You miss, I hit: Characteristic Neuroimaging Findings in Neuromelioidosis

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Abstract

Infection due to *Burkholderia pseudomallei* is a tropical disease that occurs in the monsoon season. Central nervous system involvement is not uncommon. The characteristic imaging feature of Magnetic Resonance Imaging (MRI) helps in narrowing down the differential diagnosis which is very essential as the disease is curable. We describe three cases of neuromelioidosis exhibiting a variety of clinical presentations ranging from mild to septic shock and imaging patterns can provide the initial clue to initiate the early treatment. Culture of the organism either from the body fluids or tissue biopsy is necessary to prove the condition which in turn greatly influences disease management.

Keywords: Neuromeliodosis · Neuro infection · Tropical infection

Introduction

Melioidosis is an infectious disease caused by a facultative, aerobic, motile, soil-dwelling, gram-negative bacteria named *Burkholderia pseudomallei*. It is endemic in Southeast Asia and northern Australia. In India, it is more prevalent in coastal areas. It can present in localized form or dissemination affecting Central Nervous System (CNS), lungs, liver, spleen, skin, genitourinary and musculoskeletal systems [1]. The CNS involvement of the disease is termed Neuromelioidosis. The infection spreads through inhalation, cutaneous incursion, or aspiration of the causative agent, most often during the rainy season, and is commonly seen in patients with comorbidities like diabetes mellitus, renal failure, immunosuppression, and alcohol abuse [2]. Imaging presentation varies from person to person depending on the immunity. Diagnosing this condition needs a high index of suspicion. Neuromelioidosis can manifest as a focal or diffuse dural thickening, cerebritis, encephalitis, micro or macro-abscesses, cranial nerve involvement, and dural venous sinus thrombosis. The extracranial presentation may be in the form of calvarial osteomyelitis, scalp edema or even discharging sinus or otomastoidits [3]. We present three such cases, in one of which a biopsy was necessary to confirm the diagnosis. Brain biopsy may be of great help in diagnosing this condition if clinical and radiological findings are equivocal or not conclusive [4].

Case Description

Patient 1

A 32-year-old young man presented with left-sided weakness and high-grade fever for 5 days. MRI brain was advised which showed multiple rings enhancing lesions in the right frontal lobe showing diffusion restriction, suggesting abscesses (Figures 1A-1C). Right-sided craniotomy procedure was performed and the abscess was drained. Culture from the pus showed growth of *B.Pseudomallei*. Appropriate antibiotics were given during the hospital stay and a long course of antibiotics for 6 weeks was prescribed at the time of discharge. Follow-up MRI after one month showed complete regression of the lesion. However, despite repeated instructions for taking antibiotics, the patient stopped the prescribed course. Following this, he presented with severe headache, left-sided weakness, and slurring of speech. Lumbar puncture was performed as an initial investigation which was inconclusive. Hence, MRI brain was advised. It showed irregular infiltrating enhancing linear tracts in the right temporal and parietal white matter extending to the corpus callosum (Figures 1D-1F).

There was no cranial nerve involvement or pachymeningeal thickening. A brain biopsy of the lesion was recommended as other means of diagnosing the condition were not possible. Right fronto-temporo-parietal craniotomy and neuronavigation guided stereotactic biopsy of the enhancing linear white matter tract lesions was done and a specimen was sent for culture which again proved infection by the same organism. He was again started on long-term antibiotics to which he responded dramatically. He has completely recovered and has been on regular follow up.

