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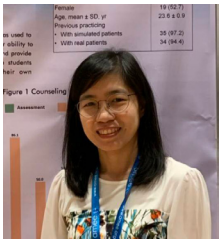
Case Report/รายงานผู้ป่วย

Orbital Cellulitis and Cavernous Sinus Thrombosis from Melioidosis: Case Report

รายงานผู้ป่วยที่มีการติดเชื้อรอบเบ้าตาและการอุดตันโพรงหลอดเลือดดำสมองจากโรคเมลิออยด์



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Abstract

A 34-year-old female patient with newly diagnosed diabetes mellitus type 2 presented with a three -day history of high grade fever, severe headache and erythematous plaque along forehead. Ocular involvement included painful proptosis of the right eye and restriction of ocular motility. The patient was administered with intravenous cetriaxone, clindamycin and oral acyclovir for two days but clinical outcome was then worsening. Hemoculture subsequently reported *Burkholderia pseudomallei*. Therefore, Ceftazidime was administered instead. MRI of the brain showed thrombophlebitis of bilateral superior ophthalmic vein, cavernous sinus thrombosis and small epidural abscess in right frontal region. Surgical pus drainage from skin abscess in forehead area was done and oral trimethoprim/sulfamethoxazole was used as a combined treatment. Venous sinus thrombosis was initially treated with subcutaneous enoxaparin and then maintained with warfarin. The clinical outcome was satisfactory with final visual acuity of 20/20 and completely healed forehead scar.

Keywords: orbital cellulitis, cavernous sinus thrombosis, melioidosis

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บทคัดย่อ

รายงานผู้ป่วยที่มีการติดเชื้อรอบเบ้าตาและการอุดตันโพรงหลอดเลือดดำสมองจากโรคเมลิออยด์

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แผนกจักษุวิทยา ศูนย์แพทย์ศาสตร์ศึกษาชั้นคลินิก โรงพยาบาลสุรินทร์ 68 ถนนหลักเมือง ตำบลในเมือง อำเภอเมือง จังหวัดสุรินทร์ 32000

ผู้ป่วยหญิงอายุ 34 ปี มาด้วยอาการไข้สูง ปวดศีรษะ มีตุ่มแดงบริเวณหน้าผาก มา 3 วัน ปวดเบ้าตาขวา ตาขวาโปน กลอกตาได้จำกัด ผู้ป่วยได้รับตรวจพบวินิจฉัยเป็นเบาหวานชนิดที่ 2 เป็นครั้งแรก ได้รับการรักษาด้วยยาปฏิชีวนะทางหลอดเลือด cetriaxone clindamycin และยา acyclovir ชนิดรับประทานได้ 2 วัน แต่อาการทางคลินิกไม่ดีขึ้น ผลเพาะเชื้อทางเลือดพบเชื้อ *Burkholderia pseudomallei* จึงได้เปลี่ยนยาปฏิชีวนะเป็น ceftazidime ผลตรวจเอกซเรย์สมองด้วยคลื่นแม่เหล็กไฟฟ้าภายหลังพบการอุดตันของเส้นเลือดดำ superior ophthalmic vein 2 ข้าง การอุดตันโพรงเส้นเลือดดำในสมอง และฝีขนาดเล็กที่สมองชั้นนอก จึงได้ผ่าตัดระบายหนองจากผิวหนังบริเวณหน้าผาก ร่วมกับการเพิ่มยารับประทาน Trimethoprim/sulfamethoxazole การรักษาการอุดตันของหลอดเลือดดำทำโดยการฉีดยาใต้ผิวหนัง enoxaparin ในช่วงแรกและการให้ warfarin การรักษาให้ผลน่าพอใจ ผู้ป่วยมีระดับการมองเห็น 20/20 และมีแผลเป็นบริเวณหน้าผาก

คำสำคัญ: การติดเชื้อรอบเบ้าตา, การอุดตันโพรงหลอดเลือดดำสมอง, เมลิออยด์

Introduction

Melioidosis is caused by *Burkholderia pseudomallei (B. pseudomallei)*. It is common in Southeast Asia especially in northeast Thailand and northern of Australia. Melioidosis manifestation varies from asymptomatic, localized infection, multiple organ abscess, bacteremia, disseminated septicemia to septic shock. Risk factors are diabetes mellitus, thalassemia, chronic kidney disease, and soil exposure. In Thailand, the incidence rate of melioidosis in 2018 was 4.28 /100,000 population and it increased in northeast Thailand (10.41 /100,000).[1] In previous report, prevalence of ocular melioidosis was from 0.49 to 1.02% of total.[2] Neurological and ocular involvements are rare but the mortality is high up to 40%. The author reported patient with orbital cellulitis and cavernous sinus thrombosis due to melioidosis. This study was approved by the Research Ethics Committee of Surin Hospital with the reference number of 41/2564.

