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Pediatrics 1982;70;137-138

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Insulin Allergy in a 19-Month-Old Boy with Newly Diagnosed Diabetes Mellitus

Systemic insulin allergy is rare and usually occurs in adults with diabetes mellitus following reinstitution of insulin therapy.^{1,2} The present case is unusual in that the systemic symptoms appeared 23 days after initial continuous treatment with insulin in a very young child.

CASE REPORT

An 18-month-old boy was seen by his pediatrician six weeks after a severe episode of varicella, with a monilial diaper rash and a three-week history of polyuria, polydipsia, polyphagia, and weight loss. The blood glucose concentration was 534 mg/100 ml and serum ketones were present. Diabetes mellitus was diagnosed. He was hospitalized and insulin therapy was instituted without incident; the patient was discharged on a daily mixed dose of regular and isophane (NPH) insulins (single-peak, beef-pork mixture, Eli Lilly & Co). He and his family were referred to our program for education and follow-up care for his diabetes.

Twenty-three days after diagnosis, when he was receiving 1 unit of regular insulin and 3 units of NPH insulin daily, small "insect bite-like" lesions appeared on his trunk approximately one hour after his insulin injection. They were not pruritic and faded as the day progressed. On the third day the lesions were urticarial and associated with angioedema of the hands and face, without respiratory symptoms. The child was admitted to the hospital for evaluation. A careful history revealed no new foods in the diet nor unusual environmental exposure. There was no family history of allergy. The parents denied any previous local reactions at the injection site. Physical examination revealed a fading rash but was otherwise unremarkable. Pertinent laboratory studies included an absolute eosinophil count of 490/cu mm at the time of presentation and serum antibody titers as shown in Table 1.

Twenty-four hours after the last injection, intradermal skin tests were performed with 0.01 unit of each of the following: single-peak beef insulin, single-peak pork insulin, monocomponent pork insulin (Eli Lilly & Co), Lilly diluent for regular insulin, and 0.9% saline solution. There was an equivalent wheal and flare reaction to all of the insulins but no reaction to the saline or the diluent (Table 2). No systemic symptoms developed.

Because continuing insulin therapy was necessary, desensitization was performed with regular single-peak pork

insulin (Eli Lilly & Co). The initial dose was 0.05 unit subcutaneously. Progressively increasing doses were given every hour for nine hours until 0.6 unit was administered, after which insulin (up to 1 unit) was administered every two to four hours for the next 36 hours. The patient was carefully observed for systemic allergic symptoms, and epinephrine, diphenhydramine, and hydrocortisone were kept at the bedside. Mild urticarial lesions appeared following injection of 0.4 unit, but no further systemic symptoms developed during the remainder of the procedure. There was local erythema following all injections.

Two days after desensitization was begun, the patient was given a mixed dose of 0.5 unit of regular and 2 units of Lente single-peak pork insulin without systemic symptoms. He continued to have occasional mild local reactions for approximately one month, but has had no further systemic symptoms.

DISCUSSION

Because insulin is a foreign protein, it is not surprising that antibody responses are observed in all diabetic patients treated with insulin. Both immunoglobulin G (IgG) and IgE specific for insulin have been detected in all patients.³ Markedly elevated levels of IgG are often associated with insulin resistance whereas IgE levels are significantly elevated in patients with systemic insulin allergy. Caution must be applied, however, in correlating serum levels of IgE with degree of allergic symptoms in as much as Ishizaka and Ishizaka⁴ have failed to correlate serum IgE concentration with the number of cell-bound IgE molecules which is believed to be the mediator of histamine release and thus, the determinant of the allergic response. In our patient, the serum level of IgE did not decrease as dramatically with desensitization as has been reported in previous cases,⁵ although the systemic symptoms disappeared completely.

It has been suggested that the ratio of IgE/IgG antibodies is an important correlate in the degree of clinical manifestation of the allergy, with IgG providing protection by "blocking".^{3,6} The results in our case do not support this theory, in that the ratio of IgE/IgG decreased only slightly following desensitization and increased dramatically two weeks later as the IgG decreased. In one report,⁷ cellular immunity was studied by blast cell transformation and it was noted that the lymphocyte response to insulin was greater in the patient with systemic insulin allergy than in patients with either local reactions or no reaction to insulin or in healthy subjects. Unfortunately, this technique was not readily available and we were unable to study this in our patient.

To our knowledge, this case represents the youngest child reported with systemic insulin allergy and one of a few who were seen following the initial

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TABLE 1. Anti-insulin Immunoglobulin E and Immunoglobulin G Titers*

	Anti-insulin IgE (cpm/ml)	Anti-insulin IgG (cpm/ml)	Ratio IgE/ IgG
Patient			
Day 1	37,723	161,725	0.23
Day 2	28,348	152,570	0.19
Day 3	26,047	173,070	0.15
Day 4	25,641	187,420	0.14
Day 16	28,916	60,655	0.48
Insulin-treated control	8,916	59,745	0.15
Nondiabetic control	Undetectable	Undetectable	

* Titers expressed as radioactive counts per minute (cpm) of ¹²⁵I-beef insulin (specific activity 120 mCi/mg) bound with 1 ml of serum.³

TABLE 2. Intradermal Testing 20 Minutes After Injection of 0.01 Units of Various Insulin Preparations

Insulin Preparation	Reaction	
	Wheal	Erythema
Single-peak regular beef	9 mm	14 mm
Single-peak regular pork	5 mm	12 mm
Monocomponent regular pork	6 mm	12 mm
Lilly diluent for regular insulin	None	None
Saline (0.9% NaCl solution)	None	None

exposure to insulin. We conclude from the skin tests that this represents a true insulin allergy in as much as the patient was equally responsive to all insulin preparations tested. We did not attempt to rule out zinc allergy, which has been reported,⁸ but did rule out other protein or diluent components with the intradermal skin tests to the monocomponent pork preparation and the diluent solution alone. Although it is a rare condition, true insulin allergy can be a life-threatening complication of insulin treatment for insulin-dependent diabetes mellitus. Rapid desensitization is an important therapeutic modality in the patient requiring continuing insulin administration. We have demonstrated that the desensitization schedule recommended by Galloway and Bressler⁹ can be successfully modified to suit individual requirements.

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REFERENCES

1. Kahn CR, Rosenthal AS: Immunologic reactions to insulin: Insulin allergy, insulin resistance and the autoimmune insulin syndrome. *Diabetes Care* 2:283, 1979
2. Lamkin N, Lieberman P, Hashimoto K, et al: Allergic reactions to insulin. *J Allergy Clin Immunol* 58:213, 1976
3. Kumar D: Anti-insulin IgE in diabetes. *J Clin Endocrinol Metab* 45:1159, 1977
4. Ishizaka T, Ishizaka K: Biology of immunoglobulin E. *Prog Allergy* 19:60, 1975
5. Mattson JR, Patterson R, Roberts M: Insulin therapy in patients with systemic insulin allergy. *Arch Intern Med* 135:818, 1975
6. Witters LA, Ohman JL, Weir GC, et al: Insulin antibodies in the pathogenesis of insulin allergy and resistance. *Am J Med* 63:703, 1977
7. Dacon-Voutetakis C, Thomaidis T, Roma E, et al: Systemic allergic reaction to initial insulin therapy in a juvenile diabetic. *Acta Paediatr Scand* 64:773, 1975
8. Feinglos MN, Jegasothy BV: Insulin allergy due to zinc. *Lancet* 1:122, 1979
9. Galloway JA, Bressler R: Insulin treatment in diabetes. *Med Clin North Am* 62:663, 1978

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