Case 8

T.C. is a 24 year old woman who presented with a severe non-productive cough in January with a worsening pruitic[1] skin rash. The patient gave a history of eczema,[2] particularly in the winter and the patient reported an allergy to "wool." Her parents told her that she had severe "cradle cap" prior to the age of 6 months and was a "colicky" baby. Her mother has a history of hay fever and her father has a history of skin rashes and asthma. On physical exam she had a papular[3] erythematous rash on her neck, wrists and antecubital and popliteal fossae (Fig. 1). Many areas were lichenified[4] (thickened) and the patient reports frequent scratching. The remainder of the physical exam was unremarkable. Laboratory studies revealed a markedly elevated serum IgE. She received topical corticosteroids and non-sensitizing moisturizing emollients, and was advised to avoid strong detergents and perfumes. The patient was prescribed hydroxyzine.[5]

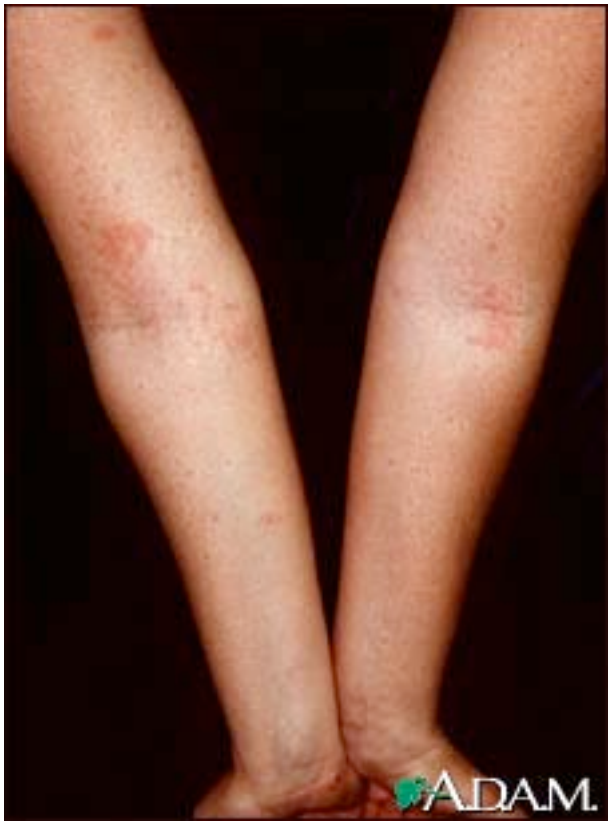

Fig. 1. Chronic rash in T.C. at age 24.

The patient did well until April when she noted the onset of nasal and eye itching associated with severe nasal congestion which was much worse than in previous spring allergy seasons. Antihistamines gave only moderate relief. She was referred to an allergist who administered skin tests and found that she had positive skin tests to tree pollen and dust mites. She was instructed in how to make her home as dust-free as possible and prescribed an inhaled nasal corticosteroid an an oral antihistamine. In addition, she was given a trial of topical tacrolimus (an immunosuppressive drug). On this program she improved and by June was relatively

Case 8, cont'd

asymptomatic. The possibility of beginning immunotherapy against dust mites and tree pollen was considered, but rejected.

[1]Itchy
[2]A general term used to describe a variety of conditions that cause an itchy, inflamed skin rash.
[3]Raised
[4]Thickened
[5]An antihistamine with mild sedating properties for severe itching

Questions for Case 8

1. Atopic dermatitis is sometimes described as the "itch that rashes." Why does scratching exacerbate the rash?

2. The pathogenesis of atopic dermatitis involves activated mast cells. Explain how mast cells become activated. Which cytokines are produced locally? What do mast cells secrete that exacerbate the rash?

3. How can inhaled allergens such as dust mites lead to an exacerbation of the skin rash?

4. The pathology of atopic dermatitis consists of infiltration of the dermis by mononuclear cells, which are chiefly T-cells, as well as macrophages and Langerhans cells (dendritic cells of the skin). Recent studies have demonstrated that human epithelial cells have the capacity to produce a cytokine that activates dendritic cells. The activated dendritic cells secrete a subset of chemokines for lymphocytes. How might these chemokines promote the accumulation and T_H2 polarization of T-cells?

5. Individuals with atopic dermatitis are predisposed to certain viral infections, such as those due to herpesvirus. Why?

6. One of the therapeutic options for atopic diseases is allergen-specific immunotherapy. Although immunotherapy improves about 80% of patients with allergies to tree pollen and dust mites, it is of little or no benefit in patients with atopic dermatitis and sometimes makes them worse. In general, how might allergen-specific immunotherapy result in amelioration of allergic symptoms?

7. Recently, the FDA issued a warning concerning the safety of topical agents that target the mTOR (mammalian target of rapamycin), such as sirolimus and tacrolimus. Studies in rats demonstrated increased incidence of lymphomas after administration of these agents, which have also been associated with up to 25 cases of malignancies in humans. Curiously, these drugs have also been used to treat some malignancies and i*n vitro* studies show that inhibition of mTOR triggers cell death in sensitive tumor cell lines. Although the mechanism by which rapamycin and its analogs might contribute to the development of malignancies is unknown, suggest a plausible mechanism.