

Case report

Hodgkin's lymphoma presenting with markedly elevated IgE: a case report

Anne K Ellis^{1,2} and Susan Waserman*¹

Address: ¹Division of Clinical Immunology & Allergy, Department of Medicine, McMaster University, Hamilton, ON, Canada and ²Division of Allergy & Immunology, Department of Medicine, Queen's University, Kingston, ON, Canada

Email: Anne K Ellis - ellis.anne@gmail.com; Susan Waserman* - waserman@mcmaster.ca

* Corresponding author

Published: 7 December 2009

Received: 27 October 2009

Allergy, Asthma & Clinical Immunology 2009, **5**:12 doi:10.1186/1710-1492-5-12

Accepted: 7 December 2009

This article is available from: <http://www.aacijournal.com/content/5/1/12>

© 2009 Ellis and Waserman; licensee BioMed Central Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Markedly elevated IgE as a manifestation of a lymphoproliferative disorder has been only rarely reported.

Case Presentation: We present the case of a 22 year old female referred to the adult Allergy & Clinical Immunology clinic for an extremely elevated IgE level, eventually diagnosed with Hodgkin's lymphoma. She had no history of atopy, recurrent infections, eczema or periodontal disease; stool was negative for ova & parasites. Chest X-ray revealed large bilateral anterior mediastinal masses that demonstrated prominent uptake on gallium scan. Mediastinal lymph node biopsy was consistent with Hodgkin's lymphoma, nodular sclerosing subtype, grade I/II.

Conclusion: Although uncommon, markedly elevated IgE may be a manifestation of a malignant process, most notably both Hodgkin's and Non-Hodgkin's lymphomas. This diagnosis should be considered in evaluating an otherwise unexplained elevation of IgE.

Background

Elevated levels of total serum IgE are associated with many diseases, including allergic bronchopulmonary aspergillosis (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 [2-4], however a marked elevation of IgE as an initial manifestation of a lymphoproliferative disease is rare, and mainly reported in IgE producing plasmacytomas; also rare (0.01% of plasmacytomas)[5]. Three cases are reported 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 during an evaluation of perennial rhinitis[6]. Here we present a patient referred for evaluation of a markedly

elevated IgE, eventually diagnosed with Hodgkin's lymphoma.

Case Presentation

A 22 year old female was referred to our allergy clinic for evaluation of an elevated IgE in the setting of a 4 year history of fatigue; diffuse pruritus and a microcytic anemia (see Table). She denied weight loss, fever, or decreased appetite. She had night sweats while taking venlafaxine for depression, which resolved upon discontinuation of this medication. She had been diagnosed by Hematology with both B₁₂ deficiency and a possible iron deficiency (serum Fe was low but ferritin and total iron binding capacity were normal (see Table)); however, treatment with B12 injections and iron replacement did not correct the anemia. Bone marrow aspiration confirmed the pres-

ence of iron stores. There was associated thrombocytosis (platelet count $592 \times 10^9/L$, reticulocytosis (retic count $100 \times 10^9/L$), elevated C-reactive protein (146.0 mg/L) and an ESR of 50 mm/hr. Quantitative immunoglobulins demonstrated an IgE level of 22,562 kU/L, prompting the referral to Allergy & Immunology. Details of her investigations are summarized in Table 1.

She had no history of recurrent infections, eczema or periodontal disease, nor was there a history of foreign travel, diarrhea or other symptoms suggestive of parasitic infection. There was no history of allergic rhinitis (seasonal or perennial), asthma, sinusitis, otitis or other allergic disease. Her physical examination was entirely normal. Skin tests were positive to trees, grass and ragweed, and careful questioning confirmed an absence of clinical symptoms aside from intermittent cough. Stool examination was

negative for ova & parasites. Spirometry and methacholine challenge revealed a mild isolated decrease in diffusion capacity, and no airway hyper-responsiveness.

After initial investigations were completed, her symptomatology remained unexplained. Investigation was extended with repeat stool examination, and a chest x-ray, which revealed large bilateral anterior mediastinal masses (see Figure 1). Further evaluation with gallium scan demonstrated prominent diffuse uptake within these lesions, and a CT of the chest & abdomen confirmed the presence of multiple enlarged anterior mediastinal lymph nodes and mild hepatomegaly. A mediastinal lymph node biopsy was consistent with Hodgkin's lymphoma, nodular sclerosing subtype, grade I/II. She was reassessed by Hematology and treatment with ABVD (adriamycin, bleomycin, vinblastine and dacarbazine) was initiated.

Table 1: Laboratory parameters upon referral to Allergy & Immunology Clinic.

Parameter	Value	Reference (Units)	Parameter	Value	Reference (Units)
Creatinine	64	50-100 umol/L	WBC	10.2	4.0-11.0 $\times 10^9/L$
Urea	2.3	3.0-6.5 umol/L	Eosinophils	0.1	0.0-0.4 $\times 10^9/L$
Sodium	140	135-145 mmol/L	Hb	103	115-165 g/L
Potassium	3.7	3.5-5.0 mmol/L	MCV	76.7	82-99 fL
Chloride	104	98-107 mmol/L	Platelet	592	150-400 $\times 10^9/L$
Total Protein	81	60-80 g/L	Retic	100	10-86 $\times 10^9/L$
Albumin	33	35-50 g/L	ESR	50	1-20 mm/hr
A/G ratio	0.7	1.4-1.6	CRP	122	<3.0 mg/L
AST	14	<35 U/L	C3	1.67	0.73-1.73 g/L
ALT	22	<28 U/L	C4	0.3	0.13-0.52 g/L
GGT	65	<32 U/L	IgA	1.6	0.70-3.52 g/L
Alk Phos	293	40-120 U/L	IgD	4	<140 mg/L
Bilirubin	5	2-18 umol/L	IgE	18 429	<120 kU/L
Ferritin	173	51-400 ug/L	IgG	13.9	6.35-14.65 g/L
CK	27	<150 U/L	IgM	1.07	0.41-2.07 g/L
LDH	308	100-220 U/L	RF	<11.0	0-15.0 IU/mL
TIBC	43	4-80 umol/L			
Fe	4	9-30 umol/L			



Figure 1
Chest x-ray, PA and Lateral views.

