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DURING INFLUENZA SEASON: ALL INFLUENZA-LIKE ILLNESSES ARE NOT DUE TO INFLUENZA: DENGUE MIMICKING INFLUENZA

Burke A. Cunha, MD*† and Muhammad Raza, MBBS*†

*Infectious Disease Division, Winthrop-University Hospital, Mineola, New York and †State University of New York School of Medicine, Stony Brook, New York

Reprint Address: Burke A. Cunha, MD, Infectious Disease Division, Winthrop-University Hospital, 222 Station Plaza North, Suite #432, Mineola, NY 11501

☐ **Abstract—Background: During influenza season, many patients present to the emergency department (ED) for evaluation with influenza-like illnesses (ILIs). ILIs are commonly due to influenza A or B, but other infections may mimic influenza in their clinical presentation. With the high volume of ILIs presenting to the ED during influenza season, the ED physician should be alert to other infections masquerading as influenza. Case Report: We report an interesting case of a 31-year-old female who presented with an ILI during influenza season. She had recently been in contact with multiple people with influenza. Her nonspecific laboratory tests done in the ED were consistent with influenza, except for a highly elevated serum ferritin level. The serum ferritin level was the key finding that led to the correct diagnosis of dengue fever, which she acquired during a recent trip to Haiti. Why Should an Emergency Physician Be Aware of This?: During influenza season, facing high patient volumes of ILIs in the ED, the ED physician needs to be aware of clinical features in ILIs that may suggest a mimic of influenza.** © **2015 Elsevier Inc.**

☐ **Keywords—thrombocytopenia; leukopenia; elevated ferritin levels**

INTRODUCTION

In the northern hemisphere, influenza season usually begins in October, peaks in February, and ends by March. Most adults ill enough to be admitted with the hospital with an influenza-like illness (ILIs) have influenza A or B. However, influenza has many mimics and a variety of infectious diseases may present as an ILI. An ILI may be defined as acute onset of fever, chills, headache, sore throat, dry cough, and severe myalgias. Parainfluenza virus, particularly HPV-3, Legionnaires' disease (LD) and adenovirus not infrequently present as an ILI-mimicking influenza (1–3). We present a case of an adult admitted via the emergency department (ED) during influenza season with an ILI initially thought to have influenza, but that was later found to be an unusual mimic of influenza.

CASE REPORT

A 31-year-old female was admitted via the ED with fever, chills, headache, and prominent myalgias in fall. She also had nausea/vomiting and fatigue for 4 days. The patient returned from Haiti a week earlier after spending 2 weeks there on a health mission. She remained well for a week after returning from Haiti, but then developed fatigue and malaise, 2 days later she developed fever/chills and headache. The patient stated she was exposed to many people with influenza and she went to an urgent care clinic and asked to be tested for influenza. Her rapid influenza diagnostic test was negative, but she was given oseltamivir based on her contact history and symptoms. She took oseltamivir for 2 days and developed rash and swelling of both hands and feet. Physical examination was unremarkable except for a maculopapular, nonblanching,

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pruritic rash and swelling on the dorsum of both hands/wrists and feet/ankles mildly pruritic. Admission laboratory tests in the ED included a white blood cell count of 2.8 k/uL, her hemoglobin and hematocrit were normal, and her platelet count was 96 k/uL (n = 160–392 k/uL), aspartate aminotransferase was 75 IU/L (n = 13–39 IU/L), alanine aminotransferase was 27 IU/L (n = 4–36 IU/L), creatine phosphokinase (CPK) was 588 IU/L (n = 42–285 IU/L) and her serum ferritin level was 2140 ng/mL (n = 10–187 ng/mL). Nasal swab viral polymerase chain reaction for 17 respiratory viruses (BioFire Diagnostics Respiratory FilmArray PCR, Salt Lake City, UT) was negative. Chest x-ray (CXR) was clear. Oseltamivir was discontinued and her extremity rash and edema resolved. Her myalgias, fatigue, headache, nausea, and vomiting completely resolved in 2 days. Her leukopenia and thrombocytopenia rapidly resolved.

