Case Report

Dural Sinus Thrombosis in Melioidosis: The First Case Report

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Melioidosis which is infection with Burkholderia pseudomallei, is an important cause of sepsis in India, southeast Asia and northern Australia. Mortality is high and treatment is problematic. Neurological melioidosis is unusual but meningoencephalitis, encephalomyelitis and brain microabscess can occur. Dural sinus thrombosis is not an uncommon cerebrovascular disorder with various etiologies. Hypercoagulable state, pregnancy, dehydration, certain blood dyscrasia and contraceptive pills are common causes however meningitis and local head & neck infections may lead to this condition. Dural sinus thrombosis complicating septicemic melioidosis has never been reported. The authors report a 42-year-old Thai man suffering from septicemic melioidosis with dural sinus thrombosis. He had high fever, headache, left hemiparesis, focal seizure and increased intracranial pressure. Diabetes and mild alcoholic cirrhosis were diagnosed in this admission. CT scan, MRI brain and MRV revealed superior saggital sinus thrombosis with complicating venous infarction over right posterior parietal lobe. Hemoculture demonstrated Burkholderia pseudomallei and CSF was acellular. Investigations for causes of dural sinus thrombosis were all negative. This patient gradually improved after treatment with ceftazidime, antiepileptic drug and heparin without clinical recurrence. Neuromelioidosis is a rare syndrome that may present as brain abscess, encephalitis or meningoencephalitis. The authors report dural sinus thrombosis associated with septicemic melioidosis. The authors' hypothesis of venous thrombosis in the presented case is sepsis induced hypercoagulable state. Physicians should be aware of cerebral venous thrombosis in case of suspicious melioidosis with neurological involvement. Prompt treatment with intravenous heparin and antibiotic is potentially effective.

Keywords: *Dural sinus thrombosis, Melioidosis, Neuromelioidosis, Venous infarction*

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Dural sinus thrombosis was an uncommon neurological disorder in the past. After the advent of non-invasive imaging methods such as magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) of the brain resulted in increased recognition of this condition[1]. The common clinical presentations are headache with increased intracranial pressure. In severe or untreated patients may develop hemorrhagic venous infarction which can produce focal deficits, seizure and impaired consciousness[2]. Pathogenesis of venous sinus thrombosis are damage to vessel wall, disorders of coagulation and stagnant flow. Damage to vessel wall consists of infection, infiltration or trauma (such as otitis, sinusitis, dental abscess, tonsillitis and tumor)[3]. However, more common problems are coagulation defects that cause hypercoagulable state. Common hereditary coagulopathies that have been identified to produce dural sinus thrombosis are deficiency of protein C, protein S, antithrombin III, factor V Leiden, and antiphospholipid antibody syndrome[1,4-6]. Pregnancy, dehydration and some blood dyscrasia also can cause stagnant blood[7]. The common drug at risk for this condition is oral contraceptive pills[8]. Common infections which have been reported associated with dural sinus thrombosis are local infection of the face such as sinusitis, otitis and mastoiditis. These may lead to secondary thrombophebitis[9]. Meningitis from infectious or carcinoma-

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tous meningitis have been reported in association with venous thrombosis[1,10]. Dural sinus thrombosis in a sepsis patient without meningitis or local cranial abscess is a very rare condition and pathogenesis may occur from a sepsis induced hypercoagulable state[11]. The authors could not identify venous sinus thrombosis associated melioidosis septicemia like in the presented case report in any research.

