

Successful Management of Deferoxamine Hypersensitivity in a Child

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ABSTRACT

A 6-year-old boy with sickle cell disease that required frequent blood transfusions experienced repeated anaphylactoid reactions with dyspnea, rhinorrhea, and angioedema within minutes after treatment with intravenous deferoxamine for his iron overload. Pretreatment with prednisone and diphenhydramine (radiocontrast medium protocol) did not prevent these reactions.

Two reports have described successful desensitization in adults with beta-thalassemia who were sensitive to deferoxamine and who were subsequently able to receive it subcutaneously. For our patient, we devised a 9-week protocol that enabled him to receive intravenous deferoxamine overnight via indwelling catheter at 3 day intervals without reactions. After pretreatment with prednisone and diphenhydramine, he was given graduated doses of deferoxamine intravenously in the pediatric intensive care unit. The initial dose was less than 1:10,000 of the target dose, based on body surface area, and was progressively increased by factors of 10, at 15–20 min intervals. Subcutaneous aqueous epinephrine (1:1000) was required to control bronchospasm twice during the desensitization. Routine treatment with terfenadine by mouth and albuterol by metered-dose inhaler was required.

To the best of our knowledge, this is the first reported desensitization with deferoxamine in a child and the first use of the intravenous route in any patient desensitized with deferoxamine.

INTRODUCTION

CHRONIC HYPERTRANSFUSION OF RED blood cells is used to prevent recurrence of vaso-occlusive complications in sickle cell patients.⁽¹⁾ Deferoxamine (DF), to control secondary hemochromatosis, has produced anaphylactoid reactions in some patients.⁽²⁾ Miller et al. in 1981⁽³⁾ and Bousquet et al. in 1983⁽⁴⁾ described "desensitization" to DF subcutaneously administered in two adult patients with beta-thalassemia. We were confronted with a child with sickle cell disease who had anaphylactoid reactions to intravenous DF.

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CASE REPORT

A 6-year-old boy with sickle cell disease was placed on a red cell hypertransfusion protocol after two cerebrovascular accidents. Biweekly infusions of DF 750 mg, each in 500 ml, were administered via an indwelling intravenous catheter over 8 h. After 15 min of the third infusion, the patient experienced throat tightness, wheezing, weeping, generalized pruritus, and periorbital edema. Subsequent infusions produced similar reactions. None of the common pretreatment protocols prevented these reactions. DF therapy was abandoned.

Skin prick tests with DF were negative, but intradermal injection of 0.02 ml 5 mg/ml DF produced a 10 mm wheal and surrounding flare. A nonexposed volunteer had a positive reaction to a 50 mg/ml intradermal test.

Beginning 18 h before desensitization, diphenhydramine 12.5 mg and prednisone 12.5 mg were given orally every 6 h and continued for 4 days. These dosages and DF dosages from Bousquet's modification of Miller's protocol⁽⁴⁾ were adjusted according to body surface area (Table 1). In the pediatric intensive care unit, each 25 ml DF infusion was given over 30 min in continuous sequence. The concentration of the 11th bottle was maintained for 24 h at 50 ml/h. Afterwards, infusions were given intermittently according to the following schedule: 12 h on, 12 h off for 2 weeks; 12 h on, 24 h off for 3 weeks; 12 h on, 36 h off for 3 weeks.

RESULTS

During the seventh and ninth doses, the patient developed rhinorrhea, sneezing, nasal pruritus, and 40% and 60% reductions in peak expiratory flow. These reactions resolved after interruption of the DF infusion and single subcutaneous injections of 0.25 ml aqueous epinephrine (1:1000).

Although infusions were tolerated after 12 h off, the first infusion after 24 h off was complicated by bronchospasm that responded to inhaled albuterol. Subsequent infusions were preceded by two inhalations of albuterol from a metered-dose inhaler administered with a reservoir bag delivery system (Inspirease, Schering Corporation, Kenilworth, NJ). No further reactions occurred. Increasing the interval between doses to 36 h initially produced rhinitis, prevented by routine oral administration of terfenadine 30 mg every 12 h. The patient was rehospitalized to extend the interval between infusions to three doses per week. He tolerated infusions after 60 h off when terfenadine was increased to 60 mg twice daily and albuterol to two inhalations four times a day.

TABLE 1. DILUTION SCHEDULE OF INTRAVENOUS INFUSIONS OF DEFEROXAMINE

<i>Bottle</i>	<i>Dilution^a</i>	<i>Concentration (mg/ml)</i>
1	0.00375	0.00015
2	0.0375	0.0015
3	0.375	0.015
4	3.75	0.15
5	12.5	0.5
6	25	1.0
7	50	2.0
8	100	4.0
9	200	8.0
10	400	16.0
11	600	24.0

^aValues given in mg DF in 25 ml 5% Dextrose in 1/4 normal saline.

DISCUSSION

We successfully administered DF intravenously at intervals as long as 3 days to a DF-hypersensitive child with sickle cell disease. Although Bousquet's patient tolerated doses every 3 but not every 4 days,⁽⁴⁾ ours experienced systemic reactions when the interval between doses was extended beyond 24 h. This may be due to a "depot" effect in subcutaneous administration. Only additions of terfenadine and albuterol enabled our patient to tolerate longer intervals between doses.

The means by which DF produces anaphylactoid symptoms in some persons is unknown. Bousquet's patient had no detectable specific serum IgE or IgG to DF coupled either to radioallergosorbant test (RAST) discs or to serum albumin and had intradermal skin test results similar to those of nonexposed controls.⁽⁴⁾ Recently Shalit et al. showed that DF in concentrations of 50–100 mg/ml caused histamine release from rat peritoneal, but not bone-marrow-derived, mast cells⁽⁵⁾ and that healthy volunteers demonstrated increasing wheal and flare reactions to intradermal DF in concentrations from 0.1 to 100 mg/ml. They concluded that DF acts nonspecifically to cause activation of connective-tissue-type mast cells. Such observations fail to explain the fact that only a minority of patients exposed to therapeutic doses of DF experience anaphylactoid reactions and fail to rule out the possibility that, in some, DF or one of its metabolites may act as a hapten in an allergic reaction.

We hope that our method enables other children who require hypertransfusion and who have anaphylactoid reactions to DF to receive the drug safely by vein.

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