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Case Report

Two uncommon cases of Pneumococcal pyomyositis

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Introduction: Pneumococcal pyomyositis is a rare disease. To our knowledge, only 28 cases of this disease have been reported in adults.

Case presentation: We report two new cases of pneumococcal pyomyositis managed at an inter-regional referral centre for bone and joint infections in the south of France. One of our patients had heterozygous sickle-cell disease, and the second had no apparent immunodeficiency. The pneumococcal pyomyositis was localized primarily to the psoas muscle and was complicated by hip arthroplasty infection in one of our cases. In the other case, it was localized to the abductor muscle, which has not been reported previously.

Conclusion: We report two new cases of this disease with favourable outcomes following long-term antimicrobial treatment and surgery debridement.

Keywords: bacteria; human; pneumococcal pyomyositis; pyomyositis; *Streptococcus pneumoniae*.

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Introduction

Pyomyositis is a rare disease that is typically caused by *Staphylococcus aureus* (Bickels *et al.*, 2002; Burdette *et al.*, 2012). Pneumococcal pyomyositis occurs in 1 % of cases of pyomyositis (4 of 452 cases; Bickels *et al.*, 2002) and is usually reported in immunodeficient individuals, such as those with human immunodeficiency virus (HIV) infection, diabetes mellitus, cancer, connective tissue diseases, cirrhosis or asplenia (Burdette *et al.*, 2012).

Here, we report two cases of pneumococcal pyomyositis managed in an inter-regional referral centre for bone and joint infections in the south of France. We also reviewed 28 cases of pneumococcal pyomyositis in adult patients reported in the literature between 1940 and 2014.

Abbreviations: HIV, human immunodeficiency virus; MALDI-TOF, matrix-assisted laser desorption-ionization time-of-flight mass spectrometry.

Case reports

Case 1

In August 2010, a 68-year-old man was admitted for fever, chills, dyspnoea, weight loss, and lumbar and right hip pain that occurred 1 month before admission. His medical history indicated that he had received a right hip prosthesis for tuberculosis coxarthrosis in 1976; the anti-tuberculosis treatment information was not available. He was treated for primary arterial hypertension by administration of candesartan cilexetil and hydrochlorothiazide. The patient did not have any malnutrition or alcoholism. This patient was born in Guinea and had lived in France for more than 30 years. He travelled for 3 months in Guinea and spent 1 month in Senegal for a family visit.

Upon admission, he presented with fever (38.5 °C) and muscle pain that had migrated secondarily to his right hip prosthesis. Laboratory investigations revealed a high C-reactive protein level (299 mg l⁻¹; normal value ≤ 5 mg l⁻¹), an elevated leukocyte count (14 000 μl⁻¹, predominantly neutrophil granulocytes), an elevated platelet count (700 000 μl⁻¹)

and severe hypochromic microcytic aplastic anaemia (6 g haemoglobin dl⁻¹ and 43 000 reticulocytes μ⁻¹). Computed tomography scans of the chest, abdomen and pelvis revealed a bilateral psoas abscess associated with hip prosthesis infection (Fig. 1) and left basal pneumonia with pleural effusion. Trans-thoracic echocardiography revealed no evidence of infectious endocarditis or valve abnormalities.

Blood cultures were performed before antibiotics were administered and were sterile. A bacterial culture of purulent fluid aspirated from the psoas abscess with a percutaneous drainage needle was positive for *Streptococcus pneumoniae*, as identified by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS) completed by an optochin disc and latex agglutination test for rapid detection of *S. pneumoniae*. Laboratory tests found no immunosuppression. Screening by a sickle-cell test and capillary electrophoresis revealed heterozygous sickle-cell disease, which was the primary cause of the microcytic anaemia.

He was treated with administration of oral rifampicin (1.2 g day⁻¹) and amoxicillin (12 g day⁻¹) for 14 days. Antimicrobial treatment was then continued by oral monotherapy with amoxicillin (12 g day⁻¹) for 5 months without any intolerance being observed. Surgical drainage of the psoas abscess and two-stage prosthesis exchange were performed on day 7 of antimicrobial treatment. A new prosthesis was inserted during the fourth month of treatment. No relapses were observed during the 4-year post-antibiotic follow-up.

