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Internal Medicine

CNS MELIOIDOSIS IN AN APPARENTLY IMMUNOCOMPETENT INDIVIDUAL- AN UNUSUAL CASE OF HEMIPLEGIA

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ABSTRACT Melioidosis, also colloquially called “Vietnamese Time Bomb” is a bacterial infection caused by *Burkholderia pseudomallei.* This highly aggressive organism can cause abscesses in any part of the body. Central nervous infectious caused by *B. Pseudmallei* mimicking stroke are extremely rare and are limited to case reports. Here we present a case of CNS Melioidosis in a 51 year old shopkeeper from Assam, presenting as hemiplegia.

KEYWORDS : CNS Melioidosis, Rare diseases, Cerebral abscesses, Indolent diseases, Tropical illnesses.

INTRODUCTION:

Melioidosis is an infectious disease that can affect both humans and animals. *Burkholderia pseudomallei,* a Gram-negative bacterium, is the disease's caussative organism. It is mostly a tropical disease, and it is particularly common in Southeast Asia and northern Australia. Melioidosis-causing bacteria can be found in contaminated soil and water. Animals and people can contract it by coming into direct contact with an infected source.(1)

More than 200,000 American soldiers who fought in Vietnam between 1965 and 1972 acquired the bacillus' latent form, and many of them are still infected today without showing any clinical signs of the disease. Therefore, melioidosis has often been referred to as "Vietnam's ticking time bomb".(2)

Immunocompromised individuals, and agricultural and construction workers who have a high chance of coming in contact with contaminated soil are at risk. Melioidosis presents a variety of clinical symptoms that vary depending on the route of entry. There have been estimates of CNS involvement ranging from 1.5 to 10%, with a high mortality rate of up to 60%. Although it is curable, relapses and recurrences are frequent. (3)

Case Report:

Mr. M, a 51-year-old gentleman, a shopkeeper by occupation, hailing from Assam, was brought to our hospital with complaints of weakness on the right side of the body, left-sided facial deviation, dysphagia, and aphasia for 15 days. There was a history of fever 3 days before the onset of weakness, which was resolved with IV Paracetamol. His history was negative for any co-morbidities but he was a chronic alcohol consumer (10-15g per day for the last 10 years).

On examination, he was conscious, oriented afebrile, and hemodynamically stable. His Heart rate was 84 beats/ minute, BP was 122/70 mmHg, and sPO2 was 99% under the room air. CNS examination revealed right hemiplegia with Power 0/5 of both right upper and lower limbs, with 7th nerve Upper Motor Neuron palsy on the right side evidenced by deviation of angle of mouth to the left side with loss of nasolabial fold and perseveration of wrinkling of the forehead.

His basic investigations on admission are given in table 1. Chest X-ray was normal. His HIV, HBsAg, and HCV tests were negative and his blood sugars were within normal limits. An MRI brain with contrast was done immediately. It was notable for conglomerated peripherally enhancing altered signal lesions in the left high frontoparietal lobe with associated significant mass effect, choline and NAA (N-acetyl aspartate) spike, and contralateral midline shift -features likely represent cerebral abscess (Figure 1). The radiologist offered necrotic high-grade glial neoplasm as the second differential. His blood cultures were negative for any organism and 2D ECHO did not reveal any valvular vegetations. The neurosurgery team was consulted and a frontoparietal craniotomy was done and drainage of the pus from the abscess and a biopsy were also obtained (Figure 2). The postoperative period was uneventful. Gram stain was notable for pus cells and Xpert MTB was negative. His pus from the cerebral abscess grew *Burkholderia pseudomallei* and he was started on IV Meropenem (1g, 8th hourly) and Co-Trimoxazole Double strength tablets, twice daily as per the Infectious diseases team. Antiepileptic drug (Brivaracetam 50mg oral, 12th hourly) was started prophylactically.

Although his speech improved after the surgery, his motor functions are yet to improve. During the first follow-up, there was a mild increment in the power in his upper limbs. The patient is currently on IV Meropenem and Oral Co-Trimoxazole and is advised to follow up regularly and be compliant with the medications.

