

IgE deficiency may indicate underlying hypogammaglobulinaemia?

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ABSTRACT

Low serum immunoglobulin E (IgE) (<2 kU/L) found during allergy investigations may be a marker for other immunodeficiency states, in particular common variable immunodeficiency. The latter is characterised by recurrent infections, mainly respiratory, resulting in structural lung damage making early diagnosis important. We looked through 4013 samples retrospectively over a 12-month period to identify samples with IgE <2 kU/L. We identified 74/4013 (1.84%) with serum IgE levels <2 kU/L. Only 20 samples had serum immunoglobulin quantification and serum electrophoresis requested. Three of these samples were from the same patient, 10/18 (56%) had one or more classes of immunoglobulin above/below reference range for age and two of these had new diagnosis of immunodeficiency. Serum IgE <2 kU/L can be a marker for hypogammaglobulinaemia or common variable immunodeficiency. As early diagnosis is important to reduce morbidity and mortality, very low serum IgE should trigger further investigation—that is, serum protein electrophoresis and immunoglobulin quantification.

INTRODUCTION

The role of immunoglobulin E (IgE) in the pathogenesis of allergic disease has been extensively researched. The dominant role of IgE has been shown to protect the host from parasitic infections, particularly helminth but apart from this little is known of its contribution to host defence. There has been some evidence that IgE antibodies play a protective role against viral, parasitic and bacterial infections;^{1 2} may be involved in tumour prevention and control;³ may play a role in the regulation of the respiratory immune response to prevent non-allergic reactive airway disease;^{1 4–6} and may protect against autoimmune diseases.^{1 4 5}

There is also suggestion that patients with IgE deficiency have an increased prevalence of multiple immunoglobulin deficits.⁴ Low IgE (<2 kU/L) found during allergy investigations may be a marker for other immunodeficiencies,⁷ including well defined immune deficiency diseases such as common variable immunodeficiency (CVID), hyper-IgM syndrome, selective IgM deficiency, IgG subclass deficiencies, ataxia telangiectasia and Bruton's or X-linked agammaglobulinaemia (XLA).¹ While Bruton's agammaglobulinaemia and ataxia telangiectasia present in infancy or early childhood, CVID can be diagnosed at any age with no sex preponderance. It is characterised by recurrent bacterial infections, mainly respiratory, resulting in irreversible structural lung damage such as bronchiectasis.⁸ Early diagnosis is important because morbidity and mortality are high and the efficacy of immunoglobulin replacement treatment is well established.^{9–16}

METHODS

We looked through 4013 samples submitted for total serum IgE quantification to the immunology laboratory at Surrey Pathology Services over the 12-month period (1 May 2011 to 30 April 2012) to identify those with IgE <2 kU/L. We then looked at these samples to see if serum immunoglobulin quantification and serum protein electrophoresis had been requested. We identified 74 samples with serum IgE <2 kU/L but only 20 of these samples had serum immunoglobulin quantification and serum protein electrophoresis requested.

We were unable to retrospectively test the remaining samples for immunoglobulin quantification and protein electrophoresis due to following reasons: 43/74 samples were not requested from within the hospital, 18/74 samples were paediatric and sample was too small and the remaining samples were time expired as samples are only kept for 3 months.

RESULTS

Out of the 20 samples that had had serum immunoglobulin quantification and protein electrophoresis, three requested were for the same patient. Corrected for this, 10/18 patients had one or more classes of immunoglobulin above/below reference range for age as follows:

- ▶ Three patients: IgG, IgA, IgM and IgE deficiency—two new cases, one patient under haematology
- ▶ One patient: IgG, IgA and IgE deficiency with known trace IgM k
- ▶ Two patients: high IgM+IgE deficiency
- ▶ Three patients: high IgA+IgE deficiency
- ▶ One patient: high IgA, high IgM+IgE deficiency.

More detailed information is given in [table 1](#).

After reviewing the results, there were two new cases of hypogammaglobulinaemia. This was a possible cause of bronchiectasis in both cases.

DISCUSSION

Do we need to test patients with very low IgE levels for possible linked antibody deficiency?

We identified 2/18 (11%) patients with hypogammaglobulinaemia. These two patients had a diagnosis of bronchiectasis. Our results confirm the investigation by Unsworth and coworkers in their work 'Immunoglobulin E deficiency: a forgotten clue pointing to possible immunodeficiency?'.⁷ They found very low IgE (≤ 2 IU/mL) in 85/2622 (3.2%) routine patient samples. Two children and four adult patients were found to have one or more classes of immunoglobulin below the age-specific reference range. In 2/6 cases, this identification led

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Short report

Table 1 Results of serum immunoglobulin (Ig) quantification and protein electrophoresis

Age	IgE kU/l	IgG g/L	IgA g/L	IgM g/L	Protein elect	Requestor	Reason
83 m	<2	1.4	<0.06	0.06	↓ γ Region	Haem	Pneumococcal septicaemia
65 f	<2	5.1	<0.24	0.31	↓ γ Region	Resp	Bronchiectasis
82 f	<2	1.8	<0.24	1.49	Trace IgM κ	Haem	NHL
76 f	<2	12.2	4.29	0.76	Normal	Resp	Allergy
27 f	<2	12.2	2.93	1.73	Normal	Immun	Allergy
25 f	<2	13.1	3.01	3.09	Normal	Immun	Allergy
79 m	<2	7.5	5.59	1.2	polyclonal IgA	GP	Autoimmune screen
69 m	<2	7.5	1.34	2.38	Normal	On call doctor	Liver screen
46 m	<2	2.2	<0.06	0.05	↓ γ Region	Resp	Bronchiectasis
60 m	<2	15.4	3.94	2.64		Immun	Allergy

Adult Ig ranges: IgE 0–81 kU/L; IgG 6–16 g/L; IgA 0.8–4 g/L; IgM 0.5–2 g/L.

f, female; GP, general practitioner; Haem, haematology; Immun, immunology; m, male; NHL, non-hodgkin's lymphoma; Protein elect, protein electrophoresis; Resp, respiratory.

to a new unsuspected diagnosis of antibody immunodeficiency. This is very similar to the findings of our study.

Antibody deficiency such as CVID continues to be overlooked as a primary cause of chronic lung disease in adults. Early diagnosis is important to reduce morbidity and mortality in this group of patients. Clues such as very low IgE may assist in early identification of antibody deficient patients.

Our follow-up plan is to prospectively request serum immunoglobulins and serum protein electrophoresis in all patients with serum IgE levels <2 kU/L and to reaudit a year later.

Take home message

Suggest check immunoglobulins in patients with IgE<2 kU/L.

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Competing interests None.

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