The Tunnel Sign Revisited: A Novel Observation of Cerebral Melioidosis Mimicking Sparganosis

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ABSTRACT

The tunnel sign has been described as a specific feature of cerebral sparganosis. We present a case of a 55-year-old gentleman found to have cerebral melioidosis and with initial imaging mimicking the appearance of sparganosis. This suggests that the tunnel sign in brain abscesses may be specific for infection by Burkholderia Pseudomallei, Spirometra Mansoni or Listeria Monocytogenes.

CASE REPORT

A 55-year-old gentleman of Southeast Asian descent presented at a routine gastroenterology outpatient appointment with a 1-day history of fever, chills and rigors. This was preceded by 1 week of headache, bilateral lower limb weakness and altered mental state in the form of increasing forgetfulness, incoherent speech and insomnia. He was previously involved in farm work. His past medical history includes type 2 diabetes mellitus (on glipizide, HbA1c 10%) as well as Child-Pugh score A liver cirrhosis secondary to chronic hepatitis C infection and alcohol use. The patient had also presented 2 months prior to colorectal surgery for a supralevator abscess and complex perianal fistula; the abscess was unable to be drained and he was treated conservatively with intravenous (IV) ceftriaxone and metronidazole that was subsequently converted to oral amoxicillin-clavulanate. He was subsequently admitted to hospital for investigation of his neurologic symptoms.

On examination, the vital signs were normal (blood pressure 121/72 mm Hg, pulse rate 80/minute, SpO2 100% on room air) and the patient was afebrile. Slow mentation was noted although he remained oriented to time, place and person. His gait was unsteady, and power was reduced (grade 4- out of 5) in the bilateral lower limbs with associated hyper-reflexia. No signs of meningism were elicited. A perianal fistula was seen, covered with an iodine dressing, and this was clean. The rest of the physical examination was unremarkable.

The full blood count showed thrombocytopenia of 77 x 109/L (normal range: 132-372 x 109/L) but with no neutrophilia present. The C-Reactive protein levels were elevated at 17 mg/L (normal range: 0-10 mg/L). No other sources of sepsis were identified on chest radiography or urine formed element examination.

An unenhanced computed tomography (CT) scan of the brain was organized, which showed extensive right frontoparietal lobe edema with high-attenuation foci (Figure 1). An urgent contrast-enhanced magnetic resonance imaging (MRI) scan of the brain was subsequently performed, which showed a highly irregular, coalescing and rim-enhancing lesion in the right frontal lobe with tubular and linear components (Figures 2 to 5). Associated mass effect and restricted diffusion were present. There was adjacent pachymeningeal
enhancement as well as erosion of the inner table of the right frontal bone. The MRI findings suggested brain abscesses, although the on-call radiologist thought they were atypical for the usual pyogenic organisms and suggested the differential diagnosis of cerebral sparganosis based on the presence of the tunnel sign.

An urgent referral to neurosurgery was organized and the patient started on IV dexamethasone and anti-epileptics. A right frontal craniotomy was performed; intra-operatively, right frontal lobe brain abscesses were found, with pus and necrotic tissue seen in the abscess cavities. Histologic findings were compatible with a brain abscess (Figures 6 and 7). The visible abscesses were drained.

Cultures of the drained pus returned growth of Burkholderia Pseudomallei, sensitive to ceftriaxone, cotrimoxazole and doxycycline. Apart from the known supraventricular abscess, no other thoracic or abdominal locus of infection was found on CT. Screen for cytomegalovirus, toxoplasma and human immunodeficiency virus was negative. The patient was reviewed by infectious disease specialists and started on a 6-week course of IV ceftriaxime. The blood cultures were negative throughout the admission.