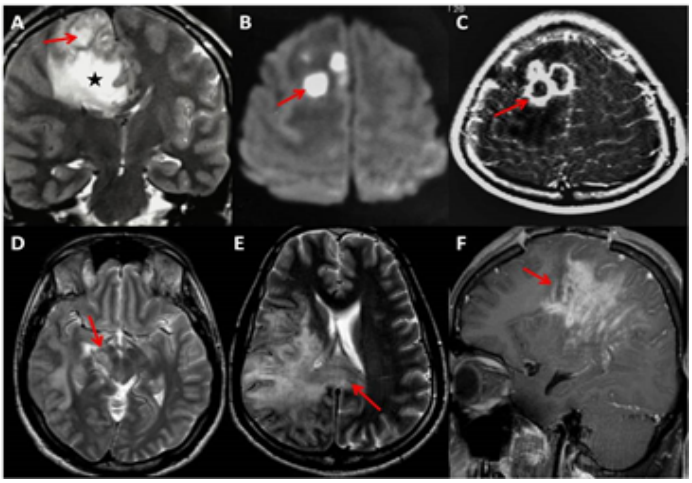

Figure 1. (1A) T2 weighted coronal section through the brain shows well-defined hyperintense lesion with a hypointense rim in the right frontal lobe (arrow) and associated vasogenic edema (asterisk). (1B) Diffusion-weighted axial section of the brain shows bright lesions in the right frontal lobe (arrow) (1C) Post-contrast T1 weighted axial section through the brain shows ring-enhancing lesions in the right frontal lobe with non-enhancing perilesional edema suggesting abscess (arrow). (1D) T2 weighted axial section of the brain shows ill-defined hyperintensity in the right cerebral peduncle involving the corticospinal tract (arrow). (1E) T2 weighted axial section through the brain shows the involvement of splenium of corpus callosum (arrow). (1F) Post-contrast T1 weighted sagittal section through the brain shows tunnel-like enhancement along the cortico-spinal tract (arrow).

Patient 2

A 52-year-old gentleman with a recent history of travel presented with left-sided trigeminal neuralgia with symptoms of pain and tingling sensation in the left cheek for 10 days. There was a history of fever for three days at the onset which responded to antipyretics. He was not a known diabetic or have any comorbidities. MRI brain was advised to assess the cause of trigeminal neuralgia. It showed subpial small irregular ring-enhancing lesions in the brainstem on the left side along the edema along the course of the corticospinal tract. Thickening and enhancement of the left trigeminal nerve was noted along with the involvement of trigeminal nerve fasciculus at the level of the middle cerebellar peduncle (Figures 2A-2H).

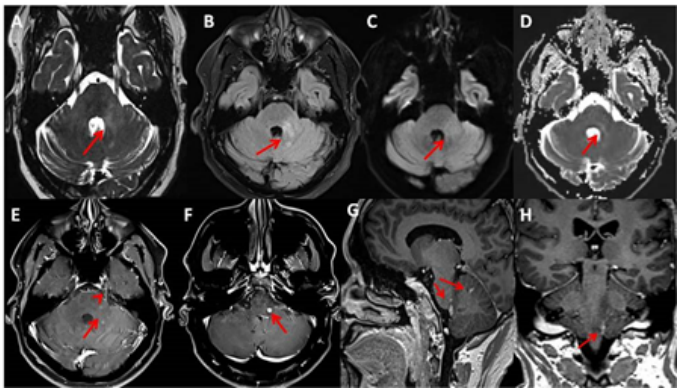

Figure 2. (2A & 2B) FIESTA and FLAIR axial section images through the brain show ill-defined patchy hyperintensities in the left middle cerebellar peduncle respectively (arrows). (2C & 2D) Axial section DWI and apparent diffusion coefficient images in the same section show no obvious diffusion restriction. (2E-2H) Axial, sagittal, and coronal post-contrast T1 weighted images through the brain show thickening and enhancement of the left trigeminal nerve (arrowhead), patchy areas of enhancing foci in the left middle cerebellar and inferior cerebellar peduncles with involvement of trigeminal nerve nucleus (arrows).