Case Report

A 42-year-old Thai man came to Phramongkutklao Hospital on June 10, 2003. He is a soldier. He presented with high grade fever and severe headache for the last ten days. Ten days prior to admission, he went to the forest for a soldier's training program. On the first day, he developed a high fever, myalgia and headache. After that his symptoms continued everyday. He got some medications from a primary doctor such as acetaminophen, naproxen, amoxyclavulonic acid for 4 days without improvement. Characteristics of headache were diffuse, throbbing and tightening and were located predominately at the bitemporal areas. Headache was progressively severe, and not relieved by analgesics. Finally he developed nausea and vomiting. Two days before admission, he developed focal motor seizures that started at the left side of the extremities for 2 minutes and after that he had mild weakness of the left arm. He was a previous healthy man with no underlying disease. He drunk alcohol heavily everyday for twenty years. He had no hematologic problem either bleeding disorder or hypercoagulable state. Other abnormal symptoms that suggested local infection of head and neck could not be identified from history reviews.

The physical examinations revealed a body temperature of 39 c, pulse rate 94/ min, respiratory rate 24/ min and blood pressure 110/65 mmHg. He had mild icteric sclera. Otherwise were within normal limit. Neurological examinations revealed drowsiness and left hemiparesis grade IV/V. Optic fundi showed engorgement of retinal veins but no burring of the optic discs. All sensory modalities and deep tendon reflex were normal. Babinski's sign was absent. He had neither stiffness of neck nor Kernig's sign. Laboratory findings showed the followings; complete blood count: hemoglobin 11 g/dL, hematocrit 31.4%, white blood cell (WBC) 12,000/mm^3 [polymophonuclear (PMN) 68%, lymphocyte 22%, monocyte 10%], platelet 251,000/mm^3. Electrolytes, calcium and magnesium were normal. Liver function tests were albumin 26 mg/dL, globulin 41mg/dL, SGOT 72 U/L, SGPT 59 U/L, total bilirubin 22 mmol/L, direct bilirubin 18 mmol/L and alkaline phosphatase 135 U/L. Urine specific gravity was 1.010. Urine osmolarity was 467 mosmol/Kg [normal range 500-800 mosmol/Kg], thus there was no evidence of dehydration in this patient. Diabetes mellitus (DM) was newly diagnosed in this patient due to high fasting plasma glucose and HbA_1C (288 mg% and 8.3 mmol/L, respectively). Coagulogram showed only prolongation of prothrombin time (PT), [international normalized ratio (INR) = 1.33], but normal partial thromboplastin time and thrombin time. Early alcoholic cirrhosis was diagnosed by history of heavy drinking, reverse albumin/globulin ratio, prolongation of PT and ultrasonography but no evidence of decompensation of liver cirrhosis. Blood examination for malaria was done due to a history of forest exposure and the result was negative. Serologic studies for leptospirosis Ab IgM, hepatitis A, B, C, ricketsial titer IgM, IgG and anti HIV were all negative. CT scan, MRI and MRV of brain were done due to severe headache and showed filling defects in superior sagittal sinus and right transverse sinus that represented dural sinus thrombosis (Fig. 1-4.). There was focal infarction at gray-white junction of right posterior parietal lobe (Fig. 5.) and no evidence of sinusitis. Lumbar puncture was done. Cerebrospinal fluid (CSF) profile revealed an opening pressure of 200 mmH_2O, protein 102 mg%, glucose 6.2 mmol/L (plasma glucose 8 mmol/L), no WBC, no red blood cell, negative for India ink and cryptococcal antigen, no organism in

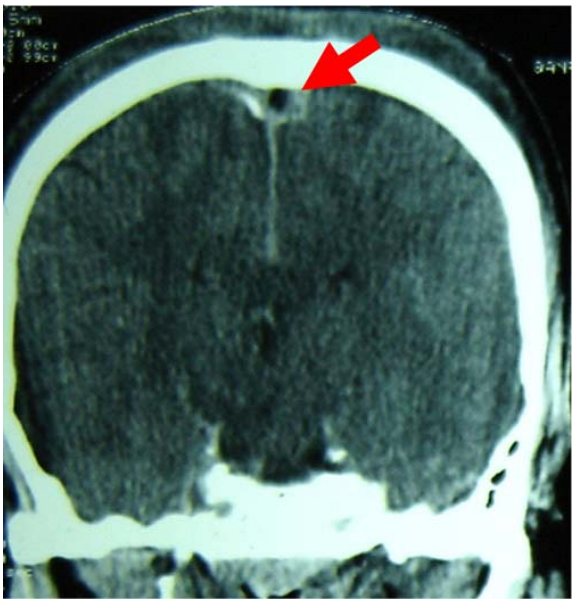

Fig. 1 Coronal CT scan brain with contrast shows clot in superior saggital sinus (arrow)

