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A report of 4 patients with Nipah encephalitis from Rajbari district, Bangladesh in the January 2004 outbreak

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Abstract

This is a report of 4 patients with Nipah encephalitis during the January outbreak in Bangladesh. The patients were from Rajbari district. The age was from 13 years to 35 years. Two of the patients were housewives and the other 2 were brothers. The patients presented with acute onset of fever, headache impaired consciousness, and seizure in one patient. On examination, all the patients were comatosed with hyporeflexia and hypotonia were seen in 3 patients. Cerebrospinal fluid was abnormal in one patient. MR imaging of brain showed confluent high signal lesions involving both gray and white matter. IgM and IgG antibodies to Nipah virus were positive in the serum and cerebrospinal fluid of all the 4 patients. There was one death. Two patients recovered with residual neurological signs, and the other patient recovered completely.

In *conclusion*, Nipah virus causes a fatal encephalitis in Bangladesh with MR imaging features different from the Malaysian outbreak.

INTRODUCTION

Nipah encephalitis is an emerging zoonotic infection first surfaced in Malaysia and Singapore in 1998/99. In Malaysia it caused a predominantly encephalitis illness, with some characteristic clinical picture such as myoclonus.[1-3] The mortality overall was 40%[3], and 9% of the survivors had relapsed encephalitis.[4] There has also been report of characteristic MRI changes in the brain in patients with acute and relapsed Nipah encephalitis.[5] The illness in Malaysia mainly affected pig farm workers, who developed the illness through contact with infected pigs.[1,2,6] Two species of large fruit bats, *Pteropus vampyrus* and *Ptoropus hympmelanus*, has been found to be reservoir of the Nipah virus.[7]

To-date, there has been 4 outbreaks of Nipah encephalitis in Bangladesh; Mehepur district in 2001, Naogoan district in 2003, Rajbari, Faridpur, Golpagonj, Manikganj, Joypurhat, Naogaon districts in January 2004, and Faridpur district in April 2004. The preliminary investigations suggest a fatal encephalitis illness, with acute respiratory distress syndrome in some patients. Direct contact with human-to-human transmission is thought to be important in the spread of disease. Ecology studies identified Indian flying foxes (*Pteropus giganteus*) to have positive antibodies to Nipah virus antigen, but not in a variety of other animals tested.[8-11] To-date, there has not been detailed clinical report of the Nipah encephalitis patients in Bangladesh. This is a report of 4 Nipah encephalitis patients from Rajbari district seen in the Dhaka Medical College Hospital, Dhaka, Bangladesh during the January 2004 outbreak.

CASE REPORTS

Patient 1

This 23-year-old housewife from Char Khankapur of Rajbari Thana of Rajbari district was referred by Faridpur Medical College Hospital, and admitted to Dhaka Medical College Hospital on 16th February, 2004. She had 3 days' history of fever, vomiting, headache, restlessness, disorientation followed by coma, and several episodes of generalized convulsions. There was no similar illness in her family. She also had no history of contact with pig, dog, bat, rat and chicken. On admission, she was febrile with temperature of 99ºF. The pulse rate was 160 per minute, blood pressure was 110/90 mm Hg, and

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respiratory rate was 40 per minute. She was deeply comatosed with Glasgow Coma Scale of 3/15. Doll's eye reflex was normal. There was no neck rigidity. The fundus examination and papillary response were normal. The limbs were hypotonic with absent deep tendon reflexes. Planter responses were bilaterally extensor. There was no other physical abnormality. Laboratory investigations showed normal full blood count and erythrocyte sedimentation rate. Blood film for malarial parasite was negative and ICT for *P falciparum* was negative. Urine examination showed albuminuria, urine red blood cell of 10-15 per high power field, leukocyte of 20-25 per high power field. Chest XR was normal. ECG showed sinus tachycardia. Blood urea, serum creatinine and electrolytes were normal. Random blood sugar was raised at 12 mmol/L. Liver function test showed raised alanine aminotransferase of 160 IU/L, aspartate aminotransferase of 140 IU/L and no other abnormality. Cerebrospinal fluid was clear with normal pressure. Protein was raised at 90 mg/dl with no other abnormality. VDRL was non reactive. IgM and IgG antibody against Nipah antigen were positive in serum and cerebrospinal fluid using enzyme-linked immunosorbent assay (ELISA). CT brain scan showed extensive low density area in both cerebral hemispheres. MR imaging of brain showed multiple confluent high signal lesions involving the gyri and subcortical white matter both insular, parietal, frontal and occipital lobes (Figure 1). Patient was given supportive treatment. She subsequently improved. On discharge one month later, she could take food but needed help to walk, and had sphincteric incontinence.

