

## CASE REPORT

## Systemic lupus erythematosus and melioidosis

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Accepted 17 June 2019

**SUMMARY**

We reported a case of a young female patient presented with sepsis and diagnosed with melioidosis and systemic lupus erythematosus (SLE) within the same admission. She presented with 1-week history of productive cough, progressive dyspnoea together with prolonged fever, arthralgia, rashes and oral ulcers. She had septicemic shock, respiratory failure requiring intubation and ventilation in intensive care unit and subsequently developed acute renal failure requiring haemodialysis. Antibiotics and immunosuppressive treatment including low-dose intravenous cyclophosphamide were commenced. She had a remarkable recovery and was discharged after 6 weeks. There was no evidence of active SLE or relapse of melioidosis during clinic follow-ups.

**BACKGROUND**

Melioidosis is a common cause of sepsis in endemic regions, especially so in immunosuppressed patients. Systemic lupus erythematosus (SLE) is an autoimmune disorder involving multiple organ inflammation, and patients are typically immunosuppressed either due to the treatment or the disease itself.

**CASE PRESENTATION**

A 26-year-old Malay female patient had presented to our hospital in April 2016 with a complaint of worsening dyspnoea 2 days prior to admission. She had prolonged fever and joints pain for 1 month. She developed productive cough, facial rashes and eye dryness 1 week prior to presentation. She was diagnosed as dengue fever at local clinic and discharged home with regular full blood counts monitoring. She did not have history of hair loss, Raynaud's phenomenon, change in mood or behaviour or seizures.

There were no previous medical illness or admissions. Further questioning revealed a history of bathing in a hot water spring 2 months earlier.

On admission, she was dehydrated and weak. There was a high-grade temperature recorded (39.4°C), and she was tachypnoeic (36 breaths/min). Oxygen saturation was 94% on nasal prong 3 L/min. There was visible malar rash over both cheeks sparing the nasolabial folds. Multiple oral ulcers were noted. Lung examination revealed coarse crackles over bilateral lower zone. An enlarged tender liver was palpable three finger breadths beneath the right costal margin. Other physical examinations were unremarkable.

**INVESTIGATIONS**

Blood investigations showed bicytopenia (normochromic normocytic anaemia, thrombocytopenia), raised transaminases (alanine aminotransferase 76 IU/L, aspartate aminotransferase 63 IU/L) with normal alkaline phosphatase and elevated urea and creatinine (27.6 mmol/L and 237 µmol/L, respectively). Antinuclear antibody and anti-dsDNA results were positive with titre of 1:320 and >400, respectively (table 1). Urine investigation showed significant proteinuria (3+). Twenty-four-hour urine protein was 0.7 g. Blood culture and sensitivity grew *Burkholderia pseudomallei* on day 3 of admission.

Chest radiograph showed heterogeneous opacities at both lung bases. Echocardiography revealed pericardial effusion (0.47 cm).

**DIFFERENTIAL DIAGNOSIS**

- ▶ Disseminated tuberculosis.
- ▶ Antineutrophil cytoplasmic antibodies vasculitis.
- ▶ Goodpasture syndrome.
- ▶ Severe sepsis with acute renal failure.

**TREATMENT**

Our patient was treated for pneumonia due to melioidosis, SLE with mucocutaneous, serosal and haematological involvement and acute renal failure secondary to rapidly progressive glomerulonephritis. She was given intravenous imipenem for 2 weeks then de-escalated to intravenous ceftazidime for another 4 weeks for induction phase. High-dose intravenous methylprednisolone was given for 3 days and changed to oral prednisolone. Intravenous cyclophosphamide (Euro-Lupus regime) was given for one cycle during admission. She was intubated for severe respiratory failure and required transient haemodialysis support.

**OUTCOME AND FOLLOW-UP**

After almost 6 weeks, the patient had a significant recovery. She was discharged with oral amoxicillin/clavulanic acid for eradication phase, prednisolone and hydroxychloroquine 200 mg daily. She had completed a total of six cycles of intravenous cyclophosphamide. Clinical and laboratory investigations confirmed no recurrence of active melioidosis infection during follow-up. There was also no clinical and laboratory evidence of relapse of SLE since discharge. Her SLE is well controlled with low-dose oral prednisolone 5 mg/day and oral mycophenolate



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**To cite:**

Che Rahim MJ, Mohammad N, Kamaruddin MI, et al. *BMJ Case Rep* 2019;12:e229974. doi:10.1136/bcr-2019-229974

**Table 1** Serial investigations results

| Investigations                  | April 2016 | May 2016 | June 2016 | May 2017 | August 2017 |
|---------------------------------|------------|----------|-----------|----------|-------------|
| Urea (mmol/L)<br>n=1.7–8.3      | 27.6       | 10.2     | 9.1       | 5.1      | 5.1         |
| Creatinine (µmol/L)<br>n=70–130 | 237        | 88       | 9.4       | 67       | 75          |
| Urine protein (g/24 hours)      | 0.7        |          |           |          |             |
| ESR (mm/hour)<br>n=1–20         | 78         | 25       | 30        | 15       | 13          |
| CRP (mg/L)<br>N <10             | >200       | Negative | Negative  | Negative |             |
| Anti-dsDNA (IU/mL)              | >400 IU    |          |           |          | 67.8        |
| C3 (g/L)<br>n=0.6–1.3           | 0.26       | 0.37     | 0.85      | 1.26     |             |
| C4 (g/L)<br>n=0.2–0.6           | 0.07       | 0.06     | 0.19      | 0.29     |             |

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

mophetil 500 mg two times a day. The patient, however, refused for renal biopsy after counselling.