Gram's and AFB staining. CSF culture was no growth. Protein C, Protien S, Antithrombin III levels were all normal and didn't show evidence of antiphos-pholipid antibody syndrome. Hemoculture revealed positive for Burkoderlia pseudomallei 2 specimens. The final diagnosis of this patient were 1) septicemic form of

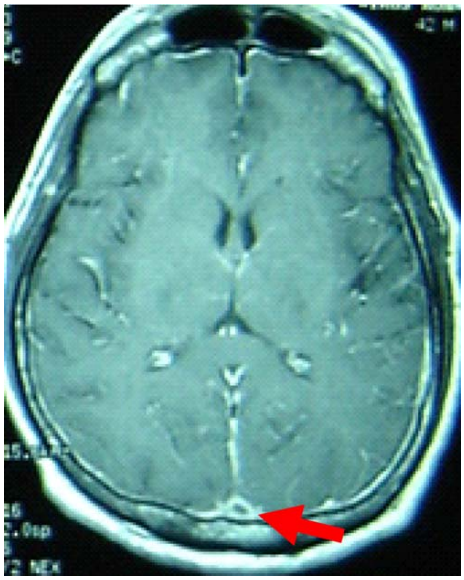

Fig. 2 Axial MR brain T1 weighted with gadolinium shows empty delta sign that represents a clot in superior sagittal sinus (arrow)

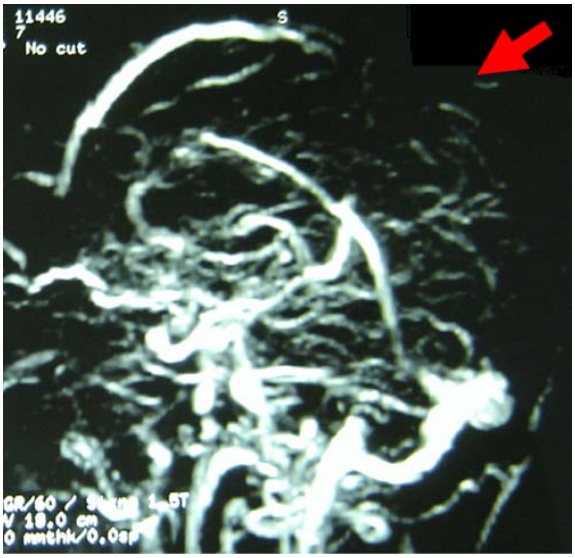

Fig. 3 Sagittal view of MR venography demonstrates absence of signal in posterior two third of superior sagittal sinus (arrow)

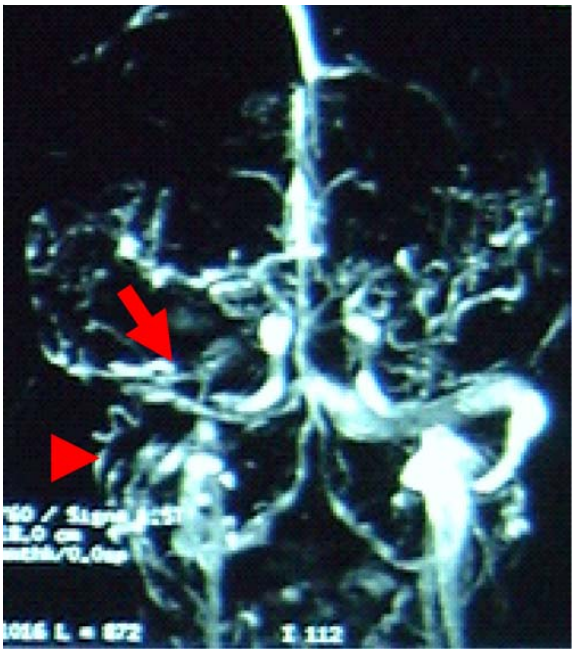

Fig. 4 Coronal view MR venography shows markedly decreased signal of right transverse sinus (arrow) and sigmoid sinus (arrow)

