous" IJVT as demonstrated by case 3. Resistance to oral anticoagulants and an increased risk of pulmonary embolism was found in these patients, with a better response to heparin as demonstrated in a study by Lieberman et al.[22]

Other treatments described for IJVT are surgical ligation to prevent propagation or pulmonary embolism and the use of fibrinolytic agents

to produce recanalization of the thrombosed vein.

Cohen et al. suggested one of the last two measures in cases where thromboembolic phenomena persist despite adequate treatment with antibiotics and anticoagulation.[8]

Further commentary is necessary on what we have labeled "spontaneous" IJVT. The basis for this involves recalling Virchow's triad for vascular thrombosis, where hypercoagulability is one of the factors. The hypercoagulable state is associated with "spontaneous IJVT." In case 3, the patient presented with isolated IJVT not associated with any other recent relevant condition. The only other pertinent event was his present and previous lower extremity superficial thrombophlebitis. This suggests a diagnosis of recurrent or migratory thrombophlebitis, which if associated with malignancy is known as Trousseau's syndrome.

Malignant neoplasms can be associated with IJVT through two coexisting mechanisms and are illustrated by cases 2 and 3. First, this may occur from a local tumor mass (primary or metastatic) diminishing the jugular blood flow sufficiently by compression to result in stasis and thrombosis or even direct invasion into the vein. Alternatively, this could result from a migratory thrombophlebitis known to occur in association with malignancies of the lung, female reproductive system, pancreas, stomach, and a wide variety of other neoplasms.[22] The pathophysiology is postulated to be a hypercoagulable state related to elevated levels of factor VIII and accelerated production of thromboplastin.[23]

Lieberman and coworkers studied the correlation between thrombophlebitis and cancer in a group of 81 patients having both.[22] In nearly 60% of these patients, thrombophlebitis was recognized prior to the discovery of the neoplasm. In approximately 50% of these patients, the carcinoma was discovered between 2 and 6 months after the initial finding of thrombophlebitis, while more than a year elapsed before the neoplasm was found in 6 patients.[22] They concluded that thrombophlebitis associated with neoplasia is characterized by a tendency to be recurrent or migratory, more resistant to anticoagulation, may often precede the diagnosis of neoplasia, and that any primary site of neoplasia is possible, although most frequently neoplasms of the lung, pancreas, and female reproductive system were involved.[22] Veins of the arm and neck were the sites commonly involved.

Therefore, spontaneous thrombophlebitis may be the first indication that an occult neoplasm is present. As a result, every patient with spontaneous thrombophlebitis must undergo a careful history, a complete physical examination, and a thorough investigation or workup to avoid missing or delaying the diagnosis of a hidden malignancy. Although all of these investigations may turn out to be negative, it is mandatory that the patient be followed closely and carefully for the early manifestations of a hidden neoplasm.

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