Case Presentation

A 34-year-old female government officer presented with history of 14 days of swelling forehead and intermittent fever. She went to a medical clinic. The diagnosis was upper respiratory tract infection and she was treated with amoxicillin clavulanate and naproxen. Three days after, she had high grade fever, severe headache, erythema edematous papule and plaque on right side of forehead, glabella and eyelid. She was admitted at a private hospital with a diagnosis of cellulitis and herpes zoster ophthalmicus. Intravenous cetriaxone, clindamycin and oral acyclovir were administered for two days but the clinical outcome was worsening. She was then referred to our hospital.

Upon presentation at the hospital, the patient was in distress condition. The vital signs were as

following: body temperature was 38.6 °C, pulse rate was100 /minute, respiratory rate was 26/minute and blood pressure was 116/79 mmHg. Her visual acuity was 20/20 in both eyes, intraocular pressure was 38 mmHg in the right eye and 18 mmHg in the left eye. Right eye showed swelling eyelid, proptosis and limited abduction. There was no relative afferent pupillary defect, no cell in anterior chamber and vitreous. Unilateral dermatomal vesicular cutaneous eruption on trigeminal branch was shown in Figure 1. Other neurological examination was unremarkable.

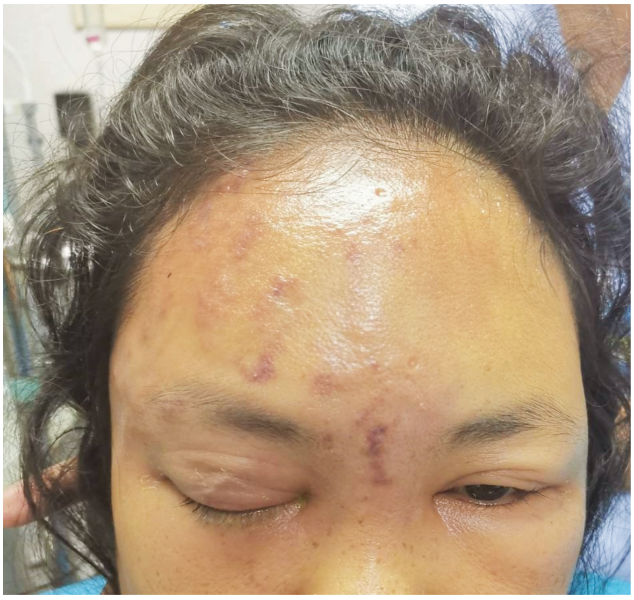

Figure 1 Clinical photograph admission day 1.

The complete blood count demonstrated: 7,200 WBCs/mm^3 (93.9% neutrophils), 37% Hct, 202,000 platelets/mm^3. The fasting blood sugar was 290 mg/dl and HbA1C was 11.9%. The prothrombin time and partial thromboplastin time were normal. Serology test for the human immunodeficiency virus was negative. Serum creatinine was 0.46 mg/dl. The liver enzyme was mild elevated with serum aspartate aminotransferase 92 U/L and alanine aminotransferase 60 U/L. Serum alkaline phosphatase was normal (68 U/L). Chest radiography showed no pulmonary infiltration. Ultrasound of upper abdomen was unremarkable.

Initial diagnosis was right orbital cellulitis with secondary glaucoma from herpes zoster ophthalmicus and newly diagnosed diabetic mellitus. The empirical treatment with intravenous cetriaxone 2 g once daily, clindamycin 600 mg 8 hourly and acyclovir 500 mg 8 hourly were administered. She was still severely febrile. Hemoculture showed gram negative bacilli in 2 specimens. Because Surin province has high incidence of melioidosis. Clindamycin and cetriaxone were

