Hong Kong College of Physicians
Case Report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign):
Hospital and Unit: Specialty:
Name of supervisor (print and sign):
Date(s) and place (hospital) of patient encounter: December 2019
Date of report submission: 10 March 2021

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: An elderly woman with fever and poor skin condition – a case of complicated MRSA bacteraemia

Case history:

An 88-year-old woman with a history of hypertension, diabetes mellitus, hyperlipidaemia, non-toxic retrosternal goitre, severe asteatotic eczema, fractured left neck of femur with previous unipolar hip arthroplasty, and right occipital meningioma was admitted for fever. She had had several admissions in the past month for unintentional weight loss and cognitive decline, with workup suggesting Alzheimer's disease. However, prior to the index admission, she had still been able to walk with a rollator indoors, though she required a wheelchair when going outdoors.

On admission, the patient was communicable but tired-looking. She presented with on-and-off fever for two days, just after her last discharge. Collateral history was obtained from the patient's domestic helper. There were no particular localizing symptoms except generalized malaise, as the patient was now too weak to stand up from bed or to ambulate.

Physical examination showed an elderly lady with a temperature of 38 degrees Celsius, blood pressure of 135/67 mmHg and heart rate of 94 beats per minute.

Passed at Council Meeting on 24 Oct 2019

Chest, cardiovascular and abdominal examinations were unremarkable but severe eczema was noted over all four limbs and the trunk. Blood tests showed leukocytosis with white blood cell count of 16.6 x 10^9/L, with neutrophil predominance. Liver and renal function tests were unremarkable. C-reactive protein was elevated to 18 mg/dL (reference: <0.76). The patient was empirically started on intravenous meropenem based on recent urine culture results after blood cultures were taken.

The fever did not respond to meropenem after 48 hours. Antibiotics were streamlined to intravenous ceftriaxone when the initial blood culture results returned to show Gram-positive cocci in clusters. Subsequent identity and susceptibility test confirmed culture positivity for methicillin-resistant *Staphylococcus aureus* (MRSA), and the patient was started on intravenous vancomycin after repeating blood cultures.

Repeat blood cultures still showed persistent growth of MRSA. A transthoracic echocardiogram did not show any evidence of infective endocarditis; the patient's family was reluctant to proceed to trans-oesophageal echocardiogram. In view of her previous hip prosthesis, ultrasound of the hip joint was arranged which did not show any evidence of effusion.

The source of the MRSA bacteraemia was presumed to be due to the poor skin condition with bacterial translocation. However, the patient showed slow clinical response despite *in vitro* sensitivity of the *Staphylococcus aureus* isolate to vancomycin. Gallium scan revealed intense uptake at C6/7 vertebrae with erosion of endplates and destroyed C6/7 disc space, suggestive of infective spondylo-disciitis. MRI of the cervical spine further confirmed findings compatible with infective spondylitis over C6-C7, with associated posterior subligamentous soft tissue thickening related to the inflammatory process, resulting in spinal stenosis. (Figure 1) Surgery was offered, but the family opted for medical therapy in view of the patient's frailty, accepting the risks of treatment failure and permanent disability. A spinal corset to immobilize the spine was prescribed by the prosthetics and orthotics team.

A peripherally inserted central catheter (PICC) was placed for prolonged administration of antibiotics as the patients showed evidence of complicated MRSA bacteraemia (i.e. presence of a hip prosthesis and evidence of metastatic infective foci). The patient completed a 6-week course of vancomycin with normalization of all inflammatory markers. Decontamination with mupirocin nasal ointment and a chlorhexidine body wash was also performed in view of nasal carriage of MRSA.

Passed at Council Meeting on 24 Oct 2019

The patient became severely deconditioned during her prolonged hospital stay and was discharged to an old age home upon completion of antibiotics. The family decided not to proceed with repeat systemic imaging due to her poor general condition. A repeat nasal swab confirmed eradication of MRSA colonization during her admission six months later for decreased general condition.

Discussion and literature review

MRSA is now endemic to most healthcare settings around the developed world, including the Asia-Pacific region, and chronic carriage in the nares and skin is common among patients.[1] Locally, there is an increasing prevalence of MRSA carriage among the elderly in Hong Kong, both in hospitals as well as in long-term care homes.[2] This case illustrates the management and complications of an invasive MRSA infection, a clinical condition that is increasingly common and associated with significant morbidity and mortality.

