Elevated IgE Is Not Always Allergic In Origin: A Case Of Hodgkin's Lymphoma Presenting With Elevated IgE

Anne K. Ellis, MD FRCPC and Susan Waserman MDMC, FRCPC

Division of Allergy & Clinical Immunology, McMaster University, Hamilton, ON, Canada

Abstract

Background: While lymphoproliferative disorders are known associations of the hyper-IgE syndrome, massive elevations of IgE as a manifestation of underlying lymphoproliferative disease is rare. **Methods:** We present a case of a patient referred to the adult allergy clinic for an extremely elevated IgE, who was ultimately diagnosed with a Hodgkin's lymphoma. **Results:** A 22 year old female was referred to our allergy clinic for evaluation of elevated IgE in the setting of fatigue, pruritus and anemia. She had a 4-year history of fatigue, insomnia and diffuse itching, initially presenting at a time of severe emotional stress. She denied weight loss, fever or decreased appetite, but described night sweats while taking venlafaxine, which resolved on its discontinuation. She was diagnosed with anemia and B12 deficiency 3 years prior; treatment with B12 injections corrected her B12 levels but not her anemia. Six months prior she was diagnosed with iron deficiency anemia; however, her hemoglobin did not rise with oral or IV iron. Bone marrow aspiration confirmed the presence of iron stores. Her anemia was microcytic with an associated thrombocytosis, reticulocytosis, elevated CRP (146.0 mg/L) and an ESR of 50 mm/hr. Quantitative immunoglobulins demonstrated an IgE level of 22,562 U/L, prompting the referral to Allergy/Immunology. She had no history of recurrent infections, eczema or periodontal disease. Stool was negative for ova & parasites. A chest X-ray revealed large bilateral anterior mediastinal masses that demonstrated prominent uptake on subsequent gallium scanning. CT of the chest/abdomen confirmed the presence of multiple enlarged anterior mediastinal lymph nodes and mild hepatomegaly. Lymph node biopsy was consistent with Hodgkin's lymphoma, nodular sclerosing subtype, grade I/II. Bone marrow aspiration showed no evidence of Hodgkin's disease in the marrow. **Conclusion:** Although uncommon, hyper-immunoglobulin E may be a manifestation of an underlying lymphoma. This diagnosis should be considered in evaluating any significant elevation of IgE.

Background

- Elevated levels of total serum IgE are associated with many diseases, including ABPA, parasitosis, atopic dermatitis, adult HIV infection, hyper-IgE (Job's) syndrome, Sézary's syndrome, IgE myeloma, and Kimura's disease[1]
- Lymphoproliferative disorders are known associations of the hyper-IgE syndrome[2-5]
- Reports of massive elevations of IgE as a manifestation of underlying lymphoproliferative disease is rare and are mostly limited to IgE producing plasmacytomas (also rare, representing 0.01% of all plasmacytomas)[4]
- Three cases are represented in the literature of Non-Hodgkin's lymphoma associated with markedly elevated levels of IgE[6-8] – one of which was asymptomatic and discovered serendipitously in the evaluation of perennial rhinitis[6].
- Here we present a case of a patient referred for elevation of a markedly elevated IgE, ultimately diagnosed with underlying Hodgkin's lymphoma.

Presentation of the Case

- A 22 year old female was referred to our allergy clinic for evaluation of elevated IgE in the setting of fatigue, pruritus and anemia.
- She had a 4-year history of fatigue, insomnia and diffuse itching, initially presenting at a time of severe emotional stress
- She denied weight loss, fever or decreased appetite, but described night sweats while taking venlafaxine, which resolved on its discontinuation
- She had been diagnosed with anemia and B12 deficiency 3 years prior; treatment with B12 injections corrected the serum B12 but not the anemia
- Six months prior she was diagnosed with iron deficiency anemia; however, her hemoglobin did not rise with oral or IV iron therapy
- Bone marrow aspiration confirmed the presence of iron stores
- Her anemia was microcytic with associated thrombocytosis, reticulocytosis, elevated CRP (146.0 mg/L) and an ESR of 50 mm/hr
- Quantitative immunoglobulins demonstrated an IgE level of 22,562 U/L, prompting the referral to Allergy & Immunology
- She had no history of recurrent infections, eczema or periodontal disease
- Stool was negative for ova & parasites
- Skin prick testing revealed …. There was no history of rhinitis, asthma or other allergic symptoms
- A chest X-ray revealed large bilateral anterior mediastinal masses that demonstrated significant uptake on subsequent gallium scanning
- CT of the chest & abdomen confirmed the presence of multiple enlarged anterior mediastinal lymph nodes and mild hepatomegaly
- Lymph node biopsy was consistent with Hodgkin's lymphoma, nodular sclerosing subtype, grade I/II
- Repeat bone marrow aspiration showed no evidence of Hodgkin's disease in the marrow
- She was treated with …..
- Chemotherapy is still in ongoing with…Response based on PET scan shows…; her IgE has decreased to: …..

Table of all chemistry, etc.

CXR, CT Chest/Abdo

Pathology slide?

Discussion

- Significant elevations of IgE are seen in various allergic diseases and parasitosis. In this case, the patient had no history of atopy, and parasitic work- up was negative
- Extreme elevations of IgE are also seen in IgE myeloma, but the patient's protein electrophoresis was normal, as was the bone marrow evaluation.
- Lymphomas are known to produce immunoglobulins, and cases have been reported of both B- and T-cell lymphomas associated with elevated IgE, but these are rare[6-8].
- Sézary's syndrome (a peripheral T-cell neoplasm characterized by a pruritic, exfoliative or infiltrated erythroderma, lymphadenopathy, and atypical T lymphocytes) has been associated with elevated circulating IgE levels when the malignant clone is a CD4+ helper phenotype and/or associated with eosinophilia[9,10].
- Elevated IgE levels (but not markedly) have also been reported in the setting of B-cell chronic lymphocytic leukemia[11] and in 2 patients with Hodgkin's disease[12].
- Our patient presented with extremely elevated levels of IgE in the setting of chronic profound fatigue and an unexplained anemia. Only the chest x-ray confirmed evidence of an underlying malignant process, underscoring the importance of this simple diagnostic test.

Conclusion

- **Although uncommon, elevated IgE may represent a manifestation of lymphoma or other lymphoproliferative disorder**
- **These diagnoses should be considered in evaluating any significant elevation of IgE**

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This paper was internally funded.