

Letters and Comments

Primary Allergy to Human Insulin in Patient With Gestational Diabetes

Hypersensitivity reactions to insulin have been reported since its introduction in therapeutics, although its frequency decreased when purified insulins (monocomponent, single peak) became available (1). Nevertheless, cases of insulin allergy do occur, being a serious problem in insulin-dependent diabetes mellitus. It was hypothesized that the use of human insulin could circumvent this problem (2), but cases of local (3) and generalized (4) allergic reactions to human insulin have been reported. Most of these appeared in patients allergic to insulins of animal origin transferred to human insulin. Primary allergy to human insulin is rare, and to our knowledge only four cases have been previously reported (5,6). We describe a case of primary local allergy to human insulin in a gestational diabetic woman treated exclusively with human insulin.

A 34-yr-old pregnant woman with no known history of glucose intolerance, drug allergy, or atopy was diagnosed with gestational diabetes at 10 wk. She had never received insulin. Islet cell antibody tests performed just after diagnosis were negative. She was placed on a normocaloric diet but insulin was required to achieve normoglycemia. Therapy was initiated with semisynthetic human insulin; intermediate at bedtime and regular preprandially (Monotard HM and Actrapid HM, Novo, Copenhagen). Two weeks later, immediate local reactions (10×10 cm, erythematous, swollen, indurated, and pruriginous lesions) developed repeatedly after insulin injections. Other human insulins (semisynthetic and recombinant DNA insulins) were used, but there was still a local reaction. An intradermal

test with regular and NPH humulin (Lilly; 0.04 IU) insulin elicited positive immediate reactions, whereas zinc did not.

Specific IgE antibodies measured by enzyme-linked immunosorbent microassay (Pharmacia, Uppsala, Sweden) gave highly positive results (8 phadebas rast U/ml, score 3). Total IgE levels were in the normal range. A skin biopsy showed a histologic pattern of urticaria. Because of the severity of the local reaction, we decided to place the patient on a desensitization protocol. A schedule of intradermal injections of human insulin (regular humulin) at increasing concentrations, starting with 10^{-5} IU administered at 30-min intervals, was used. No reaction was observed either during the desensitization procedure or after reintroduction of the usual insulin program. However, 48 h later, less intense local lesions reappeared, becoming weaker after some weeks. Specific IgE antibodies decreased, matching the clinical course.

It is not known why human insulin is immunogenic, although changes in tertiary structure have been suggested to be related to its immunogenicity. The appearance of de novo specific IgG and IgE insulin antibodies without clinical manifestations is common (40 and 10%, respectively; 7), but primary allergy to human insulin is exceptional. This study adds a new case to the four previously reported. Note that although rare, this entity is possible, so allergy to insulin must be suspected in patients on insulin treatment even when treated with human insulin.

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Hyperglycemia and Toxic Oil Syndrome in Spain

The toxic oil syndrome (TOS) was described in Spain in 1981 and was related to the ingestion of adulterated rapeseed oil. It is a new illness of multisystemic character whose etiology and pathogenesis has constituted controversial problems (1-5).

In 1986, we observed that many TOS patients showed greater prevalence of hyperglycemia than was average among the Spanish population (6). A study of 734 TOS patients and 1474 control subjects, both groups from the Villaverde district (Madrid, Spain), enabled us to prove that the incidence of hyperglycemia (insulin-dependent [type I] and non-insulin-dependent [type II] diabetes mellitus and impaired glucose tolerance) in TOS patients reached 13%, whereas in the control subjects,

it was 3.8% ($P < 0.001$). The diagnostic procedure and criteria were established according to the World Health Organization (7).

Moreover, the determinations of plasma insulin, C-peptide, and islet cell antibodies were carried out. All of them were normal in both groups. On the other hand, the pancreatic lesions detected in deceased TOS patients (2) did not coincide with those commonly described in diabetes mellitus by pathologists (8).

In our opinion, even though associations and statistical correlations do not prove causation, to suffer from TOS entails a high risk of having hyperglycemia. Finally, in this study, we described a new type of hyperglycemia that has not been previously reported.

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