With a high degree of suspicion of neuromelioidosis, Cerebrospinal Fluid (CSF) analysis was recommended. It showed normal glucose and protein levels. CSF PCR confirmed the diagnosis. Serum angiotensin-converting enzyme level was normal which was done to rule out sarcoidosis. Serum glucose continued to be normal. Liver and renal function tests were normal. Screening of the liver and spleen by ultrasound to rule out any abscess showed no abnormality. He was treated with broad-spectrum antibiotics following 6 weeks of antibiotics at the time of discharge. Repeat MRI following the treatment showed near complete resolution of the lesions (Figures 3A-3H). The patient completely recovered from the disease and is on follow-up.

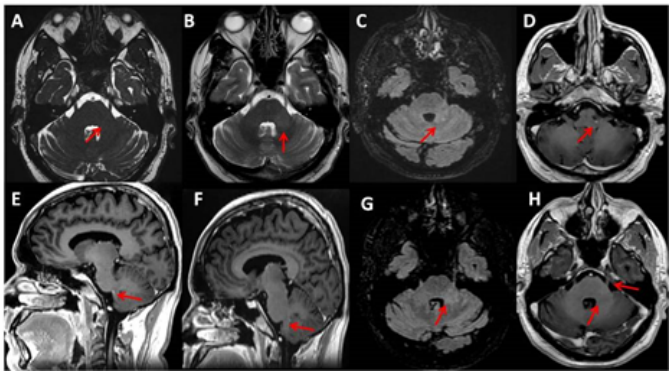

Figure 3. Follow-up MRI after one month (3A-3C) FIESTA and T2 weighted images through the brain show resolving hyperintensity in the left middle cerebellar peduncle (arrow) respectively (3D & 3E) axial and sagittal section of the brain show reduction in the size of the enhancing focus in left inferior cerebellar peduncle (arrow) (3F-3H) Follow-up MRI after 2 months show significant resolution of the left middle and inferior cerebellar peduncle lesions and normal left trigeminal nerve (arrow).

Patient 3

A 41-year-old man came with a history of fever with chills for 20 days, headache for 15 days, and sudden onset of left-sided weakness for seven days. He was admitted to some other hospital for these symptoms. In suspicion of tubercular meningitis, he was started on antitubercular treatment along with steroids for which he did not show any improvement. He was shifted to our hospital which is a tertiary care center for further management. No significant family or history. No history of any travel in the recent past. On examination, he was conscious and alert, obeying commands, with no speech output, dolls eye movement was present, and pupils were reactive. Left upper and lower limb power was 2/5 and right upper and lower limb power was 4/5 respectively.

MRI was advised which showed T2/ Fluid Attenuated Inversion Recovery (FLAIR) intensity involving the posterior limb of the right internal capsule, corona radiata, mid-brain on the right side, right middle cerebellar peduncle, cortex, subcortical white matter of right superior and middle frontal gyri, precentral gyrus with multiple ill-defined coalescent nodular enhancement and mild diffusion restriction with tunneling with a possible diagnosis of neuromelioidosis (Figures 4A-4H).

CSF analysis showed slightly raised glucose and protein levels. Mycobacterium tuberculosis complex was not detected on GeneXpert. Gram stain showed no bacteria, few pus cells, no fungal elements filaments, negative for acid fast bacilli and normal adenosine deaminase. Antinuclear Antibody Profile, C-Antineutrophil Cytoplasmic Antibodies (ANCA) and P-ANCA was normal. Biopsy was further advised. A stereotactic biopsy with CRW frame for the right thalamo-peduncular lesion was performed and sent for histopathology study. The culture showed growth of The patient withstood the procedure well. The post-operative period was uneventful. The patient was treated with antibiotics Injection Meropenem and septran DS, antiepileptics, antihypertensives, antacids, analgesics, antiemetics, and other supportive measures. The patient is discharged in stable condition with the advice of Injection Meropenem and septran for 6 weeks and other medications as mentioned above.

