

Parkinsonism due to isolated substantia nigra involvement in probable Japanese encephalitis

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Abstract

Parkinsonism due to an isolated lesion of the substantia nigra following a febrile illness is a rare entity. Anecdotal reports in the literature implicate substantia nigra as peculiarly susceptible to flaviviruses. Here we report a case of isolated substantia nigra involvement in a probable Japanese encephalitis patient who presented with post-encephalitic parkinsonism.

INTRODUCTION

Infective encephalitis is common in developing countries including the Indian subcontinent. Isolated substantia nigra involvement is described in St.Louis encephalitis and Japanese encephalitis.¹⁻⁴ We report a patient who presented with parkinsonian features following a febrile illness and had isolated substantia nigra involvement on neuroimaging.

CASE REPORT

A 22 year old man from an area where Japanese encephalitis is endemic was admitted to our hospital with a one month history of intermittent fever, headache and vomiting. One week after the onset of fever he developed progressive stiffness of all four limbs that made him bedbound. This was associated with decreased volume of speech, inability to open the mouth and tremulousness in all four extremities, the jaw and the perioral region. His medical history was unremarkable. The neurological examination revealed masking of the face, reduced blink rate and hypophonia. His vertical eye movements were restricted. Marked rigidity and resting tremor were present in all four limbs. Tremor of the tongue and peri-oral region subsided during sleep. The motor and sensory examinations were normal. Slit lamp examination for Kayser-Fleisher (KF) ring was negative. The remaining systemic examination was normal. Laboratory examination showed mild anemia, polymorphonuclear pleocytosis with normal erythrocyte sedimentation rate (ESR), serum

transaminases, blood sugar, urea and creatinine levels were within normal range. Malarial parasite and Widal test for typhoid was negative. Serological testing for Hepatitis B surface antigen, Human immunodeficiency virus (HIV), West Nile, dengue, varicella zoster and measles was negative. Serum Immunoglobulin M (IgM) antibody and Haemagglutination Inhibition (HAI) titre against Japanese encephalitis was negative. Cerebrospinal fluid (CSF) examination revealed protein of 60 mg/dl, sugar of 3.6 mmol/L and 50 cells per μ L (all lymphocytes). CSF Gram's stain, acid fast bacilli (AFB), India ink preparation and CSF IgM antibody against Japanese encephalitis was negative. Electromyography and nerve conduction velocity were within normal limits. Computerised tomography (CT) of the brain was normal. Brain magnetic resonance imaging (MRI) showed symmetric lesions in the midbrain confined to substantia nigra. The lesions were hyperintense on T2 and hypointense on T1 weighted images. There was no lesion elsewhere in the brain including thalamus. There was no restriction on diffusion weighted images nor enhancement on gadolinium contrast injection (Figure 1). Technetium-ethyl cysteinate dimmer (99m Tc-ECD) brain Single Photon Emission Computed Tomography (SPECT) study of brain showed normal perfusion including midbrain area.

A diagnosis of post-encephalitic parkinsonism caused probably by Japanese encephalitis virus was made based on the clinical picture and neuroimaging finding. The patient was treated with the dopamine agonist ropinirole 0.5 mg

