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

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Executive Summary

Background: Reports are rare of markedly elevated IgE as a manifestation of a lymphoproliferative disorder.

Case Summary: We present a case of a 22 year old female referred to the adult allergy clinic for an extremely elevated IgE level, ultimately diagnosed with Hodgkin's lymphoma

• She had no history of 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 scanning.

• 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. This diagnosis should be considered in evaluating an otherwise unexplained 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 complications of the hyper-IgE syndrome[2-5]

• Reports are rare, however, of massive elevations in IgE as a complication or manifestation of an underlying lymphoproliferative disease, and are mostly limited to IgE producing plasmacytomas (in themselves rare, representing only 0.01% of all plasmacytomas)[4]

• 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 in the evaluation of perennial rhinitis[6].

•Here we present a patient referred for elevation of a markedly elevated IgE, ultimately diagnosed with 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 a 4 year history of fatigue, diffuse pruritus and a microcytic anemia

• She denied weight loss, fever or decreased appetite, but did have night sweats while taking venlafaxine, which resolved upon its discontinuation

• She had been diagnosed with both B12 and a presumed iron deficiency ; treatment with B12 injections, and iron replacement did not correct the anemia

• Bone marrow aspiration confirmed the presence of iron stores

• There was associated thrombocytosis, reticulocytosis, 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

•She had no history of recurrent infections, eczema or periodontal disease

Table 1: Laboratory parameters upon referral assessment in Allergy & Immunology Clinic

Parameter	Value	Reference	(Units)	Parameter	Value	Reference	(Units)
Creatinine	64	50-100	umol/L	WBC	10.2	4.0-11.0	x10^9/L
Urea	2.3	3.0-6.5	umol/L	Eosinophils	0.1	0.0-0.4	x10^9/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	x10^9/L
Total Protein	**81**	60-80	g/L	Retic	**100**	10-86	x10^9/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

• Stool was negative for ova & parasites

• Skin prick tests were positive to trees, grass and ragweed; however there was no history of rhinitis, asthma or other allergic disease

• Spirometry and methacholine challenge revealed a mild isolated decrease in DCO, and no airway hyper-responsiveness

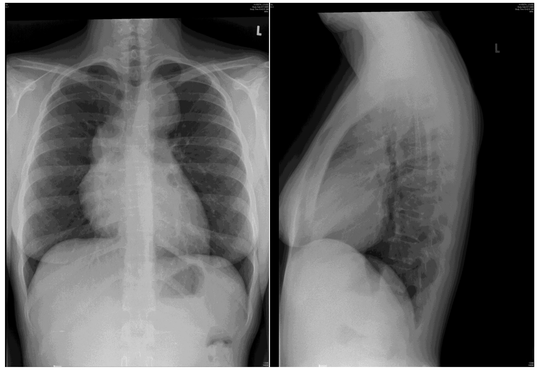
• Chest X-Ray revealed large bilateral anterior mediastinal masses that demonstrated prominent uptake on gallium scanning

• 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

• Ongoing treatment with ABVD (adriamycin, bleomycin, vinblastine and dacarbazine) has resulted a partial response based on PET scan FDG uptake; IgE has decreased to 4,014 kU/L

Figure 1: Chest X-ray of anterior mediastinal lymphadenopathy



Discussion

• Significant elevations of IgE are seen in various allergic conditions and parasitosis. In this case, the patient had no history of atopy, and parasitic work- up was negative

• Marked 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) has been associated with elevated IgE when the malignant clone is a CD4+ helper phenotype and/or associated with eosinophilia[9,10]. Abnormal cytokine profiles with increased IL-4 contribute to the hyperIgE[9]

• Elevated IgE levels (but not marked) 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. The diagnostic utility of this simple test was underscored in the process.

Conclusions

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

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