CASE REPORT

Oesophageal cancer presenting as Lemierre's syndrome caused by *Streptococcus anginosus*

Mohammed Osman,¹ Saqib Hasan,² Ghassan Bachuwa¹

¹Hurley Medical Center, Flint, Michigan, USA
²Infectious Disease, Hurley Medical Center, Flint, Michigan, USA

Correspondence to
 Dr Ghassan Bachuwa,
 gbachuwa2@hurleymc.com

Accepted 30 March 2017

SUMMARY

A 59-year-old man presented to the emergency department with complaints of dysphagia, right-sided neck swelling, fever and chills. Physical examination was remarkable for fever and tender swelling over the right side of the neck. Laboratory investigations revealed leucocytosis with neutrophilia. CT of the neck showed right internal jugular vein thrombosis with an overlying abscess and a nodular opacity in the right lung apex with air locules. He underwent surgical drainage of the neck abscess. Aerobic cultures from the drainage and blood cultures grew *Streptococcus anginosus*. Given his initial complaint of dysphagia, upper endoscopy was performed which showed a mass in the upper oesophagus. Histopathology confirmed squamous cell carcinoma. The patient received 6 weeks of antibiotics therapy.

BACKGROUND

Lemierre's syndrome (LS) (postanginal sepsis) is a septic thrombophlebitis of the internal jugular vein secondary to upper respiratory tract infection with *Fusobacterium necrophorum* as the identified pathogen.¹

Streptococcus anginosus belongs to a group carrying the same name which contains two other streptococci, *S. constellatus* and *S. intermedius*. To our knowledge, three cases of LS secondary to *S. constellatus* and three cases secondary to *S. intermedius* have been described in the literature.^{2–7}

The associations between *S. anginosus* and its carcinogenic role in the pathogenesis of oesophageal cancer has been postulated in different studies.^{8–10}

To our knowledge, our case will be the first to report of LS secondary to *S. anginosus* as an initial presentation of squamous cell carcinoma of the oesophagus.

CASE PRESENTATION

A 59-year-old man with no medical history presented to the emergency department with complaints of swelling of the right side of the neck, fever, chills and difficulty swallowing. Two months before his presentation, the patient noted pain on swallowing that ultimately progressed to difficulty swallowing solids and then to liquids. Ten days before admission, the patient noticed a painful right-sided neck swelling. He reported 25 pounds weight loss over the preceding months. The patient was a chronic alcoholic with an 80 pack-year smoking history.

Physical examination revealed a temperature of 38.2°C, erythema, diffuse swelling and tenderness over the right side of the neck. There were coarse crackles over the right upper lung zone. Mouth examination revealed only three remaining teeth with no signs of infection.

INVESTIGATIONS

Haematological and biochemical laboratory parameters were notable for leucocytosis with neutrophilia and left shift.

CT angiography (CTA) of the neck revealed thrombosis of the right internal jugular vein (figure 1). CT of the neck shows air-containing soft tissue swelling in the right supraclavicular region (figure 2). Nodular opacity in the right lung apex with air locules suspicious for an abscess was detected on CT of the neck (figure 3).

Cultures of the blood and the abscess drainage were positive for *S. anginosus*. Upper gastrointestinal endoscopy revealed squamous cell carcinoma in the upper oesophagus.

TREATMENT

The patient was intubated due to impending respiratory failure secondary to upper airway obstruction. He was started empirically on vancomycin, cefepime and clindamycin. Based on culture and sensitivity results, antibiotics were changed to ceftriaxone and metronidazole. The patient received a 6-week course of antibiotics.

Figure 1 Axial section of CT angiography of the neck showing absence of contrast in the right internal jugular vein (arrow) indicating thrombosis of the right internal jugular vein.

CrossMark

To cite: Osman M, Hasan S, Bachuwa G. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-219661

Figure 2 Coronal section of the CT neck with contrast showing air in the soft tissue with swelling in the right supraclavicular region.

OUTCOME AND FOLLOW-UP

The hospital course was complicated by ventilator-associated pneumonia with highly resistant *Pseudomonas aeruginosa* that was treated with piperacillin-tazobactam. The patient required tracheostomy due to persistent upper airway obstruction. The patient improved clinically and repeat blood cultures were

Figure 3 Coronal section of the CT neck showing air filled opacity in the upper lobe of the right lung (arrow).

negative. On discharge, the patient was tracheostomy dependent.

