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Holmes Tremor Following Midbrain Abscess in an Immunocompromised Patient: A Case Report

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Abstract:

Holmes tremor (HT) is a rare occurrence due to insults located at the midbrain. We are reporting a case of HT, which occurred in a retroviral disease patient who presented with a 1-week history of fever associated with third and fourth cranial nerve palsy. Magnetic resonance imaging of the brain revealed a midbrain lesion favoring abscess with blood investigations revealed positive serology for toxoplasmosis. The patient was started on toxoplasmosis treatment coupled with a six-week course of antibiotics. Following one-month post-treatment, the patient complained of a tremor that characteristics of HT with repeated computed tomography brain revealed resolving brain abscess. This case highlights an important reminder of potential neurological sequelae due to midbrain abscess and the importance of recognition of HT. The management of HT is challenging, involving the initial use of dopaminergic agonists with a potential role of deep brain stimulation in refractory cases.

Key Words:

Brain abscess, deep brain stimulation, dopamine agonists, immunocompromised host, tremor

Key Message:

This case highlights an important reminder of potential neurological sequelae of Holmes tremor in a patient with midbrain abscess and challenges in management.

Gordon Holmes first described Holmes tremor (HT) in 1904.[1] It was previously labelled by various names, including rubral tremor, midbrain tremor, thalamic tremor, and Benedict's tremor. However, a nomenclature based on localization was later found to be misleading as some cases are being reported with lesions outside the typical areas.[2,3]

HT is described as a low frequency (less than 4.5 Hz), irregular tremor which combined resting, kinetic, and postural components.[4] HT may be accompanied by various other neurologic symptoms in varying degrees, such as hemiparesis, ataxia, bradykinesia, dystonia, dysarthria, cranial nerve involvement, rigidity, and even psychiatric disorder.[4] In addition, the tremor can be a combination of Parkinson's Disease and cerebellar tremor.[5] There is also a time gap of 1–24 months, which typically existed between lesion identification or insult and tremor manifestations.[2,6]

We are reporting a case of a newly diagnosed retroviral disease (RVD) patient with midbrain abscess who presented with third and fourth cranial nerve palsies, which subsequently developed typical HT one month after admission. This case highlights an important reminder and recognition of HT in RVD patients with brain abscesses.

Case History

Our case is a 41-year-old lady with no known medical illness, presented with a fever of one week duration, giddiness, and right-sided diplopia. Neurological examination shows right sided third and fourth cranial nerve palsy with normal cerebellar function without evidence of unilateral hemiparesis. Other systems were unremarkable. She was a divorcee and works as a home maker.

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On presentation, her white cell count was 3.8 x10^9/L, predominantly neutrophils with low lymphocytes count and elevated C- reactive protein (CRP). Her blood cultures grew Flavobacterium indolences (query significance), and her serology Toxoplasma IgG was reactive with a titre of 1 in 160. The cerebral spinal fluid (CSF) examination was unremarkable with CSF protein and sugar values of 217 mg/L (3.8 mmol/L), respectively. No growth was obtained from her CSF, with negative culture for Mycobacterium tuberculosis, fungal, cryptococcal and cytomegalovirus. Her RVD screen returned positive for human immunodeficiency virus (HIV) with a CD4 count of 7 cells/μL.

Initial contrasted computed tomography (CT) brain showed a faint rim enhancing midbrain lesion [Figure 1a]. On magnetic resonance imaging brain, the characteristic of the midbrain lesion was in favor of an abscess with restricted diffusion [Figure 2a, b], smooth rim enhancement on gadolinium-enhanced T1-weighted MR images [Figure 3a], and low signal rim intensity with profound vasogenic edema on T2-weighted images [Figure 3b].

Diagnosis of midbrain abscess secondary to toxoplasmosis in newly diagnosed RVD patient was made. Antitoxoplasmosis treatment was started with both pyrimethamine and clindamycin during the intensive and maintenance phases. Also, she was given an empiric 6-week treatment course of intravenous ceftriaxone and metronidazole covering for the bacterial cause of the abscess. Furthermore, highly active antiretroviral therapy was started after completing the one-month anti-toxoplasmosis treatment with oral tenofovir-emtricitabine and efavirenz.

She made a good recovery in the ward with no more fever, headache, and improvement of diplopia. However, after 1 month of admission, she developed a persistent unilateral hyperkinetic tremor of the left upper limb, which subsided during sleep. The tremor appeared to be of low frequency and high amplitude, which persist at rest, postural, and movement. There was no rigidity, bradykinesia, or cerebellar signs. Her third-nerve palsy persisted, with an improvement of fourth-cranial nerve palsy. Other cranial nerve functions are normal. Repeated contrasted CT brain done showed that the previously seen midbrain lesion was significantly smaller [Figure 1b]. Repeated blood parameters showed improvement in CRP and no new growth on blood culture with a reducing trend of toxoplasmosis titer (1 in 4). Diagnosis of HT was made secondary to midbrain abscess.

She was started on oral levodopa-carbidopa 120/25 mg TDS, which increased to 250/25 mg TDS 2 weeks later. During follow-up, after 1 month of levodopa-carbidopa 250/25 mg TDS, she showed only mild improvement in her symptoms, but she able to continue with daily activities. However, her third nerve palsy persisted. She was not keen on a trial of other medications for the tremor.