Infectious Diseases Society of America (IDSA) guidelines suggest that, due to the severe consequences of untreated MRSA infections, *Staphylococcus aureus* bacteraemia should never be dismissed as merely a contaminant. Repeat blood cultures should be obtained and a meticulous search performed to look for possible sources of infection and evidence of complicated infections.[3] In many patients, poor skin condition and infected drip sites are common sources of bacteraemia.[4] Once bacteraemia is established, *Staphylococcus aureus* may easily colonize and form biofilms in the heart and on prosthetic devices. For all patients with MRSA bacteraemia, therefore, echocardiogram is warranted to look for infective endocarditis.[3] Furthermore, haematogenous spread to metastatic sites around the body is a common complication of *Staphylococcus aureus* bacteraemia. Particular caution is thus needed in patients with prosthetic implants as infection of the prosthesis with *Staphylococcus aureus* can result in persistent bacteraemia and treatment failure. Systemic imaging, with a whole-body Gallium scan, or a PET-CT scan, is useful to look for foci of infection that may require drainage or other surgical interventions.[4]

A significant proportion of cases of pyogenic spondylo-disciitis are due to haematogenous spread. Compared to other pathogens, MRSA is particularly associated with risk of relapse and treatment failure despite antibiotic treatments, and is independently associated with risk of future disability.[5] In young and otherwise fit patients, therefore, early surgical treatment in combination with intravenous antibiotics

Passed at Council Meeting on 24 Oct 2019

is often warranted to eliminate the infective focus, restore functionality of the spine and alleviate pain and other symptoms.[6] The clinical decision is necessarily more difficult in the elderly, who are often not optimal candidates for major surgery under general anaesthesia due to their co-morbidities. In such patients, as in our case, conservative management with aggressive intravenous antibiotics as well as spinal immobilization should be provided, with close monitoring for spinal instability and neurological deterioration.[5]

Intravenous vancomycin remains the first-line treatment of choice for most cases of MRSA bacteraemia.[3] There is an increasing role for newer MRSA agents, such as intravenous daptomycin or ceftaroline, for the treatment of MRSA bacteraemia. These novel agents have a superior pharmacokinetic profile with excellent tissue penetration and high blood levels, as well as greater tolerability with a significantly lower risk of nephrotoxicity, and may be associated with better outcomes.[7] Worldwide, there is concern of increasing minimum inhibitory concentrations (MIC) due to *Staphylococcus aureus* to vancomycin, a phenomenon known as "MIC creep", with an increased risk of vancomycin failure, necessitating the utilization of newer, alternative antibiotic choices.[8]

Guidelines typically recommend at least four to six weeks of intravenous antibiotics for complicated MRSA bacteraemia, which includes patients with high risk for relapsing or metastatic infections. This includes patients with a prosthetic implant, such as a prosthetic heart valve or orthopaedic implant, as well as those with evidence of a metastatic focus of infection.[3] However, intravenous access often becomes a significant issue during prolonged treatment for MRSA bacteraemia, as such patients often have a background of poor skin condition. A PICC or central venous catheters can be inserted for antibiotic treatment, as in our patient. Small studies have suggested that an early switch from intravenous to oral treatments for MRSA, such as linezolid, trimethoprim-sulfamethoxazole or clindamycin, with or without adjuvant rifampicin, at two weeks may be non-inferior to continued parenteral antibiotics for patients with MRSA bacteraemia.[9] While such a treatment strategy can be considered for select patients, especially those with very difficult venous access, this should not be adopted as routine clinical practice due to the lack of well-conducted large-scale studies.

MRSA infections can relapse despite treatment with antibiotics. Sometimes, it is unclear whether these episodes are due to flare-up of an incompletely treated infection, or represent *de novo* infections, which may be due to persistent skin and

nasal colonization. Thus, decontamination should be considered in patients who are proven to have MRSA nasal carriage. Several trials have demonstrated the efficacy of decontamination with mupirocin nasal ointment and whole-body washing with chlorhexidine, though repeated courses of treatment are often needed.[10] This is also important from a public health perspective to prevent the spread of MRSA infections in the community and in long-term care facilities. This was clearly a relevant concern for our patient, who required discharge to an old age home due to her frailty.

This case illustrates the multitude of concerns salient to a case of MRSA bacteraemia. On the individual level, in-depth investigations and aggressive treatments are needed to prevent treatment failure, disability and other morbidities. On the public health perspective, MRSA is a multi-drug resistant organism (MDRO) that can cause both community and nosocomial outbreaks. The proper management of a patient with MRSA infection has important impact on patient outcomes as well as implications on infection control and healthcare costs.

Tables and figures (where applicable) (no more than two figures)