Dense left hemiplegia was noted in the immediate post-operative period, which improved with physiotherapy at the point of discharge 2 weeks later. However, 3 weeks after discharge, surveillance contrast-enhanced CT scan showed recurrent abscesses in the surgical cavity (Figure 8). The patient was re-admitted for a re-open craniotomy and excision of the right frontal lobe abscess, with thick brown fluid drained intra-operatively. A 4-week course of IV meropenem and a 6-month course of oral cotrimoxazole were completed. At last review a year later, the patient had residual left-sided weakness (power 4+ of 5) and sleep disturbances but was otherwise well. MRI at this point showed complete resolution of the original abscesses with right frontal lobe encephalomalacia (Figure 9).

DISCUSSION

**Etiology & Demographics:**

The causative organism for Melioidosis is *Burkholderia Pseudomallei*, a gram-negative, aerobic and motile bacillus which has been described as having a “safety pin” appearance. The bacterium is able to withstand harsh environments and survive in moist and dry conditions, and is estimated to be 165,000 cases per annum, although the disease is likely to be under-reported due to poor access to appropriate diagnostic techniques [1]. In India, China, Brazil and Malawi [1,4], the global incidence is estimated to be 165,000 cases per annum, although the disease is likely to be under-reported due to poor access to proper diagnostic techniques [4]. In Singapore alone, 550 cases were reported over a 10-year period, with spikes in incidence related to rainfall levels and the monsoon season [5]. Case-fatality rates in excess of 50% have traditionally been reported [4], although more recent case series have shown reductions to less than 10% possibly related to improvements in diagnosis and management [6]. A male predominance has been described [1]. The disease is more common in the 4th to 6th decade of life, with only 1/5 of all cases in Thailand occurring in children less than 14 years of age [2].

Routes of entry into the human body include skin abrasions, inhalation or aspiration. Several risk factors, both related to the environment and host, have been identified. These include a history of soil/water exposure (e.g. rice farmers in Thailand), diabetes mellitus, chronic renal/lung/granulomatous disease, alcoholism and steroid use [1,2].

**Clinical & Imaging Features:**

The clinical presentation is protean and dependent on the locus of infection. Pulmonary involvement is most commonly seen, with presentation as either a pneumonia or pleural effusion [1,6]. Other sites of involvement include the genitourinary (prostatic abscesses in particular), skin, bloodstream, musculoskeletal and neurological systems in descending order of prevalence. Of note, neurological involvement is noted in approximately 5% of cases [1].

Multiple case series and reports have been published on central nervous system melioidosis; a recent case series from China showed that patients commonly presented with fever, headache, seizures and motor weakness. Associated neutrophilia is often present [8].

Definitive microbiological diagnosis can be made by culturing and isolating the bacterium on Ashdown’s medium. Serological tests are poorly sensitive and specific, particularly in endemic areas that show high prevalence of seropositivity [1].

On imaging, cerebral melioidosis typically presents as a pyogenic abscess with either solitary or multifocal ring-enhancing lesions accompanied by surrounding vasogenic edema and mass effect, predominantly hypodense on CT. On MRI, these are typically T2 hyperintense, T1 hypointense and show restricted diffusion on diffusion weighted imaging (DWI) [8–16]. No published apparent diffusion coefficient (ADC) ranges are available. A variety of enhancement patterns and shapes are possible; the lesions may be cyst-like, linear, nodular and coalescent [8]. Spread conforming to white matter tracts and cranial nerve pathways has also been seen [11]. Rapidly progressive lesions may be a feature [8].

Associated extra-axial involvement may be demonstrated in the form of leptomeningeal enhancement, subdural empyema, epidural abscesses [13,15], calvarial/vertebral osteomyelitis or subgaleal abscesses [8,17]. Concomitant sinusitis has been reported in a Singaporean series [16]. Dural venous sinus thrombosis may also be present [8]. Outside of the head and neck, other abscesses may also be found in the lungs and abdominal viscera, particularly the prostate gland [6,18,19].