Case 2

In April 2014, a 72-year-old man was admitted to the Emergency Department of the University Hospital in Marseille for fever. He had a medical history of multiple degenerative age-related arthrosis, which happened 10 years before the current episode. He did not have trauma or apparent immunodeficiency state. He had practiced aquatic gymnastics during the week before his admission. A clinical examination did not reveal any abnormalities. Laboratory investigations showed a high C-reactive



Fig. 1. Computed tomography scan of the bilateral psoas abscess of pneumococcal pyomyositis in case 1.

protein level (299 mg l⁻¹), an elevated leukocyte count (21 000 μl⁻¹, predominantly neutrophil granulocytes), a normal platelet count (187 000 μl⁻¹) and normal haemoglobin (13 g dl⁻¹). Blood cultures were positive for *S. pneumoniae*, as identified by MALDI-TOF MS completed by optochin disc and latex agglutination tests for rapid detection of *S. pneumoniae*. The pneumococcal urinary antigen test was positive.

He was treated with the oral antibiotic amoxicillin-clavulanate acid (3 g day⁻¹). He developed first crackles in his right lung base. Chest radiology did not reveal any abnormalities. On day 3 of treatment, he developed painful erythema of the left thigh and left groin pain, and a fever of 39 °C. Laboratory investigations showed the following changes: an elevated C-reactive protein level (206 mg l⁻¹), an elevated leukocyte count (13 000 μl⁻¹, predominantly neutrophil granulocytes) and a normal platelet count (150 000 μl⁻¹). Magnetic resonance imaging of the left hip revealed arthritis and an abscess of the left adductor brevis muscle (Fig. 2).

Surgical debridement of the adductor was performed using a direct internal approach. He was treated with a combination of intravenous amoxicillin and gentamicin for 3 days, and the treatment was then switched to intramuscular ceftriaxone (2 g day⁻¹) and oral rifampicin (900 mg day⁻¹) for 1 month. The patient was discharged at 4 weeks after surgical drainage and was prescribed the oral antibiotics amoxicillin (9 g day⁻¹) and rifampicin (900 mg day⁻¹) for 5 weeks without any intolerance being observed. We did not observe any relapse at the 6-month post-antibiotic follow-up. Echography at the 4-month post-antibiotic follow-up revealed a normal adductor brevis muscle.

Discussion and Conclusion

Here, we report two cases of pneumococcal pyomyositis managed in our centre. In PubMed/Medline, Web of Science and Google Scholar, we used the following keywords ('pneumococcal pyomyositis', '*Streptococcus pneumoniae*' and 'pyomyositis') with limits of the English and French language.

With the exception of paediatric cases, two hypocomplementaemia cases (Ekdahl *et al.*, 1995) and one case report of a 75-year-old woman that has been cited in previous studies (Collazos *et al.*, 1996), only 28 cases of pneumococcal pyomyositis have been reported in the literature (Table 1).

Of these 28 adult cases of pneumococcal pyomyositis that have been reported, four of the patients (14 %) were over 65 years of age and 16 (57 %) were immunodeficient, comprising three (11 %) patients with splenectomy, three (11 %) with HIV infection, seven (25 %) with chronic alcoholism, one with diabetes mellitus, one with Hodgkin's lymphoma recurrence (this case had also underwent a splenectomy), one with metastatic thyroid neoplasia and one