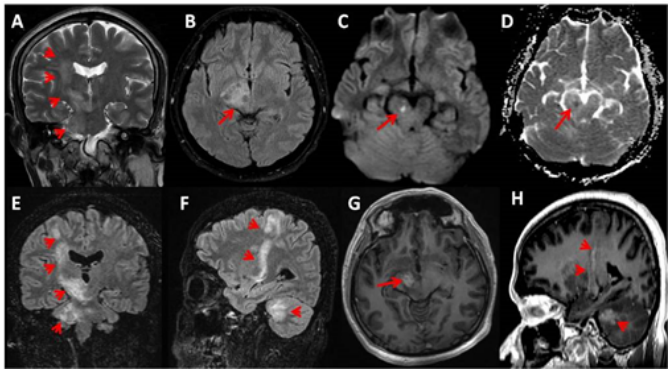

Figure 4. (4A) T2 weighted coronal section of the brain shows hyperintensity along the right corticospinal tract (short arrows). (4B) FLAIR axial image of the brain shows bulky and hyperintense right cerebral peduncle (arrow). (4C & 4D) DWI and ADC images axial section through the brain show patchy areas of restricted diffusion in right cerebral peduncle (arrows). (4E & 4F) Coronal and Sagittal FLAIR images through the brain show hyperintensity along the right corticospinal tract and middle cerebellar peduncle (short arrows) respectively depicting tunnel sign. (4G & 4H) Post-contrast T1 weighted axial and sagittal images show enhancing foci in the right cerebral peduncle (arrow) and track-like enhancement along the corticospinal tract (short arrows) respectively.

Discussion

Melioidosis occurs predominantly in a wet environment and has a close association with rainfall. Moist clay soil and pooled surface water promote the growth of the organism. The major mode of spread of infection is through inoculation of B.Pseudomaleii through cut wounds. Another common route of spread is through inhalation/ aspiration, especially during tropical monsoonal storms and rainfall [5,6]. Ingestion of water contaminated with the organisms also causes the disease. Information of the history of travel to the places where the organisms are more prevalent is very useful and essential in diagnosing the condition. The disease also has a predilection to individuals with diabetes, renal disorders, immunosuppression, alcoholism, and thalassemia due to poor cell-mediated immune response resulting in defective neutrophil function. The spread of infection into the central nervous system is mainly through the hematogenous route but can also occur through the nasal route along the olfactory and trigeminal nerves [7]. Mortality of more than 20% of patients has been reported with neuromelioidosis [8]. B. Pseudomallei may remain latent and can get reactivated later in life [9].

Patients with neuromelioidosis present with fever, headache, seizure, cognitive dysfunction, cranial nerve palsy including neuralgia, and focal neurological deficit depending on the site of involvement. Trigeminal neuralgia is common among all other neuralgias. It may also manifest as having stroke-like symptoms or septic shock [10].

The most common neuroimaging presentation is the formation of tiny cerebral abscesses often involving frontal and parietal lobes. These Microabscesses tend to merge and tend to tunnel or track along the white matter tracts. These will have surrounding vasogenic edema which may cause mass effects. They appear hypodense on CT and show peripheral enhancement on contrast CT. MRI shows central diffusion restriction of the abscess with ring-like enhancement. There may be marco-abscess with or without conglomeration of the lesions. The most characteristic imaging finding in neuromelioidosis is the involvement of white matter tracks including corpus callosum,cortico-spinal tracts, and cerebellar peduncles [7, 8, 11]. The involvement of the corticospinal tract with linear tract-like enhancement is called Tunnel sign (Figure 5) [12].

The infection may initially present with abscess formation or cranial nerve involvement and then may involve the cortico-spinal tract on progression.

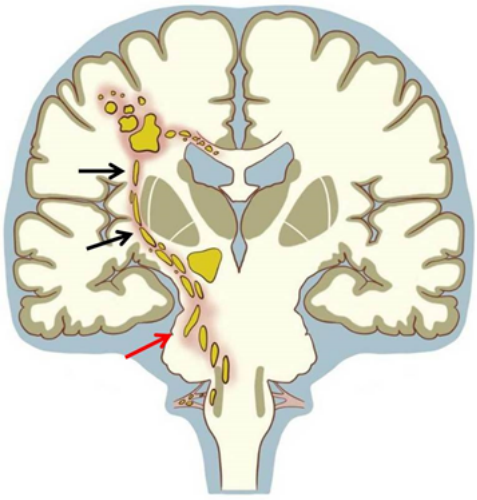

Figure 5. Coronal section of the brain showing involvement of cortico-spinal tract (black arrow) and trigeminal nerve nucleus (red arrow).