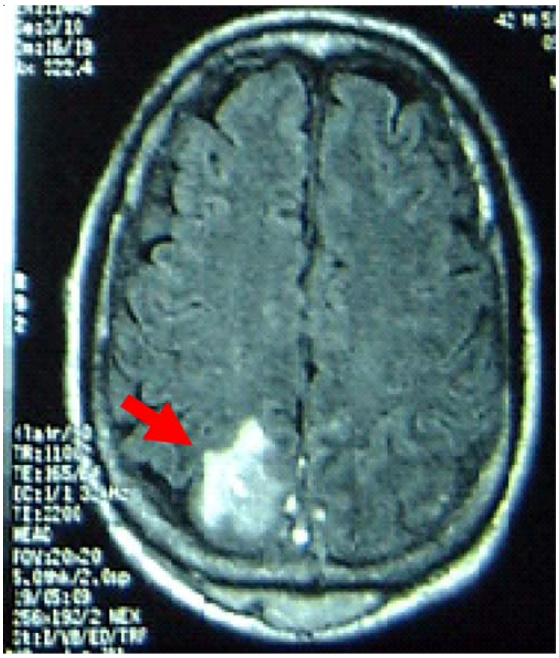

Fig. 5 Axial FLAIR MR brain imaging reveals a hyper-intensity lesion at right posterior parietal lobe that represents venous infarction (arrow)

melioidosis (caused fever and clinical sepsis) confirmed by hemoculture 2) superior saggital sinus and right sigmoid sinus thrombosis (caused diffuse headache, high CSF pressure, confirmed with MRI and MRV) 3) venous infarction at right parietal region (caused seizure and mild left hemiparesis), 4) DM and early alcoholic cirrhosis.

Treatment of the presented patient was intravenous ceftazidime (for melioidosis), intravenous heparin (for venous sinus thrombosis) and phenytoin (for seizure prevention). Fever and headache were improved within 1 week. There was no seizure recurrence. Two weeks after treatment, he was discharged from our hospital without fever or neurological deficit.

Discussion

Melioidosis is an infection caused by *Burkholderia pseudomallei*, which is an aerobic gram negative bacilli, free living, small, motile, saprophyte normally found in soil. Human contact with the disease is through soil contamination of skin abrasion, ingestion or inhalation. This organism has characteristics in gram stain as bipolar staining or safety pin appearance[12]. This infection is quite common in tropical areas especially South East Asia including Thailand[13-15]. It can affect any host but is more common in diabetes and alcoholism[12].

Clinical manifestations may be acute, subacute or chronic, localized form as abscess or more severe generalized as septicemia[12]. However, melioidosis correlate with high morbidity and mortality and the need long term antibiotic such as cotrimoxazole and ceftazidime[12,15]. Melioidosis of the head and neck can present as parotid abscess, acute sinusitis, acute supurative lymphadenitis and chronic suppurative otitis media causing meningoencephalitis[16].

Neurological manifestation of melioidosis or neuromelioidosis is an unusual condition (about 5%) with very high mortality. It can cause brain abscess (at cerebrum, cerebellum, brainstem and spinal cord), encephalitis and meningoencephalitis[17-27]. Melioidosis may produce thrombophebitis but usually is secondary to sinusitis, brain abscess or meningitis. The presented patient was diagnosed with melioidosis septicemia, superior saggital sinus and right sigmoid sinus thrombosis with venous congestion and hemorrhagic infarction. Many investigations were done searching for the cause of dural sinus thrombosis which were all negative. There was no evidence of sinusitis, otitis, mastoiditis, soft tissue infection of the face, brain abscess, meningitis and hereditary coagulopathies that might be the leading cause of venous sinus thrombosis. The authors' hypothesis of this condition of the presented patient was sepsis induced acquired hypercoagulable state.

