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Lemierre syndrome - a forgotten complication of acute tonsillitis

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Abstract
Lemierre syndrome, also known as postanginal sepsis, is an illness characterized by the development of a fusobacterial septicaemia with multiple metastatic foci following an attack of acute tonsillitis. It typically affects previously healthy adolescents and young adults who, following an attack of sore throat, become acutely ill with hyperpyrexia, rigors and multiple metastatic abscesses. The clinical picture tends to vary widely because of the possible involvement of a number of body systems and organs in the disease process. This serious complication of oropharyngeal sepsis had a mortality rate in excess of 90 per cent in the pre-antibiotic era. Although now rarely seen and often forgotten, it remains a potentially life-threatening condition. We present four cases of post-tonsillitis fusobacterial septicaemia to illustrate the variability of the clinical presentation and stormy clinical course frequently associated with this rare syndrome.

Key words: Lemierre syndrome; *Fusobacterium necrophorum*; Tonsillitis

Introduction

Lemierre (1936) described a condition known as 'post-anginal septicaemia' which affected mainly young adults and adolescents. In his description of the condition, he quoted: 'The appearance and repetition several days after the onset of a sore throat (and particularly of a tonsillar abscess) of severe pyrexia attacks with an initial rigor, or still more certainly the occurrence of pulmonary infarcts and arthritic manifestations, constitute a syndrome so characteristic that mistake is almost impossible'. Other features described by Lemierre include unilateral swelling of the lateral aspect of the neck, renal impairment, hepatic dysfunction, mastoiditis, thyroiditis, suppurative peritonitis, psoas abscess and abscess of the deep muscles of the buttock. The diagnosis was established by the isolation of an anaerobic bacteria *Bacillus funduliformis* (later reclassified as *Bacillus necrophorum* and more recently as *Fusobacterium necrophorum*) from blood culture and purulent effusion. Of the 20 cases studied by Lemierre, 18 succumbed as a direct result of the disease.

Alston (1955) used the term necrobacillosis (based on the name *Bacillus necrophorum*) to describe the infection and reviewed 21 cases recorded in Great Britain between 1933 and 1954. He was personally involved in the management of 12 of the patients. Of these, seven died of the disease and five survived.

With the widespread use of antibiotics, this syndrome has been reduced both in its incidence and its mortality rate.Of the 23 cases reported worldwide over a 15-year period between 1974 and 1989 reviewed by Sinave *et al.* (1989), only two patients died. As only sporadic cases have been reported in recent literature, the syndrome is no longer well recognized as a complication of tonsillitis even in the major text books of Otolaryngology. Nevertheless, awareness of the characteristic features of this syndrome is important as it will lead to a prompt diagnosis and early treatment with antibiotics which have good anti-anaerobic activity while awaiting bacteriological confirmation.

We have recently managed two patients with post-tonsillitis fusobacterial septicaemia both of whom presented with otolaryngological complications (*Cases 1* and *2*). A search of the recent hospital microbiology records showed four other patients who had fusobacterial septicaemia, two of whom had evidence of preceding tonsillitis in keeping with the diagnosis of Lemierre syndrome. These two cases are also presented and discussed (*Cases 3* and *4*).

Case reports

Case 1

A previously healthy 32-year-old man was admitted with a three-day history of a painful left-sided neck swelling, increasing dyspnoea, cough, fever, rigor, lethargy and a pleuritic chest pain. Two weeks prior to his admission he had developed a sore throat which was treated with a course of pencillin by his GP with good resolution of this symptom.

On examination, he was jaundiced and looked acutely unwell. He had a temperature of 39.5°C, a blood pressure of 95/55 mmHg and a pulse rate of 110 per minute. There was a diffuse, firm, tender swelling extending from the angle of the mandible to the clavicle along the left side of the neck (Figure 1). Oral examination showed oedema of the fauces and the oropharyngeal wall. The tonsils themselves were no longer inflammed. The chest was clear to auscultation but the patient complained of a right-sided pleuritic chest pain on deep inspiration. Abdominal examination revealed tenderness of the liver and spleen both of which were just palpable.

