Influenza A Infection and Anaphylaxis in a Pediatric Patient Hospitalized for Asthma Exacerbation

ERIC J. CHOW, MD, MS, MPH; IVONA SEDIVA, MD

ABSTRACT

Influenza infections can cause a variety of different systemic problems beyond respiratory symptoms. A 4-year-old boy with a history of atopy, infected with influenza A, presented to our hospital with an asthma exacerbation developed symptoms of anaphylaxis. He was treated with a full course of oseltamivir and symptoms resolved without recurrence of allergic reaction. Infections have been implicated as causes of anaphylaxis but this has mostly been limited to parasites. While viral infections have been documented as causes of urticarial rashes, anaphylaxis due to viral infection has only been reported once, in an adult patient. There have not been any reports of anaphylaxis related to influenza infections. Early recognition and treatment of patients with influenza may prevent progression of systemic allergic reactions.

KEYWORDS: influenza, anaphylaxis, urticaria, allergy, asthma

INTRODUCTION

Influenza infections are a major cause of morbidity and mortality every year. Between 2015 to 2016, there were 24.6 million cases of influenza, 95.9 per 100,000 patients requiring hospitalization and almost 12,000 cases resulted in death.[1] Symptoms can include fever, cough, rhinitis, headaches and myalgias.[2] While skin manifestations of viral infections are common, they are an uncommon presentation in patients infected with influenza.[3] Influenza is a known precipitant of asthma exacerbation; however, anaphylaxis attributed to influenza has not previously been reported.[4] In this report we describe a case of anaphylaxis associated with influenza A infection in a pediatric patient hospitalized for an asthma exacerbation.

CASE REPORT

Our patient is a 4-year-old boy with a history of moderate persistent asthma and eczema who presented to the hospital with rhinorrhea, cough and shortness of breath, worsening over a two-day period. He was tachypneic with a fever of 39.2°C. He had decreased aeration on auscultation and combined diffuse inspiratory and expiratory wheezes. He had his baseline eczematous rash but no other skin findings. Respiratory viral testing was positive for influenza A by rapid influenza test (Xpert; Cepheid, Sunnyvale, CA). No other laboratory studies were drawn at the time of admission. Standard treatment for his asthma exacerbation was initiated, including beta agonist inhaler treatments and oral corticosteroids. His tachypnea persisted, with intermittent hypoxia. He was given continuous albuterol, magnesium and a normal saline bolus and admitted to the pediatric intensive care unit (PICU) for further management.

The patient's work of breathing improved with continued treatment of his asthma. He was also started on oseltamivir. Four hours later, the patient developed a diffuse urticarial skin eruption encompassing his trunk, face and extremities. He had no swelling or vomiting. Initially, his respiratory status remained stable. He was given intravenous (IV) diphenhydramine, which resulted in improvement of his rash. After a 2-hour observation period, he was transferred to the pediatric floor. Upon arrival, the patient redeveloped diffuse urticaria and became hypoxic to 80% on room air with significantly increased work of breathing. He was placed on a non-rebreather mask and was treated for anaphylaxis. The patient was given intramuscular epinephrine, IV ranitidine, albuterol and IV corticosteroids and he was transferred back to the PICU. Over the next 2 hours, his rash and work of breathing improved. His asthma improved and he had no further rash during his hospitalization. He was discharged home on hospital day three. Since discharge, his fever resolved and he completed his course of oseltamivir without further allergic symptoms. He has not had any further anaphylactic reactions since discharge.

During his hospitalization, the patient only ate food that he had previously tolerated. Latex gloves are not used in the hospital. An allergist has followed the patient in the outpatient setting and reports intermittent compliance with his home asthma controller medications. He has been seen in the emergency department for asthma symptoms four times a year prior to this hospitalization, with only one prior hospitalization. His asthma triggers included dust mites, dogs, mold, pollen and smoke exposure. The patient has a notable allergy to latex. He had a non-urticarial skin reaction when touching tomatoes but this had been localized to his mouth and hands. He had received inactivated influenza vaccines during the 2015–2016 and 2016–2017 influenza seasons without any adverse reactions. Allergy testing 2 years prior was notable for allergic reaction to dust mites, dog dander, mold, cats and pollen. During an outpatient follow-up, the allergy test was repeated and showed no change in test results.

DISCUSSION

Anaphylaxis is a systemic reaction to an allergen through the triggering of T helper 2 cells, activating mast cells and basophils. The resulting symptoms are life threatening.[5] The most common allergens include food, insect stings, and medications.[6] The diagnosis of anaphylaxis is based on the clinical presentation of cardiovascular, dermatologic, respiratory and gastrointestinal symptoms.[5] Three criteria were established to help physicians diagnose anaphylaxis generally involving two or more organ systems with or without the presence of a likely or known allergen.[7] There are two documented cases of anaphylaxis to oseltamivir, both in adults.[8,9] Our patient, however, completed his course of oseltamivir without any further reactions and thus the medication was unlikely the cause of the anaphylaxis experienced in the hospital.

A review of the literature showed that while bacterial, parasitic and viral infections, including influenza, have been implicated in the development of urticarial rashes, reports of infections causing anaphylaxis have been limited to case reports, mostly involving parasitic infections.[10] Only one case of a patient with anaphylaxis and associated viral upper respiratory infection (URI) symptoms was reported. This 64-year- old female had symptoms of cough and rhinitis without known exposures to antigens who developed anaphylactic shock.[11] Anaphylactic shock reoccurred when she developed URI symptoms within the same year; however, no viral testing was reported at the time of her symptoms.

The mechanism for allergic response following mast cell and basophil activation involves allergen-IgE interaction followed by a release of mediators including tryptase, tumor necrosis factor and histamine.[12] Mechanisms for influenza activation of the body's allergic response have been proposed. Influenza infects the body through the respiratory tract. The lung parenchyma is lined with cells that serve as a first line of defense against invading pathogens including macrophages, dendritic cells and mast cells.[13] Activation of mast cells leads to degranulation, which in turn promotes inflammatory responses and further recruitment of mast cells. Influenza A and other viruses are known causes of asthma exacerbation.[14] In patients with asthma, the accumulation of mast cells in the lung leads to worsening respiratory symptoms.[15] Grunewald et al suggest that viruses like influenza A can directly activate mast cell degranulation through IgE and viral antigen interaction.[16] Molecular mimicry is another plausible mechanism whereby viral antigens cross react with IgE specific to other allergens. In some cases, viral infections produce sufficient inflammatory response that they activate T helper 2 cell and subsequent allergic response. Future studies will be needed to further understand the complex molecular explanations for these interactions.

CONCLUSION

Recognizing influenza A and other viral infections as potential causes of systemic allergic response is required to reduce patient morbidity and mortality. Studies have shown that viral infections can induce pathways that trigger allergic reactions. This case of influenza A infection associated with anaphylaxis highlights the need to treat allergic symptoms early in patients with known history of atopy and viral respiratory infections.

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Authors

Eric J. Chow, MD, MS, MPH, Departments of Medicine and Pediatrics, Warren Alpert Medical School of Brown University; Rhode Island Hospital and Hasbro Children's Hospital, Providence, RI.

Ivona Sediva, MD, Department of Pediatrics, Warren Alpert Medical School of Brown University; Division of Pediatric Critical Care, Hasbro Children's Hospital, Providence, RI.

Correspondence

Dr. Eric J Chow
Departments. of Medicine and Pediatrics,
Rhode Island Hospital, Hasbro Children's Hospital
245 Chapman Street, Suite 100, Providence, RI 02905
401-444-6072
Fax 401-444-8804