DISCUSSION:

India is rapidly becoming a melioidosis hotspot due to its suitable climate and sizable diabetic population. Melioidosis has a variable clinical history and can be docile in some people.(4)

The many symptoms of melioidosis, including severe pneumonia and sepsis, purulent skin abscesses, intra-abdominal abscesses, and neurological abnormalities, can mirror those of tuberculosis, typhoid fever, and malaria. The bacterium can have up to seven different morphotypes, each of which has different pathogenicity, making identification difficult.(2)

Analysis of the *Burkholderia pseudomallei* genome revealed that the bacterium acquired a large number of genes coding for various exotoxins involved in tissue necrosis. Among these toxins, Hautbergue et al. identified a deadly *Burkholderia* toxin, namely *Burkholderia* Lethal Factor 1 (BLF1). Its toxicity is immense, since an intraperitoneal injection of one hundred millionths of a gram is enough to kill a mouse. Nanomolar concentrations of this toxin also kill macrophages in culture, which absorb it by pinocytosis.(2)

The most significant risk factor for melioidosis is diabetes mellitus, which has been shown to multiply the relative risk of infection by up to 100 times in several age groups in northeast Thailand. Diabetes mellitus, pre-existing renal disease, thalassemia, and occupational exposure to soil and water have all been shown in case-control studies from Thailand to be definite risk factors for melioidosis and bacteremic melioidosis. Malignancy, immunosuppression, and excessive alcohol consumption are further known risk factors for melioidosis.(5) Our patient had alcohol consumption as the only risk factor.

The recovery of a *B. pseudomallei* isolate by culture from blood, sputum, cerebrospinal fluid, or other bacteriology specimens, play a significant role in the confirmation of a diagnosis of melioidosis. Indirect haemagglutination assay (IHA) can be used to provide serological evidence of infection, although seroconversion is unlikely to happen early enough to influence treatment decisions made during the admission stage of a severe, acute infection. ELISA-based or indirect immunofluorescent (IFAT) tests have increased the sensitivity

and specificity, but false negative results still happen occasionally.(6)

CNS melioidosis seems to have a unique etiology. Hematogenous transmission of the bacterium to the CNS is crucial to the disease's mechanism of action. A study by Wongwandee et al. investigation shows that blood is the most frequent sample used to isolate B. pseudomallei. The blood-brain barrier and the blood-CSF barrier are two of the cellular barriers that circulating bacteria can breach through the transcellular, paracellular, or Trojan horse approaches.(7)

Due to its high sensitivity, contrast-enhanced MRI is the preferred neuroimaging study for CNS melioidosis. If done early, a brain CT scan might look normal. Therefore, if CNS melioidosis is still on the differential diagnosis, additional MRI scan should be performed. The most accurate way to determine CNS melioidosis is through culture from the CNS specimen. These sources include 1) brain tissue, 2) CSF, and 3) pus from an epidural abscess, subdural collection, or brain tissue. However, it can be challenging to collect the material from a pathogenic area like the brainstem. The diagnosis can then be established based on the presentation of the CNS disorders and are confirmed by positive cultures from additional specimens.(6,7)

It is prudent to note that our patient did not have blood cultures positive for *Burkholderia*, although his pus from cerebral abscess grew the organism. The patient likely had a seedling of the organisms earlier in his life, which got reactivated now, causing cerebral abscess with neurological deficits.