DISCUSSION

Her presentation was that of an ILI, and influenza was the most likely diagnosis based upon her influenza contact history and ILI symptoms, leukopenia, and thrombocytopenia. In adults ill enough to be hospitalized, influenza A can be essentially ruled out if thrombocytopenia is not present. That the nasal swab was negative for influenza, as well as other respiratory viruses, could be explained on the basis of antecedent oseltamivir therapy or specimen timing, i.e., relatively late in the course of her illness. The rash of her hands/feet was difficult to explain and suggested parvovirus B 19. Rash is uncommon with adult influenza and when it occurs in children it is usually maculopapular and truncal and does not usually involve the extremities. It was thought that because of the pruritic nature of the rash, that it could be due to the neuraminidase inhibitor that she was taking (4–6). Although cutaneous and neurologic adverse side effects of oseltamivir are most common in children, it was not unreasonable to consider that the rash was a possible cutaneous manifestation of oseltamivir.

The key clue to the final diagnosis was a highly elevated serum ferritin level. The patient had no underlying disorders associated with elevated ferritin levels. There are many causes of highly and persistently elevated ferritin levels, e.g., liver disease and renal insufficiency. However, relevant to the differential diagnosis of an ILI, the key diseases are dengue and LD. Dengue fever should only be considered in the differential diagnosis of an ILI in recently returned travelers from dengue-endemic areas. From the experience gained in the swine influenza (H_1N_1) epidemic of 2009−2010, we reported that elevated serum ferritin levels are not a characteristic feature of influenza A in adults. In fact, the finding of a high serum ferritin level during the 2009−2010 swine flu pandemic effectively ruled out influenza and always suggested an alternate diagnosis, e.g., LD.

This case should be of interest to ED physicians facing large numbers of patients during influenza season who present to the ED with ILIs. It is important for ED physicians to quickly differentiate influenza A from dengue fever in hospitalized adults. The most important reason has to do with infection-control considerations to prevent spread of influenza in the ED to other patients and staff. Secondly, influenza A should be treated as soon as it is diagnosed in the ED. There is no specific therapy for dengue fever. In “walking well” adults with an ILI who are not ill enough to be admitted, testing is not necessary. This patient’s illness was compatible with influenza, but an unusual feature was the hand/foot rash that was ascribed to a cutaneous manifestation or oseltamivir therapy (4–6). For ED physicians, history is important. In this case, favoring influenza was a history of recent contact with influenza, and favoring dengue was the travel history to Haiti. Because rash is not a feature of influenza, the case was a diagnostic dilemma because dengue has a rash that is typically truncal, not an extremity rash. Therefore, the nonspecific laboratory findings were all that ED physicians had for a rapid presumptive diagnosis. Her routine nonspecific laboratory findings provided the key clue that eventually led to the consideration of another diagnosis, i.e., dengue fever. While dengue fever may present with the same signs and symptoms as influenza, and many of the laboratory abnormalities, both dengue fever and influenza A are associated with leukopenia, relative lymphopenia, thrombocytopenia, and a unelevated erythrocyte sedimentation rate and C-reactive protein. Serum transaminases and the serum CPK levels may be elevated in both influenza A and dengue fever. Highly elevated serum ferritin levels were the key nonspecific laboratory clue in this case, pointing away from the diagnosis of influenza A (7,8).

During the swine flu (H_1N_1) in 2009–2010 pandemic, LD was the other infection most likely to mimic influenza A in hospitalized adults (7–10). In this case, against the diagnosis of LD was leukopenia and thrombocytopenia, which are not features of LD, and the CXR was negative. Because influenza was unlikely based on the serum ferritin level, further consideration was given to her recent trip to Haiti. Although the rash of dengue fever is typically truncal, dengue titers were ordered. Dengue antibody titers were highly elevated, i.e., her dengue IgM titer was 8.59 (n ≤ 1.64) and her dengue IgG titer was 9.57 (n ≤ 1.64), confirming the diagnosis of dengue fever.

Mild elevations of serum ferritin may be part of the acute-phase response, but very high or prolonged elevations of serum ferritin levels indicate the elevation is