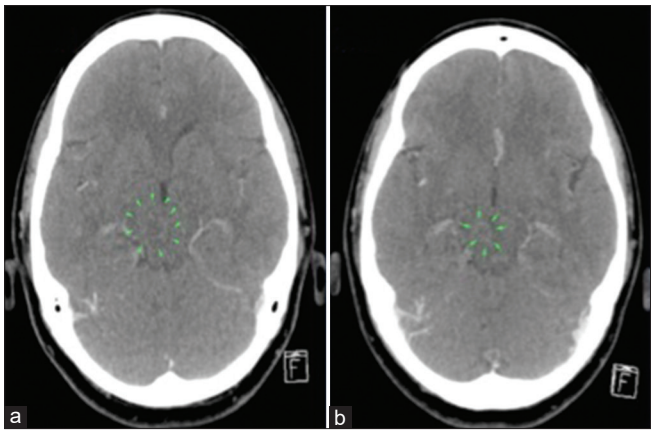

Figure 1: Axial contrasted CT brain image done during early admission showing faint rim enhancing midbrain lesion (a). Following 1-month treatment, repeated axial-contrasted CT brain image showing significant size reduction (b)

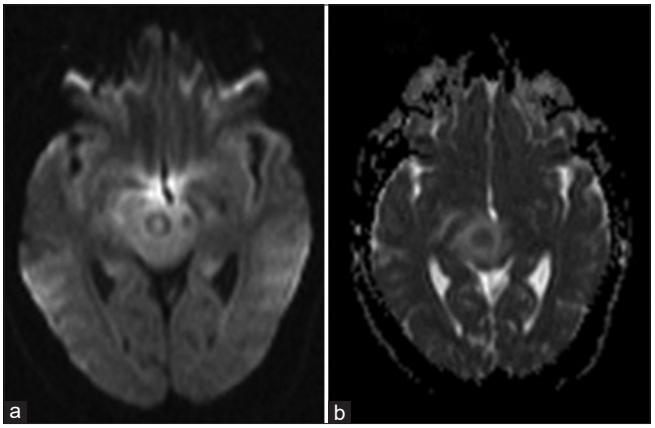

Figure 2: Central portion of the midbrain lesion with restricted diffusion in favor of an abscess as evident by the central high signal intensity on diffusion-weighted imaging (DWI) (a) and central low signal intensity on apparent diffusion coefficient (ADC) (b)

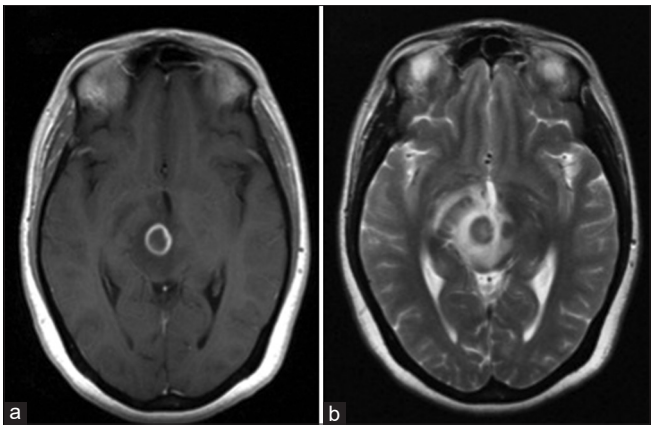

Figure 3: Peripheral (rim) portion of midbrain lesion characteristic of an abscess with smooth rim enhancement on gadolinium enhancement T1-weighted image (a) and low signal intensity rim with associated profound edema on T2-weighted image (b)

Discussion

Our patient developed the symptoms suggestive of left-sided-HT 1 month after being diagnosed with abscesses at the right midbrain. Lesions in this area resulted in third and fourth cranial nerve palsies, which appeared early in presentation and subsequently led to HT development.

It is suggested that based on clinical correlation and imaging studies, the pathogenesis of HT includes the combination of lesions at the nigrostriatal pathway and cerebello-thalamic pathways.[3,6] Furthermore, dynamic uptake studies with positron emission tomography and single-photon emission computerized tomography (SPECT) scan suggest that pathogenicity in HT seems to originate from a presynaptic dopaminergic deficit as objectified by a severe unilateral decrease in radiotracer uptake.[2,3] However, another retrospective study suggests a heterogenicity in the pathogenesis of HT, where their group of patients did not show any significant interhemispheric radiotracer uptake, which might explain poor response to levodopa in a portion of patients in their study (two out of six).[3]

Etiologies of HT are myriad, including hemorrhage, ischemic stroke, infections, vascular malformations, tumors, trauma, and demyelinating disease.[3,6] There are also reports of patients with HT who had preexisting spinocerebellar ataxia and later developed nigrostriatal deficit.[7] HT also reported in a patient with existing Parkinson's Disease developed HT after cerebellar infarct.[8] The most common lesion is located at the thalamus, followed by the midbrain. Other structures which may be involved include pons, medulla, and cerebellum, with a unique combination for each patient.[3,6]

Treatment of HT is challenging with variable results. Levodopa should be tried in all patients, and it was suggested that treatment response could be predicted by a dopaminergic deficit on DaTSCAN SPECT.[2,3,6] Alternative medications include dopaminergic agonists, anticholinergic drugs, clonazepam, levetiracetam, topiramate, and carbamazepine, although responses are limited and variable.[3,6] Deep brain stimulation (DBS) of the ventralis intermedius (VIM) or thalamotomy may provide a good response in refractory HT.[6] Moreover, case reports showed that DBS was also done at VIM in combination with globus pallidus internus, subthalamic nucleus, ventralis oralis anterior, and ventralis oralis posterior, successively.[6]

Conclusion

HT is a very rare occurrence. To our awareness, there was no epidemiologic study done except for small-scale descriptive studies of retrospective case reports. The most frequent lesions are located at the thalamus and brain stem, and pathogenesis may involve a combination of the nigrostriatal pathway and cerebello-thalamic pathways insults such as brain abscess in our case. Treatment is shown to be challenging with variable results with a trial of levodopa in all patients with a potential role of DBS in refractory HT.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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