

Influenza B presenting with bicytopenia in an adult – An unusual presentation and failure of antimicrobial stewardship by a practicing physician

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ABSTRACT

Influenza is a very common cause of upper respiratory illness, rarely presented with bicytopenia, and is being wrongly treated with antimicrobials many-a-times. We report a case of 36-year-old North-Indian man, physician by profession who presented with a 5-day history of typical upper respiratory tract symptoms (sore throat, irritative cough, hoarseness of voice, coryza) and high-grade fever for which he took antibiotics (initially levofloxacin for 2-days, followed by azithromycin) after self-prescription. He developed hematological involvement (leukopenia and thrombocytopenia) for which he was admitted. Throat swab tested positive for Influenza B by RT-PCR. This case highlights a rare presentation of influenza as bicytopenia which rapidly improved with oseltamivir given for 5-days. This is also a classic case of lack of antimicrobial stewardship practice by a physician while self-treating viral pharyngitis. There is a pressing need to create more awareness regarding appropriate use of antimicrobial resources among doctors, only then will others follow.

Keywords: Antimicrobial stewardship, flu, leukopenia, oseltamivir, thrombocytopenia, viral fever

Introduction

Influenza is a contagious respiratory illness caused by the influenza virus. Typical uncomplicated influenza begins with an abrupt onset of symptoms after an incubation period of 1-2 days. Initially systemic symptoms predominate—feverishness, chilliness, or frank chills, headache, myalgia, malaise, and/or anorexia. These systemic symptoms usually persist for 3-days, following which only the respiratory symptoms predominate.^[1] Routine laboratory findings are non-specific, as are for most viral infections. Among the three major subtypes of influenza: Type A, B, and C, type A is more associated with pandemic spread

and more severity in the form of H1N1 (swine flu). Influenza B is likely to have more leukopenia and thrombocytopenia than influenza A.^[2,3] Antimicrobials are mostly used inappropriately for any viral infection including viral rhinitis/pharyngitis due to lack of stewardship practices.

We, here, report an unusual case of influenza B pharyngitis with bicytopenia who cured with oseltamivir and highlight antimicrobial stewardship practices in the doctor's community.

Case presentation

A 36-year-old man, doctor by profession and resident of North-India, was apparently well till 5-days back. He developed throat congestion, myalgia, and mild fever (documented as 100°F in axilla, without any chills or rigors) for which he took Tab. levofloxacin and paracetamol after self-prescription. Next day he also developed rhinorrhoea associated with hoarseness

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of voice. He continued his daily job activities including exercise in the form of running. On day-3, he developed high-grade fever (103°F), dry irritating cough with production of yellow sputum, severe prostration, and loss of appetite, following which he changed antibiotic to Tab. azithromycin, added fexofenadine-levocetizine, and did routine blood investigations. He had no chills and rigor, headache, bone pain, retro orbital pain, back pain, joint pain, rashes, or any bleeding manifestation. His laboratory reports suggested neutropenia (722/mm³) and thrombocytopenia (70340/mm³), for which he was admitted.

He did not have any previous significant medical/surgical history. He had traveled to outstation 2-days before the onset of fever and had been exposed to flu patients among family members where flu outbreak was going on. He had no vaccination history against influenza or streptococcus pneumoniae.

On physical examination, throat erythema with mucoid exudates were noticed on the posterior pharyngeal wall. Systemic examination was unremarkable. His hemogram showed bicytopenia. His liver function test suggested mild transaminitis (SGPT- 77 units/L; SGOT- 81 units/L); kidney function test and his chest X-ray was normal. Rapid card tests (ICT) for enteric fever, malaria, and dengue were negative. Next day, throat and nasopharyngeal swabs were taken and RT-PCR came out to be positive for Influenza B. Peripheral blood smear examination showed no presence of any atypical cells. His serum creatine phosphokinase level was normal.

His old records were reviewed from the hospital records (baseline obtained at the time of his joining the services at our hospital, 2 years prior) and showed normal hemogram as well as liver and kidney functions.

At presentation, based on the history and examination, possibility of viral infection (viremia with hematological involvement) was kept, especially H1N1 (2009 pandemic strain) since there was predominance of systemic manifestations (fever, malaise, myalgia) and type A influenza is the more prevalent subtype. Clinically it is easy to differentiate the two (viral vs bacterial) using the Centor and Modified Centor criteria scores.^[4,5] Here the score was 1 and thus the possibility of bacterial pharyngitis was kept very low (5–10%) and as such, the patient should not have been treated on the line of suspected GAS pharyngitis if the antimicrobial stewardship practices (ASP) had been adhered to.^[5-7] Another very common cause of febrile bicytopenia in our region is dengue which also has an acute picture. However, the possibility was kept very low in view of the time of the year (March) and the presence of localizing (upper respiratory tract) symptoms.

