Septic thrombophlebitis of the internal jugular and subclavian veins treated with percutaneous mechanical thrombolysis

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Introduction: Treatment of septic thrombophlebitis of the jugular vein may include both medical and surgical interventions. Historically, the goal of surgical interventions was not the restoration of blood flow through the affected vessel.

Case presentation: We present a case of a 19-year-old male with septic thrombophlebitis who, despite appropriate antibiotic treatment, experienced symptomatic thrombus progression. Percutaneous thrombolytic procedures were performed, successfully restoring blood flow without triggering clinically significant bacteraemia or septic emboli.

Conclusion: Thrombolysis may have a role in select patients, especially those with co-existent thrombophilia or progressive thrombus development despite medical treatment.

Keywords: antibiotics; anticoagulation; Lemierre’s disease; septic thrombophlebitis; thrombolysis.

Introduction

Septic thrombophlebitis of the jugular vein develops following pharyngitis and frequently seeds metastatic abscesses to the lungs and elsewhere. Similar syndromes of suppurative thrombophlebitis also occur in peripheral veins (commonly associated with intravenous catheterization) and the vena cava (always associated with central lines). The responsible organisms depend on the infection’s site of origin. Jugular septic thrombophlebitis draws from the oral flora, with the most common causative agent being the anaerobic Fusobacterium. In the peripheral veins or vena cava, Staphylococcus, a member of normal skin flora, is the more common pathogen. Streptococcus, Enterobacteriaceae, Candida and even assorted viruses have also been reported (Huntington & Sewall, 2007). Thrombophlebitis with Fusobacterium bacteraemia and metastatic abscesses is known as Lemierre’s disease. Aspects of treatment are controversial. Aggressive antibiotic therapy is the mainstay for management of this condition, but surgical interventions may be employed (Karkos et al., 2009; Riordan, 2007).

Case report

A 19-year-old otherwise healthy male African immigrant presented with a 3-day history of fever, severe left-sided neck pain, mild discomfort radiating to his left arm and a sore throat. He had been suffering from fever, rhinorrhoea and a non-productive cough for 1 week. These symptoms progressed to include abdominal pain, left-sided chest pain, sore throat and neck pain. His vital signs at presentation were a temperature of 37.9°C, blood pressure 138/69 mmHg, pulse 80 and respiratory rate 16 min⁻¹. His neck was exquisitely tender and distended on the left side; although the lymph nodes were enlarged, they were non-tender. This clinical picture was suspicious for septic thrombophlebitis, so blood was collected and the patient sent for computed tomography (CT) (Fig. 1); once the results had been read, the patient was admitted directly to the hospital.

Investigations

The CT imaging was consistent with septic thrombophlebitis of the left jugular vein involving the supraclavicular and upper mediastinal regions, with occlusion of the jugular, left
subclavian and portions of the left axillary veins. Collateral venous flow was present. No abscess or fluid collection was identified, and no evidence of septic emboli was seen (Fig. 1).

- C-reactive protein and leukocytes were elevated at 119 mg l$^{-1}$ and $11 \times 10^3$ cells mm$^{-3}$, respectively. Haemoglobin was 12.3 mg dl$^{-1}$. Blood cultures had no growth. Partial thromboplastin time was prolonged at 47.9 s with a low positive for the lupus inhibitor screen. Cardiolipin IgG and IgM, and $\beta_2$-glycoprotein IgG and IgM were all negative.

Duplex ultrasound demonstrated extension of the thrombus into the left brachial vein on hospital day 3.

**Diagnosis**

**Treatment**

On admission, the patient received intravenous piperacillin/tazobactam (3.375 g intravenously every 6 h) to cover both oral streptococci and *Fusobacterium*. In addition, aspirin was given and subspecialty consultations were requested.

On hospital day 2, vancomycin was added to the antibiotic regimen to expand coverage to methicillin-resistant *Staphylococcus aureus*. CT of the chest showed no evidence of septic emboli, and blood cultures had no growth. Heparin and warfarin were initiated.

The patient began experiencing increasing upper extremity pain on hospital day 3. Duplex ultrasound demonstrated extension of the thrombus into the left brachial vein.

Percutaneous lytic therapy was performed: rheolytic thrombectomy followed by catheter-directed lysis for 24 h (total tissue plasminogen activator dose 22 mg) (Ballehanina et al., 2012; Grommes et al., 2011; Kim et al., 2006). Repeat venography demonstrated significant resolution of the thrombus with excellent patency through the brachial, axillary, subclavian and innominate veins.

Following the procedure, on hospital day 5, the patient experienced severe nausea and was found to have acute kidney injury (creatinine 3.03 mg dl$^{-1}$; up from 0.7 mg dl$^{-1}$ 3 days earlier). This was believed to represent contrast-induced nephropathy, but, because of the potential contribution of vancomycin to acute kidney injury, both the vancomycin and piperacillin/tazobactam were stopped and intravenous ertapenem was initiated via a central venous catheter.

**Outcome and follow-up**

The patient improved slowly and was discharged on hospital day 17 with an additional 2-week outpatient course of oral clindamycin (300 mg every 6 h) and daily warfarin. Anticoagulation with warfarin was continued for 6 months.