On magnetic resonance spectroscopy (MRS), the lesions are expected to appear similar to typical pyogenic abscesses,
with lipid (0.8-1.2 ppm), lactate (1.3 ppm) and amino acid (0.9 ppm) peaks and low N-acetyl-aspartate (NAA) and choline levels [20]. However, an atypical case of melioidosis has been reported [10] with lack of the aforementioned peaks and paradoxically increased choline-to-NAA ratio.

No studies featuring perfusion weighted imaging (PWI) findings have been reported, but the lesions are expected to show the absence of increased perfusion in the enhancing rim on the relative cerebral blood volume (rCBV) maps [20,21].

**Treatment & Prognosis:**
Melioidosis is a difficult infection to treat due to the bacterium’s resistance to a wide-range of antibiotics, including aminoglycosides, penicillins and rifamycins. Ceftazidime-based regimens are most widely used in the intensive-phase. Eradication-phase regimens include the use of agents such as cotrimoxazole, chloramphenicol and amoxicillin-clavulanate [1,22].

Apart from the high mortality associated with cerebral melioidosis, significant morbidity post-event is also known. Of 12 patients in an Australian series, 3 patients died, 6 patients had residual weakness and only 3 patients made a full recovery [23]. Recurrent infections are possible; in a series of 540 patients with melioidosis of any site in Australia, a recurrence rate of 6% was found out of the 465 patients who survived the initial episode [6].

**Differential Diagnoses:**
The differential diagnosis of subcortical or deep white matter ring-enhancing lesions in the brain is well-known and wide-ranging, including gliomas, metastases, typical pyogenic abscesses and demyelinating disease [24]. However, to the best of our knowledge, tubular enhancement in a linear or curvilinear fashion – the tunnel sign – has not yet been described in these common pathologies. It was originally suggested to be a specific sign of cerebral sparganosis [25]. We have found that it may also be demonstrated in cerebral melioidosis, as this case illustrates, as well as in cerebral listeriosis [26]. We propose that the tunnel sign, if seen, may be a specific finding for these three etiologic agents. The distinguishing features of sparganosis and listeriosis are outlined below.

**Sparganosis**
This is a rare zoonotic disease caused by the larvae of the parasite Spirometra Mansoni. The disease is reported chiefly in East Asia and associated with a history of ingestion of raw meats (e.g. frog, snake, fish) or contact with contaminated water [27,28]. Treatment is by surgical excision of the worm or, less effectively, with antiparasitic agents such as praziquantel [29]. The clinical course may be acute or chronic [7] and may also be seen in children [30]. Peripheral eosinophilia may be found but this is not a common feature [30].

Imaging appearances depend partially on the chronicity of disease as well as on the live status of the parasite [31]. Acutely, perilesional edema may be present with corresponding CT hypodensity and T2 hyperintensity, similar to the appearance of melioidosis and listeriosis. Apart from the tunnel sign mentioned above, beaded enhancement patterns and migration of the enhancement [7,30–33] may also be seen. The tunnel and migration signs are associated with live worms and portend a poorer prognosis [7].

It has also been reported that hyperdense components on unenhanced CT (HU 50-70) may correspond to a live parasite [33]. This finding is present in our presented case of cerebral melioidosis and cannot be used to distinguish the two.

Stigmata of chronicity may be present, which would not be seen in either Burkholderia or Listeria infections. For instance, punctate calcifications may be noted on CT, possibly representing degenerated larvae [31,33]. Cortical atrophy and ventricular dilatation may also be noted [30,33].

DWI iso-hypointensity may be seen, in contradistinction with the restricted diffusion of melioidosis or listeriosis abscesses [32,34,35]. MRS may show slightly elevated choline and significantly decreased NAA levels, similar to that of neoplasms or granulomas [34,35]. PWI may show the absence of significantly increased perfusion to the lesion and to the surrounding tissue [35].

