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Case Report

INFLUENZA B VIRUS PRESENTING AS SEVERE ACUTE RESPIRATORY ILLNESS-A CASE SERIES

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ABSTRACT
Influenza B virus is known to cause mild illness in humans however; sometime it may cause severe respiratory illness (SARI) in certain individuals. It is rarely investigated in patients hospitalized for Severe Acute Respiratory Illness. Here, we are reporting 3 cases presented as SARI and found to be Influenza B positive. To best of our knowledge, this is the first case report of influenza B virus infection presenting as SARI from India which will help the clinicians and epidemiologist to consider it as one of the important etiology and monitor the disease spectrum. More aggressive search for Influenza B virus in patients hospitalized with SARI is needed.

Key Words: *Influenza B, Severe Acute Respiratory Illness, Pneumonia, Nasopharyngeal Aspirate*

INTRODUCTION
Influenza virus causes febrile respiratory illness and greatly affects hundreds of thousands of people worldwide each year. In most cases, influenza infections are self limiting mild illnesses lasting 4-5 days with predominantly upper respiratory symptoms (Ramsey and Kumar (2011). Mainly two types of influenza virus are pathogenic to human; influenza A and B. Influenza A is associated with wide range of pathology from mild to severe and influenza B causes mild illness**.** Acute Respiratory Illness (ARI) e. g. pneumonia caused by influenza B virus is uncommon and has been rarely reported in children and previously healthy adults (Lu *et al.*, (2004)**.** Few studies report that influenza B is associated with severe disease in children which might be fatal, and cause encephalitis/ encephalopathy, influenza-associated myositis (IAM), and acute respiratory distress syndrome (ARDS) (Li *et al.*, (2008)**.** During routine influenza surveillance, we found a series of three patients of severe acute respiratory illness (SARI) who were positive for influenza B infection.

CASES
Case 1
A 26 months old male child presented with complains of high fever (102^0F), mild non-productive cough and vomiting (two episodes in 2 days) for two days. He was admitted in Intensive Care Unit of paediatric department due to sudden onset of breathlessness. There was no history of seizures. Measles, Polio and DPT vaccines were administered. However, swine flu vaccine was not administered. There was no history of influenza like illness (ILI) or any respiratory illness in any family member.
On physical examination following findings were reported; pulse rate -normal; respiratory rate -56/min, heart rate - 180/min, blood pressure-110/68mm Hg. Bilateral wheezing and coarse crepitation on right side of the chest were present. Computed tomography scan (CAT) of thorax showed right sided pyopneumothorax and similar results with Chest radiography (CXR). Blood, pleural fluid and urine samples were negative on fungal and bacterial culture. Haemogram showed; Haemoglobin (Hb) -8gm%, total leucocyte count (TLC)-7600/mm^3, differential leucocyte count (DLC)- neutrophile (N) 52

Lymphocyte (L) 46 Eosinophile (E) 1 Monocyte (M) 1. Patient was diagnosed as a case of severe pneumonia.

Nasopharyngeal aspirate (NPA) was collected in Viral Transport Media (VTM) on 2nd day of admission. Sample was processed and RNA was extracted from 200µl clinical samples using High Pure Viral Nucleic Acid Extraction kit (Roche, Germany) according to manufacturer's instructions. One step real time RT-PCR was done for diagnosis of influenza A and B viruses by using group specific primers targeted to conserve matrix gene (M) for influenza A and nucleocapsid protein gene (NP) for influenza B (WHO protocol (2009)**.** The test result was positive for Influenza B and negative for Influenza A. Sample also tested negative for other respiratory viruses; respiratory syncytial virus (RSV), human meta-pneumovirus (hMPV), Para-influenza viruses 1, 2, 3 and 4 (PIV-1,2,3 and 4), Adenovirus (ADV) and human Bocavirus (hBoCA) by multiplex real-time RT PCR. Multiplexing was done in three panels. Detection of RSV and hMPV in panel-I was done by using gene specific primers targeted to nucleoprotein gene for both RSV and hMPV (Jokela *et al.*, (2010), PIV-1,2,3 and 4 in panel-II by primers targeted to HA-NA gene (Templeton *et al.*, 2004), ADV and hBoCA viruses in Panel-III using primers targeted to gene hexon gene for ADV and nucleocapsid for hBoCA (Sanghavi *et al*., (2012). Patient recovered and was discharged on day 14th after admission.