DISCUSSION

LS was first described by the French bacteriologist Andre-Alfred Lemierre in 1936 who labelled his observation as 'anaerobic post anginal septicaemia'.¹ It was not until 1983 that the disease was labelled as 'Lemierre's syndrome' by Shannon *et al* in his description of a case of oropharyngeal septicaemia.¹¹ The syndrome is classically described in young patients with a mean age of 20 years.^{12 13} The incidence of this rare disease is increasing in the last 10 years possibly due to change in the pattern of antibiotic prescription or increase in bacterial resistance.¹² In a large prospective study in Denmark, the incidence of the disease was 14.4 cases per million per year in 15–24 years of age and it was rare in adults over 40 years of age, with an incidence of 1.4 cases per million per year.¹³

E. necrophorum is the classical culprit of LS, with reported incidence of 63%.¹³ Other organisms causing the syndrome have been described and include *Staphylococcus*, *Streptococcus* and *Klebsiella*.^{4 7 12 14 15}

The syndrome presents initially as upper respiratory tract infection with sore throat being the most commonly observed complaint.^{12 16} Neck pain, which develops secondary to internal jugular vein thrombosis or neck abscess, is the second common presenting symptom.^{11 12 16–19} Atypical presentations include otalgia, otorrhoea, arthritis, dental pain, seizures and blindness in rare cases with extension to cranial venous sinuses.^{12 16 20}

The diagnosis of LS needs a high index of suspicion, and it is crucial for starting early therapy. The proposed criteria for the diagnosis are symptoms of upper respiratory tract infection, thrombosis of the internal jugular vein with subsequent septic emboli with bacteraemia and isolation of the causative bacteria in blood cultures.^{1 11 12 16–19 21–23}

In our case, the causative organism was *S. anginosus*, a member of the anginosus group (previously was named as milleri group) of streptococci which also includes *S. intermedius* and *S. constellatus*.²⁴ Virtually all strains (93%) of *S. intermedius* are non-haemolytic while 38% of *S. constellatus* and 12% of *S. anginosus* are β -haemolytic.^{25 26} *S. anginosus* group are normal flora of the oral cavity and genitourinary tract.²⁷ They are known for their association with purulent infection, which usually occurs after local disruption of the mucosal barrier that leads to ulceration, perforation, inflammation and surgery.^{27 28}

The DNA of *S. anginosus* has been linked to malignancy of the upper gastrointestinal tract.⁸ Moreover, the bacteria has been isolated in oesophageal dysplasia and cancer tissues and the bacterial DNA fragments are frequently found in samples from oesophageal and gastric cancers as well as oesophageal dysplasia suggesting *S. anginosus* infection or colonisation happen in the initial phases of the cancerous process, and it is related to carcinogenesis through induction of inflammation which promotes the cancerous process.^{8–10}

The infection in our case probably originated at the site of oesophageal cancer with subsequent invasion of the blood stream and involvement of the internal jugular vein leading to septic thrombophlebitis.

The cornerstone of therapy is prolonged course of antibiotics.¹² Although the final choice of antimicrobial therapy must be based on the result of culture and sensitivity, clinical judgement is crucial for the initial decision while awaiting the results of the culture.^{12 13} Suggested empiric antibiotic therapy includes

clindamycin, ampicillin-sulbactam, piperacillin-tazobactam or a combination of penicillin G with metronidazole.^{12 13 18 19 22 29}

There is no agreement on the use of anticoagulation, and no clear guidelines exists. An acceptable approach is to reserve the use of anticoagulation for patients with underlying thrombophilia, clot extension to cranial sinuses or poor clinical response to antibiotics.^{13 18 30 31} A recent systematic review found a rise in the rate of anticoagulation to 68% from 21% to 23% which was observed in previous systematic reviews.^{17 22}

In the presence of abscesses, surgical drainage is usually considered in the form of incision and drainage.^{18 19 29} An old surgical approach at the time of Lemierre was ligation of the internal jugular veins which is rarely used in the modern era unless there is persistent septic embolisation.^{18 32}

Learning points

- *Streptococcus anginosus* should be considered as a causative organism for Lemierre's syndrome.
- Oesophageal cancer can be associated with *S. anginosus* bacteraemia.
- Antibiotics and abscess drainage are the cornerstones of treatment for Lemierre's syndrome; anticoagulation can be used in special situations.