**Listeriosis**
*Listeria Monocytogenes*, a gram-positive non-spore-forming bacillus with a predilection for the intracellular space, is the offending agent. Brain abscesses are a rare manifestation, with only 56 cases reported from 1968 to 2011 [36]. Main risk factors for infection include ingestion of contaminated food and impaired host immunity. Treatment with ampicillin-based regimens is most commonly employed, with alternative options in trimethoprim-sulfamethoxazole, gentamicin, linezolid and rifampicin. Mortality rates of 40% have been reported with *Listeria* brain abscesses, similar to that of melioidosis [36].

The imaging findings of cerebral listeriosis are almost identical to that of melioidosis, presenting with the typical features of a pyogenic abscess [36]. Tubular enhancement patterns reminiscent of the tunnel sign have also been demonstrated [26,37–40] and diffusion tensor imaging (DTI) studies have shown that the lesions correspond to white matter fiber tracts [37,38]. MRS findings are also as expected for pyogenic abscesses [36].

It has been suggested that the extent of involvement in *Listeria* infections is less extensive compared to that of melioidosis [38]. Involvement of contiguous extra-axial structures in the form of subgaleal abscesses and calvarial osteomyelitis appears to be less commonly reported compared to cerebral melioidosis.

**Pathological Considerations**
The tunnel sign as originally described for cerebral sparganosis corresponds to the inflammatory reaction around the parasite in situ [25]. *Listeria Monocytogenes* has been shown to spread intra-axonally in in-vitro studies [41] and its linear pattern of spread along white matter tracts accounts for its worm-like appearance. Although no DTI studies have been
performed for cerebral melioidosis, the bacterium has been shown to travel along axon conduits [42,43] and is expected to mimic the patterns of spread of Listeria. To the best of our knowledge, such tunnel-like patterns of enhancement have yet to be reported in other neurotropic organisms such as *Herpesviridae* and *Borrelia*.

**TEACHING POINT**

Tubular enhancement in a linear or curvilinear pattern – the tunnel sign – is an unusual appearance of brain abscesses. Its presence may be specific for infection by one of three etiologic agents - *Burkholderia pseudomallei*, *Spirometra Mansoni* or *Listeria Monocytogenes*.

**REFERENCES**


17. Kuan Y, How S, Ng T, Fauzi A. The man with the boggy head: cranial melioidosis. Singapore medical journal 2010; 51:e43-5. PMID: 20358143


Figure 1: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: A) Subtle erosion of the inner table of the right frontal bone is present (arrow) with associated lytic changes. B) On the initial CT, an ill-defined hypodensity is seen in the right frontal lobe with mass effect. Hyperdense foci are also seen within (HU 50, arrow, up to 0.7 x 0.5 cm in size), read as hemorrhagic stigmata, although this has been reported in sparganotic infections [33].
TECHNIQUE: Axial non-contrast CT, Siemens Sensation 64, 330 mAs, 120 kV, 3.00mm slice thickness

Figure 2: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: A) T2-weighted axial MRI. An irregular lesion with predominantly central hyperintensity and peripheral iso-/hypointensity (arrow, up to 4.6 x 2.6 cm in axial dimensions) is noted, surrounded by extensive edema. B) Gradient recalled echo sequence (GRE) shows susceptibility foci (arrow, up to 0.5 x 0.5 cm in size) corresponding to the hyperdense areas on the previous CT, likely representing hemorrhage.
TECHNIQUE: Siemens Aera 1.5T. Ax T2: TE 112, TR 4380, 5 mm slice thickness, non-contrast. Ax GRE: TE 22, TR 629, 5 mm slice thickness, non-contrast.
Figure 3: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: A and B) DWI and corresponding ADC map. The core of the lesion shows features of restricted diffusion (arrows).
TECHNIQUE: Siemens Aera 1.5T. Ax DWI/ADC: TE 97, TR 4400, 5 mm slice thickness, B = 0/1000.

