Pandemic H1N1 influenza with atypical presentation: Encephalopathy and severe thrombocytopenia

Sir,

A 43-year-old male, employee in an office of a teaching hospital, presented in the emergency room (ER) with history of high-grade fever and body ache for 10 days and altered sensorium for 1 day. For the current illness, he was treated with analgesic and antipyretic on an outpatient basis during his previous visits. On examination in ER, his GCS E3V3M4, heart rates 110/m, blood pressure 138/80 mmHg, respiratory rate 16–18/m, temperature 38.8°C, peripheral edema, urine output 50–60 mL/h and signs for meningitis were absent. At the time of admission, his arterial blood gas analysis on venturi mask (0.4 FiO_2) showed pH 7.38, paO_2 86 mmHg, $paCO_2$ 35.9 mmHg, HCO_3^- 21.9 mmol/L, BD -2.8, Na^+ 142 mEq/L, K^+ 3.4 mEq/L, Cl^- 103 mEq/L and lactates 1.8 mmol/L. Because of worsening of sensorium and unable to protect his airway, endotracheal intubation was done and he was kept on mechanical ventilation and shifted to the intensive care unit for further care. Empirically, ceftriaxone i.v. was started along with other supportive care. Routine laboratory investigations revealed Hb 11.6 g/dL, Hct 35.3%, TLC 12300 cells/µL, platelets 28000 cells/µL, S. creatinine 1.7 mg/dL, S. bilirubin 5.3 mg/dL (total), 4.2 mg/dL (direct), AST/ALT 264/107, alk phosphtase 915, PT 13.5 s (11.5 s), aPTT 44.1 s (c: 26.8 s) and INR 1.16, CPK 66 U/L, LDH 1200 U/L. Peripheral blood smear was negative for hemolysis. Chest X-ray findings were within normal limits. Magnetic resonance imaging head revealed normal study. Cerebrospinal fluid (CSF) study could not be done due to thrombocytopenia.

In further diagnostic work-up, dengue (IgM ELISA), malaria (blood peripheral smear for parasite and malarial antigen) and serology for other infective agents (HBsAg, HAV, HEV, HIV and IgM ELISA for Leptospira) were ruled out. Meanwhile, due to the ongoing epidemic of H1N1 influenza, endotracheal aspirate were sent for possible H1N1 infection and samples was found positive for H1N1 influenza viral infection by the reverse transcription polymerase chain reaction (RT-PCR) method (Applied Biosystem™). Oseltamivir at a dose of 75 mg twice daily was added in his treatment on the third day of ICU admission. His fever settled out, sensorium and thrombocytopenia also showed improvement by fifth day of ICU admission [Table 1]. No platelet transfusion was required and it was observed that after starting oseltamivir the platelet count improved from 30 to 360 x 10^3 cells/µL. The patient was weaned from the ventilator and extubated. He showed speedy recovery after receiving oseltamivir and was discharged from the ICU in the next 5 days. His total duration of ICU stay was10 days.

Infection due to H1N1 influenza is commonly presented with flu-like symptoms, while in the severe form this may manifest as pneumonia and respiratory failure. Recently, few cases of atypical presentation like encephalopathy due to H1N1 have been reported worldwide, mainly in childhood, including extensive cortical–subcortical

Table 1: Clinical course of patient during ICU stay

Clinical features	Days of illness					
	Day 10	Day 13	Day 15	Day 17	Day 19	Day 20
	ICU Day 1	ICU Day 3	ICU Day 5	ICU Day 7	ICU Day 9	ICU D10
Fever (max. °C)	39.4	38.8	38	37.8	37	37
GCS	10	-	13	15	-	-
Total leukocyte count (x10^3)	12.3	10.6	9.8	8.9	9.1	7.8
Platelets (x10^3)	24	30	57	201	346	360
Serum bilirubin (total/direct)	5.3/4.2	2.8/1.3	-	1.2/0.9	1.0/0.4	-
AST/ALT (IU/L)	264/107	165/67	-	-	40/35	-
INR	1.16	-	1.08	-	1.09	-
Serum creatinine (mg/dL)	1.7	1.3	1.3	1.2	1.3	1.2
Oseltamivir (75 mg BD)	-	+	+	+	-	-

GCS = Glasgow coma scale; AST / ALT = Aspartate aminotransferase/ alanine aminotransferase ; INR = International normalized ratio

necrosis with high morbidity and mortality.[1-4] From India also, there is a case report of encephalitis-like findings in a patient of H1N1 influenza.[5] The underlying mechanism of encephalopathy in H1N1 infection still remains unclear, with multiple theories including host immune response and genetic susceptibility, and CSF findings are usually not helpful in the diagnosis.[4,6,7] Our case had late-onset (second week) encephalopathy as opposed to early-onset (within 48 h) encephalopathy found in patients with influenza A and B, which may reflect different mechanism of pathogenesis.[8] Also, in pandemic H1N1 influenza, frequent abnormal laboratory parameters are high lactate dehydrogenase, creatine kinase, aminotransferases and white blood cells.[5,9] Although thrombocytopenia is not uncommon and may be present in up to 20% of the hospitalized patients with H1N1 influenza, severe thrombocytopenia is very infrequent.[5,9] Our case had atypical presentation of H1N1 influenza with encephalopathy and severe thrombocytopenia. Because of such variable presentations of H1N1 virus, patients with viral fever, with or without flu-like symptoms, should be suspected and screened for H1N1 virus infection, especially in the presence of thrombocytopenia that could mimic dengue fever.

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