The authors could not find a previous report of cerebral dural sinus thrombosis associated with melioidosis septicemia without brain abscess, sinusitis or meningitis. So the presented patient might be the first case of dural sinus thrombosis in melioidosis septicemia.

Conclusion

This is the first case report of melioidosis septicemia associated with dural sinus thrombosis. Intravenous ceftazidime and heparin were used with rapid improvement of both conditions. The authors' hypothesis of pathogenesis of venous thrombosis is sepsis induced acquired hypercoagulable state. Physicians should be aware of cerebral venous thrombosis in cases of suspicious meliodosis with neurological involvement. Prompt treatment with intravenous heparin and antibiotics is potentially effective.

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การอุดตันของ Dural Sinus ในโรค Melioidosis: รายงานผู้ป่วยรายแรก

สุชาดา นิยะสม, พาสิริ สิทธินามสุวรรณ, เจษฎา อุดมมงคล, จิตถนอม สุวรรณเตมีย์

โรค Melioidosis เกิดจากการติดเชื้อ Burkholderia pseudomallei ซึ่งยังเป็นโรคที่มีอัตราตายและพิการสูง จึงเป็นปัญหาสาธารณสุขที่สำคัญ ภาวะความผิดปกติทางระบบประสาทจากโรคนี้ (Neurological melioidosis) พบไม่บ่อย ลักษณะที่พบได้แก่ เยื่อหุ้มสมองและสมองอักเสบ (meningoencephalitis), สมองและไขสันหลังอักเสบ (encephalomyelitis) และฝีในสมอง (brain microabscess) สำหรับภาวะการอุดตันของ Dural sinus เป็นโรคหลอดเลือดสมองที่พบไม่บ่อย ซึ่งไม่เคยพบรายงานผู้ป่วยที่มีการอุดตันของ Dural sinus ร่วมกับโรค Melioidosis ที่มีการติดเชื้อในกระแสเลือดมาก่อน คณะผู้รายงานจึงขอเสนอรายงานผู้ป่วยรายหนึ่งที่มีภาวะทั้งสองร่วมกัน ผู้ป่วยชายไทยอายุ 42 ปี มีไข้สูง ปวดศีรษะ แขนขาซีกซ้ายอ่อนแรง ชักเฉพาะที่ และมีความดันในโพรงกะโหลกสูง ผู้ป่วยได้รับการวินิจฉัยว่าเป็นเบาหวานและโรคตับแข็งจากการดื่มสุรา ผลการตรวจ CT scan สมอง, MRI สมอง และ MRV พบลักษณะ superior sagittal sinus thrombosis และมีการตายของเนื้อสมองบริเวณ parietal lobes ด้านขวา เนื่องจากหลอดเลือดดำอุดตัน การเพาะเชื้อจากเลือดพบเชื้อ Burkholderia pseudomallei ไม่พบการติดเชื้อจากการตรวจน้ำไขสันหลัง จากการตรวจค้นเพิ่มเติมไม่พบสาเหตุอื่น ๆ ที่เป็นสาเหตุของการอุดตันของ dural sinus หลังให้การรักษาด้วยยา ceftazidime, antiepileptic drug และ heparin ผู้ป่วยมีอาการดีขึ้นตามลำดับ และไม่เกิดอาการซ้ำ สมมติฐานของคณะผู้รายงานเกี่ยวกับสาเหตุของการเกิดภาวะอุดตันของ dural sinus ในผู้ป่วยรายนี้คือการติดเชื้ออาจมีผลกระตุ้นให้เลือดแข็งตัวได้ง่าย