**Discussion**

Diagnostic criteria for Lemierre’s disease are not clearly established. While some authors require radiological confirmation and *Fusobacterium*-positive cultures (Karkos et al., 2009), others suggest a history of anginal illness in the preceding 4 weeks or compatible clinical findings, evidence of metastatic lesions in lungs or another remote site and evidence of internal jugular vein thrombophlebitis, or isolation of *F. necrophorum* or *Fusobacterium* sp. from blood cultures or a normally sterile site are needed for a diagnosis of Lemierre’s disease (Riordan, 2007). Lungs are the most common site for metastatic abscesses (80 %), followed by joints (17 %), with hepatic or splenic abscesses a distant third (2.7 %) and other sites extremely rarely (Chirinos et al., 2006).

However, in some series, only a third of patients have positive blood cultures (Hagelskjaer et al., 1998), and Lemierre himself described cases without metastatic lesions. The case presented here occurred in the context of recent pharyngitis in a patient of the age typical of Lemierre’s disease patients, with evidence of septic thrombophlebitis of the internal jugular vein but showing no metastatic lesions. As relying on a microbiological diagnosis, rather than a clinical diagnosis, may delay initiation of treatment and increase morbidity and mortality (Chirinos et al., 2006), this patient was given a presumed diagnosis of septic thrombophlebitis.

Treatment of Lemierre’s disease is best accomplished via a multidisciplinary approach. Collaboration between infectious

*Fig. 1. CT of the patient's chest with a filling defect in the left subclavian and jugular veins, with collateral backfilling evident (medial and lateral margins of clot indicated by arrows).*
disease specialists, radiologists, otolaryngologists and thoracic surgeons is essential for rapid diagnosis and a positive therapeutic outcome (Kuppalli et al., 2012).

Choice of antibiotic is dependent on the likely organisms and is culture directed where possible. Given the need to treat for β-lactamase-producing *Fusobacterium* and oral streptococci, monotherapy with carbapenem, ampicillin-sulbactam, antipseudomonal penicillins or clindamycin is an appropriate option, as is combination therapy of metronidazole and ceftriaxone (Kuppalli et al., 2012). Carbapenems have limited central nervous system penetration; metastatic abscesses of the central nervous system – although extremely rare – must be ruled out prior to their use. In situations in which skin infections are suspected (e.g. precedent central venous instrumentation), an additional spectrum of coverage must be considered. Retrospectively, in the present case, the addition of vancomycin was probably superfluous. The duration of antibiotic treatment should be 3–6 weeks (Kuppalli et al., 2012).

The use of anticoagulation in septic thrombophlebitis is controversial (Bondy and Grant, 2008), even in the presence of laboratory findings suggestive of a thrombophilia (Kaushik et al., 2008). Septic thrombophlebitis is rare; as a result, a strong evidence base to guide clinicians is lacking. A single, small randomized trial, however, showed no benefit (Brown et al., 1999); routine use of anticoagulation is not currently recommended (Kuppalli et al., 2012). At the time of his hospitalization, the present patient had laboratory evidence suggestive of thrombophilia and significant clot progression despite antibiotic therapy; warfarin was indicated in his case for treatment of the co-incident coagulopathy. *Fusobacterium* has been reported to trigger aspirin-reversible platelet aggregation; although the clinical benefit of aspirin in this condition has not been demonstrated, it represented an intervention with low risk potential in this patient so was utilized (Huntington & Sewall, 2007).

Often surgical treatment is needed. Drainage of purulent fluid collections and debridement of necrotic tissue is essential in Lemierre’s disease. Such conditions were not present in our patient. Additionally, in the pre-antibiotic era, ligation or resection of the infected internal jugular vein was often performed to stem the tide of bacteraemia and the resultant spread of metastatic abscesses. Since the advent of effective antibiotics, these latter two procedures are uncommon and are reserved for cases with severe sepsis or recurrent septic emboli despite medical treatment (Chirinos et al., 2002). The use of percutaneously placed intravascular coils has been reported as an effective alternative to ligation (Lim et al., 2010).

Historically, the goal of surgical interventions was not the restoration of blood flow through the affected vessel: ligation and excision ensured a lack of flow with the intent of preventing septic emboli. The use of thrombolytics was not indicated. More recently, percutaneous mechanical antithrombotic procedures – with or without medical thrombolysis – have been employed (Kar & Webel, 2014; Krauthamer & Milefchik, 2004). With the symptomatic progression of our patient’s thrombosis in the context of a presumed coagulopathy, these more aggressive percutaneous interventions were undertaken. Blood flow was restored successfully, without evidence of triggering clinically significant bacteraemia or septic emboli. The current case represents only the third report, to the best of our knowledge, of the use of percutaneous interventions in the management of septic thrombophlebitis.

Lemierre’s disease may be increasing in incidence, although this is perhaps merely reflective of reporting bias (Ramirez et al., 2003; Riordan, 2007). This has prompted speculation that the increase could be due to changing prescribing habits away from empirical antibiotic use for patients presenting with pharyngitis (Karkos et al., 2009). However, considering the low incidence of septic thrombophlebitis, this is not a valid excuse to abandon antibiotic stewardship programmes, which are attempting to slow the increase in antimicrobial resistance (Huttner et al., 2014).

Septic thrombophlebitis remains an uncommon condition. Prompt recognition and treatment are essential to prevent the associated morbidity and mortality. In addition to aggressive antibiotic treatment, percutaneous mechanical thrombolysis has a role in a subset of these patients.

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**References**


