

Hypereosinophilia Associated with Echinacea Use

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Abstract: Echinacea, believed by herbal practitioners to enhance the immune system, is one of the most widely used herbal supplements in the United States. Like most herbal products, it lacks strict FDA regulation and more information is needed about its potential adverse reactions. Here, we report the case of a patient with eosinophilia of unclear etiology whose condition resolved after cessation of this supplement. We feel this likely represents an IgE-mediated allergic process to echinacea.

Key Words: echinacea, eosinophils, hypereosinophilia

Echinacea, the purple cone flower of the Asteraceae family, has been used for centuries for its reported immune stimulatory effects and is currently one of the most commonly used herbal supplements. In 2002, echinacea was consumed by 40% of people in the United States who used herbal products.¹ A recent meta-analysis evaluated the immune-enhancing effects of echinacea in humans and found that it decreased the odds of developing a cold by 58% and reduced the duration of a cold by an average of 1.4 days, though other studies have not shown it to be effective in treating upper respiratory tract infections.^{2,3}

Case Report

A 58-year-old white male was referred for eosinophilia found on a routine complete blood count. The patient's only complaint at the time was of having a several week history of mild crampy abdominal pain, with occasional nausea and diarrhea. His past medical history included a long history of controlled asthma and

allergic rhinitis, hyperlipidemia, resolved hepatitis B infection, cholelithiasis, an inguinal hernia, and a hiatal hernia. He denied any smoking, alcohol, or illegal drug use, and his family history was noncontributory. Physical exam was unremarkable.

Medications included esomeprazole, sildenafil citrate, ezetimibe/simvastatin, aspirin, cetirizine, fluticasone nasal spray, olopatadine eyedrops, calcium supplements, and glucosamine. He had also started taking echinacea supplements several weeks prior around the time his abdominal pain started. He otherwise had an allergy to iodine.

Labs revealed a white blood cell count of 24,900/ μ L with 74% eosinophils, for an absolute eosinophil count of 17,800/ μ L (normal <350 eosinophils/ μ L). The rest of the differential included 7% neutrophils, 11% lymphocytes, and 11% monocytes. His hemoglobin was 12.7 g/dL, with a platelet count of 208,000. Serum chemistries were normal except for slightly elevated creatinine, which normalized a few weeks later. Liver function tests and lactate dehydrogenase levels were also normal. Of note, he had a very elevated Immunoglobulin E (IgE) level of 1390 IU/mL (normal <114 IU/mL).

An extensive evaluation was initiated. Bone marrow aspirate showed a mildly hypercellular bone marrow, marked eosinophil hyperplasia with mild atypia, and trilineage hematopoiesis with normal maturation. No evidence of myeloproliferative disease, lymphoma, or

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Key Points

- In 2002, echinacea was consumed by 40% of people in the United States who used herbal products.
- Although it is unclear if echinacea has true immunostimulatory effects in humans, it is widely used by the general public for its supposed health benefits.
- We urge physicians to be aware of the possibility of severe allergic reactions to echinacea, especially in view of its widespread use.

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infection was noted. Flow cytometry revealed increased eosinophils, but no monoclonal B cell population, aberrant T cell antigen expression, or increased immunophenotypic blasts. Bone marrow cytogenetics were also normal. Tests for adrenal insufficiency and parasitic and connective tissue disorders were also negative, including evaluation for human immunodeficiency virus (HIV), systemic lupus erythematosus, scleroderma, Wegener granulomatosis, celiac disease, *Clostridium difficile*, *Bartonella*, *Toxocara*, *Coccidioides*, *Cryptococcus*, and *Brucella*. Stool ova and parasite studies and serologic testing for IgG antibodies against *Strongyloides* antigens were also negative.

Since the cause of hypereosinophilia was not readily apparent at first, the patient was treated for hypereosinophilic syndrome, a disorder characterized by persistent eosinophilia with no evident cause, and signs or symptoms of organ involvement by eosinophilic infiltration. Both hydroxyurea and imatinib were tried, but the only effective therapy was prednisone. Any attempt to taper prednisone resulted in increasing eosinophil counts and worsening nausea and diarrhea. Three years after treatment had started, the patient mentioned that he had stopped taking echinacea supplements but had continued taking the rest of his medications. Two weeks after echinacea discontinuation, his eosinophil counts and IgE levels were checked, and they had markedly improved to almost normal levels. Prednisone was quickly tapered off, and, at the patient's last visit, he continued to have normal eosinophil counts and IgE levels six months after discontinuation of the supplement.

Discussion

Although it is unclear if echinacea has true immunostimulatory effects in humans, it is widely used by the general public for its supposed health benefits, and because it is felt to be a natural and "safe" supplement. Like many herbal products, Food and Drug Administration (FDA) regulation is lacking and the full spectrum of side effects is not known, but several adverse reactions have been reported, including possible allergic reactions. The first reported case of anaphylaxis associated with echinacea use was thought to be secondary to an IgE-mediated process.⁴ The patient described in this case had pharyngeal irritation almost immediately after ingesting echinacea. She was found to have positive skin prick testing with aqueous echinacea solution, and radioallergen sorbent testing (RAST) of her serum confirmed the presence of echinacea-binding IgE, which supports echinacea as the cause of her anaphylaxis. The same author of the previous case of anaphylaxis also reviewed 51 adverse events associated with echinacea use, and 26 cases suggested possible IgE-mediated

hypersensitivity, including 4 cases of anaphylaxis, 12 cases of acute asthma, and 10 cases of urticaria/angioedema.⁵

Other authors have also reported possible allergic reactions to echinacea. One study evaluated echinacea efficacy and safety in treating upper respiratory tract infections in children.³ Two of the 407 children involved in the study had croup symptoms shortly after taking echinacea, which could have been due to an allergic reaction. Also, a very recent Swedish study evaluated adverse reactions associated with complementary medicine substances, and found echinacea-containing products to be associated with several cases of anaphylaxis, angioedema, and urticaria.⁶ Although the above information is anecdotal and should be interpreted carefully, it does provide evidence of the possibility of an IgE-mediated hypersensitivity reaction to echinacea.

Conclusion

It is known that patients with atopy are at higher risk for developing more frequent or severe allergic reactions, and this may have been a factor in our patient's reaction to echinacea.⁷ This case highlights the importance of a thorough medication history (including prescription medications, over-the-counter drugs, vitamins, and herbal products) during evaluation of eosinophilia. To our knowledge, this is the first reported case of eosinophilia in a human patient associated with echinacea use. Although it is possible that our patient had another etiology for eosinophilia besides an allergic reaction to echinacea, the temporal relationship of the patient's eosinophilia and elevated IgE levels to echinacea use, and normalization of these parameters after cessation of echinacea use, strongly suggests a causal relationship. We urge physicians to be aware of the possibility of severe allergic reactions to echinacea, especially in view of its widespread use.

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