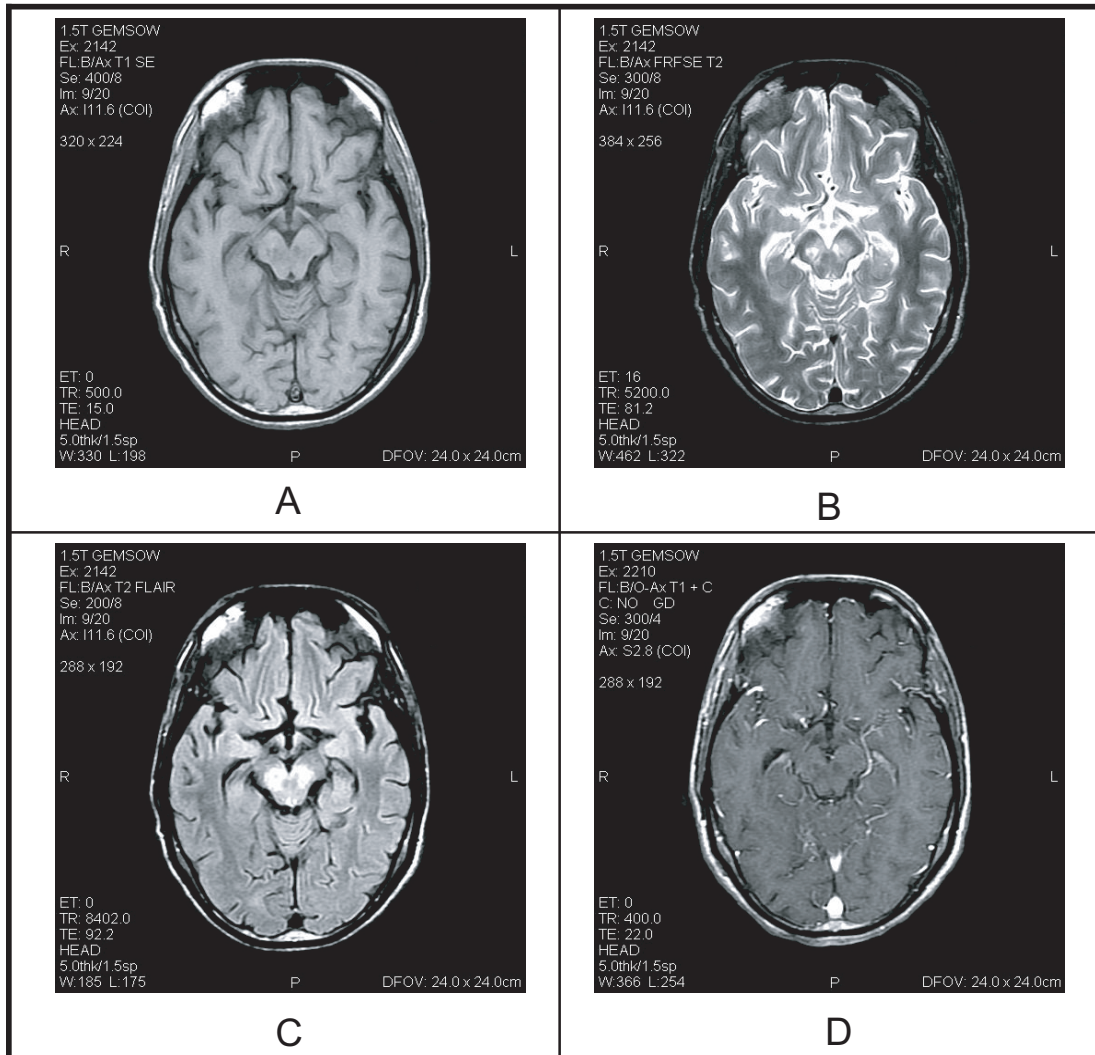


Figure 1: **A.** MRI T1 weighted image shows bilateral hypointensities in substantia nigra of midbrain. **B.** T2 weighted image shows bilateral hyperintensities in substantia nigra of midbrain. **C.** T2 Flair image shows bilateral hyperintensities in substantia nigra of midbrain. **D.** T1 weighted image with contrast shows no contrast enhancement.

thrice a day (TDS). He showed marked clinical improvement in speech, decreased tremulousness and rigidity. He was able to walk with minimal support within one month of treatment. Repeat brain MRI 2 months after the onset of illness showed diminution in the lesion size on T2 weighted images. On follow-up at 6 months, the patient was independent in all the activities of daily living. Parkinsonian features (mask like facies, reduced blink rate of 3 per minute, a short shuffling gait with minimal stooped posture, cogwheel rigidity in upper limbs and resting tremors) along with emotional incontinence were the positive findings on examination.

DISCUSSION

Japanese encephalitis, a mosquito borne infection of central nervous system is the leading cause of viral encephalitis in South East Asia.^{5,6} These infections may lead to residual sequelae in 30-60% of cases in which various types of movement disorders are described. Parkinsonism and dystonia are two major movement disorders described as sequelae of Japanese encephalitis.⁷ On MRI, thalamus, basal ganglia and brainstem involvement are seen in 88%, 41% and 37% respectively.⁸ SPECT studies show initial hyperperfusion in the acute encephalitic phase

in the thalamus and putamen followed by hypoperfusion of the thalamus, frontal cortex and the lentiform area in the postencephalitic phase.⁹ Isolated lesion of the substantia nigra following central nervous system infection are unusual, although there have been case reports of isolated substantia nigra involvement on T2 weighted MRI caused by arboviruses in India^{1,2,3} and St. Louis virus in Texas.⁴

Here we report a patient with an isolated lesion in the substantia nigra on MRI. In a patient from an endemic area for Japanese encephalitis in the monsoon period, febrile illness followed by parkinsonian features can be suggestive of Japanese encephalitis. In the case we present, viral diseases that have been associated with parkinsonian features such as measles, varicella zoster, polio and HIV were ruled out by appropriate tests. Serum and CSF was tested for the common arboviral infections; Japanese encephalitis, West Nile and dengue virus, all of which were negative. Despite this, we still suggest this case to be from underlying Japanese encephalitis as sensitivity of serological tests is between 70-75%.^{10,11} It is important to note that the sensitivity of these tests decreases with delay in getting the tests done.¹² SPECT study of the patient showed no perfusion defect in the substantia nigra pars compacta. This may be one of the indicators of early improvement with therapy as was evident in our patient.

Our patient had marked clinical improvement though mild rigidity, monotonous voice and residual bilateral substantia nigra lesions on MRI persisted after 2 month of illness. In one study, 2 out of 15 patients of Japanese encephalitis with substantia nigra involvement, when followed for 3 to 5 years had persistent parkinsonism along with associated residual lesions in the substantia nigra with negative Japanese encephalitis antigen and antibody in CSF.² The loss of dopaminergic neurons was possibly considerable with the surviving dopaminergic nigral neurons being unable to compensate sufficiently.

In summary, patients presenting with features of encephalitis followed by parkinsonian features who show isolated T2 weighted hyperintensity of the substantia nigra should be evaluated for Japanese encephalitis. In patients who present later in the course of illness, the tests for Japanese encephalitis may be negative as the sensitivity of the tests decreases with time.

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