CASE REPORT

INTRACEREBRAL COINFECTION WITH *BURKHOLDERIA PSEUDOMALLEI* AND *CRYPTOCOCCUS NEOFORMANS* IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Irenawati Samad, Margaret Choon Lee Wang and Vui Heng Chong

Department of Medicine, Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, Bandar Seri Begawan, Brunei Darussalam

Abstract. Infections are a serious complication in patients with systemic lupus erythematosus (SLE), and are an important cause of morbidity and mortality. SLE patients are particularly susceptible to infection due to immune suppression from underlying disease or treatment. Most infections are due to common bacterial organisms. Clinicians also need to be aware of the possibility of polymicrobial infections as these may cause diagnostic delay and affect outcomes. We report the case of an intra-cerebral coinfection with *Burkholderia pseudomallei* and *Cryptococcus neoformans* in a 34-year-old woman with SLE. The diagnosis in this case was delayed since coinfection was not suspected.

Keywords: *Burkholderia pseudomallei*, fungal infection, intra-cerebral abscess, melioidosis, meningitis

INTRODUCTION

Infections are a serious cause of morbidity and mortility in patients with systemic lupus erythematosus (SLE) (Hellman *et al*, 1987). Approximately 50% of patients with SLE will have at least one infection (Hellman *et al*, 1987). Infections may be related to immunologic defects caused by the disease or therapy used to manage SLE (Hellman *et al*, 1987). Most infections in SLE patients are caused by common bacterial organisms; fungal infections are generally less common (Hellman *et al*, 1987). Melioidosis endemic in the tropics, is rarely seen in SLE patients (Badsha *et al*, 2001). Clinicians need to consider the possibility of polymicrobial infections in these patients to avoid diagnostic delays and untoward outcomes. We report a rare case of intra-cerebral coinfection with *Burkholderia pseudomallei* and *Cryptococcus neoformans* in a 34-year-old woman with SLE.

Correspondence: Vui Heng Chong, Department of Medicine, RIPAS Hospital, Bandar Seri Begawan BA 1710, Brunei Darussalam.
E-mail: chongvuih@yahoo.co.uk

CASE REPORT

A 34-year-old woman was diagnosed nine months previously with SLE and class IV nephritis based on the American College of Rheumatology Criteria. She was 16 weeks pregnant at the time of diagnosis and the pregnancy was terminated. She was started on prednisolone therapy 40mg daily and slowly tapered down to a

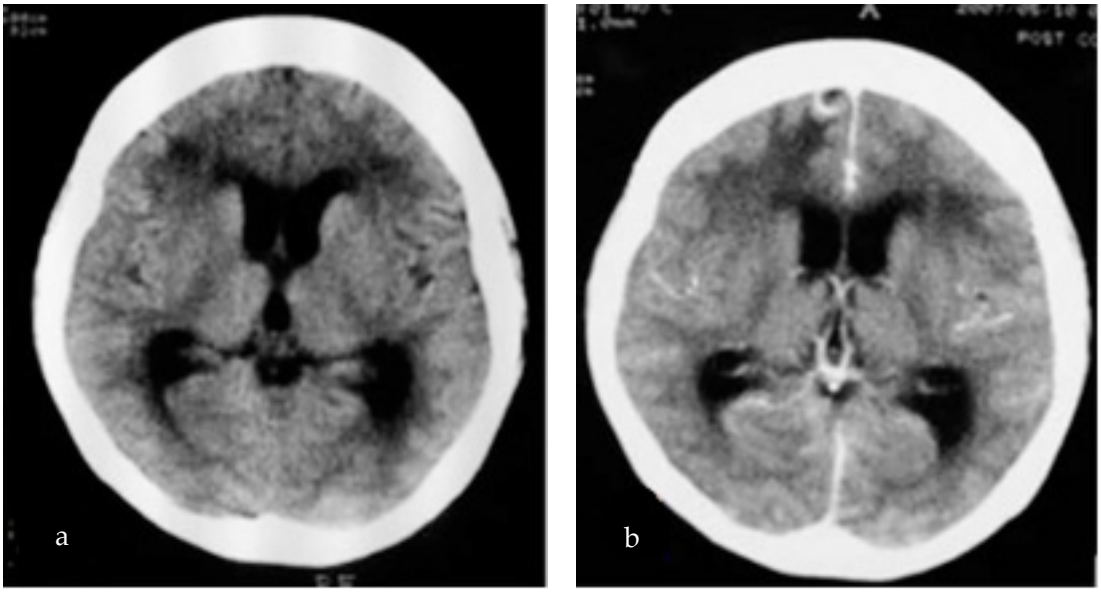

Fig 1–a) Axial computed tomography scan showing hydrocephalus; b) scan showing dilated ventricles and a ring enhancing right frontal lesion.

maintenance dose of 15 mg per day.