Involvement of the cortico-spinal tract may result in limb paresis. Cranial nerve palsy or neuralgia in neuromelioidosis is not uncommon. Involvement of fifth, third, sixth and seventh are common. Thickening and enhancement of the nerve with or without associated adjacent meningeal thickening may be seen on imaging. The cranial nerve nucleus may be involved. Cranial nerve involvement and enhancement are better appreciated on heavily T2-weighted sequences like 3D Fast Imaging Employing Steady-State Acquisition (FIESTA) [9]. Patients may complain of neuralgia related to the corresponding cranial nerve. MR spectroscopy shows findings similar to a bacterial abscess which includes, lipid/ lactate and amino acid peaks with low N-acetylaspartate and choline peaks. It can even present as encephalitis showing enhancement without any abscess formation. Mere leptomeningeal thickening or enhancement is uncommon. All these findings reverse following appropriate treatment.

The extradural disease may be seen in the form of collection. Cases of scalp, orbital, and parotid abscess due to B.Pseudomallei have been reported. Mastoiditis was associated in one of our cases. Spinal involvement is seen as longitudinally extensive transverse myelitis like a picture. Screening of the chest by X-ray and abdominal viscera by ultrasound are done as imaging workup to look for systemic disease.

Neuromelioidosis should be differentiated from Tuberculosis (TB), neurobehcet's disease, spargonisis and listeriorsis. Microabscesses with conglomeration show similar imaging findings to TB. However, TB shows more predilection to basal cisternal spaces and in neuromelioidosis, white matter tract and cranial nerve involvement is more common than in tuberculosis [13]. Another important disease that mimics neuromelioidosis is neurobehcets disease, a multisystem vasculitic condition. Cortico-spinal tract or brain stem involvement is very commonly seen in neurobehcets disease [14]. Presence of a history of fever and recent travel favor neuromelioidosis. Behçet's disease is associated with HLA-B51 and HLA-B5. The radiological finding of tunnel signs is also seen in spargonisis and listeriosis. Spargonisis is a parasitic infection that also shows a typical imaging feature named Tunnel sign indicating the migration of the live worm. CT may demonstrate hyperdense components corresponding to live parasites and calcifications. In listeriosis, the involvement of the neuroparenchyma or extra-axial space is not extensive as compared to melioidosis [11].

CSF analysis shows normal glucose, high protein, lymphocytosis. CSF PCR is very helpful awaiting biopsy to initiate early treatment. Culture from CSF, blood, pus, or tissue is necessary to prove B.Pseudomaleii infection. A blood culture may not grow organisms if the patient is already on antibiotics. In such cases, culture from tissue biopsy samples of the diseased brain parenchyma is required to confirm the diagnosis as seen in our patient discussed in case 3. This is done following navigation protocol using MRI. Treatment of choice in neuromelioidosisis antibiotics along with supportive therapy. Antibiotics used to treat the condition include meropenem, trimethoprim-sulphamethoxazone, and doxycycline. In case of a cerebral abscess, surgical drainage of the abscess may be required.

Conclusion

A recent history of travel, seasonal, involvement of cranial nerve, abscess, and tunnel sign on imaging warrant a high degree of suspicion for neuromelioidosis. Characteristic imaging findings should be promptly recognized in the background of a typical clinical profile to avoid delay in the initiation of appropriate treatment. Diagnosis of the disease is important before initiating any treatment as neuromelioidosis is an emerging, under-diagnosed and treatable disease. MRI helps in diagnosing the condition as well as for follow-up to assess the progression or regression of the disease.

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