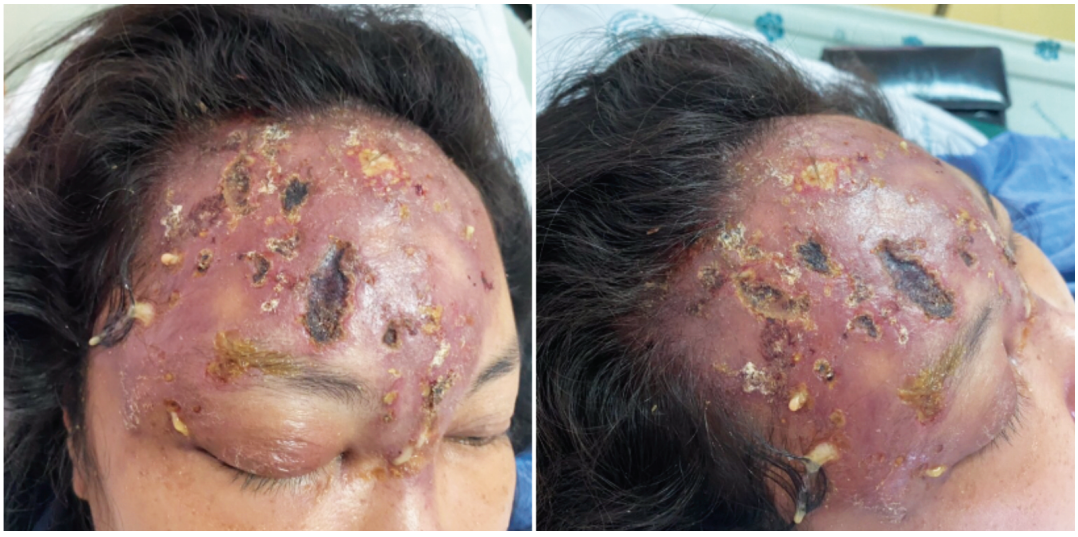

Figure 2 Violaceous swollen plaque with area of pus and necrotic skin is presented on forehead and eyelid.

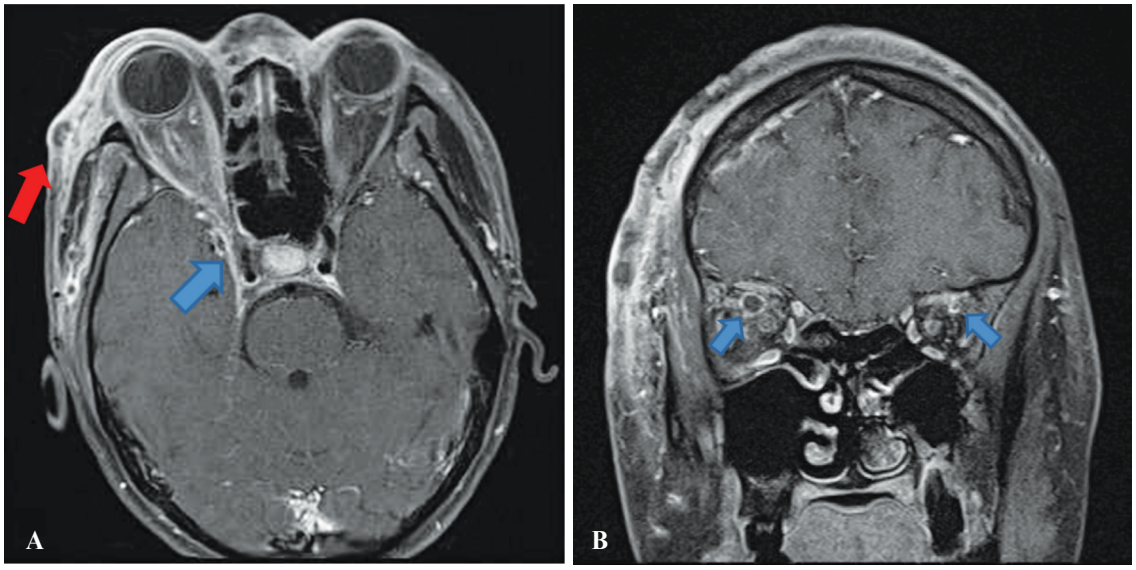

Figure 3 (A) Axial MRI (T1) showing thrombophlebitis of superficial veins along bilateral frontal scalps right temporalis (red arrow) and preseptal spaces with right exophthalmos and right cavernous sinus thrombosis (blue arrow).
(B) Coronal MRI (T1) showing diffuse enhancement of bilateral optic nerves and thrombophlebitis of bilateral superior ophthalmic veins (blue arrow).