Three months after the diagnosis of SLE the patient was admitted to the hospital with septicemia secondary to *B. pseudomallei* infection. This was treated with four weeks of intravenous ceftazidime 2 g TID and amoxicillin-clavulanic acid 1.2 g TID, followed by oral doxycycline 100 mg bid and amoxicillin-clavulanic acid 625 mg bid for a planned duration of six months. At that point, she was on prednisolone 15 mg daily and her SLE was stable with normal C3 and C4 levels.

She represented three months later in septic shock with respiratory distress requiring intubation and ventilator support. At that time she was then on prednisolone 7.5 mg daily. On admission she had an elevated erythrocyte sedimentation rate of 30 mm/hr and her C3 and C4 levels were normal. Urine analysis was negative for white and red blood cells and casts; but was positive for 1+protein. She had a single generalized seizure and an urgent non-contrast computed tomography (CT) scan of the brain revealed mild hydrocephalus (Fig 1a). Both blood and cerebrospinal fluid (CSF) cultures grew out *B. pseudomallei* with a sensitivity pattern similar to when the organism was first isolated six months previously. CSF analysis was negative for *Cryptococcus neoformans*. She was retreated with four weeks of intravenous ceftazidime 2 g TID and amoxicillin-clavulanic acid 1.2 g TID, followed by doxycycline 100 mg bid and amoxicillin-clavulanic acid 625 mg bid. Further inquiry revealed that she had missed her medications on several occasions. Her condition improved and she was discharged on treatment, including anti-epileptic medication.

She continued to complain of mild intermittent headache when she was seen two weeks later. At that time her serum C3 and C4 levels were normal. A repeat

Table 1
Summary of the reported cases of SLE and melioidosis.

Authors (Year)	Age/Gender	Comorbid/Risks	Immunosuppression	Diagnosis	Treatment		Outcomes
					Intensive	Eradication	
Christenson-Bravo *et al* (1986)	62/F	SLE Diabetes mellitus Cirrhosis	Prednisolone	Meningitis	Penicillin Chloramphenicol Amikacin Moxalactam	None	Died
Badsha *et al* (2001)	29/F	SLE	Prednisolone	Fever	Ceftazidime	Co-trimoxazole/ Doxycycline	Alive
	20/F	SLE	Prednisolone	Fever	Ceftazidime	Co-trimoxazole/ Doxycycline	Alive
	43/F	SLE/ Hypertension Acute renal failure Peritoneal dialysis (temporary)	Prednisolone	Fever Peritonitis	Ceftazidime	Doxycycline/ [a]Amoxicillin- Clavulanic acid	Alive
Vachvanichsanong *et al* (2002)	14/F	SLE	Prednisolone	Brain abscess	[b]Co-trimoxazole	Co-trimoxazole	Alive
Present case (2012)	34/F	SLE	Prednisolone	Meningitis Cryptococcus abscess	Ceftazidime/ Amoxicillin- Clavulanic acid	Amoxicillin- Clavulanic/ Doxycycline	Alive

[a]Trimethoprim-sulfamethoxazole allergy; [b]ceftazidime allergy.

CT scan done four weeks after discharge showed a frontal lobe ring enhancing lesion (Fig 1b). After detailed discussion, the patient agreed to a craniotomy where a right frontal abscess was drained. The CSF culture again isolated *B. pseudomallei* and histology revealed chronic inflammatory changes and *Cryptococcus neoformans* spores. She was treated with 14 days of amphotericin B at 1 mg/kg daily followed by oral fluconazole 200 mg daily for eight weeks. She was given another course of anti-melioidosis therapy for four weeks followed by oral maintenance therapy for a further six months. She was encouraged to be compliant with her medication. She completed her anti-melioidosis therapy and has been well without any seizures or relapse of either the melioidosis or cryptococcal infections.

DISCUSSION

Melioidosis, caused by a gram-negative bacillus (*B. pseudomallei*) is associated with significant mortality, particularly the septicemic form (Currie and Antsey, 2011). Melioidosis is endemic to Southeast Asia and Northern Australia (Suputtamongkol *et al*, 1994; Currie and Anstey, 2011). It has also been reported in non-tropical countries as an imported case. Contact with soil or contaminated water through activities such farming, gardening and swimming with open wounds is a known risk factor (Currie and Anstey, 2011). Patients with chronic underlying diseases such as diabetes mellitus, are particularly at risk (Currie and Antsey, 2011). Use of immune suppressing therapy is also a risk factor (Currie and Antsey, 2011).

