

Case Report

Correspondence

Mark K. Huntington
mark.huntington@usd.edu

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

Muna Ashraf,¹ Chad Laurich^{2,3} and Mark K. Huntington^{1,4}

¹Sioux Falls Family Medicine Residency Program, Center for Family Medicine,
1115 East 20th Street, Sioux Falls, SD 57105, USA

²Sanford Vascular Associates, 1305 W 18th Street, Sioux Falls, SD 57105, USA

³Department of Surgery, University of South Dakota Sanford School of Medicine,
1400 W. 22nd Street, Sioux Falls, SD 57105, USA

⁴Department of Family Medicine, University of South Dakota Sanford School of Medicine,
1400 W. 22nd Street, Sioux Falls, SD 57105, USA

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

Abbreviations: CT, computed tomography.

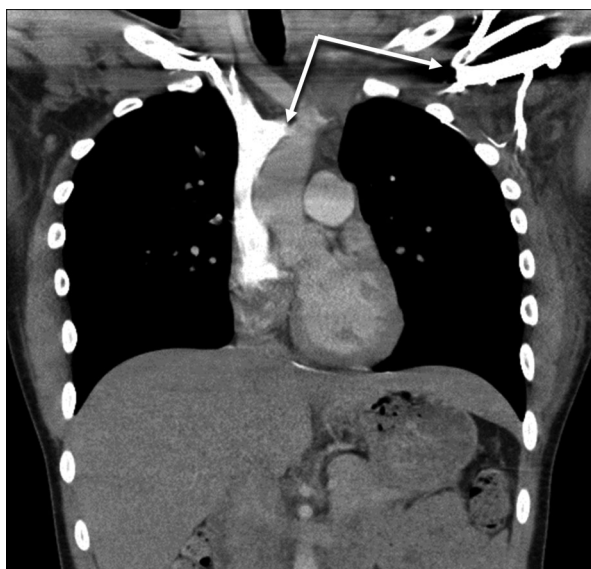


Fig. 1. CT of the patient's chest with a filling defect in the left subclavian and jugular veins, with collateral backfilling evident (medial and lateral margins of clot indicated by arrows).

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 $11 \times 10^3 \text{ cells mm}^{-3}$, 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 β_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) (Ballehaninna *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

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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