Figure 4: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: A) Axial T1-weighted non-contrast. The lesion is predominantly hypointense (dashed arrow) with isointense components (solid arrow). B) Axial FLAIR post-contrast. A ring-enhancing cyst-like component is seen anteriorly (solid arrow, 2.1 x 1.9 cm) with perilesional edema. A smaller satellite lesion is also seen posteriorly (dashed arrow, 1.0 x 0.8 cm).
TECHNIQUE: Siemens Aera 1.5T. Ax VIBE: TE 4.77, TR 9.87, 3 mm slice thickness, non-contrast. Ax FLAIR +C: TE 84, TR 7000, 5 mm slice thickness, 14 mls gadoterate meglumine (Dotarem ®).
Figure 5: A 55-year-old gentleman with cerebral melioidosis

FINDINGS: Axial, coronal and sagittal post-contrast images showing a highly irregular, coalescing lesion with ring-enhancing as well as tubular, linear/curvilinear components, measuring up to 7.0 x 4.0 x 4.8 cm. Examples of the tunnel sign are shown (solid arrows). Anteriorly, there is associated pachymeningeal enhancement (dashed arrow) and involvement of the right frontal bone (curved arrow), suggesting contiguous spread of infection.

TECHNIQUE: Siemens Aera 1.5T. Ax VIBE+C: TE 4.77, TR 9.87, 3 mm slice thickness, 14 mls gadoterate meglumine (Dotarem®). Cor T1+C: TE 17, TR 663, 5 mm slice thickness, 14 mls gadoterate meglumine (Dotarem®). Sag T1+C: TE 17, TR 635, 5 mm slice thickness, 14 mls gadoterate meglumine (Dotarem®).
Figure 6: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: Abscess with hemorrhage bordered by granulation tissue.
TECHNIQUE: Low-magnification photomicrograph (Hematoxylin & eosin stain; 40x)

Figure 7: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: Abscess with adjacent gliotic brain parenchyma to the left.
TECHNIQUE: Intermediate-magnification photomicrograph (Hematoxylin & eosin stain; 100x)

Figure 8: A 55-year-old gentleman with cerebral melioidosis
FINDINGS: A) Immediate post-operative MRI. This axial T1-weighted post-contrast image shows the surgical cavity with residual abscesses (dashed arrow). Note the absence of significant enhancement along the margins of the cavity (solid arrow). B) Contrast-enhanced CT 3 weeks after the initial admission now shows irregular enhancement along the margins of the surgical cavity (solid arrow, measuring up to 4.9 x 3.5 cm). This was proven to be a recurrent abscess on re-open craniotomy.
TECHNIQUE: 8a) GE Signa HDxt 1.5T. Ax 3D BRAVO Post contrast: TE 3.736, TR 9.504, 3 mm slice thickness, 15 mls gadoterate meglumine (Dotarem®). 8b) Axial post-contrast CT, Philips iCT 256, 300 mAs, 120 kV, 3.00mm slice thickness, Omnipaque 350 50 mls.
Figure 9: A 55-year-old gentleman with cerebral melioidosis

FINDINGS: MRI 1 year later. A) Axial T2-weighted image shows complete resolution of the abscesses and encephalomalacia of the right frontal lobe (arrow). B) Axial T1-weighted post-contrast image demonstrating resolution of the previously seen enhancing lesions.

TECHNIQUE: GE Optima MR450w 1.5T. Ax T2 FRFSE Prop: TE 112.896, TR 5250.74, 5 mm slice thickness, non-contrast. Ax T1 3D BRAVO+C: TE 4.804, TR 11.588, 3 mm slice thickness, 14 mls gadoterate meglumine (Dotarem ®).