Results of the haematological and biochemical investigations were as follows. Full blood count: haemoglobin

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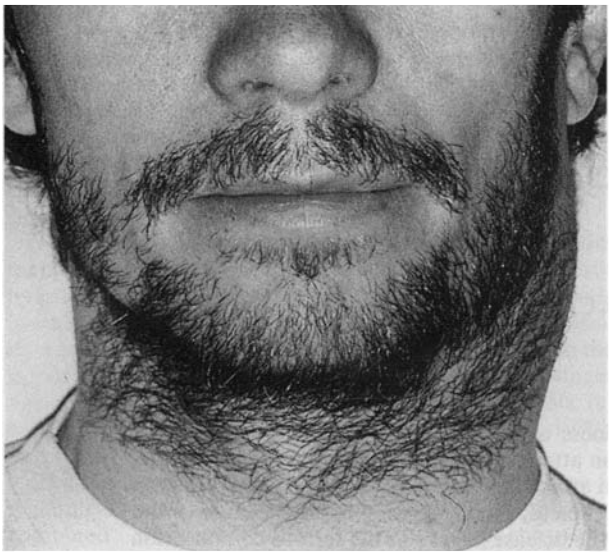

FIG. 1

Photograph of the patient in *Case 1* demonstrating unilateral left-sided neck swelling along the sternocleidomastoid.

13.4 g/dl; white blood count 17.2 x 10^9/l (42 per cent neutrophils, 44 per cent lymphocytes and eight per cent monocytes); platelet count 419 x 10^9/l; erythrocyte sedimentation rate: 93 mm/h. Liver function tests: total bilirubin 89 μmol/l (normal range = 3-22); alkaline phosphatase 216 i.u./l (38–126); alanine transaminase 1285 i.u./l (7–56); aspartate transaminase 953 i.u./l (5–35). The urea and eletrolytes results were within normal limits.

A monospot test for infectious mononucleosis was positive and the diagnosis was supported by subsequent detection of IgM and IgG antibody to Epstein-Barr viral capsid antigen in the serum. Hepatitis screen for HBsAg and Hepatitis A IgM were negative and chest X-ray was normal. Ultrasound scan of the neck swelling showed a large, mainly solid, complex mass with a few small hypoechoic areas. An ultrasound guided aspiration of one of the hypoechoic areas yielded 1 ml of pus.

The patient was commenced on intravenous metronidazole and cefuroxime and kept under close observation. Both the blood culture taken at the time of admission and the culture from the neck aspirate subsequently grew *Fusobacterium necrophorum* sensitive to metronidazole and penicillin. The same intravenous regime was therefore continued for a total of one week. The temperature remained persistently raised above 38.5°C over the first three days followed by intermittent spikes of pyrexia until day seven when he became completely afebrile. His general clinical improvement correlated well with the fall in his temperature. The patient was discharged on day nine with a further two-week course of oral metronidazole. He lost nearly two stones in weight through the short course of the illness.

He was kept under regular review in the outpatient clinic and it was noted that the neck swelling reduced in size very gradually over the subsequent three weeks. The liver function returned to normal after six weeks with no further evidence of hepatosplenomegaly.

Comment

Fusobacterial septicaemia secondary to infectious mononucleosis is rare and very few cases have previously been described (Adams *et al.*, 1983; Dagan and Powell, 1987; Shek *et al*, 1988). One needs to be aware that a positive monospot test alone is not sufficient to confirm the diagnosis of infectious mononucleosis in the presence of fusobacterial septicaemia as a false-positive result may occur (see *Case 3*). Serological confirmation is necessary before infectious mononucleosis is incriminated as the primary cause of the septicaemia.

Case 2

An 11-month-old baby girl was admitted with five-day history of lethargy, poor feeding, fever and a 24 hour history of fluctuating consciousness. She was seen by her GP two days previously who diagnosed acute tonsillitis and started her on a course of amoxicillin without any improvement in her symptoms.

On examination, she looked flushed, unwell and sleepy with a temperature of 40.2°C and a pulse rate of 150 per minute. The tonsils were enlarged and inflammed. A tender 2 cm firm swelling was also noted just superior to the right zygoma. There was no evidence of erythema of the overlying skin. Due to presence of wax deep in the right external auditory canal, the tympanic membrane was not visualized.

The results of the haematological investigation on admission were as follows: haemoglobin 10.5 g/dl; white blood count 22.9 × 10^9/l (79.6 per cent neutrophils, 14 per cent lymphocytes and 5.4 per cent monocytes); platelet count 606 × 10^9/l. Liver function tests and the urea electrolytes results were within normal limits. Examination of the cerebral spinal fluid following a lumbar puncture showed no evidence of a meningitis.