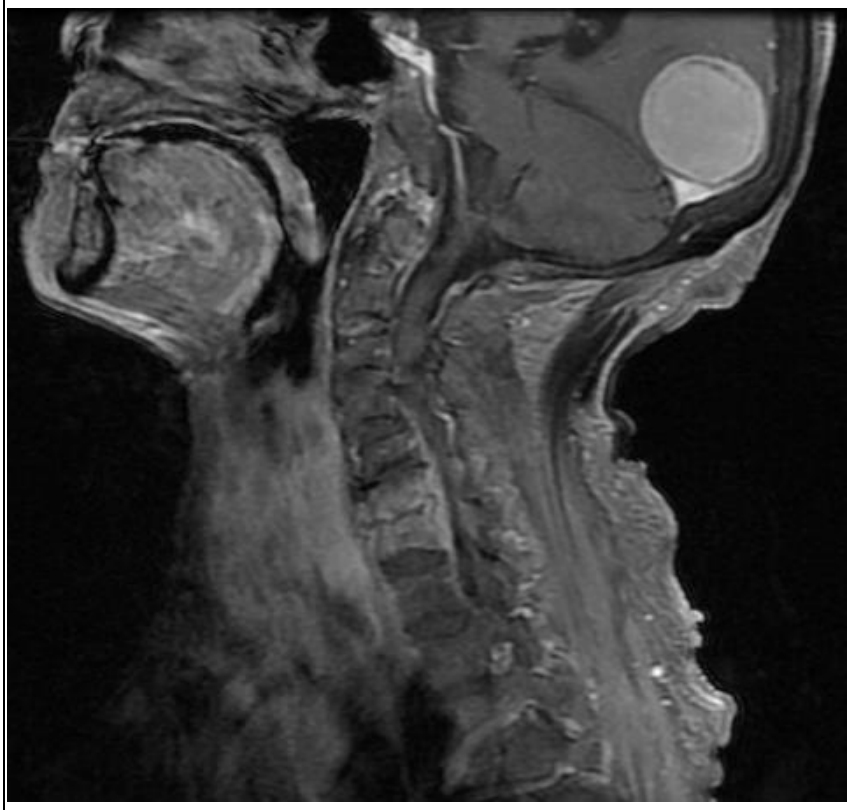

Figure 1. T1 sagittal image of cervical spine, post-contrast. Significant motion artefacts degraded the image quality but contrast enhancement can be seen at C6-7 with surrounding soft tissue swelling. The known occipital lobe meniongioma is included in the image.

Reference (not more than 10)

1. Chen, C.J., Huang, Y.C. New epidemiology of Staphylococcus aureus infection in Asia. *Clin Microbiol Infect*. 2014;20(7):605-23.
2. You, J.H.S., Choi, K.W., Wong, T.Y., Ip, M., Ming, W.K., Wong, R.Y., et al. Disease Burden, Characteristics, and Outcomes of Methicillin-Resistant Staphylococcus aureus Bloodstream Infection in Hong Kong. *Asia Pac J Public Health*. 2017;29(5):451-61.
3. Liu, C., Bayer, A., Cosgrove, S.E., Daum, R.S., Fridkin, S.K., Gorwitz, R.J., et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clin Infect Dis*. 2011;52(3):e18-55.
4. Bassetti, M., Trecarichi, E.M., Mesini, A., Spanu, T., Giacobbe, D.R., Rossi, M., et al. Risk factors and mortality of healthcare-associated and community-acquired Staphylococcus aureus bacteraemia. *Clin Microbiol Infect*. 2012;18(9):862-9.
5. Ascione, T., Balato, G., Di Donato, S.L., Pagliano, P., Granata, F., Colella, G., et al. Clinical and microbiological outcomes in haematogenous spondylodiscitis treated conservatively. *Eur Spine J*. 2017;26(Suppl 4):489-95.
6. Skaf, G.S., Domloj, N.T., Fehlings, M.G., Bouclaous, C.H., Sabbagh, A.S., Kanafani, Z.A., et al. Pyogenic spondylodiscitis: an overview. *J Infect Public Health*. 2010;3(1):5-16.
7. Geriak, M., Haddad, F., Rizvi, K., Rose, W., Kullar, R., LaPlante, K., et al. Clinical Data on Daptomycin plus Ceftaroline versus Standard of Care Monotherapy in the Treatment of Methicillin-Resistant Staphylococcus aureus Bacteremia. 2019;63(5).
8. Diaz, R., Ramalheira, E., Afreixo, V., Gago, B. Evaluation of vancomycin MIC creep in Staphylococcus aureus. *J Glob Antimicrob Resist*. 2017;10:281-4.
9. Jorgensen, S.C.J., Lagnf, A.M., Bhatia, S., Shamim, M.D., Rybak, M.J. Sequential intravenous-to-oral outpatient antibiotic therapy for MRSA bacteraemia: one step closer. *J Antimicrob Chemother*. 2019;74(2):489-98.
10. Sai, N., Laurent, C., Strale, H., Denis, O., Byl, B. Efficacy of the decolonization of methicillin-resistant Staphylococcus aureus carriers in clinical practice. *Antimicrob Resist Infect Control*. 2015;4:56.

No of words in Case History and Discussion (excluding references): 1453

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

_____

(signature of Trainee)

Endorsed by Supervisor *

_____

(signature of Supervisor)

* Supervisors must go over the Case Report with the Trainees, advise Trainees whether further amendments are necessary, review the Originality/ Similarity Report prepared by Trainees, adherence to the required format, sign on the report and remind Trainees on issues related to copyright and plagiarism.