**DISCUSSION**

Melioidosis is caused by *B. pseudomallei*, a gram-negative bacillus. It is endemic in Southeast Asia (Malaysia, Thailand, Cambodia, Myanmar, Laos and Vietnam) and North Australia with some reports of cases in Central America, Caribbean, China, Taiwan, the Middle East and South Asian countries. Common mode of transmission includes inhalation of contaminated dusts or entry into blood stream via wounds or skin abrasions. Clinical presentation may vary from acute presentation with rapid progression of the sepsis leading to death to a chronic, relapsing course. Pneumonia is the most common clinical presentation. Others include septicaemia, musculoskeletal involvement or organic abscess. Fever of unknown origin may be one of presentation prior to the diagnosis of melioidosis.<sup>1,2</sup>

Blood agar or Ashdown’s medium cultures are definitive if the organisms are isolated. Serological investigation includes indirect fluorescence antibody titre for IgM antibody. Treatment comprises two phases: intensive/induction phase and eradication phase. Duration of intensive phase is at least 2 weeks with the duration extended to 4 to 6 weeks in deep infection. The choice of antibiotics includes intravenous carbapenems and ceftazidime with the latter used in non-life threatening melioidosis. Bactrim with folic acid are adjunct antibiotic in those with severe infection and deep focal infections (neurological, prostate, bone and joint involvement). Eradication phase lasts up to 5 months, with antibiotic options including oral Bactrim plus oral doxycycline or oral amoxicillin/clavulanic acid in those intolerant to the former combination and in pregnancy.<sup>1,2</sup>

SLE is an autoimmune disorder characterised by multiple organ inflammation which has predilection towards young patients. It is associated with significant morbidity and mortality. Diagnosis is based on clinical and laboratory parameters with patients fulfilling four or more criteria (at least one clinical and one laboratory criteria) in accordance to the latest recommendation published by Systemic Lupus International Collaborating Clinic (SLICC) committee in 2012.<sup>3</sup> Treatment includes corticosteroids, hydroxychloroquine, azathioprine and mycophenolate mofetil. Treatment with intravenous cyclophosphamide is recommended in patients with lupus nephritis

class III and IV, rapidly progressive glomerulonephritis and class V disease which failed to respond with mycophenolate mofetil.<sup>4</sup>

Infection is the major cause of morbidity and mortality in patients with SLE, particularly in developing countries with pneumonia as a major cause. Factors that contribute to infection in patients with SLE include the degree of disease severity, abnormalities in humoral and cellular immune response and the use of immunosuppressive drugs and glucocorticoids as treatment regimes.<sup>5</sup>

Our case report reflected a complicated management of severe melioidosis infection with concomitant active SLE with suspected renal involvement. Multiple immunosuppressive agents used for the treatment of acute SLE put the patient at risk of worsening sepsis. Thus, the induction phase of antibiotic treatment was extended due to the above concern. Fortunately, she recovered from the infection, and SLE remission was achieved. Possible factor that might have contributed to her recovery was the decision to use the low-dose, Euro-Lupus intravenous cyclophosphamide regime than the higher dose, National Institutes of Health (NIH) monthly regime.

Studies have shown that the Euro-Lupus regime is as efficacious as the NIH regime with less frequency of serious infections in certain white European subpopulation.<sup>6,7</sup> However, there are no studies as of now to support the use of this regime in severe sepsis. This should prompt further studies to ascertain the safest, most efficacious immunosuppressive therapy in lupus nephritis patients with severe sepsis.

Our case report is also the first to report a successfully treated patients with SLE and severe kidney injury with concomitant severe melioidosis infection. A previous prevalence study in Malaysia reported a case of melioidosis bacteraemia in a 16-years-old patient with lupus nephritis. She presented with fever and seizure and was treated with imipenem. Unfortunately, the patient succumbed.<sup>8</sup>

The limitation of this case report was the absence of renal biopsy to confirm lupus nephritis. However, it should not cast any doubt that this patient had SLE with lupus nephritis as evidenced by clinical and laboratory criteria which satisfied the SLICC diagnostic criteria and subsequent improvement of symptoms and renal function after being given immunosuppressive drugs.

**Learning points**

- ▶ Severe melioidosis in a newly diagnosed systemic lupus erythematosus (SLE) is an uncommon presentation.
- ▶ Concomitant sepsis in acute SLE flares posed a challenge in the management.
- ▶ Immunosuppression in patients with acute SLE needs to be balanced with the risk of infection.
- ▶ Close monitoring of infection relapse is needed whenever immunosuppressive agents are given.
- ▶ Further studies are needed in determining the best immunosuppressive therapy for rapidly progressive glomerulonephritis in sepsis.

**Contributors** MJCR drafted the manuscript. NM, MIK and WSWG edited the manuscript. WSWG approved the final manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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