Ongoing treatment with ABVD has resulted in a partial response based on PET scan FDG (F-18 fluorodeoxyglucose) uptake; IgE has decreased to 4,014 kU/L.

Discussion

Significant elevations of IgE are seen in various allergic conditions, parasitosis, and rarely, in lymphoproliferative malignancies. Specifically, extreme elevations of IgE have been documented in the setting of multiple myeloma, and B-cell lymphomas. In this case, the patient had no history of atopy, or parasitic infection and she had a normal protein electrophoresis and bone marrow evaluation.

Lymphomas are known to produce immunoglobulins, and rarely, cases have been reported of both B- and T-cell lymphomas associated with elevated IgE [6-8]. Sézary's syndrome (a peripheral T-cell neoplasm) has been associated with elevated IgE and/or eosinophilia when the malignant clone is of the CD4+ helper phenotype and produces an abnormal amount of the cytokine IL-4[9,10]. Modestly elevated IgE has also been reported in B-cell chronic lymphocytic leukemia[11] and in 2 patients with Hodgkin's disease (1 case of nodular sclerosing, one case of mixed cellularity, levels were 675 IU/mL and 310 IU/mL, respectively)[12].

Conclusion

Markedly elevated IgE may rarely present as an initial manifestation of a lymphoproliferative disorder such as a lymphoma. These patients may be referred for evaluation of allergy or immunodeficiency, such as hyperIgE syn-

drome. This patient had unexplained fatigue and anemia, and only chest X-ray was suggestive of a malignant process. Underlying lymphoproliferative disease should always be considered when evaluating an otherwise unexplained significant elevation of IgE, particularly when features of allergy or parasitosis are distinctly lacking. Specific work-up of significantly elevated IgE levels should be tailored to the clinical features of the case, but in this circumstance a serum LDH and a CXR helped to reveal the underlying causative lymphoma.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AKE and SW both saw this patient in an outpatient Allergy/Immunology clinic. AKE wrote the first draft of the manuscript and SW and AKE jointly worked on several subsequent revisions to the manuscript. Both AKE and SW contributed to the comments raised upon peer review and the final revised, accepted version of the manuscript. Both authors have read and approved the final manuscript.

Acknowledgements

No external funding was received to support this publication.

References

1. Ownby D: **Clinical significance of IgE.** In *Allergy principles and practice* Edited by: Adkinson NF Jr, Bochner BS, Busse WVV, Holgate SJ, Lemankse RF Jr. Mosy Year book, Inc, St Louis; 2003:1087-1101.
2. Gorin LJ, Jeha SC, Sullivan MP: **Burkitt's lymphoma developing in a 7-year-old boy with hyper-IgE syndrome.** *J Allergy Clin Immunol* 1989, **83**:5-10.
3. Leonard GD, Posadas E, Herrmann P: **Non-Hodgkin's lymphoma in Job's syndrome: a case report and review of the literature.** *Leuk Lymphoma* 2004, **45**:2521-2525.
4. Lin SJ, Huang JL, Hsieh KH: **Hodgkin's disease in a child with hyperimmunoglobulin E syndrome.** *Pediatr Hematol Oncol* 1998, **15**:451-454.
5. Jako JM, Gesztesi T, Kaszas I: **IgE lambda monoclonal gammopathy and amyloidosis.** *Int Arch Allergy Immunol* 1997, **112**:415-421.
6. Young MC, Harfi H, Sabbah R: **A human T cell lymphoma secreting an immunoglobulin E specific helper function.** *J Clin Invest* 1985, **75**:1977-1982.
7. Miyake S, Yoshizawa Y, Ohkouchi Y: **Non-Hodgkin's lymphoma with pulmonary infiltrates mimicking miliary tuberculosis.** *Intern Med* 1997, **36**:420-423.
8. Koutsonikolis A, Day N, Chamizo W: **Asymptomatic lymphoma associated with elevation of immunoglobulin E.** *Ann Allergy Asthma Immunol* 1997, **78**:27-28.
9. Borish L, Dishuck J, Cox L: **Sezary syndrome with elevated serum IgE and hypereosinophilia: role of dysregulated cytokine production.** *J Allergy Clin Immunol* 1993, **92**:131.
10. Spinozzi F, Cernetti C, Gerli R: **Sezary's syndrome: a case with blood T-lymphocytes of helper phenotype, elevated IgE levels and circulating immune complexes.** *Int Arch Allergy Appl Immunol* 1985, **76**:282-285.
11. Neuber K, Berg-Drewniock B, Volkenandt M: **B-cell chronic lymphocytic leukemia associated with high serum IgE levels and pruriginous skin lesions:successful therapy with IFN- α 2b after failure on IFN- γ .** *Dermatology* 1996, **192**:110-115.
12. Samoszuk M: **Reed-Sternberg cells of Hodgkin's disease with eosinophilia.** *Blood* 1992, **79**:1518-1522.

Publish with **BioMed Central** and every scientist can read your work free of charge

"BioMed Central will be the most significant development for disseminating the results of biomedical research in our lifetime."

Sir Paul Nurse, Cancer Research UK

Your research papers will be:

- available free of charge to the entire biomedical community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours — you keep the copyright

Submit your manuscript here:
http://www.biomedcentral.com/info/publishing_adv.asp