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Burkholderia Pseudomallei</th>
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<tbody>
<tr>
<td>Incidence</td>
<td>Globally – 165,000 cases per year (estimated)</td>
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<tr>
<td>Cerebral melioidosis 5% of cases</td>
<td></td>
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<tr>
<td>Gender Ratio</td>
<td>More commonly in males</td>
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<tr>
<td>Age Predilection</td>
<td>Predominantly 4th to 6th decades of life</td>
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<tr>
<td>Risk Factors</td>
<td>Environment – wet seasons, soil/water exposure</td>
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<tr>
<td></td>
<td>Host – diabetes mellitus, steroid use, chronic disease</td>
</tr>
<tr>
<td>Treatment</td>
<td>Ceftazidime-based antibiotic regimens</td>
</tr>
<tr>
<td>Prognosis</td>
<td>High mortality and morbidity rate</td>
</tr>
<tr>
<td></td>
<td>Mortality rate as high as 50% previously</td>
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</tbody>
</table>

Findings on Imaging

*General features:*
- Solitary/Multifocal
- Ring-enhancing
- Variety of shapes (e.g. cyst-like, linear, nodular, coalescing)
- Rapidly progressive
- Prominent extra-axial involvement

*CT:*
- Hypodense with mass effect

*MRI:*
- T2w: Hyperintense
- T1w: Hypointense
- DWI: Restricted diffusion
- MRS: Similar to pyogenic abscesses (lipid, lactate and amino acid peaks)

Table 1: Summary of demographic and clinical features of melioidosis.
Neuroradiology: The Tunnel Sign Revisited: A Novel Observation of Cerebral Melioidosis Mimicking Sparganosis

<table>
<thead>
<tr>
<th>General Features/Contrast Enhancement Patterns</th>
<th>Melioidosis</th>
<th>Sparganosis</th>
<th>Listeriosis</th>
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<tbody>
<tr>
<td>• Solitary/Multifocal</td>
<td>• Similar to melioidosis</td>
<td>• Similar to melioidosis, but less prominent extra-axial involvement</td>
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<tr>
<td>• Ring-enhancing</td>
<td>• Migration of enhancement</td>
<td></td>
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<tr>
<td>• Variety of shapes (e.g. cyst-like, linear, nodular, coalescing)</td>
<td>• Cortical atrophy and volume loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Rapidly progressive</td>
<td>• Prominent extra-axial involvement</td>
<td></td>
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</tbody>
</table>

| CT                                             | • Hypodense with mass effect                  | • Hypodense with mass effect                  | • Hypodense with mass effect                  |

| MRI (T1/T2/DWI)                                | • T2w: Hyperintense                           | • T2w: Hyperintense                           | • T2w: Hyperintense                           |
|                                                | • T1w: Hypointense                            | • T1w: Hypointense                            | • T1w: Hypointense                            |
|                                                | • DWI: Restricted diffusion                   | • DWI: Iso-/hypointensity                     | • DWI: Restricted diffusion                   |

| PWI                                            | • Not reported. Likely to have normal rCBV in the enhancing rim | • Normal rCBV in lesion and surrounding tissue | • Not reported. Likely to have normal rCBV in the enhancing rim |

| MRS                                            | • Similar to pyogenic abscesses (lipid, lactate and amino acid peaks) | • Slightly elevated choline and decreased NAA | • Similar to pyogenic abscesses (lipid, lactate and amino acid peaks) |

Table 2: Differential diagnosis of cerebral melioidosis. The key distinguishing features are highlighted in bold.

ABBREVIATIONS

ADC = apparent diffusion coefficient  
CT = computed tomography  
DWI = diffusion weighted imaging  
DTI = diffusion tensor imaging  
FLAIR = fluid attenuation inversion recovery  
FRFSE = fast recovery fast spin echo  
GRE = gradient recalled echo  
IV = intravenous  
L = liter  
MRI = magnetic resonance imaging  
MRS = magnetic resonance spectroscopy  
NAA = N-acetyl-aspartate  
PWI = perfusion weight imaging  
rCBV = relative cerebral blood volume  
VIBE = volumetric interpolated breath-hold examination

KEYWORDS

Tunnel Sign; Cerebral; Melioidosis; Sparganosis; Listeria; MRI

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