substituted with ceftazidime 2 g 8 hourly to covering melioidosis. The final hemoculture exhibited *B. pseudomallei*. Five days after admission, her ocular and systemic condition became deteriorated. The wound at right forehead appeared erythematous with suppurative collection. (Figure 2) A bedside surgical drainage was performed and 20 mL purulent content was collected. *B. pseudomallei* was also identified from pus. MRI of the brain and orbit which was performed five days after admission revealed extensive thrombophlebitis along both superior ophthalmic veins, superficial veins along both frontal scalps, right temporal region, right zygomatic temporalis, right preseptal space, right upper-lower eyelids and right facial vein. Concurrent with those findings, cavernous sinus thrombosis and focal epidural abscess in right frontal region were also observed. (Figure 3 A, B) The patient was treated with subcutaneous enoxaparin for 7 days and then maintenance with warfarin.

After 14 days of intravenous ceftazidime, fever persisted. Therefore, oral sulfamethoxazole-trimethoprim (240/1200 mg) 12 hourly was added. She was successfully treated with a 6-month course of eradication phase of oral trimethoprim-sulfamethoxazole and a 2-month course of warfarin monitoring a target international normalized ratio (INR) of 2-3. Her comorbid diabetes mellitus type 2 was also controlled with mixed insulin, glipizide and metformin. Her visual acuity was stable 20/20 and fundus showed mild non proliferative diabetic retinopathy in both eyes.

Discussion

Eye involvement in melioidosis is an uncommon manifestation. Sixty three percent presented with ocular symptom and 56% progressed together with disseminated septicemia melioidosis from bacteremia.[2] Our patient presented with orbital cellulitis and subsequently developed septicemia. She also had

Table 1 Summary reported cases of ocular melioidosis with intracranial extension

Reference	Patient information	Symptom and sign	Risk factor	Investigation	Imaging	Treatment	Outcome
Wong and Ng[3]	42 years Singaporean male, forklift driver	Fever, left sided headache for 1 week blurred vision and orbital cellulitis left eye	Newly diagnosed DM	Nasal swab, pus from sinus, hemoculture: *B. pseudomallei* preseptal abscess	CT orbit/sinus: bilateral ethmoid sinusitis, left frontal sinus empyema and preseptal abscess	Frontal sinus drainage, intravenous ceftazidime, imipenam and chloramphenicol	Ruptured mycotic aneurysm, death from pulmonary empyema and chloramphenicol
Mohd et al[4]	45 years Malay male	Painful proptosis and swelling of forehead	DM	Pus from forehead, hemoculture: *B. pseudomallei*	Frontal sinusitis, orbital cellulitis, parotid gland abscess and subdural abscess	Surgical drainage, intravenous ceftazidime 2 g IV every 8 hours, metronidazole 500 mg every 8 hours, fluconazole 400 mg OD	Death from septic shock
Jusoh et al[5]	55 years Malay male, shopkeeper	Low grade fever for 3 weeks and left eye swelling for 5 days (orbital cellulitis with blindness)	Newly diagnosed DM	Eye swab from fistula, hemoculture: *B. pseudomallei*	CT brain/orbit: left sphenoidal sinusitis, left orbital abscess with extension to left temporal lobe	Ceftazidime 2 g IV every 8 hours, trimethoprim/ sulfamethoxazole 650 mg bid for months	VA no PL
Tirakunwichcha and Vaivanijkul[6]	18 years Thai male	Orbital cellulitis, left orbital apex syndrome and parotid gland abscess	None	Tissue biopsy from parotid gland and cavernous sinus: *B. pseudomallei*	parotid gland abscess, orbital cellulitis with extension to orbital apex and cavernous sinus	Craniectomy, surgical drainage, ceftazidime 2 g IV every 8 hours, trimethoprim/ sulfamethoxazole for 1 month then doxycycline 200 mg OD, augmentin (625), amoxicillin (250) TID	VA 20/100
Kogilavaani et al[7]	11 years Malay girl	Fever with bilateral orbital abscess progress to have weakness right upper and lower limb	None	Pus, hemoculture: no growth, melioid titer = 1:160	CT brain/ orbit: orbital abscess, cavernous sinus thrombosis and subdural abscess	Bifrontal craniotomy, ceftazidime 1.2 g IV every 8 hours for 6 weeks then trimethoprim/ sulfamethoxazole for 5 months	VA 6/6 both eyes and no neurological deficit

