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CASE REPORT

H1N1 Encephalitis 'Sans' Flu: A Case Report

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ABSTRACT

Influenza H1N1 infection is a viral infection with a seasonal preponderance, usually presents with flu-like symptoms, and rarely has extra-respiratory manifestations. It has taken a pandemic form on few occasions in the past. Involvement of the Central Nervous System (CNS), though rare, is described.

We describe a 42-year immunocompromised woman who presented with an acute febrile rapidly progressive encephalopathic illness without the usual flu-like symptoms. Instead, she had widespread Magnetic Resonance Imaging (MRI) brain changes resulting in a fatal outcome. Such an encephalitic presentation of H1N1 infection without respiratory involvement has never been reported. *J Microbiol Infect Dis 2021; 11(3):166-169.*

Keywords: *H1N1 Infection, Encephalitis, Magnetic Resonance Imaging*

INTRODUCTION

Influenza due to H1N1 infection is a viral infection with a seasonal preponderance, and respiratory symptoms are the usual initial presenting symptoms. Other systemic involvement has also been described, and CNS is no exception. Patients with prior comorbidities are prone to severe infections [1,2]. CNS involvement can be of varied presentations such as encephalitis, encephalopathy, seizures, acute disseminated encephalomyelitis, transverse myelitis, Guillain-Barre syndrome, or treatment-related complications like Reye's syndrome [3-7].

The MRI features can be typical, diffuse cerebral edema, diffuse cortical involvement, bilateral symmetrical thalamic involvement, or features suggestive of focal encephalitis [8]. Splenial lesions, involvement of brainstem, cerebral white matter, and cerebellum have also been reported [9,10]. We report a case of H1N1 infection who presented with a febrile illness with no flu-like symptoms and rapidly developing features of encephalitis and MRI brain showing few atypical areas of involvement which is not usually described.

CASE

A 42-year woman developed acute febrile illness associated with moderate headache and vomiting. There were no accompanying flu-like symptoms, dyspnea, chest pain, pain abdomen, or dysuria. She was operated on for Pituitary Macroadnoma by transnasal-transsphenoidal route in 2009, underwent gamma-knife radiosurgery in 2012, and was on treatment for Ulcerative Colitis and Diabetes Mellitus for the past 04 years. Her Ulcerative Colitis was in remission. She was receiving Azathioprine 100 mg, Mesalamine 3.6 gm, Levothyroxin 50 mcg, Tab Hydrocortisone 15 mg, Metformin 2 gm daily, and oral contraceptive pills for contraception. She took symptomatic treatment for her fever at home. On the third day of fever, she developed altered sensorium and rapidly became stuporous, after which she was brought to a tertiary care hospital. She was noted to have a temperature of 103 ^{0}F, tachycardia, respiratory rate of 22/min with normal blood pressure, and SpO2 of 95% on room air. There was no pallor, icterus, cyanosis, rashes, petechiae, or lymphadenopathy. CNS examination revealed an unconscious patient with GCS of E1M4V1; right pupil 3mm and left pupil 2mm, both not reacting; moving limbs to noxious stimuli with

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bilaterally extensor plantar response. Chest examination revealed bilateral vesicular breath sounds with no adventitious sounds. Other systems were unremarkable. She was intubated in view of her poor GCS and was placed on mechanical ventilation. Initial investigations revealed normal hematological and biochemical parameters except for a mild rise in transaminases and 72 mg/dl random blood sugar.

Peripheral smear and Paracheck for malaria, NS1Ag, and IgG/IgM for dengue were negative. Her initial Chest X-Ray was normal. She was started on broad-spectrum injectable antibiotics with Ceftriaxone and Vancomycin along with intravenous Acyclovir and Artesunate. She was also given injectable Dexamethasone, Inj Sodium Valproate, IV Dextrose, Tab Levothyroxine, Tab Metformin, and Inj Paracetamol, along with supportive care. Her contrast-enhanced MRI Brain showed T2/FLAIR hyperintensities involving bilateral posterior basifrontal region, mammillary bodies, the anterior column of fornices, hypothalamus, anterior thalamus on the left side, and splenium of the corpus callosum with diffusion restriction of above areas and no contrast enhancement (Figure 1). Cerebrospinal fluid (CSF) examination revealed clear CSF with a white blood cell count of 08/cumm, red blood cell count of 120/cumm, protein of 58 mg/dl, sugar of 93 mg/dl (blood sugar of 112 mg/dl) and globulin was not raised. Injectable Thiamine was added to the treatment with a remote differential of Wernicke's encephalopathy after her MRI brain. Her condition remained critical with continuous high-grade fever, persistent comatose state, and on ventilatory support. Her arterial blood gas, urine routine, and microscopy, and serum procalcitonin were normal. Her platelet count reduced marginally from 1.6 lakhs to 1.2 lakhs, and transaminases gradually normalized. Because of no clinical improvement, MRI brain was repeated, which showed an increase in the size of the lesions seen previously, along with the involvement of bilateral basal ganglia and the right side of the midbrain (Figure 2). Her urine culture showed no growth, and blood culture grew Pseudomonas aeruginosa, sensitive to Colistin. Weil-Felix and Widal tests were negative, and the throat swab for H1N1 by Taqman Reverse Transcriptase - Polymerase Chain Reaction (PCR) was positive. Her antibiotics were modified, and Tab Oseltamivir was also added. Despite all possible efforts, her condition went downhill, and she finally succumbed on day 5 of hospitalization. CSF for Herpes Simplex Virus 1 & 2 by Deoxy Ribonucleic Acid – PCR and Japanese Encephalitis virus IgM by Enzyme-linked Immunosorbent Assay were negative (received post-mortem).