A diagnosis of acute tonsillitis was made but the cause of the right-sided 'suprazygomatic' swelling remained obscure. Further questioning revealed that she had had a fall two days previously and had bumped her head over the right temporal region. A haematoma was therefore thought to be a possible cause of the swelling. A blood culture was taken and the patient was started on intravenous flucloxacillin and cefuroxime and kept under

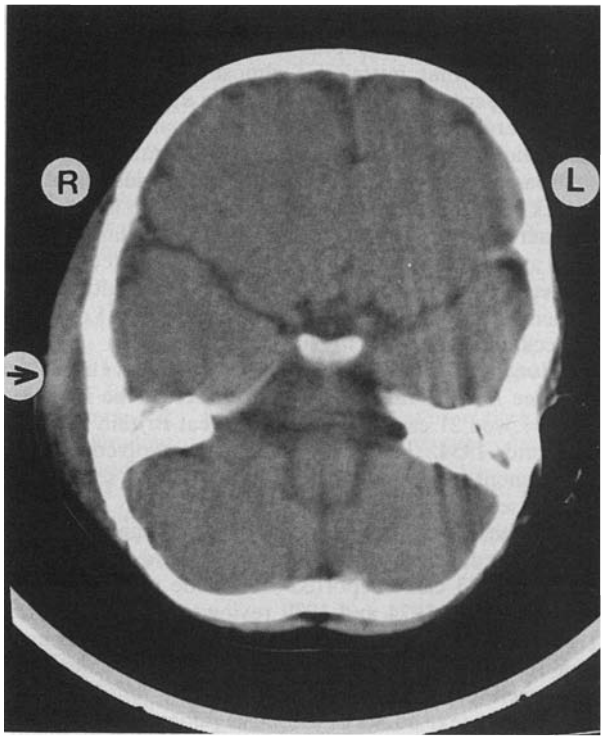

FIG. 2

CT scan of the patient in *Case 2* demonstrating subcutaneous abscess collection running along the outer aspect of the right side of the skull (arrowed).

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close observation. Twelve hours later, she developed a discharge from the right ear and the swelling above the right zygoma was noted to have increased in size and had extended posteriorly to the superior aspect of the right pinna pushing it laterally. A diagnosis of acute mastoiditis with zygomatic extension of the abscess was suspected and the patient was prepared for exploration and drainage of the abscess under anaesthesia. A preliminary CT scan showed mucosal thickening of the right mastoid air cells and a subcutaneous collection running along the outer aspect of the right side of the skull from just superficial to the mastoid process to the temporal region (Figure 2).

At operation, an abscess filled with offensive smelling pus was found deep to the temporalis extending anteriorly along the zygomatic arch. A cortical mastoidectomy revealed a well pneumatized air cell system filled with granulation tissue extending superiorly over the roof of the external auditory canal. More mucopus was aspirated from the middle ear after a myringtomy. Due to the smell of the pus, an anaerobic infection was suspected and metronidazole was added to her intravenous treatment regime.

Blood culture taken at the time of admission showed *Fusobacterium necrophorum* sensitive to metronidazole. Intravenous treatment with metronidazole was therefore continued for a total of seven days. The temperature continued to swing and remained above 38°C before returning to normal after five days. The patient made a slow but otherwise uneventful recovery. There was no evidence of any hearing impairment on review in the clinic three months later.

Comment

Fusobacterial septicaemia following tonsillitis is uncommon in children and only a few cases have previously been described in those under the age of 10 years, the youngest being five years old (Alston, 1955; Sinave *et al.*, 1989). The association of mastoiditis with fusobacterial septicaemia is also very rare (Lemierre, 1936; Alston, 1955; Barlett and Gorbach, 1976). Another unusual feature demonstrated here is the initial presentation of the abscess anteriorly over the zygoma rather than the more usual posterior route to the mastoid antrum.

Case 3

A previously healthy 17-year-old was admitted with a six-day history of sore throat and swollen glands in the neck followed by a three-day history of fever and rigor, and a one-day history of diarrhoea, severe abdominal pain and pleuritic chest pain.

On examination, she appeared acutely unwell with a temperature of 40.6°C, a pulse rate of 120 per minute and a blood pressure of 100/60 mmHg. Multiple tender lymph nodes were palpable on both sides of the neck and the tonsils and fauces were noted to be inflammed. Chest examination showed decreased air entry into both bases with coarse crepitation. Abdominal palpation revealed generalized tenderness with heptomegaly and splenomegaly.