PL = perception of light; VA = visual acuity

Table 2 Summary reported cases of cerebral sinus thrombosis complicated melioidosis

Reference	Patient information	Symptom and sign	Neurological symptom	Risk factor	Investigation	Imaging	Treatment	Outcome
Niyasom et al[9]	42 years Thai male, soldier	Fever, severe headache for 10 days	Focal seizure of left extremities and weakness of left arm	Newly diagnosed DM, early alcoholic cirrhosis	Hemoculture: *B. pseudomallei*	CT, MRI, MRV brain: dural thrombosis and focal right posterior parietal lobe	Intravenous ceftazidime and phenytoin, heparin	No neurological deficit
Nayak et al[10]	23 years Indian male, student	Progressive diplopia on the left for 9 months and progressive hearing loss of left ear for 6 months	Multiple cranial nerve palsy	None	Surgical biopsy tissue culture: *B. pseudomallei*	MRI brain: pachymeningitis, left sigmoid and transverse sinus thrombosis	Ceftazidime 2g IV every 6 hours for 6 weeks, and then trimethoprim-sulfamethoxazole regimen for 6 months	Recovery symptoms
Abeysundara et al[11]	69 years Sri Lankan male, businessman	Fever, multiple painful lumps on scalp for 3 weeks, left mature cataract	Confusion without neurological defect	DM	Pus from scalp, CSF, hemoculture: no growth, melioid titer change from 1:160 to 1:1200	CT chest: multiple abscess both lungs MRI brain: multiple cerebral, cerebellar abscesses, and superior sagittal venous-sinus thrombosis	Meropenem 1g IV every 8 hours for 4 weeks (prior diagnosis) switch to meropenem 2g IV every 8 hours, trimethoprim-sulfamethoxazole 320/1600 mg BID for 2 weeks then doxycycline 100 mg BID, trimethoprim-sulfamethoxazole 320/1600 mg BID for 5 months and warfarin for 3 months	Healed scalp abscess

unilateral dermatomal vesicular cutaneous eruption on trigeminal branch, proptosis and restricted ocular movement. Even though orbital cellulitis and HZO were treated with empirical therapy and antiviral agent, the clinical became worse. She was newly diagnosed with type 2 diabetes and experienced septicemia. Although history of soil contact was unclear, melioidosis was suspected in this case. The gold standard for diagnosis of melioidosis is isolation of *B. pseudomallei* from blood, pus, sputum, or other clinical specimens. However, culture has a low diagnostic sensitivity in patient with melioidosis. Serology essay for detection 4-fold rising titer antibody by indirect hemagglutination test (IHA test) or ELISA maybe helpful for diagnosis. Previous studies reported five patients (four males and one child) with orbital cellulitis from melioidosis with intracranial involvement. (Table 1) [3-7] Three patients had diabetes. Most of patients had declined condition after suggested empirical treatment. Four patients needed surgical debridement. Similarly, pus drainage was necessary in our patient. The outcome of ocular and neural involvement melioidosis was unsatisfactory. One patient suffered from blindness and two patients died from septic shock and hospital- acquired pneumonia. Early diagnosis, prompt treatment as well as surgical drainage of abscess are keys to treatment success.

The pathogenesis of neuromelioidosis includes hematogenous spreading, direct brainstem extension from cranial nerve, nasal pathway and skin inoculation.[8] Cerebral sinus thrombosis in neuromelioidosis is unusual. Three cases were reported. (Table 2) [9-11] Two of patients were diabetes, presented with high grade fever. The last patient presented with progressive multiple cranial nerve (III, VII, VIII, IX, X) involvement. Our patient was also developed bilateral superior veins and cavernous sinus thrombosis from septicemia. Hypercoagulable condition and vasculitis were not identified in this patient.

Treatment of melioidosis composes of two phases. In intensive phase, intravenous ceftazidime, imipenem or meropenem are used for 10-14 days. In case of neurological melioidosis, bone, joint, deep seated collection infection the intravenous antibiotics treatment is extended to 4-8 weeks and combined with trimethoprim-sulfamethoxazole. In eradication phase, trimethoprim-sulfamethoxazole is used for 3- 6 months.[12,13]

Conclusion

Ocular melioidosis with neurological involvement had high mortality rate and poor visual outcome consequence. It can be presented in variable manifestation. Risk factor evaluation and awareness is important for making the early diagnosis and effective management.

Acknowledgement

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