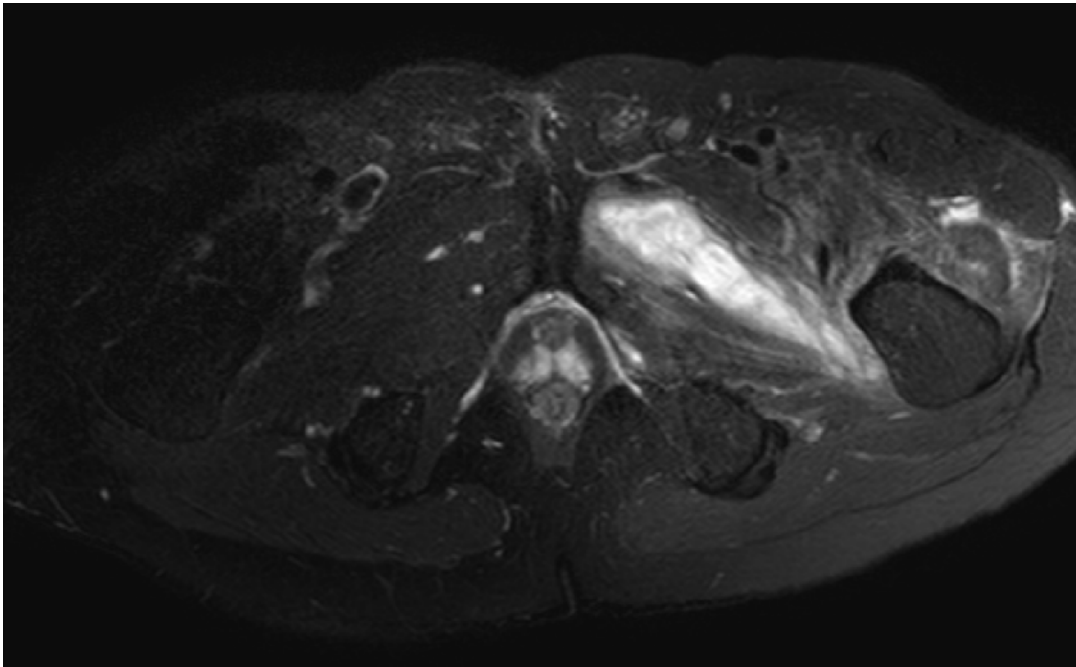


Fig. 2. Magnetic resonance imaging of the adductor muscle abscess of pneumococcal pyomyositis in case 2.

with inflammatory rheumatism. Nine cases reported in the literature did not identify any risk factors. With regard to our two cases, the first had heterozygous sickle-cell disease and the second had no apparent immunodeficiency. Both of our patients had arthrosis and one of our patients had a hip prosthesis, which has not been reported in the literature as a risk factor of pneumococcal pyomyositis. It should be considered as a risk factor for future observation.

Our two patients have not been vaccinated with pneumococcal vaccine. Zadroga *et al.* (2012) reported one case of pneumococcal pyomyositis in an immunocompromised patient who had previously received a *S. pneumoniae* vaccine. It would be interesting to study, in the perspective of infectious diseases, the effectiveness of pneumococcal vaccination in preventing this unusual disease.

Pneumococcal pyomyositis is frequently localized to the psoas muscle, as reported in 10 cases in the literature (36 %) (Baddour *et al.*, 2001; Bruggeling & Houwing, 1992; Collazos *et al.*, 1996; Jimenez-Lucho & Quinn, 1985; Levine *et al.*, 1982; Nakazato *et al.*, 1999; Oliver *et al.*, 2000; Orrison *et al.*, 1977; Scott & Schmidt, 1989; Simpson *et al.*, 2009) (Table 1). One of our cases had primary pyomyositis localized to the psoas muscle complicated with hip arthroplasty infection. In the other case, it was localized to the abductor muscle, which has not been reported previously.

Respiratory infection has been reported to be the main infection associated with pneumococcal pyomyositis, as

reported in six cases in the literature (Collazos *et al.*, 1996; Ejlertsen & Døssing, 1997; Granowitz *et al.*, 1992; Nakazato *et al.*, 1999; Oliver *et al.*, 2000; Peetermans *et al.*, 1993), followed by meningitis, which has been reported in five cases of pneumococcal pyomyositis (Levine *et al.*, 1982; Orrison *et al.*, 1977; Robertson-Mackay & al-Hillawi, 1993; Scott & Schmidt, 1989; Simpson *et al.*, 2009).

Of the 28 cases of pneumococcal pyomyositis, 56 % were documented by identification of *S. pneumoniae* in deep biopsy cultures. *S. pneumoniae* has rarely been isolated from blood cultures (only 4 of 18 cases) (Collazos *et al.*, 1996; Ejlertsen & Døssing, 1997; Levine *et al.*, 1982; Robertson-Mackay & al-Hillawi, 1993). One of our cases had a positive blood culture, and the other had a positive needle aspiration culture.

The two isolates of *S. pneumoniae* in our cases were identified by MALDI-TOF MS as described previously (Seng *et al.*, 2013), as well as an optochin test and a latex agglutination test. To the best of our knowledge, MALDI-TOF MS [i.e. Microflex with Biotyper (Bruker Daltonik) and the VITEK MS system (bioMérieux)] is an early and accurate tool to identify *S. pneumoniae* from other *Streptococcus mitis* groups (Branda *et al.*, 2013; Dubois *et al.*, 2013; Werno *et al.*, 2012).

In general, pneumococcal pyomyositis has a good outcome with antibiotic treatment (Table 1). Of the 28 cases of pneumococcal pyomyositis that have been reported, one died (Orrison *et al.*, 1977), 20 were cured following

Table 1. Review of 28 cases of pneumococcal pyomyositis in adult patients reported in the literature

Age	(years)	Treatment	Sex	First author	Risk factor(s) and co-morbidities	Site	Clinical association	Outcome
47	M	Alcoholism, splenectomy, Gaucher's disease		Iliopsoas abscess	Meningitis	Died	Antibiotics and surgical drainage	Orrison <i>et al.</i> (1977)
50	M	Alcoholism		Psoas abscess	Meningitis	Cured	Chloramphenicol, penicillin and surgical drainage	Levine <i>et al.</i> (1982)
40	M	Alcoholism		Psoas abscess	Trauma	Cured	Penicillin and surgical drainage	Jimenez-Lucho & Quinn (1985)
66	F	None		Psoas abscess	Meningitis	Cured	Penicillin and surgical drainage	Scott & Schmidt (1989)
69	F	None		Psoas abscess		Cured	Clindamycin and surgical drainage	Bruggeling & Houwing (1992)
44	M	None		Lower leg and pectoral abscess	Arthritis and pneumonia	Cured	Penicillin, ceftriaxone and surgical drainage	Granowitz <i>et al.</i> (1992)
54	F	Inflammatory rheumatism		Gluteus abscess	Pneumonia	Cured	Ampicillin and surgical drainage	Peetermans <i>et al.</i> (1993)
36	M	Splenectomy		Deltoid abscess	Meningitis	Cured	Penicillin and surgical drainage	Robertson-Mackay & al-Hillawi (1993)
Unknown	M	None		Unknown	Unknown	Unknown	Unknown	Gamboa <i>et al.</i> (1995)
72	F	None		Shoulder abscess	Respiratory tract infection	cured	Penicillin	Collazos <i>et al.</i> (1996)
39	M	None		Unknown	Unknown	Unknown	Unknown	Giladi <i>et al.</i> (1996)
53	M	None		Shoulder and bicep abscess	Arthritis, pneumonia	Cured	Penicillin and surgical drainage	Ejlertsen & Døssing (1997)
Unknown	M	Thyroid neoplasia		Unknown	Unknown	Unknown	Unknown	Fernández-Miera (1998)
47	F	Alcoholism		Psoas abscess	Respiratory tract infection, septic shock	Cured	Imipenem-ciclastin, penicillin and surgical drainage	Nakazato <i>et al.</i> (1999)
62	F	None		Psoas abscess	Cellulitis	Cured	Meropenem, cefuroxime and percutaneous drainage	Oliver <i>et al.</i> (2000)
64	M	None		Psoas abscess	Respiratory tract infection	Unknown	Metronidazole, tobramycin, cefotaxime and surgical drainage	Oliver <i>et al.</i> (2000)
Unknown	–	None		Iliopsoas and iliacus abscess	Sacroiliitis and osteomyelitis	Unknown	Unknown	Baddour <i>et al.</i> (2001)
Unknown	–	HIV		Unknown	Unknown	Unknown	Unknown	Chatterjee & Al-Hihi (2007)
32	F	HIV		Unknown	Unknown	Cured	Antibiotics and surgical drainage	Garcia-Lechuz <i>et al.</i> (2007)
44	M	None		Unknown	Unknown	Cured	Surgical drainage	Garcia-Lechuz <i>et al.</i> (2007)
68	M	Alcoholism		Unknown	Unknown	Cured	Antibiotics and surgical drainage	Garcia-Lechuz <i>et al.</i> (2007)
48	M	Alcoholism		Unknown	Unknown	Cured	Antibiotics and surgical drainage	Garcia-Lechuz <i>et al.</i> (2007)
59	M	Chronic obstructive pulmonary disease		Unknown	Unknown	Cured	Antibiotics and surgical drainage	Garcia-Lechuz <i>et al.</i> (2007)
40	F	HIV		Unknown	Unknown	Cured	Antibiotics and percutaneous drainage	Garcia-Lechuz <i>et al.</i> (2007)
37	M	None		Psoas abscess	Meningitis	Cured	Amoxicillin, ceftriaxone and metronidazole	Simpson <i>et al.</i> (2009)
55	M	Diabetes mellitus		Quadriceps and adductor abscess	Unknown	Unknown	Amoxicillin, gentamycin and surgical drainage	Guerrier <i>et al.</i> (2011)
47	M	Hodgkin's lymphoma and splenectomy		Shoulder abscess	Unknown	Cured	Cephalexin	Zadropa <i>et al.</i> (2012)
52	M	Alcoholism, hepatitis C virus infection		Knee abscess	Trauma	Cured	Ceftriaxone and moxifloxacin	Zadropa <i>et al.</i> (2012)

M, male; F, female.

treatment and the outcomes were unknown for seven. Surgical drainage was performed in 17 cases and needle aspiration in two (Table 1). Antibiotic treatment was given in 22/23 cases, and one case was treated with surgery only, without antibiotic treatment. β -Lactams were used in most cases. Multidisciplinary management is necessary for the successful treatment of pneumococcal pyomyositis. One patient in this case series required a second surgery with a large debridement because of septic shock and necrosis of the muscle (Guerrier *et al.*, 2011). Our two patients benefitted from surgical drainage and long-term antibiotic treatment, after which they were cured and did not experience recurrence, as determined several months later. None of the 28 reported cases in the literature showed a reduced sensitivity to penicillin. Similarly, the pneumococcal isolates from our patients showed no resistance to penicillin.

In summary, pneumococcal pyomyositis is a rare disease. We have reported two new cases of this disease with favourable outcomes following long-term antimicrobial treatment and surgery debridement.

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This study was approved by the institutional research ethics board, and a written informed consent form was signed by the patients. The authors declare they have no conflicts of interest.

References

- Baddour, V. T., Hugenberg, S. T., Brandt, K. D. & Yang, E. L. (2001). Pneumococcal pyomyositis: a patient with diagnostic problems and complications. *J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis* 7, 21–29.
- Bickels, J., Ben-Sira, L., Kessler, A. & Wientroub, S. (2002). Primary pyomyositis. *J Bone Joint Surg Am* 84-A, 2277–2286.
- Branda, J. A., Markham, R. P., Garner, C. D., Rychert, J. A. & Ferraro, M. J. (2013). Performance of the Vitek MS v2.0 system in distinguishing *Streptococcus pneumoniae* from nonpneumococcal species of the *Streptococcus mitis* group. *J Clin Microbiol* 51, 3079–3082.
- Bruggeling, W. & Houwing, A. (1992). [Primary pneumococcal abscess in the psoas muscle]. *Ned Tijdschr Geneesk* 136, 481–482, (in Dutch).
- Burdette, S. D., Watkins, R. R., Wong, K. K., Mathew, S. D., Martin, D. J. & Markert, R. J. (2012). *Staphylococcus aureus* pyomyositis compared with non-*Staphylococcus aureus* pyomyositis. *J Infect* 64, 507–512.
- Chatterjee, S. & Al-Hihi, M. (2007). Pneumococcal pyomyositis in a patient infected with human immunodeficiency virus. *Am J Med* 120, e5–e6.
- Collazos, J., Fernández, A., Martínez, E., Mayo, J. & de la Viuda, J. M. (1996). Pneumococcal pyomyositis: case report, review of the literature, and comparison with classic pyomyositis caused by other bacteria. *Arch Intern Med* 156, 1470–1474.
- Dubois, D., Segonds, C., Prere, M.-F., Marty, N. & Oswald, E. (2013). Identification of clinical *Streptococcus pneumoniae* isolates among other alpha and nonhemolytic streptococci by use of the Vitek MS matrix-assisted laser desorption ionization-time of flight mass spectrometry system. *J Clin Microbiol* 51, 1861–1867.
- Ejlertsen, T. & Døssing, K. (1997). Pneumococcal pyomyositis secondary to pneumonia. *Scand J Infect Dis* 29, 520–521.
- Ekdahl, K., Truedsson, L., Sjöholm, A. G. & Braconier, J. H. (1995). Complement analysis in adult patients with a history of bacteremic pneumococcal infections or recurrent pneumonia. *Scand J Infect Dis* 27, 111–117.
