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In January, a 58 year old male with a history of refractory multiple myeloma presented to the emergency department after 4 days of fever, rigors, severe fatigue, chills, dry non-productive cough, and expiratory wheezing. A CT scan showed bilateral patchy infiltrates. A nasopharyngeal (NP) swab was collected and a rapid influenza A/B PCR test was performed, which was negative. A molecular multiplex test for respiratory pathogens (RP) was performed on the same NP swab and was also negative. The patient had received the influenza vaccine two weeks prior.

The patient was admitted for further evaluation. The next day, he experienced tachycardia and worsening hypoxia, requiring intubation and admission to ICU for respiratory failure. A bronchoscopy was performed and the bronchoalveolar lavage (BAL) fluid was collected and sent for multiplex RP testing. The BAL was positive for influenza A (2009/H1N1).

What could explain the discordant rapid influenza PCR and multiplex RP results?

A. The NP swab was improperly collected.
B. The virus is no longer present in the NP.
C. His recent vaccination led to a false positive result on the BAL.
D. Multiplex RP testing is more sensitive if performed on BAL than NP swab.
E. A and B

Answer and Explanation

The correct answer is E. Influenza A virus infections are characterized by the rapid onset of fever, cough, upper respiratory symptoms, headache, and malaise. Transmitted via respiratory droplet, the influenza virus preferentially infects respiratory epithelial cells via sialic acid receptors. Following infection of the nasopharynx, viral replication peaks within 48 hours and occurs in both the upper and lower respiratory tract. Damage to the respiratory epithelium leads to exudation of fluid into the airways and can lead to hypoxemia and respiratory failure. Neuraminidase inhibitors such as oseltamivir are the most common antiviral therapies, as they are active against both influenza A and B viruses. Complications following primary influenza infection can arise, such as secondary bacterial or viral pneumonia, especially among immunocompromised populations.

The concentration of virus is highest in the nasopharynx within the first few days of symptom onset and can be detected in most respiratory secretions. Nasopharyngeal swabs are the preferred specimen type for influenza testing; however the sensitivity is dependent on proper specimen collection. Unlike direct fluorescent antibody testing, which determines the quality of a specimen by the number of ciliated epithelial cells present, molecular methods do not provide the same the specimen quality check leading to potential false negative results due to improper sample collection.

In this particular patient case, the negative result on the rapid influenza PCR test and the multiplex RP may be due to multiple factors:

Answer A: Could be correct, as the NP swab, if collected improperly, could lead to a false negative result.
Answer B: Could be correct, as the negative NP swab and subsequent positive BAL is likely an indication of the pathogenesis of the virus. Infection with the influenza virus begins in the upper respiratory tract and progresses to the lower respiratory tract as the infection develops. The optimal specimen type for the detection of influenza virus is ultimately where the virus is actively replicating. In this case, the BAL provided a more accurate test result as it better reflected the stage of influenza infection in this patient (i.e., lower respiratory tract disease).

Answer C: Incorrect. If the patient received the nasal FluMist vaccine, the live attenuated virus could lead to false positive results from the NP swab. As the NP swabs were negative for influenza, this is unlikely to be the case. In addition, false positive results due to recent FluMist vaccination are typically positive for all influenza viral targets (i.e., influenza A, influenza B and all typing targets available). Further, based on the age and immunocompromised status of the patient, he most likely received the influenza vaccine by intramuscular injection, which does not cause false positive influenza results.

Answer D: Incorrect, while the overall sensitivity is high for detecting influenza viruses on multiplex RP panels, studies have shown that NP swabs have either equal\(^3\) or slightly increased\(^4\) sensitivity than lower respiratory samples such as the BAL.

Answer E: This is the most correct answer, as identifying potential negative results due to improper specimen collection or inappropriate specimen type can be challenging to distinguish. It is likely that the BAL represented a better specimen, given the progression and severity of the patient’s symptoms. However, improper collection technique is a common problem when trying to attain a true nasopharyngeal swab and certainly could be a contributing factor in this case.

References


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