Contributors MO: carried out the literature review, wrote the initial draft of the manuscript, revised it critically, collected the images, approved the final version to be published and made sure all the information presented in the manuscript was accurate. SH and GB: edited the manuscript, revised it critically, approved the final version to be published and made sure all the information presented in the manuscript was accurate.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Lemierre A. On certain septicaemias due to anaerobic organisms. *The Lancet* 1936;227:701–3.
- 2 Benhayoun M, Llor J, Van-Den-Abbeele T, et al. [Bilateral jugular thrombosis in Lemierre syndrome]. *Arch Pediatr* 2003;10:1071–4.
- 3 Righini CA, Karkas A, Tourniaire R, et al. Lemierre syndrome: study of 11 cases and literature review. *Head Neck* 2014;36:1044–51.
- 4 Shimada M, Morinaga Y, Kitazaki T, et al. A severe case of Lemierre syndrome with *Streptococcus constellatus* infection. *Jpn J Infect Dis* 2014;67:488–9.
- 5 Chemlal K, Caby I, Memain N, et al. *Streptococcus intermedius* Lemierre syndrome: an unusual association. *Presse med* 2000;29:1601–2.
- 6 Juárez Escalona I, Díaz Carandell A, Aboul-Hons Centenero S, et al. Lemierre syndrome associated with dental infections. Report of one case and review of the literature. *Med Oral Patol Oral Cir Bucal* 2007;12:394–6.
- 7 Gupta S, Merchant SS. Rare Lemierre's Syndrome: But life threatening—A case report with *Streptococcus intermedius*. *Case Rep Med* 2012;2012:624065.
- 8 Sasaki H, Ishizuka T, Muto M, et al. Presence of *Streptococcus anginosus* DNA in esophageal Cancer, dysplasia of esophagus, and gastric Cancer. *Cancer Res* 1998;58:2991–5.
- 9 Nariakiyo M, Tanabe C, Yamada Y, et al. Frequent and preferential infection of *Treponema denticola*, *Streptococcus mitis*, and *Streptococcus anginosus* in esophageal cancers. *Cancer Sci* 2004;95:569–74.
- 10 Han XY, Kamana M, Rolston KV. Viridans streptococci isolated by culture from blood of cancer patients: clinical and microbiologic analysis of 50 cases. *J Clin Microbiol* 2006;44:160–5.
- 11 Shannon GW, Ellis CV, Stepp WP. Oropharyngeal *Bacteroides melaninogenicus* infection with septicemia: Lemierre's syndrome. *J Fam Pract* 1983;16:159–60.
- 12 Karkos PD, Asrani S, Karkos CD, et al. Lemierre's syndrome: A systematic review. *Laryngoscope* 2009;119:1552–9.
- 13 Hagelskjaer Kristensen L, Prag J. Lemierre's syndrome and other disseminated *Fusobacterium necrophorum* infections in Denmark: a prospective epidemiological and clinical survey. *Eur J Clin Microbiol Infect Dis* 2008;27:779–89.
- 14 Shah RK, Wofford MM, West TG, et al. Lemierre syndrome associated with group A streptococcal infection. *Am J Emerg Med* 2010;28:643.e5–643.e8.
- 15 Tsai YJ, Lin YC, Harnd DJ, et al. A Lemierre syndrome variant caused by *Klebsiella pneumoniae*. *J Formos Med Assoc* 2012;111:403–5.
- 16 Ridgway JM, Parikh DA, Wright R, et al. Lemierre syndrome: a pediatric case series and review of literature. *Am J Otolaryngol* 2010;31:38–45.
- 17 Johannesen KM, Bodtger U. Lemierre's syndrome: current perspectives on diagnosis and management. *Infect Drug Resist* 2016;9:221–7.
- 18 Eilbert W, Singla N. Lemierre's syndrome. *Int J Emerg Med* 2013;6:40.
- 19 Wright WF, Shiner CN, Ribes JA, et al. Lemierre syndrome. *South Med J* 2012;105:283–8.
- 20 Hoffman MA, Birge ND, Chatterjee A, et al. Lemierre-like syndrome: a series of unique cases. *Clin Pediatr* 2010;49:893–6.
- 21 Moreno S, García Altozano J, Pinilla B, et al. Lemierre's disease: postanginal bacteremia and pulmonary involvement caused by *Fusobacterium necrophorum*. *Rev Infect Dis* 1989;11:319–24.
- 22 Riordan T. Human infection with *Fusobacterium necrophorum* (Necrobacillosis), with a focus on Lemierre's syndrome. *Clin Microbiol Rev* 2007;20:622–59.
- 23 Holm K. "A syndrome so characteristic" Molecular and clinical studies of *Fusobacterium*. 2015;128:1–87.
- 24 Summanen P. Recent taxonomic changes for anaerobic gram-positive and selected gram-negative organisms. *Clin Infect Dis* 1993;16(Suppl 4):S168–S174.
- 25 Ruoff KL. *Streptococcus anginosus* ('*Streptococcus milleri*'): the unrecognized pathogen. *Clin Microbiol Rev* 1988;1:102–8.
- 26 Whitley RA, Beighton D, Winstanley TG, et al. *Streptococcus intermedius*, *Streptococcus constellatus*, and *Streptococcus anginosus* (the *Streptococcus milleri* group): association with different body sites and clinical infections. *J Clin Microbiol* 1992;30:243–4.
- 27 Chen CC, Teng LJ, Kaiung S, et al. Identification of clinically relevant viridans streptococci by an oligonucleotide array. *J Clin Microbiol* 2005;43:1515–21.
- 28 Giuliano S, Simone G, Rubini G, et al. *Streptococcus anginosus* group disseminated infection: case report and review of literature. *Infez Med* 2012;20:145–54.
- 29 Noy D, Rachmiel A, Levy-Faber D, et al. Lemierre's syndrome from odontogenic infection: Review of the literature and case description. *Ann Maxillofac Surg* 2015;5:219–25.
- 30 Phan T, So TY, Ty S. Use of anticoagulation therapy for jugular vein Thrombus in pediatric patients with Lemierre's syndrome. *Int J Clin Pharm* 2012;34:818–21.
- 31 Hoehn KS. Lemierre's syndrome: the controversy of anticoagulation. *Pediatrics* 2005;115:1415–6.
- 32 Lemierre A, Grégoire R, Laporte A, et al. Les aspects chirurgicaux des infections à bacillus funduliformis. 1938.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow