CASE REPORT

A complication of meningitis and infective endocarditis due to *Streptococcus pyogenes*

Kosuke Inoue,¹ Akiyoshi Hagiwara,² Akio Kimura,² Norio Ohmagari³

¹Endocrinology and Diabetes Center, Yokohama Rosai Hospital, Yokohama, Japan

²Department of Emergency Medicine and Critical Care, National Center for Global Health and Medicine, Tokyo, Japan

³Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan

Correspondence to

Dr Kosuke Inoue,
kosuke.inoue1989@gmail.com

Accepted 29 June 2017

SUMMARY

We described a rare case of meningitis and infective endocarditis (IE) due to *Streptococcus pyogenes*. An 80-year-old woman was admitted to our hospital with unconsciousness. Glasgow Coma Scale was E1V3M5. We diagnosed her with acute meningitis due to *S. pyogenes* and started treatment using ceftriaxone. In spite of the improvement of her unconscious state, she developed a new-onset systolic murmur on day 13, and echocardiography revealed severe mitral valve regurgitation with vegetation. Therefore, we also diagnosed her with IE and continued the antibiotics for 6 weeks after we confirmed the negative blood cultures. The patient was finally transferred to another hospital for rehabilitation 57 days after admission. Considering that the number of *S. pyogenes* infections has been reported to increase in Japan and worldwide, we need to be more careful about the rare complication of meningitis and IE due to *S. pyogenes*.

BACKGROUND

Streptococcus pyogenes is an important pathogen that causes severe infections such as bacteraemia, necrotising fasciitis and streptococcal toxic shock syndrome (STSS), as well as a variety of acute infections such as soft tissue infections and pharyngitis.¹ It can cause meningitis and infective endocarditis (IE), which are also life-threatening complications of *S. pyogenes* infections.^{2,3} Although these two complications are still uncommon, the number of *S. pyogenes* infections has been reported to increase in Japan and worldwide.^{1,4-6} Here, we describe a rare case of both meningitis and IE due to *S. pyogenes*. It is getting important to consider the complication of these two diseases from the clinical and epidemiological perspectives.

CASE PRESENTATION

An 80-year-old woman was admitted to our hospital unconscious. The last reported normal interaction with the patient was 2 days before admission when a neighbour had a routine conversation with her. On the day of admission, the neighbour found the patient lying on the floor of her house and called an emergency medical service. The patient had a medical history of hypertension. On admission, her body temperature was 39.2°C, blood pressure was 156/98 mm Hg and pulse rate was 128 bpm. Her Glasgow Coma Scale was E1V3M5 and peripheral oxygen saturation was 80% on room air. Physical examination showed bilateral miosis (1.5 mm

each), absence of light reflex in both pupils and bilateral wheeze in the end-tidal phase. She also demonstrated right incomplete hemiplegia and her National Institutes of Health Stroke Scale was 21. Her Babinski and Chaddock signs showed plantar responses. We did not detect any heart murmurs, conjunctival haemorrhage, Roth spots, splinter haemorrhage, Osler's nodes or Janeway lesions.

INVESTIGATIONS

Laboratory testing on the admission day showed: serum white blood cells, $25.52 \times 10^3/\mu\text{L}$ (neutrophils, 95.9%); C reactive protein, 34.03 mg/dL; procalcitonin, 15.62 ng/mL; aspartate aminotransferase, 90 IU/L; alanine aminotransferase, 29 IU/L; lactate dehydrogenase, 420 IU/L; creatine kinase (CK), 560 IU/L; CK-MB, 31 IU/L; blood urea nitrogen, 37.3 mg/dL; creatinine, 1.34 mg/dL and fibrin degradation product, 51.6 µg/dL. Her brain natriuretic peptide and troponin I were 5007 pg/mL and 19.19 ng/dL, respectively. Examination of cerebrospinal fluid (CSF) on the second day after admission showed: initial pressure, 22 cmH₂O; cell count, 616/µL; protein, 67 mg/dL and glucose, 79 mg/dL (serum glucose, 206 mg/dL). ECG showed a slight ST-segment elevation and negative T waves at II, III, aVf and V3-V6. Transthoracic echocardiography revealed systolic dysfunction of the apical segments of the left ventricle with an ejection fraction of 50%. No definite vegetation or valvular disease was detected in transoesophageal echocardiography. We did not detect any abnormalities in abdominal CT. MRI on day 5 after admission revealed numerous sporadic lesions with high intensity on diffusion-weighted and T2-weighted imaging and low intensity on an apparent diffusion coefficient map in the areas of the bilateral cerebral hemisphere, thalamus, basal nucleus, brainstem and cerebellar hemisphere (figure 1).

DIFFERENTIAL DIAGNOSIS

We assumed that her unconsciousness was caused by meningitis and multiple infarction in her brain. She had no episode of drinking alcohol, taking drugs and trauma. She did not have hypoglycaemia, uraemia, endocrinopathy and electrolyte disorders. The abnormalities in ECG and echocardiography implied that she had takotsubo cardiomyopathy. Although we could not deny the possibility of acute coronary syndrome (ACS), it was hard to perform a coronary angiography in her severe condition.

CrossMark

To cite: Inoue K, Hagiwara A, Kimura A, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220847

Figure 1 Magnetic resonance imaging (MRI) on day 5 after admission. There are numerous sporadic lesions with high intensity on diffusion-weighted imaging (3.0 T; TR 6000 ms, TE 86 ms) at the bilateral cerebral hemisphere, thalamus, basal nucleus, brainstem and cerebellar hemisphere. T, tesla; TE, echo time; TR, repetition time.

TREATMENT

We introduced ceftriaxone (2 g every 12 hours) and supportive mechanical ventilation on the admission day (figure 2). Gram staining of two sets of blood samples obtained on the admission day revealed streptococcus-like gram-positive cocci on day 2 after admission, and, considering the possibility of infection with penicillin-resistant *S. pneumoniae*, we added vancomycin (0.5 g every 12 hours). On day 5 after admission, cultures of them showed *S. pyogenes* growth. Therefore, we replaced treatment with ampicillin (2 g every 6 hour) and clindamycin (600 mg every 8 hours). Gram staining and culture of CSF, which could be obtained after the introduction of ceftriaxone, did not show microbiological evidence of *S. pyogenes*. On the day of admission, to treat the cardiac dysfunction and multiple infarction in her brain, we initiated heparin (10 000 U/day) in addition to furosemide (20 mg/day) because we thought that the benefit of anticoagulation for such diseases would overcome the risk of intracerebral haemorrhage. Her unconsciousness gradually improved and we removed mechanical ventilation on day 7 after admission. Spontaneous improvement of systolic dysfunction of the apical segments of the left ventricle and normalisation of ECG implied that she had takotsubo cardiomyopathy rather than ACS.

OUTCOME AND FOLLOW-UP

However, on day 13 after admission, she suddenly developed an apical systolic murmur. Transthoracic and transoesophageal echocardiography revealed new-onset moderate mitral valve regurgitation with vegetation (figure 3). Based on Duke's criteria,⁷ we diagnosed her with IE. Since the patient and her family declined surgical intervention, we continued the treatment with antibiotics for a total of 6 weeks after we confirmed the negative blood cultures. Her cardiac and neurological dysfunction gradually improved, and she was finally transferred to another hospital for rehabilitation on day 57 after admission (figure 2).

DISCUSSION

Based on a review of the literature, this is the first description of the complication of meningitis and IE due to *S. pyogenes*. The present case initially showed meningitis and multiple infarction in her brain, which could be explained as the complication of IE; the bacterial dissemination to the central nervous system and the shower embolism to the brain.⁷ Therefore, although we did not detect a portal of entry and a definite vegetation in her early clinical course, we assume that she had IE at first, and developed the cerebral complications which caused her unconsciousness. IE became obvious later through the destruction of mitral valve.

S. pyogenes is an uncommon cause of both meningitis and IE.¹ Indeed, meningitis due to *S. pyogenes* accounts for less than 1% of all bacterial meningitis cases,^{8,9} and it usually occurs after upper respiratory infection or neurosurgical conditions.^{2,10} Similarly, *S. pyogenes* accounts for only 5% of all causative microorganisms for IE.¹¹ Upper respiratory infection or soft tissue infection precede IE due to *S. pyogenes*.² A nationwide cohort study in the Netherlands suggested that they found 24 cases (2%) of IE in 1025 patients with all bacterial meningitis and only one case was due to *S. pyogenes* although the detail was not described.¹² From these epidemiological data, we assumed that IE was the primary cause of her clinical course in the present case, although we could not completely deny another hypothesis; IE might be secondary to bacterial meningitis.

Both meningitis and IE have severe outcomes. A review of 41 adult cases with meningitis due to *S. pyogenes* showed that the mortality rate was 27% and neurological sequelae were observed in 36% of the surviving patients.³ Moreover, a review of 15 cases of children with IE due to *S. pyogenes* showed that the mortality rate was 27% and that the embolic phenomenon was observed in 73% of the children, including 5 (33%) with cerebral embolism.¹³ Therefore, it is important to diagnose and treat them as soon as possible in spite of their rarity.

Figure 2 Clinical course. We introduced ceftriaxone (2 g every 12 hours) with a support of mechanical ventilation on the day of admission. Her unconsciousness and systolic dysfunction of the apical segments of the left ventricle gradually improved and mechanical ventilation was removed on day 7. On day 13, she suddenly had systolic murmur at the apex area, and echocardiography showed a new-onset severe mitral valve regurgitation with some vegetation. We continued the treatment with antibiotics for a total of 6 weeks after we observed negative results for bacterial growth on blood cultures. She was finally transferred to another hospital for rehabilitation on day 57 after admission.

Figure 3 Transthoracic echocardiography on day 20 after admission. The left image shows the new-onset severe mitral valve regurgitation. The right image shows the vegetation on the mitral valve (arrow).

The incidence of *S. pyogenes* bacteraemia has been increasing during the past decade, especially owing to the injection of illicit drugs and nosocomial outbreaks in nursing homes.^{1 4} In Japan, the reported number of STSS, a severe invasive infection mainly caused by *S. pyogenes* (about 70% of all pathogens of STSS), was 270 in 2014, although the number was around 100 in the early 2000s according to National Institute of Infectious Diseases.^{5 6} Moreover, Ikebe *et al* analysed the *emm* genotype of 249 *S. pyogenes* isolates from STSS patients and found that specific genotypes such as *mefA*-positive *emm1* isolates were related with the increase of STSS in Japan since 2011.¹⁴ Although we did not analyse the genotypes of *S. pyogenes* in the present case, this epidemiological trend implies that currently we need to treat more patients with a variety of infectious diseases due to *S. pyogenes*. In other words, as the present case described, we need to be more careful about the rare complication of meningitis and IE for patients with *S. pyogenes* bacteraemia.

Learning points

- It is important to consider the possibility of infective endocarditis (IE) for patients with *Streptococcus pyogenes* bacteraemia even when a definite vegetation is not detected by transoesophageal echocardiography.
- Both meningitis and IE due to *S. pyogenes* have severe outcomes, which should be diagnosed and treated as soon as possible.
- Considering the increasing number of *S. pyogenes* infection worldwide during the past decade, we need to be more careful about the rare complication of meningitis and IE due to *S. pyogenes*.

Acknowledgements We thank Kazuhisa Mezaki (National Center for Global Health and Medicine) for his helpful advice.

Contributors KI treated the patient and wrote this manuscript. AH and AK gave a helpful advice for the treatment of the patient. NO also contributed to the treatment and finally reviewed the manuscript.

Funding This work was supported in part by the Yokohama Rosai Hospital and National Center for Global Health and Medicine.

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 Bennett JE, Dolin R, Blaser MJ, *et al*. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. Netherlands: Elsevier Health Sciences, 2014.
- 2 Stevens DL, Bryant AE. In: Ferretti JJ, Stevens DL, Fischetti VA, eds. *Severe group A Streptococcal Infections, in Streptococcus pyogenes: basic Biology to Clinical Manifestations*. Oklahoma, USA: University of Oklahoma Health Sciences Center, 2016.
- 3 van de Beek D, de Gans J, Spanjaard L, *et al*. Group A streptococcal meningitis in adults: report of 41 cases and a review of the literature. *Clin Infect Dis* 2002;34:e32–e36.
- 4 Zakikhany K, Degail MA, Lamagni T, *et al*. Increase in invasive Streptococcus pyogenes and Streptococcus pneumoniae infections in England, December 2010 to January 2011. *Euro Surveill* 2011;16.
- 5 National Institute of Infectious Diseases. Infectious Agents Surveillance Report (IASR) Vol. 36. 2015 <http://www.nih.go.jp/niid/ja/group-a-streptococcus-m/group-a-streptococcus-iasrtpc/5843-tpc426-j.html> (accessed 28 Apr 2017).
- 6 Infectious Disease Surveillance Center. Infectious Diseases Weekly Report (IDWR) Vol. 12. 2012 <http://idsc.nih.go.jp/disease/invasiveA/idwr201212.html> (accessed 28 Apr 2017).
- 7 Nessler LA, Launey Y, Mallédant Y. Infective endocarditis. *N Engl J Med* 2013;369:784–5.
- 8 Meisal R, Andreasson IK, Høiby EA, *et al*. Streptococcus pyogenes isolates causing severe infections in Norway in 2006 to 2007: emm types, multilocus sequence types, and superantigen profiles. *J Clin Microbiol* 2010;48:842–51.
- 9 Santos MS, Ribeiro GS, Oliveira TQ, *et al*. Burden of group A streptococcal meningitis in Salvador, Brazil: report of 11 years of population-based surveillance. *Int J Infect Dis* 2009;13:456–61.
- 10 Sommer R, Rohner P, Garbino J, *et al*. Group A beta-hemolytic Streptococcus meningitis: clinical and microbiological features of nine cases. *Clin Infect Dis* 1999;29:929–31.
- 11 Selton-Suty C, Célard M, Le Moing V, *et al*. Prevalence of Staphylococcus aureus in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis* 2012;54:1230–9.
- 12 Lucas MJ, Brouwer MC, van der Ende A, *et al*. Endocarditis in adults with bacterial meningitis. *Circulation* 2013;127:2056–62.
- 13 Weidman DR, Al-Hashami H, Morris SK. Two cases and a review of Streptococcus pyogenes endocarditis in children. *BMC Pediatr* 2014;14:227.
- 14 Ikebe T, Tominaga K, Shima T, *et al*. Increased prevalence of group A Streptococcus isolates in streptococcal toxic shock syndrome cases in Japan from 2010 to 2012. *Epidemiol Infect* 2015;143:864–72.

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