Results of haematological and biochemical investigation were as follows. Full blood count: haemoglobin 11.0 g/dl; white blood count 6.7 $\times$ 10^9/l (84 per cent neutrophils, 5 per cent lymphocytes, 8 per cent monocytes); platelet count 253 $\times$ 10^9/l. Liver function tests: bilirubin 25 (3–22), alkaline phosphotase 203 (38–126), alanine transaminase 333 (7–56) and aspartate transaminase 349 (5–35). Urea and electrolytes results were all within normal limits.

A monospot test for infectious mononucleosis was positive. A provisional diagnosis of infectious mononucleosis was made and the patient was treated symptomatically with analgesia and was closely observed.

Over the subsequent 48 hours, her condition deteriorated with frequent episodes of rigors, increasing abdominal tenderness and peripheral cyanosis. Abdominal ultrasound showed a large lobulated liver with multiple microabscesses. The spleen was also enlarged but the kidneys and pancreas both appeared normal. Chest X-ray showed bilateral pleural effusion. Blood culture confirmed a growth of *Fusobacterium necrophorum* sensitive to metronidazole and cefuroxime. The patient was therefore started on intravenous cefuroxime, gentamicin and metronidazole. Due to increasing abdominal tenderness and peritonitis, a laparotomy was performed which showed an engorged liver with multiple hepatic abscesses. The spleen was enlarged but did not show any focal abnormality. She had a rather stormy post-operative course and spent two weeks in the intensive therapy unit with respiratory failure requiring mechanical ventilation and repeated drainage of the pleural effusion. Her temperature remained persistently above 39°C over the next two weeks despite continuation of intravenous antibiotics. She made a very slow clinical recovery and was eventually discharged three weeks later. Further serological test for IgG and IgM antibodies to Epstein-Barr viral capsid antigen were negative suggesting that the initial monospot test result was in fact a false-positive result.

Serial chest X-ray and abdominal ultrasound showed that the radiological changes of the lungs and the liver took a further three months to resolve.

Comment

A false-positive monospot test may occur in fusobacterial septicaemia which may confuse or delay management decisions. Serological test is therefore necessary before a final diagnosis is achieved and before infectious mononucleosis is implicated as a primary cause of Lemierre syndrome as in *Case 1*.

Case 4

A 23-year-old woman presented with a two-week history of sore throat, neckache and generalized myalgia followed by a one-day history of diarrhoea, vomiting and right hip pain. On examination, she appeared clinically dehydrated with a temperature of 40°C. Abdominal examination showed signs of generalized peritonitis.

Results of haematological investigation were as follows: haemoglobin 11.4 g/dl; white blood count 17.22 $\times$ 10^9/l (neutrophils 95.3 per cent; lymphocytes 2.9 per cent, monocytes 1.4 per cent); platelet count 462 $\times$ 10^9/l. Liver function tests and electrolytes were within normal limits. Chest X-ray showed a small left pleural effusion.

The patient was commenced on intravenous cefuroxime and metronidazole and prepared for a laparotomy. At operation, 2 l of pus was found in the peritoneal cavity. The source of infection was not identified although a walled-off large bowel perforation was considered a possibility and a loop ileostomy was performed. The patient was admitted to the intensive therapy unit post-operatively. A blood culture taken at the time of admission showed a growth of *Fusobacterium necrophorum* sensitive to metronidazole. Despite continuation of the intravenous antibiotics regime which included metronidazole, her condition continued to deteriorate with increasing right-sided hip pain and development of a right buttock swelling. The swelling was explored and 200 ml of pus was drained from an abscess deep to the gluteus maximus which

extended directly from the hip joint. The patient made a slow clinical recovery after the second operation and was discharged three weeks later. She was subsequently readmitted for reversal of the loop ileostomy followed by an uneventful recovery.

Comment

This and the previous case demonstrate the serious nature of the metastatic complications of the infection which may involve multiple sites. Early identification and drainage of any purulent collection as well as prolonged intravenous antibiotics are essential.

Discussion

Fusobacteria spp. form a major part of the normal flora of the human upper respiratory tract and are found in large numbers in the gingival crevice and subgingival plaque of all healthy adults (Duerden, 1990). Inflammation of the tonsils may allow pathogenic transformation of the oral commensal and their invasion of the tonsillar and peritonsillar veins giving rise to the septicaemia. It is therefore hardly surprising that oropharyngeal sepsis is a common cause of fusobacterial septicaemia. Cases arising from dental abscess, mastoiditis, sinusitis and oral ulcer have also been described (Lemierre, 1936; Barlett and Gorbach, 1976; Quinn and Guernsey, 1985). Members of the genus are also found in the female genital tract and the large bowel. This may account for a small number of cases of fusobacterial septicaemia seen in the puerperium, following abortion and after bowel surgery (Alston, 1955).

Central to the pathogenesis of Lemierre syndrome is the spread of the septic thrombophlebitis of the tonsillar and peritonsillar veins to the internal jugular vein. The thrombophlebitic internal jugular vein acts as the focus for persistent bacteraemia and as the origin of multiple septic emboli to distant sites. It also accounts for the frequent presentation of the characteristic swelling and tenderness in the neck along the course of the vein as described by Lemierre and demonstrated by the patient in *Case 1*. In the absence of a neck swelling, the presence of a thrombophlebitic internal jugular vein may not be clinically obvious but may be demonstrated by special imaging techniques such as CT scan (Albertyn and Alcock, 1987), digital subtraction angiogram (Anand and Morrison, 1987), Doppler ultrasound and gallium scan (Yu and Norante, 1980).

The onset of symptoms frequently coincides with the apparent clinical resolution of the sore throat, hence the term 'postanginal sepsis' is often used to describe the syndrome. Rigor and high fever, often in excess of 40°C, are nearly always present. Septic pulmonary foci occur in up to 97 per cent of cases (Sinave *et al.*, 1989) and manifest as pleuritic chest pain, dyspnoea and occasionally as haemoptysis. Other pulmonary sequelae include pleural effusion (*Case 3*) and less frequently empyema. Metastatic septic joint effusion (*Case 4*) is also a frequent complication. Deranged liver function tests are common and may be associated with frank jaundice (*Case 1*). Meningitis (Alston, 1955; Adams *et al.*, 1983), mastoiditis (Lemierre, 1936; Alston, 1955; *Case 2*) endocarditis (Adams *et al.*, 1983) and adult respiratory distress syndrome (Cosgrove *et al.*, 1993) have also been described. Abdominal complications such as metastatic liver abscesses (*Case 3*) and purulent peritonitis (*Case 4*) were described by Lemierre in his original article but have rarely been reported since.

The diagnosis of Lemierre syndrome is primarily clinical, supported by bacteriological findings. Chest X-ray frequently shows nodular shadowing, cavitation and pleural effusion. Abdominal ultrasound may demonstrate hepatomegaly, splenomegaly and occasionally the presence of hepatic microabscesses. Special imaging technique to demonstrate the presence of a thrombophlebitic internal jugular vein as described above is not routinely employed as it does not normally alter the management of the patient unless one is contemplating ligation of the internal jugular vein or institution of anticoagulant therapy. However, frank abscess formation may occur in the neck in relation to the thrombophlebitic internal jugular vein and may require surgical drainage (Oleske *et al.*, 1976; Yousem *et al.*, 1985). Ultrasound scan is therefore extremely useful in the presence of a neck swelling to confirm or exclude the clinical suspicion of an abscess.

Although *Fusobacterium necrophorum* is usually sensitive to both metronidazole and benzylpenicillin *in vitro*, experience has shown that metronadazole results in an earlier and more definite clinical improvement than penicillin, probably due to its good penetration of tissue (Mitre and Rotheram, 1974; Vogel and Boyer, 1980; Seidenfeld *et al.*, 1982; Hudson *et al.*, 1984; Moore-Gillon *et al.*, 1984). Prolonged intravenous administration of antibiotics is usually necessary because of the persistent nature of the sepsis and bacteraemia. As metronidazole is very well absorbed, it can be given orally once improvement is obtained. Clinical response may be very gradual and the temperature may remain high for a prolonged period. In the critical stages of the illness, supportive treatment in an intensive therapy unit is often needed.

With appropriate antibiotics and good supportive measure, full recovery without sequelae is usual. Ligation of the thrombophlebitic internal jugular vein was frequently practiced in the pre-antibiotic era but is now rarely required except in cases not responding to conservative measures (Anand and Morrison, 1987). The presence of any purulent collection in the neck, joints, chest and abdomen will usually require drainage in order to palliate symptoms and to obtain bacteriological specimens. Anticoagulation has been used but is of unproven clinical benefit (Dagan and Powell, 1987). Late presentation and delayed diagnosis has resulted in fatalities (Seidenfeld *et al.*, 1982).