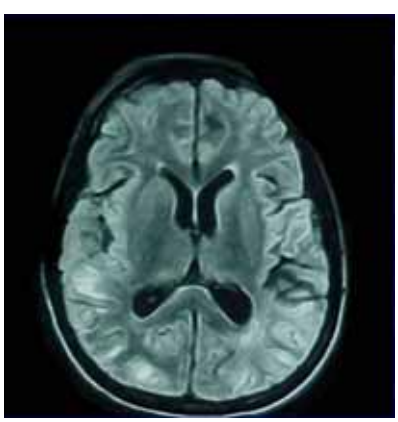

Figure 1: Axial fluid attenuated inversion recovery MR image showing multiple confluent lesions involving the gyri and subcortical white matter both insular, parietal, frontal and occipital lobes.

Patient 2

This 35-year-old multiparous housewife from Rajbari Sadar of Rajbari district was admitted to Dhaka Medical College Hospital on 25th February, 2004. She presented with 12 days history of fever, headache, followed by behavioral abnormalities with incoherent speech, withdrawal from usual household activities and disorientation. There was no history of similar illness in the family and no contact with pig, dog, bat, rat or chicken. On admission, she was febrile with temperature of 101ºF. The pulse was 80 per minute, and blood pressure was 110/60 mm Hg. Her Glasgow Coma Scale was 8/15. Fundus examination was normal and pupil was reactive to light. The muscle tone was increased, reflexes were reduced, and plantar responses flexor. There was no other physical abnormality. Laboratory investigations showed raised white count of 15,000/cmm with neutrophil if 84% and erythrocyte sedimentation rate of 50 mm in first hour. Malarial Parasite was not found. Liver function test showed raised alanine aminotransferase of 126 IU/L. Blood urea and electrolyte, serum creatinine, blood sugar, urine examination, chest XR, ECG were all normal. Cerebrospinal fluid appearance was clear with normal pressure, normal biochemistry and microscopic examination. IgM and IgG antibody against Nipah antigen were positive in both serum and cerebrospinal fluid (ELISA). MR imaging of brain showed multiple confluent high signal lesions in the gray and white matter of insular, temporal, frontal and parietal lobes in T2-weighted and fluid attenuated inversion recovery sequences (Figure 2). The corresponding areas showed hypointensity on T1-weighted sequence. Patient was given supportive treatment. She subsequently improved with cognitive impairment on discharge.

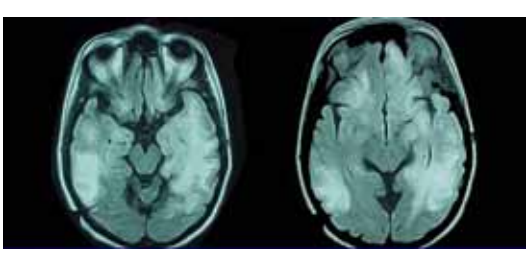

Figure 2: Axial fluid attenuated inversion recovery MR image showing multiple confluent lesions in the white matter both temporal, frontal and parietal lobes. There are also involvement of the gray matter in left insular, both frontal, and right parietal lobes.

Patient 3

This 13-year-old boy from Goalanda of Rajbari district was admitted to Dhaka Medical College Hospital on 22nd of January, 2004. He was referred from Goalanda Thana Health Complex. He has 6 days history of fever, headache followed by restlessness and unconsciousness, and an episode of vomiting. His elder brother suffered from the same illness and subsequently passed away. He had no contact with pig, dog, bat, rat or chicken. On admission, he was febrile with temperature of 102ºF. The pulse was 100 per minute, blood pressure was 100/50 mm Hg, and respiratory rate was 20 per minute. There was no neck rigidity and Kernig's sign was absent. The Glasgow Coma Scale was 8/15. Fundus examination was normal, pupils were reactive to light, and doll's eye reflex was normal. Muscle tone was diminished, deep tendon reflexes and superficial abdominal reflex were absent. Plantar response was bilaterally flexor. There was no other physical abnormality. Investigations revealed raised erythrocyte sedimentation rate of 50 mm in first hour. Malaria parasite was not detected. Serum alanine aminotransferase was raised at 120 IU/L. Blood urea and electrolytes, serum creatinine, blood sugar, chest XR were all normal. Urine showed albuminuria. ECG revealed sinus tachycardia. Cerebrospinal fluid was clear with normal pressure. The biochemistry and microscopic examination were normal. IgM and IgG antibody to Nipah antigen were positive in both serum and cerebrospinal fluid (ELISA). MR imaging of brain showed high signal lesions in the insular, parietal and occipital subcortical white matter (Figure 3). Patient was given supportive treatment with few doses of acyclovir and dexamethasone. The patient recovered completely.

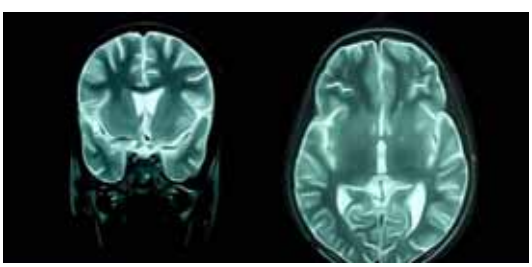

Figure 3: Coronal and axial T2-wighted MR image showing discrete high signal lesion in both insular. High signal lesions were also seen in right parietal and occipital subcortical white matter.

