

Hypersensitivity to IFN- α

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Key words: hypersensitivity; IgE; IgG; interferon-alpha.

● INTERFERON (IFN)- α is currently the only therapy of proven benefit for patients with chronic hepatitis C (1). Rare cases of acute hypersensitivity reactions have been reported in manufacturers' product enclosure sheets (2, 3), but a search of the medical literature did not yield any reports.

The patient was a 47-year-old Filipino man with a history of chronic hepatitis C and hypertension. He was initially treated with IFN alfacon-1 9 μ g, subcutaneously (SQ), three times per week for 2 months, but he developed depression that necessitated discontinuation of the medication.

Approximately

8 months later, an attempt to re-establish

An acute reaction in a patient with hepatitis C.

IFN- α therapy was initiated with IFN- α 2b 3 million units, SQ, three times per week. The patient was awakened by mild generalized pruritis 1 day after the second injection.

Within a few hours after the third dose of IFN- α 2b, he developed dyspnea and diffuse urticaria. The prescribing physician advised him to discontinue the injections.

Positive findings on examination included an enlarged liver, mild right upper quadrant tenderness, and urticaria on his arms, legs, and trunk, with no evidence of angioedema. The urticaria resolved, and he continued all of his medications except IFN- α . He did not return for skin testing.

An investigation by the enzyme-linked immunosorbent assay (ELISA) was undertaken to measure IgE and IgG antibodies to IFN alfacon-1 and IFN- α 2b. Washings, incubations, and coatings of the

microtiter wells were performed by standard methods (4). The patient was found to have an IgE titer of <1:5, and an IgG titer of >1:1000 to IFN alfacon-1 titer of 1:100 to IFN- α 2b (Fig. 1).

Hypersensitivity reactions to human recombinant proteins have been well defined to products such as human insulin and granulocyte-macrophage colony-stimulating factor (5). These reactions are probably secondary to B-cell recognition of an alteration in tertiary protein structure and subsequent antibody production, as the T cells recognize the primary amino-acid sequence, which remains conserved between natural and recombinant proteins.

In this study, we have attempted to identify the antibodies responsible for a hypersensitivity reaction to IFN- α . IgG antibody against IFN- α was demonstrated by ELISA. We could not confirm the presence of IgE antibody against IFN- α . Although hypersensitivity reactions can occur secondary to IgE-mediated mast-cell degranulation, it is possible that this patient's reaction was secondary to a different immunopathogenesis. The temporal relationship between the administration of

the IFN product and the onset of symptoms is not typical of an IgE-mediated reaction. In summary, recombinant and natural human proteins, such as the formulations of IFN- α , may induce specific antibody-mediated hypersensitivity reactions, but other mechanisms may also play a role. As new human proteins are introduced for therapeutic indications, other immunologic hypersensitivity reactions are likely to be described.

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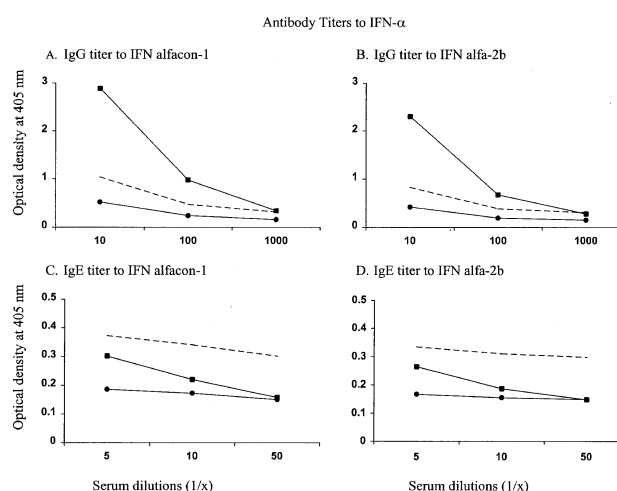


Figure 1. Solid squares (■) represent mean optical density readings of patient's serum at corresponding dilutions; solid circles (●) represent mean values of control patient's serum; dashes (---) identify level above which values are twice those of control. IgG titer to IFN alfacon-1 (graph A) reached greater than or equal to 1:1000, while IgG titer to IFN alfa-2b (graph B) was 1:100. IgE titers to IFN alfacon-1 (C) and IFN alfa-2b (D) were less than 1:10.

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Sensitization to synthetic yarns

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Key words: IgE antibody; immunoblot; occupational allergy; synthetic yarn.

• We report the case of a machinist in a synthetic textile plant. The subject was a 49-year-old female nonsmoker who presented with a 4-year history of work-related dry cough, wheeze, and chest tightness. The symptoms were particularly associated with her work in the vicinity of the looms. Her cough improved with inhaled corticosteroids, strongly supporting an asthmatic aetiology.

Samples were collected from the workplace, including dust from around the loom, and any soluble proteins present were extracted into 0.1 M ammonium bicarbonate for use in RAST, SDS–PAGE analysis, immunoblotting, and precipitating antibody detection. Precipitating antibodies

to the extract were identified by double diffusion in agarose.

Proteins in the extract were separated by SDS–PAGE (12% acrylamide). The gels were immunoblotted and the binding of serum IgE to the proteins was visualized by a chemiluminescent detection technique.

Specific IgE antibodies were present in the patient's sera to aqueous extracts of yarn (RAST score: 2.5), to dust from the loom (RAST score: 3.6), and to a mixed RAST disc of house-dust mite, cat fur, and grass pollens (RAST score: 11.2). Control atopic serum did not have IgE antibodies to the occupational extracts. In addition, the worker showed precipitating antibodies to the yarn extracts. The immunoblot detected two intensely stained bands at approximately 97 400 Da and a fainter band at approximately 29 000, but not in the two control sera (Fig. 1).

We present the case report of a worker in a textile mill processing inorganic fibres who presented occupationally related respiratory symptoms. The subject had specific IgE to a proteinaceous component of the yarn and loom dust. Immunoblot analysis showed

that the IgE antibodies were binding to two proteins present in the extracts of yarn. The material safety data sheet of the yarn suggested that the yarn was 1% w/w of an organic material that was a lubricating coating of the yarn, but we were unable to obtain further details regarding this material. These data suggest that this worker had become sensitized to a proteinaceous component of a yarn coating from her workplace that became aerosolized during the work process. We suggest that the possibility of sensitization should be considered during the risk assessment of work with this type of material.

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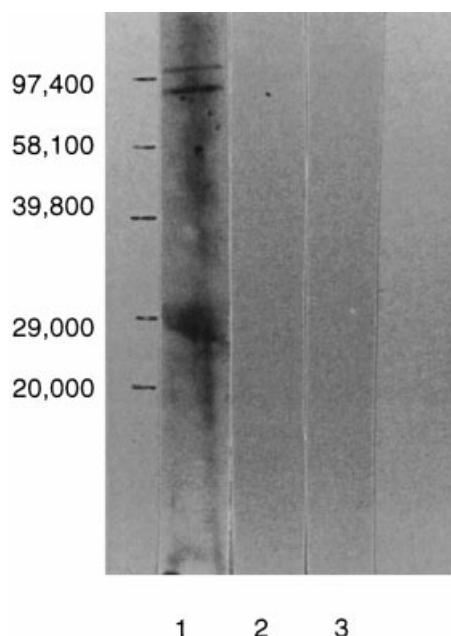


Figure 1. Serum immunoblot of yarn extract separated by reduced 12% SDS–PAGE. Lane 1) patient sera; lanes 2 and 3) control sera.