The recommended treatment for melioidosis consists of either carbapenam monotherapy or a combination of ceftazidime and amoxicillin-clavulanic acid therapy for at least two weeks during the intensive phase (Currie and Anstey, 2011). This is followed by continuing treatment with trimethoprim-sulfamethoxazole monotherapy or a combination of doxycycline and amoxicillin-clavulanic acid or ciprofloxacin for an additional 12 to 20 weeks during the eradication phase. Relapse during or after apparently successful treatment was reported to occur in 13-23% of patients at a median of 6-8 months after stopping treatment (So *et al*, 1983; Chaowagul *et al*, 1993; Suputtamongkol *et al*, 1994). In our patient, the reason for the relapse was most likely noncompliance with therapy.

Melioidosis is rarely reported in patients with SLE (Christenson-Bravo *et al*, 1986; Badsha *et al*, 2001; Vachvanichsanong *et al*, 2002). A literature search only revealed three reports of melioidosis in patients with SLE (Table 1). Not all the patients had active SLE disease when they were diagnosed with melioidosis. In our case, the use of prednisolone therapy was probably a major risk factor for melioidosis/cryptococcus coinfections. With the exception of the case reported by Christenson-Bravo *et al* (1986), all the other patients with SLE and melioidosis reported in the literature, including ours, survived. In the case reported by Christenson-Bravo *et al* (1986), the patient was treated with a non-standard regime when ceftazidime based therapy was not yet a standard treatment.

Unlike melioidosis, fungal infections are more common in patients with SLE (Chen *et al*, 2007; Tristano, 2010). Among invasive fungal infections, cryptococcus and aspergillus infections are the two most common fungal infections in SLE patients (Chen *et al*, 2007; Tristano, 2010). A recent literature review revealed 57 cases of cryptococcal meningitis in SLE

patients (Tristano, 2010). To our knowledge, intra-cerebral coinfections with *B. pseudomallei* and *Cryptococcus neoformans* in an SLE patient has not been previously reported. In our case a dual infection was not suspected until after surgery. Whether the underlying melioidosis had predisposed to the cryptococcus infection or the cryptococcus infection contributed to the melioidosis treatment failure is unknown. It is likely the infections were related to the use of prednisolone since the SLE was not active.

In conclusion, our case highlights the importance to considering a polymicrobial infection in a SLE patient whose condition does not improve despite appropriate treatment.

REFERENCES

Badsha H, Edwards CJ, Chng HH. Melioidosis in systemic lupus erythematosus: the importance of early diagnosis and treatment in patients from endemic areas. *Lupus* 2001; 10: 821-3.

Chaowagul W, Suputtamongkol Y, Dance DA, Rajchanuvong A, Pattara-Arechachai J, White NJ. Relapse in melioidosis: incidence and risk factors. *J Infect Dis* 1993; 168: 1181-5.

Chen HS, Tsai WP, Leu HS, Ho HH, Liou LB. Invasive fungal infection in systemic lupus erythematosus: an analysis of 15 cases and a literature review. *Rheumatology* (Oxford). 2007; 46: 539-44.

Christenson-Bravo B, Rodríguez JE, Vázquez G, Ramírez Ronda CH. *Pseudomonas pseudomallei* (melioidosis): acute septicemia and meningitis in patient with systemic lupus erythematosus. *Bol Asoc Med PR* 1986; 78: 347-9.

Currie B, Anstey N. Treatment and prognosis of melioidosis. [Online]. UpToDate 19.3. September 2011. [Cited 2012 Apr 15]. Available from: URL: http://www.uptodate.com/contents/treatment-and-prognosis-of-melioidosis

Hellman DB, Petri M, Whiting-O'Keefe Q. Fatal infections in systemic lupus erythematosus: The role of opportunistic organisms. *Medicine* 1987; 66: 341-8.

So SY, Chau PY, Leung YK, Lam WK, Yu DY. Successful treatment of melioidosis caused by a multiresistant strain in an immunocompromised host with third generation cephalosporins. *Am Rev Respir Dis* 1983. 127: 650-4.

Suputtamongkol Y, Hall AJ, Dance DA, *et al*. The epidemiology of melioidosis in Ubon Ratchatani, northeast Thailand. *Int J Epidemiol* 1994; 23: 1082-90.

Tristano AG. Cryptococcal meningitis and systemic lupus erythematosus: a case report and review. *Rev Chilena Infectol* 2010; 27: 155-9.

Vachvanichsanong P, Dissaneewate P, Prukprasert P, *et al*. Melioidosis and brain abscess in a girl with systemic lupus erythematosus. *Infect Dis Clin Prac* 2002; 11: 211-3.