Patient 4

This 18-year-old male from Goalanda of Rajbari district was admitted to Dhaka Medical College Hospital on 22nd of January, 2004. He was the older brother of the Patient 3, and was referred by Goalanda Thana Health Complex. He presented with 6 days history of fever, headache, non productive cough and restlessness followed by coma. He was a fish farm laborer and had no contact with pig, dog, bat, rat or chicken. On examination, he was febrile with temperature of 102°F. The pulse was 68 per minute, blood pressure was 90/50 mm Hg, respiratotory rate was 24 per minute. There was no neck rigidity and Kernig's sign was absent. He was deeply comatosed with Glasgow Coma Scale of 4/15. Fundus examination was normal and pupillary response to light was sluggish. The limbs were hypotonic with diminished deep tendon reflexes and flexor planter response both sides. There was no other physical abnormality. Investigations revealed reduced hemoglobin of 11.7 gm/dl. Erythrocyte sedimentation rate was 22 mm in the first hour. Serum alanine aminotransferase was raised at 219 IU/L. Blood urea and electrolytes, serum creatinine, blood sugar were all normal. Urine showed albuminuria. Cerebrospinal fluid was traumatic. IgM and IgG antibody to Nipah antigen were positive in both serum and cerebrospinal fluid (ELISA). He was started on intravenous acyclovir and dexamethasone. The patient expired on the next day.

DISCUSSION

The diagnosis of Nipah encephalitis was based on the case definition adopted by the investigation team for the January-April 2004 outbreak. Probable case was a patient who had fever and neurological signs, living in the same district as a laboratory-confirmed case after 15 December 2003. A laboratory-confirmed case was a case positive for Nipah IgM antibody after 15 December 2003.[10] All the 4 patients in this report has positive IgM and IgG antibody to Nipah virus in both serum and cerebrospinal fluid. However, although they were all from Rajbari, which was the outbreak district, Patients 3 and 4 were from Gaolanda, which was the village where 12 of the 23 cases in the January 2004 outbreak were from. Patients 1 and 2 were from Rajbari Thana and Rajbari Sadar. Both villages were about 10 km from Goalanda. Patients 1 and 2 denied visiting Goalanda during the outbreak period, and had no contact with other encephalitis patients.

The patients presented with an acute illness of 3-12 days, with encephalitis symptoms of fever, headache, impaired consciousness and vomiting, and seizure in one patient. On examination, the patients were deeply unconscious with Glasgow Coma Scale of less than 10. The predominant encephalitis illness is similar to that seen during the previous outbreak in Malaysia[1,2,12] and Singapore.[13] Hyporeflexia and hypotonia were seen in 3 of our patients. Hyporeflexia with hypotonia were seen in 56% of patients during the Malaysian outbreak.[2] Spinal root involvement probably contributed to the hyporefleixa.[14] On the other hand, segmental myoclonus, seen in 32-54% of the patients during the Malaysian outbreak, was not seen among our patients. Hyporeflexia with hypotonia and segmental myoclonus were distinctive features of Malaysian Nipah encephalitis.[2,12]

MR imaging was a sensitive and specific diagnostic tool for evaluating Nipah encephalitis during the Malaysian outbreak. The MR imaging during acute Nipah encephalitis consisted of discrete high-signal-intensity lesions, measuring 2-7 mm, disseminated throughout the brain, mainly in the subcortical and deep white matter of the cerebral hemisphere. The changes were thought to reflect widespread microinfarctions from underlying vasculitis of cerebral small blood vessels.[5] On the other hand, the MR imaging of our patients were that of confluent high signal lesions involving both gray and white matter, more like that of the relapsed and late-onset encephalitis seen in Malaysia. The pathology in relapsed and late-onset encephalitis in Malaysia was that of focal encephalitis.[5,15] The differences in MR imaging and clinical manifestation reflect differences in underlying pathology process. The Nipah virus in Bangladesh was said to have 95% RNA homology to that causing the outbreak in Malaysia.[10] It is not unexpected that the pathology and clinical manifestations of Nipah encephalitis in Bangladesh is not identical to that in Malaysia.

A study of 32 fatal human cases during the Malaysian outbreak showed that other than central nervous system, pathological changes were also seen in lung, heart, kidney, spleen and lymph node.[16] Although encephalitis was the predominant feature during the previous Singapore outbreak, 3 of the 11 patients presented with atypical pneumonia.[13] Chest XR abnormality was also found in 24% of the Seremban patients in the Malaysian outbreak.[12] A previous report from the April 2004 outbreak in Faridpur district, Bangladesh showed that a number of patients had bilateral infiltrates in chest XR consistent with acute respiratory distress syndrome.[11] Only one of our 4 patients has cough, and none has Chest XR abnormality. As for involvement of other organs, the liver enzyme and urine abnormalities in our patients could be due to non-specific changes of very ill patients.

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