Broad intrinsic antimicrobial resistance in *B. pseudomallei* makes prolonged therapy necessary for cure. This therapy entails an intravenous intensive phase using ceftazidime (2-3 g or 40 mg/kg/dose every 8 hours intravenously), meropenem (1 g or 25 mg/kg every 8 hours intravenously), or imipenem, followed by an oral eradication phase, typically using trimethoprim-sulfamethoxazole (10/50 mg/kg, up to 320/1600 mg, 12 hourly). Revised 2020 Darwin Guidelines recommend minimum of 8 weeks of intensive phase followed by 6 weeks of oral eradication phase, in case of CNS melioidosis.(8)

Even in situations with ample resources, melioidosis of the CNS can rapidly result in death, with case fatality rates reaching 50%. (9) It can leave the affected patients with gross morbidities and severe functional disabilities. Its recurrence should be kept in mind and the clinicians need to ensure that the patients are compliant with the therapy. Despite being endemic in tropical areas, this life-threatening condition needs to be taken into account by clinicians in temperate areas, especially in cases of returning travellers who have certain comorbidities.

Declarations:
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Ethical approval: Not required.

Table 1: Basic investigations of the patient on admission.

Test Parameters	Patient's data	Normal Range
Complete blood count:		
Haemoglobin	10.6 (grams/deciliter)	11.5-16.5 (grams/deciliter)
Total White blood cell count	4.98* 103 /mm3	4-11 103 /mm3
Neutrophils	66%	40-80%
Lymphocytes	24%	20-40%
Monocytes	6%	02-10%
Platelet count	332*103 /mm3	150-450 103 /mm3
ESR	22	0-20 mm/hr
Liver Function tests:		
Total Bilirubin	0.6 mg/dL	0.0-1.3 mg/dL
Direct bilirubin	0.4 mg/dL	0.0-0.5 mg/dL
Indirect Bilirubin	0.2 mg/dL	0.0-1.2 mg/dL
SGOT/ AST	22 U/L	<31 U/L
SGPT/ ALT	18 U/L	<34 U/L
Alkaline Phosphatase	68 U/L	<98
Gamma Glutamyl Transpeptidase (GGTP)	31 U/L	<140 U/L
Renal Function Tests		
Urea	22 mg/dl	13-43 mg/dl
Creatinine	0.6 mg/dl	0.6 - 1.1 mg/dl
Random Blood Sugar	95 mg/dl	<140 mg/dl

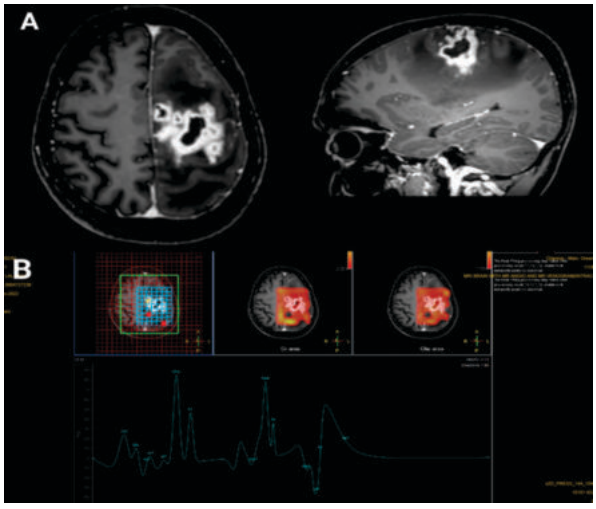

Figure 1: Contrast enhanced MRI brain showing conglomerated peripherally enhancing altered signal lesions in the left high frontoparietal lobe with associated significant mass effect(A), and choline and NAA (N-acetyl aspartate) spike (B)

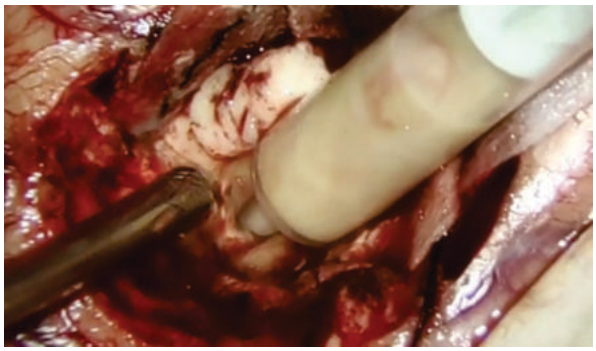

Figure 2: Intra-operative image of cerebral abscess drainage.

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