



Cough and a sore throat – more than just swine flu?

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Reviewer

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Fusobacterium infection should be considered in the pathogenesis of recurrent pharyngitis and can lead to Lemierre's syndrome if left untreated.

Case history

A 25-year-old non-smoking warehouse worker presented to the acute medical take with a five-day history of worsening symptoms including anorexia, lethargy, myalgia, swinging fevers and night sweats. He had been seen by his general practitioner at the start of this illness and commenced on oseltamivir to treat presumed H1N1 influenza; subsequent hospital referral was prompted by worsening oral intake, dyspnoea, productive cough and pleuritic chest pain. There was no past medical history of note except the patient's report of having suffered from a severe sore throat causing odynophagia a fortnight previously, along with a bout of milder pharyngitis in the weeks prior to this. On admission the patient was febrile (38.1°C), tachycardic (120 bpm) and hypotensive (106/61 mmHg). Pulmonary examination demonstrated globally reduced air entry and expansion with right basal bronchial breathing. Routine bloods (Table 1) were consistent with systemic sepsis and multi-organ dysfunction including acute renal failure, early disseminated intravascular coagulation and type 1 respiratory failure. Plain chest radiograph (Figure 1) showed extensive ill-defined consolidation. The patient was diagnosed with bilateral community-acquired pneumonia on a possible background of H1N1 influenza and commenced on intravenous fluid resuscitation and dual

antibiotic therapy (co-amoxiclav and clarithromycin) as per hospital guidelines.

Despite optimal medical management the patient deteriorated over the next 12 hours with worsening hypotension and hypoxaemia, necessitating transfer to a High Dependency Unit for cardio-respiratory support. Urinary *Legionella* and *Pneumococcal* antigens along with H1N1 viral PCR were negative. Blood cultures taken on admission grew anaerobic Gram-negative rods, subsequently characterized as *Fusobacterium necrophorum* sensitive to co-amoxiclav and metronidazole. Whole-body computerized tomography performed to identify a thrombotic focus for infection confirmed the presence of a left internal jugular vein thrombosis with widespread bilateral lung consolidation and pleural effusions (Figure 2). Intercostal chest drain insertion was performed for the larger right effusion to optimize respiratory function and subcutaneous dalteparin started for the jugular vein thrombosis. A diagnosis of Lemierre's syndrome was made on the basis of the clinical findings.

The patient improved enough to return to a general medical ward after five days, and was subsequently discharged home with improving biochemical markers after four weeks in hospital. He received a total of seven weeks' broad-spectrum intravenous antibiotic therapy and has been continued on oral anticoagulation for three months with ongoing outpatient medical follow-up.

Discussion

Descriptions of post-anginal anaerobic septicaemia following a sore throat can be found in the medical literature from the beginning of the 20th century; it

Table 1
Blood results on admission (reference values in italics)

Hb	13.1 g/dL	(13.0–17.0)	PT	12.9 sec	(9.0–15.0)
WCC	$13.9 \times 10^9/L$	(3.7–11.1)	APTT	30.0 sec	(25.0–35.0)
Plts	$21 \times 10^9/L$	(150–400)	Fibrinogen	5.51 g/L	(1.8–4.5)
Sodium	131 mmol/L	(135–145)	corr.Calcium	2.3 mmol/L	(2.15–2.70)
Potassium	3.1 mmol/L	(3.3–4.4)	Magnesium	1.0 mmol/L	(0.7–1.0)
Chloride	91 mmol/L	(101–112)	Bilirubin	47 mol/L	(3–17)
Bicarbonate	25.4 mmol/L	(21–31)	AST	44 iu/L	(16–50)
Urea	27.4 mmol/L	(3.0–6.5)	ALP	201 iu/L	(42–114)
Creatinine	241 mol/L	(55–105)	GGT	21 iu/L	(12–62)
CRP	375 mg/L	(0–6.0)	Albumin	21 g/L	(32–50)
ABG	pH 7.45 pO ₂ 7.63 kPa pCO ₂ 3.33 kPa (taken on room air)				

was Lemierre, though, who clearly defined a syndrome linking recurrent pyrexia, rigors, septic thrombophlebitis and distal embolic infarcts (e.g. pulmonary) following a sore throat to be 'so characteristic that mistake is almost impossible'.¹ The case frequency and high mortality rate reported by Lemierre declined with the advent of widespread antibiotic usage for bacterial pharyngitis, leading his syndrome to be labelled as another forgotten disease. However, recent work has suggested that its incidence may be rising again, perhaps as a result of concern regarding antibiotic overuse and resistance, changes in prescribing practice and even reduction in the number of tonsillectomies now being performed.^{2–4}

Fusobacterium necrophorum is the most common pathogen associated with Lemierre's syndrome; a recent review labelled it as responsible for 68% of cases in the published literature, while 86% grew any member of the *Fusobacterium* species.³ Despite initial claims (including by Lemierre himself) that the organism was part of the normal oral flora, it is now acknowledged that