- Fernández-Miera, M. F. (1998). [Non-tropical pyomyositis: review of a case]. *An Med Interna Madr Spain* 15, 211–213 (in Spanish).
- Gamboa, F., Sánchez-Burson, J., Gómez-Mateos, J. & Marenco, J. L. (1995). Bacterial pyomyositis due to *Streptococcus pneumoniae* in a previously healthy man. *Scand J Rheumatol* 24, 396.
- García-Lechuz, J. M., Cuevas, O., Castellares, C., Pérez-Fernández, C., Cercenado, E., Bouza, E. & Network, S. P. S. (2007). *Streptococcus pneumoniae* skin and soft tissue infections: characterization of causative strains and clinical illness. *Eur J Clin Microbiol Infect Dis* 26, 247–253.
- Giladi, M., Sada, M. J., Spotkov, J. & Bayer, A. S. (1996). Pneumococcal psoas abscess: report of a case and review of the world literature. *Isr J Med Sci* 32, 771–774.
- Granowitz, E. V., Donaldson, W. R. & Skolnik, P. R. (1992). Gas-forming soft tissue abscess caused by *Streptococcus pneumoniae*. *Am J Med* 93, 105–107.
- Guerrier, G., Carrieres, P.-A., Resiere, D., Labrada-Blanco, O. & Crombé, C. (2011). [Unusual cause of primary pyomyositis in a diabetic patient: *Streptococcus pneumoniae*]. *Ann Fr Anesthésie Réanimation* 30, 761–762 (in French).
- Jimenez-Lucho, V. E. & Quinn, E. L. (1985). Pneumococcal psoas abscess. *Scand J Infect Dis* 17, 427–429.
- Levine, J. F., Hiesiger, E. M., Whelan, M. A., Pollock, A. A., Simbekoff, M. S. & Rahal, J. J. (1982). Pneumococcal meningitis associated with retroperitoneal abscess. A rare complication of lumbar puncture. *JAMA* 248, 2308–2309.
- Nakazato, T., Kitahara, M., Watanabe, K., Kikuchi, T., Imazu, Y. & Inoue, K. (1999). Pneumococcal psoas abscess. *Intern Med Tokyo Jpn* 38, 63–66.
- Oliver, A., Sabán, J., Pujol, I., Peromingo, R., Tarragó, D., Galindo, J. & Meseguer, M. A. (2000). Pneumococcal psoas abscess: report of two cases. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis* 6, 168–169.
- Orrison, W. W., Labadie, E. L. & Ramgopal, V. (1977). Fatal meningitis secondary to undetected bacterial psoas abscess. *J Neurosurg* 47, 755–760.
- Peetermans, W. E., Buyse, B. & Vanhoof, J. (1993). Pyogenic abscess of the gluteal muscle due to *Streptococcus pneumoniae*. *Clin Infect Dis Off Publ Infect Dis Soc Am* 17, 939.
- Robertson-Mackay, F. & al-Hillawi, A. H. (1993). Pyomyositis complicating pneumococcal meningitis. *Postgrad Med J* 69, 64–65.
- Scott, B. D. & Schmidt, J. H. (1989). Pneumococcal meningitis due to psoas abscess. *South Med J* 82, 1310–1311.
- Seng, P., Abat, C., Rolain, J. M., Colson, P., Lagier, J. C., Gouriet, F., Fournier, P. E., Drancourt, M., La Scola, B. & Raoult, D. (2013). Identification of rare pathogenic bacteria in a clinical microbiology laboratory: impact of matrix-assisted laser desorption

ionization-time of flight mass spectrometry. *J Clin Microbiol* **51**, 2182–2194.

Simpson, M. A., Keston, P., Bridges, A. & Macleod, M. (2009). Bacterial meningitis associated with a complex ischiorectal abscess. *J Clin Neurosci* **16**, 1682–1683.

Werno, A. M., Christner, M., Anderson, T. P. & Murdoch, D. R. (2012). Differentiation of *Streptococcus pneumoniae* from nonpneumococcal

streptococci of the *Streptococcus mitis* group by matrix-assisted laser desorption ionization-time of flight mass spectrometry. *J Clin Microbiol* **50**, 2863–2867.

Zadroga, R. J., Zylla, D., Cawcutt, K., Musher, D. M., Gupta, P., Kuskowski, M., Dincer, A. & Kaka, A. S. (2012). Pneumococcal pyomyositis: report of 2 cases and review of the literature. *Clin Infect Dis* **55**, e12–e17.