

INSULIN ALLERGY

CASE REPORT, WITH RESPONSE TO BOILED INSULIN

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ALTHOUGH insulin resistance in diabetes mellitus has been reported not infrequently, and its management is mentioned in standard medical and pediatric textbooks, a case of generalized allergy to insulin rarely is encountered. The term "insulin allergy" denotes a specifically acquired altered antigenic response to insulin protein, in contradistinction to insulin sensitivity, which denotes an altered physiologic response. Three types of insulin allergy are usually mentioned: mild local reactions, severe local reactions, and generalized reactions, i.e., severe urticaria with angioneurotic edema, circulatory failure, asthma, arthralgia, and gastrointestinal symptoms.

The incidence of generalized reactions to insulin is estimated at 1 to 1,000 cases of diabetes mellitus. Stone and associates,¹ found two cases in 2,949 patients admitted for treatment of diabetes mellitus in eight years. A special relationship between atopy and diabetes mellitus was not found by Siegal and Herzstein² in a study of 400 severe diabetics and 227 controls.

In the management of insulin allergy, Dolger^{3, 4} suggested either rapid desensitization to insulin or a simpler method of using boiled regular or crystalline insulin, the vial of insulin being immersed in boiling

water for fifteen minutes. The molecular weight of insulin being approximately equal to that of egg albumin, he stated boiling the insulin for fifteen minutes resulted in a loss of only 10 to 20 per cent of its activity, and he reported a patient with insulin allergy treated with boiled insulin who eventually tolerated unboiled insulin. Hollindar and Zinn⁵ reported a case of urticaria from insulin where denaturing the insulin by boiling failed to improve the patient's condition, but, in the following case, boiling the insulin resulted in immediate disappearance of all signs of a severe generalized insulin allergy.

CASE REPORT

J. L. W., an 11-year-old white female, was admitted to Midland Memorial Hospital with diabetic acidosis, pharyngitis, and a blood sugar of 488 mg. per cent. She had a history of polydipsia, polyphagia, polyuria, and weight loss over two months, but no family history of diabetes or allergy. Within twenty-four hours her acidosis and dehydration had responded to intravenous fluids and regular insulin 25 units intravenously, stat, and 105 units given in divided doses hypodermically. The day following admission, the blood sugar was 209 mg. per cent. The urine showed only a trace of acetone, 2 + sugar, and she was taking food and liquids well by mouth. A moderately red, slightly raised, urticarial eruption with considerable itching had developed on

From the Mast Clinic.

her left arm (where the early injections of insulin had been given) approximately eighteen hours after admission. The itching improved with oral Chlor-Trimeton 4 mg. every six hours, but the rash would come and go on her thighs, buttocks, neck, arms, and body.

Approximately thirty-six hours after admission, the urine was noted to have turned a cloudy, reddish brown, very similar to that of a patient with acute glomerulonephritis. This urine specimen had a specific gravity of 1.022, a 2+ albumin, 3+ sugar, negative acetone, and was loaded with red blood cells. Her face appeared slightly puffy, but no generalized edema was noted. Blood pressure remained 98/60. Nonprotein nitrogen was 26 mg. per cent. Two days later the urine was clear, and showed only a trace of sugar. Corrected sedimentation rate was 14 mm. per hour.

She was discharged from the hospital seventy-two hours after admission on 40 units of NPH and 15 units of regular insulin at lunch and supper. Two days after discharge, she was seen in the office, feeling well, with no rash, itching, or edema. The urine was clear except for a trace of sugar, and fasting blood sugar was 109 mg. per cent. She weighed 82 $\frac{1}{4}$ pounds. On the following day, her mother noticed her eyelids becoming puffy and her ankles swelling. She had gained 5 $\frac{1}{2}$ pounds (weight 87 $\frac{3}{4}$ pounds). Physical examination showed generalized edema of the face, eyelids, abdominal wall, arms, and 4+ edema of the ankles. The blood pressure was 96/60. She had received 60 units of NPH insulin that morning. She was put to bed, and her insulin was changed from NPH insulin to regular beef insulin, but no improvement was noted after forty-eight hours.

She was then given 20 units t.i.d. of regular beef insulin that had been boiled fifteen minutes. The next day she voided 2,500 c.c. and the following day another 2,500 c.c. The edema disappeared, and her weight

dropped to 84 pounds. This boiled insulin was continued for three weeks and limited activity allowed. She had slowly gained to 87 pounds, a return to her "normal" weight, and no edema was noted. Then in addition to boiled insulin, 0.1 c.c. (4 units) of regular, unboiled beef insulin was given; in twenty-four hours she had gained 3 pounds and had developed generalized edema, not quite as severe as on the first occasion. Her urine showed no red cells, white cells, casts, or albumin, but did have a 3+ sugar. Only boiled, regular insulin was continued and she promptly lost 2 pounds in two days. Her insulin requirements by this time had dropped to regular insulin, 15-10-15.

One month later she developed pharyngitis, which responded well to Terramycin 500 mg. stat and 250 mg. every four hours for four days. In three weeks another bout of pharyngitis occurred. Treatment was begun with 800,000 units of fortified penicillin intramuscularly daily. She weighed 92 pounds prior to treatment. On the second day she had become edematous, and had gained 2 pounds. No rash or itching had appeared. Terramycin was substituted, and her weight returned to normal within two days. She then was admitted to the Houston Children's Hospital under the care of C. W. Daeschner, M.D., for desensitization to insulin. Following her discharge she has remained in good health taking 40 units of NPH insulin daily, and in three months has exhibited no evidence of insulin allergy.

Comment.—Fortunately, insulin resistance did not develop in this girl. Allergy to protamine or to individual species of insulin has been suggested as possible causes of insulin allergy, but, in this case, edema, urticaria, and weight gain followed the use of beef or mixed regular or crystalline insulin. It would seem that the allergy was to the insulin itself, regardless of species or preparation. Local cutaneous allergy ap-

peared within eighteen hours of the first dose of insulin. From her history, she never had received insulin previously. The local itching and urticaria were controlled by oral Chlor-Trimeton. Within five days of the onset of insulin therapy, generalized edema and a gain of 5 pounds had occurred, which did not respond to a change from pork to beef to crystalline insulin. However, within twenty-four hours of the use of boiled, regular insulin, a diuresis followed and she lost 5 pounds. She remained symptom-free on boiled regular insulin for three weeks, but again became edematous and gained 2 pounds following the use of 0.1 c.c. (4 units) of regular unboiled insulin.

SUMMARY

A case of generalized insulin allergy in an 11-year-old white girl, consisting of generalized edema, ur-

ticaria, and a weight gain of 5 pounds, responded well to the emergency treatment of boiled, regular insulin. The patient ultimately was desensitized to insulin, enabling her to take commercial NPH insulin.

REFERENCES

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