Figure 1
Plain chest radiograph on admission demonstrating widespread consolidation in keeping with a bilateral pneumonic process

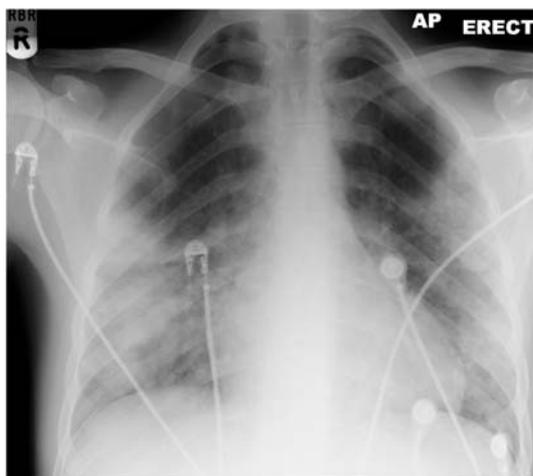


Figure 2
Axial CT image demonstrating a filling defect in the left internal jugular vein (circled) consistent with thrombosis



Fusobacterium should always be considered a pathogen, particularly when isolated in culture from sterile sites. Lemierre's syndrome classically occurs in young adult men, with the proposed pathological sequence of events being that the organism causes tonsillitis and peritonsillar abscess before invading the lateral pharyngeal space and deep neck structures (including the internal jugular vein) to cause complications such as bacteraemia, thrombophlebitis and deep abscess formation. Predisposing factors described in the medical literature for developing Lemierre's syndrome have included trauma to the oropharynx (allowing direct invasion by *Fusobacterium*), concurrent infection with Epstein-Barr virus and acquired or inherited thrombophilic states.

The place of anticoagulation in Lemierre's syndrome is unclear; no objective evidence exists to establish its usefulness in managing thrombosis associated with the infection,⁵ and any decision to start treatment is generally extrapolated from personal clinician experience with other conditions that cause septic embolic phenomena. Antibiotic therapy should provide appropriate anaerobic and beta-lactamase resistant cover with typical therapeutic choices including co-amoxiclav, piperacillin-tazobactam and/or metronidazole. Various studies have shown *Fusobacterium necrophorum* to be reliably sensitive to these antibiotics; by contrast there is evidence of resistance to penicillins (2%) and particularly macrolides (15%) among UK isolates referred for analysis in recent years,⁴ while *Fusobacterium necrophorum* also tends to be intrinsically resistant to gentamicin, quinolones and tetracyclines.

Considering the antibiotics commonly prescribed for bacterial pharyngitis in the primary care setting, this profile of resistance may be of particular relevance if assessing a patient who has presented with either recurrent or deteriorating symptoms of pharyngitis despite apparent treatment. Indeed, there is a significant body of evidence implicating *Fusobacterium necrophorum* in the pathogenesis of conventional bacterial pharyngitis. A number of prospective studies have demonstrated that when cultured for *Fusobacterium necrophorum* can be identified in around 10% of all routine throat swabs received by a microbiology laboratory,^{6,7} comparing favourably with the most common organism and textbook cause of bacterial pharyngitis, group A beta-haemolytic

Streptococcus (isolated in 11–13% of cultures in the same studies). The results also highlight an increased prevalence of *Fusobacterium necrophorum* in young adults with pharyngitis, where in one study the organism was responsible for 77% of positive cultures in swabs taken from those patients between 11 and 25 years in age.⁷ Furthermore, in those cases where swabs have been taken for persistent sore throat it would appear that *Fusobacterium necrophorum* is most likely to be the cause regardless of age.^{6,8} As such, it can be argued with some conviction that *Fusobacterium necrophorum* should be included routinely in the laboratory work-up of pharyngitis, particularly in cases that might be considered high-risk for the organism – for example, young adults and individuals with persistent sore throat. Consideration should also be given to the clinical history and background when deciding upon antibiotic therapy for bacterial pharyngitis, bearing in mind the potential resistance of *Fusobacterium necrophorum* to both penicillins and macrolides.

Lemierre's syndrome is an uncommon condition and yet one that should not be missed given the classical nature of its clinical history and presentation, alongside a mortality rate of 5% in a typically young and fit population. Unfortunately, despite a rising incidence, many clinicians are unlikely to have heard of a case or even the common causative organism, *Fusobacterium necrophorum*. This knowledge is particularly relevant in the primary care setting as *Fusobacterium necrophorum* is increasingly recognized in the pathogenesis of sore throat – notably persistent or recurrent cases – and will often be resistant to commonly prescribed antibiotics. By maintaining an appropriate degree of clinical suspicion there is the potential to diagnose and treat these patients early and effectively to the benefit of all.

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