Conclusions

Fusobacterial septicaemia should be suspected when a previously healthy adolescent or young adult develops a severe septicaemic illness after an initial sore throat. The full clinical picture may be variable depending on the site or sites of involvement of the septic emboli. The syndrome as described by Lemierre (1936) more than half a century ago still applies and almost all the features reported by Lemierre have been demonstrated by the cases we have presented here. Management of the patient often requires close collaboration between the physician, the surgeon, the microbiologist, the radiologist and the intensivist. Early diagnosis, appropriate antibiotics with good anti-anaerobic activity, prompt recognition and drainage of any purulent collection and good general supportive measures are the keys to successful outcome of the treatment.

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References

Adams, J., Capistrant, T., Crossley, K., Johanssen, R., Liston, S. (1983) *Fusobacterium necrophorum* septicemia. *Journal of the American Medical Association* **250:** 35.

Anand, V. K., Morrison, M. V. (1987) Thrombophlebitis of the jugular vein. *Ear, Nose and Throat Journal* **66:** 41–46.

Albertyn, L. E., Alcock, M. K. (1987) Diagnosis of internal jugular vein thrombosis. *Radiology* **162:** 505–508.

Alston, J. M. (1955) Necrobacillosis in Great Britain. *British Medical Journal* **II:** 1524–1528.

Bartlett, J. G., Gorbach, S. L. (1976) Anaerobic infections of the head and neck: symposium on infectious disease of head and neck. *Otolaryngologic Clinics of North America* **9:** 655–678.

Cosgrove, E. F., Colodny, S. M., Pesce, R. R. (1993) Adult respiratory distress syndrome as a complication of postanginal sepsis. *Chest* **103(5):** 1628–1629.

Dagan, R., Powell, K. R. (1987) Postanginal sepsis following infectious mononucleosis. *Archives of Internal Medicine* **147:** 1581–1583.

Duerden, B. I. (1990) The bacteroidacea: bacteroides, fusobacteria and leptotrichia. In *Topley and Wilson's Principles of Bacteriology, Virology and Immunology.* Vol. 2, Ch. 2. (Parker, M. T., Duerden, B. I., eds.), Edward Arnold, London, p 28.

Hudson, S., Maddocks, A. C., Stacey, A. (1984) Necrobacillosis. *British Medical Journal* **288:** 1915–1916.

Lemierre, A. (1936) On certain septicaemias due to anaerobic organisms. *Lancet* **1:** 701–703.

Mitre, R. J., Rotheram, E. B. (1974) Anaerobic septicemia from thrombophlebitis of the internal jugular vein. *Journal of the American Medical Association* **230(8):** 1168–1169.

Moore-Gillon, J., Lee, T. H., Eykyn, S. J., Phillips, I. (1984) Necrobacillosis: a forgotten disease. *British Medical Journal* **288:** 1526–1527.

Oleske, J. M., Starr, S. E., Nahmias, A. J. (1976) Complications of peritonsillar abscess due to *Fusobacterium necrophorum*. *Pediatrics* **57(4):** 570–571.

Quinn, P., Guernsey, L. H. (1985) The presentation and complication of odontogenic septic shock. *Oral Surgery, Oral Medicine and Oral Pathology* **59:** 336–339.

Seidenfeld, S. M., Sutker, W. L., Luby, J. P. (1982) *Fusobacterium necrophorum* septicemia following oropharyngeal infection. *Journal of the American Medical Association* **248(11):** 1348–1350.

Sinave, C. P., Hardy, G. J., Fardy, P. W. (1989) The Lemierre syndrome: suppurative thrombophlebitis of the internal jugular vein secondary to oropharyngeal infection. *Medicine* **68:** 85–94.

Shek, M., Karamali, A., McGuire, N., Seifert, P., Alperin, N. (1988) Bacterial sepsis with *Fusobacterium necrophorum*. *Archives of Internal Medicine* **148:** 2303.

Vogel, L., Boyer, K. M. (1980) Metastatic complications of *Fusobacterium necrophorum* sepsis – two cases of Lemierre's postanginal septicemia. *American Journal of Diseases of Childhood* **134:** 356–358.

Yau, P. C., Norante, J. D. (1980) Thrombophlebitis of the internal jugular vein secondary to pharyngitis. *Archives of Otolaryngology* **106:** 507–508.

Yousem, D. M., Scatarige, J. C., Gayler, B. W., Siegelman, S. S. (1985) CT demonstration of postanginal sepsis. *Journal of Otolaryngology* **14(5):** 333–335.

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