However bacterial superinfection could not be ruled out at presentation and hence azithromycin was not stopped. He was also started on Tab. paracetamol, fexofenadine, and adequate oral hydration. Once the PCR confirmed Influenza B and procalcitonin was <0.5 ng/mL, he was started on Cap. oseltamivir (75 mg BD for 5-days) and azithromycin was

discontinued. The bicytopenia resolved over next 3 days along with the other symptoms. Two days later, he joined his duty in the hospital.

Discussion

This is the case report of a RT-PCR proven adult influenza B patient presented with bicytopenia (leukopenia plus thrombocytopenia) and recovered with oseltamivir. This emphasised the lack of ASP in doctor's self-prescription.

There is no definitive clinical criteria to differentiate amongst the different influenza types. Two studies found no differences in clinical presentation by influenza type, while other studies did detect differences.^[8] For example, myalgia (as well as elevated CPK-NAC), sore throat, and hoarseness are reportedly more common among patients with influenza B than those with influenza A.^[2,9] Even in our case, these were amongst the initial and predominant presenting complaints. However, in our case, CPK levels were within normal limits.

The mechanism of bone marrow suppression seen in viral illnesses is variable, and a number of different mechanisms have been proposed depending upon the virus involved.^[10] Leukopenia is more commonly seen in influenza B infections (32.1% cases compared to 8.1% cases in influenza A).^[2] The mechanism of this cell line depletion has been found to be cytokine mediated apoptosis based on studies done in mice.^[10] Mild thrombocytopenia is an usual finding in influenza with counts being typically lower in influenza B than influenza A.^[2,11] The exact mechanism is still unclear.^[12] There have been very few case reports (<10) of adult influenza cases presenting with thrombocytopenia <100000/mm³. Also, there have been only a few case reports of pancytopenia associated with influenza A, with majority being in pediatric population.^[13] As is consistent with observations in other case reports, the counts rapidly improved with oseltamivir and a complete recovery was noticed in our case also on follow up in OPD 1-week later.^[14]

Clinically it is not difficult to differentiate between bacterial and viral pharyngitis. Signs and symptoms most indicative of GAS pharyngitis (absence of cough, fever >38°C, swollen tender anterior cervical nodes, tonsillar swelling or exudate and predominance in children and younger adults) have been used to calculate the modified Centor score.^[15] In our case, the modified Centor score was 1 which indicates a probability of 5–10% for GAS pharyngitis and thus ideally no further antibiotics or throat cultures should have been done, contrary to what was done in our case, depicting lack of ASP even among doctors' community.^[15] Pharyngitis and influenza like illnesses are amongst the most common cause of OPD visits to a general practitioner in the winters and greater awareness is needed regarding the judicious use of antimicrobials and laboratory services.

Influenza is a very common illness and CDC estimates that influenza has resulted in between 39-56 million illnesses, and

between 24–62,000 deaths in 2019–2020 season in the US alone.^[3,16] As compared to influenza A, influenza B has been relatively neglected by the healthcare fraternity. This is a result of early studies that concluded that influenza B posed less of a disease burden than influenza A.^[16] Furthermore, because of the ability of influenza A to cause severe pandemics, it is more frequently a topic of media coverage than influenza B. However, in the last 2 decades, there have been numerous studies from around the world to suggest that influenza B also has substantial public health burden, contrary to the popular perception.^[16] It thus becomes important to know the uncommon and thus, potentially misleading presentations of this common disease entity. This will reduce unnecessary antibiotic usage, investigations, and hospitalizations on a larger scale.

The anti-viral neuraminidase inhibitor, oseltamivir is known to have a higher efficacy against Influenza A compared to Influenza B when measured in terms of days of febrile illness and virus persistence but has clinical effectiveness for both when compared to non-treated groups.^[17,18] This case highlights the possible role of oseltamivir in the rapid recovery of the hematological abnormalities associated with influenza. There is a lack of studies that address this aspect. Ours is an isolated case report and there is a need for further studies on the role of neuraminidase inhibitors in hematological recovery of influenza patients. This becomes more important since oseltamivir and its role is being questioned in the management of influenza and the drug has recently been downgraded in the WHO list of essential medicines.^[19]

Take home messages

- Influenza B can have varied presentations such as bicytopenia.
- The cytopenia that occurs with influenza responded well to neuraminidase inhibitor (oseltamivir), however there is lack of sufficient credible literature to draw any meaningful conclusion.
- Modified Centor criteria to clinically differentiate viral and bacterial pharyngitis is still not used in real world practice.
- Doctors community will have to be proactive in antimicrobial stewardship practices, then only others will follow.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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