Case 2

A 55 years old male presenting with complaints of high to moderate fever, sore throat, body ache, and fatigue since four days was hospitalised. He also complained of severe productive cough, expectoration and breathlessness at the time of admission. He was a known case of Chronic Obstructive Pulmonary Disease (COPD) for last 10 years with 2 – 3 episodes of exacerbations every year. He was a smoker but not alcoholic. Swine flu vaccine was not administered. There was no history of influenza like illness (ILI) or any respiratory illness in any family member.

His respiratory rate was 42/min with bilateral equal air entry and bronchial breathing with bilateral wheezing all over the chest. Chest X ray showed bilateral hyperinflation of lungs. To rule out bacterial infection sputum, blood and NPA were collected for bacterial and fungal culture and were negative. Sputum test for AFB (acid fast bacteria) and reaction to Purified protein derivative/Mountx test were negative. Haemogram showed Hb-10.1gm%, TLC- 7600/ cmm and DLC-$N_{54}L_{40}M_5$. NPA was collected, processed and examined on fourth day of admission for detection of respiratory viruses as described in detail for case-1. Sample was positive for influenza B virus by real time PCR while negative for other respiratory viruses. Patient showed improvement after one week and was discharged on day 10th after admission.

Case-3

A four and half years old male child with chief complaints of high fever (102^0-103^0 F), severe cough, fatigue, headache, difficulty in breathing and vomiting (three episodes/day) since three days, was admitted to Department of Paediatrics. He was already a known case of acute lymphoblastic leukemia (ALL). Measles, Polio and DPT vaccines were administered. There was no history of respiratory illness in family.

At the time of admission Respiratory rate, Heart rate and Blood pressure were 36/min, 106/min, and 110/68mm of Hg, respectively. Reduced air entry on right side, bilateral wheezing and crepitation on right side of chest were found. Radio diagnosis results showed the presence of right sided hydropneumothorax. Blood, pleural fluid and urine samples were negative for the presence of any bacteria, fungus or parasite. Haemogram showed Hb-3.6gm%, TLC-14.45n/mm^3, DLC-$P_{23}L_{67}$. Clinical diagnosis was made as severe pneumonia with concomitant illness of ALL. NPA was collected for detection of respiratory viruses. The patient was found to be positive for influenza B virus by real-time PCR and negative for other respiratory viruses. Patient recovered after 14 days and discharged.

NPA from all three cases were inoculated on MDCK (Madin Darby Canine Kidney) cell lines for culture. After 4-5 days of inoculation cytopathogenic effects (ballooning, roundening, hyperpigmentation and then

degeneration) were observed in the cell lines. Presence of influenza B virus was confirmed by Haemagglutination Inhibition method and all three were sero-typed as influenza B, Victoria lineages.

DISCUSSION

Influenza B and seasonal flu are understudied, having been overshadowed by concerns over pandemic influenza H1N1. Sometimes they cause serious complications; most frequently pulmonary which includes primary viral pneumonia, and exacerbations of chronic underlying pulmonary diseases such as COPD and asthma. Immunocompromised individuals and pregnant women are on greater risk and poses major challenge to hospitals.

In present study all three cases described above presented as SARI. Two of them had co-morbid illness (ALL and COPD) that greatly enhances the susceptibility to seasonal influenza virus infection as reported in previous studies. Patients at the extremes of ages are at highest risk for hospitalization and mortality during seasonal epidemics. Izurieta HS et al (Izurieta *et al.,* (2000) described that patients with chronic medical illness such as heart disease, lung disease, diabetes, renal disease, rheumatologic disease, dementia, and stroke are at high risk for influenza complications, regardless of age. Patients with diffuse large B-cell lymphoma developed acute respiratory distress syndrome caused by Influenza B virus infection (Namendys-Silvio *et al.,* 2011). In a retrospective study of 100 immunocompromised patients with influenza, 60.4% of patients were admitted to ICU, 34.3% required mechanical ventilation and 45.4% died; of these 20% had influenza B virus infection (David *et al.,* (2010).

Influenza B may cause severe illness in some patients in contrast to the previous studies reporting influenza B infection as milder. As patients admitted to hospital due to SARI are rarely tested for influenza B, the incidence of admission due to this virus might be greatly underestimated. Therefore, a more aggressive search for Influenza B virus in patients with SARI might be needed.

Consent

Written informed consent was obtained from the patients/ guardians before taking samples. The proposed study was cleared from Institutional ethical committee.

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