DISCUSSION

H1N1 infection usually presents with fever and flu-like symptoms, and in few patients, it can be complicated with the involvement of other organ systems, including the CNS [1,2]. We did not come across any report of H1N1 infection with CNS involvement without the usual initial upper respiratory symptoms. MRI involvement of the thalamus, brainstem, and splenium have been described in the literature [8-10]. However, involvement of the basifrontal region, mamillary bodies, and fornices can occur, as in our case. The possibility of rapid CNS involvement in our case could have been possible due to the immunocompromised state and prior CNS surgery. Notwithstanding, the absence of respiratory symptoms and extensive CNS involvement as depicted in the MRI in our case makes it one of its kind.

Testing for H1N1 infection during the seasonal preponderance in the endemic region is advised in patients with acute febrile illness, even when presenting without respiratory symptoms, especially in immunocompromised patients.

Conclusion

Most guidelines for suspicion of H1N1 infection include respiratory symptomatology as the predominant manifestation. Acute encephalitis without respiratory symptomatology is presently not known. It is recommended that H1N1 infection be looked for even in an acute encephalitic presentation during the seasonal preponderance of influenza-like illness. The question of whether empirical therapy can be given pending investigations needs further elaboration.

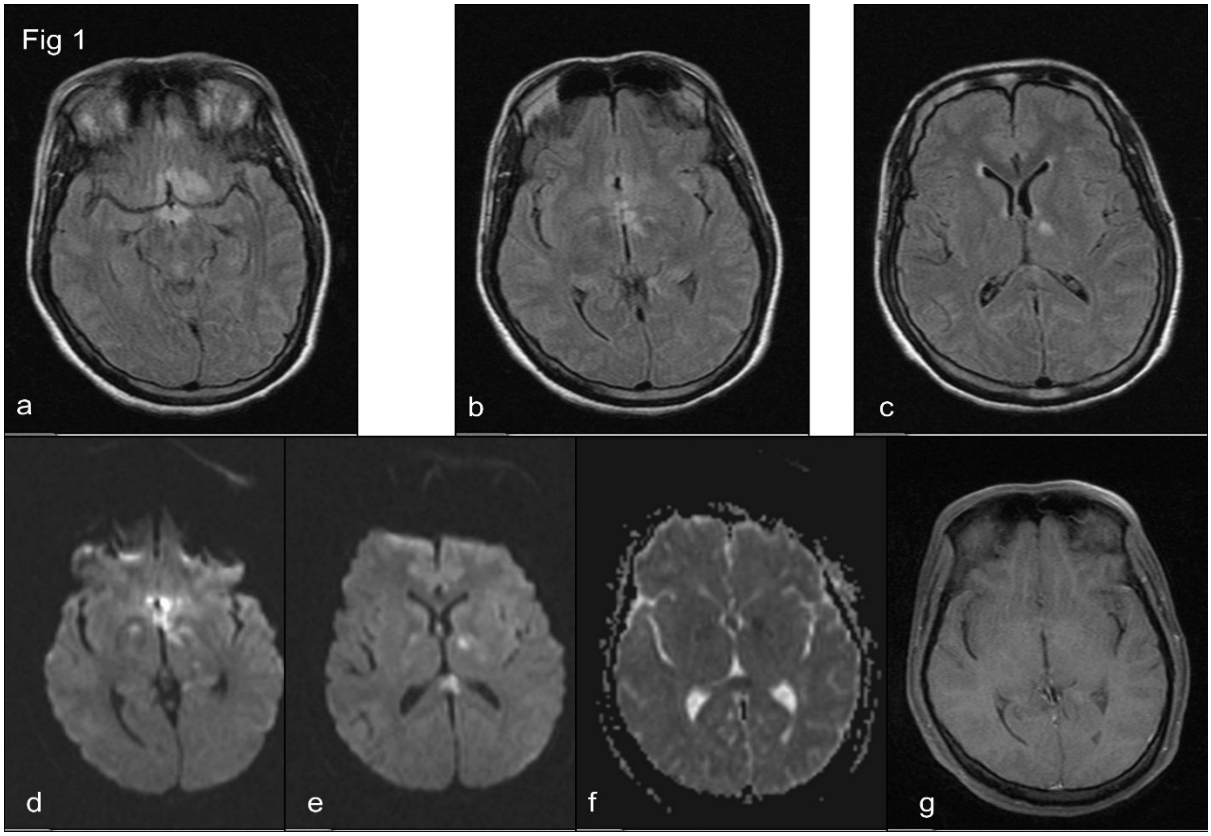

Figure 1. Contrast-enhanced MRI Brain on day 3 of illness showing FLAIR hyperintensities (a to c) involving basifrontal region, mamillary bodies, anteromedial thalamus, and genu of the internal capsule on the left side and splenium of the corpus callosum; with diffusion restriction and ADC mismatch (d to f) and no contrast enhancement (g)

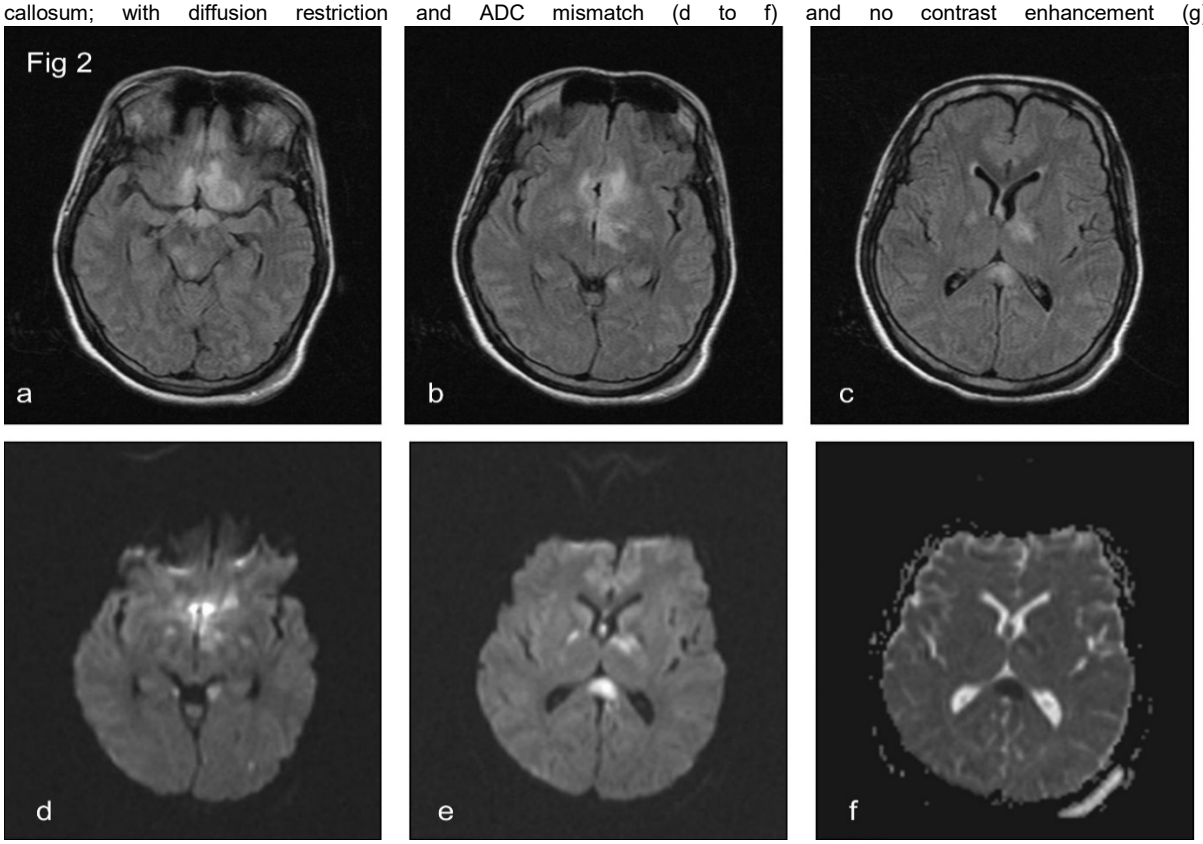

Figure 2. Repeat MRI Brain on day 6 of illness showing an increase in FLAIR hyperintensities as compared to previous MRI in fig 1 (a to c) with additional involvement of anterior column of fornices, medial temporal lobe, genu of the internal capsule on the right side & midbrain with diffusion restriction and ADC mismatch (d to f).

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