NOTE

Allergic Reaction to DDAVP in Diabetes Insipidus: Successful Treatment with Its Graded Doses

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Abstract

A case of hypersensitivity reaction to 1-desamino-8-D-arginine vasopressin (DDAVP) as observed in a patient with diabetes insipidus is reported. This patient was successfully treated with conventional doses of DDAVP after receiving gradually increasing doses.

1-Desamino-8-D-arginine vasopressin (DDAVP) has been widely used to treat diabetes insipidus since it can be administered intranasally and has a potent and prolonged antidiuretic effect with few side effects (Cobb et al., 1978; Marek et al., 1978). It is also considered unlikely for DDAVP to cause allergic reactions because of its nature as a synthetic compound (Cobb et al., 1978; Marek et al., 1978). We report here a patient with diabetes insipidus who developed an erythematous rash probably associated with both vasopressin tannate in oil and DDAVP but who was later successfully treated by administering gradually increasing doses of DDAVP.

Case report

A 49-year-old woman had a seven-year history of diabetes insipidus as previously reported (Hirata et al., 1975). In brief, on the first admission to our hospital in May 1971, a diagnosis of idiopathic diabetes insipidus was made and treatment with chlorpropamide and hydrochlorothiazide was started. Vasopressin tannate was not used because she had developed urticaria and generalized erythema after its intramuscular injection. On the second admission in February 1973, xanthomata were noted in the eyelids and the cervical regions, of which biopsies revealed histiocytic proliferation. Prednisolone was immediately introduced for histiocytosis X along with oral antidiuretic drugs. However, she was again admitted to the hospital in July 1978 for the present study because of solid masses in both axillae (rt 16 × 12 cm and lt 15 × 10 cm) with poor control of polydipsia and polyuria. She had a plethoric moon face with a temperature of 38°C and blood pressure of 168/90 mm Hg. Laboratory results included increased erythrocyte sedimentation rate (24 mm in first hour), haemoglobin concentration 13.6 g/dl, white cell count 12.7 × 10⁹/μl with a normal differentiation, normal serum electrolyte and normal liver and renal functions. Daily urine volume varied from 2200 to 3400 ml with nocturia on
antidiuretics. Plasma from the patient showed no discernible binding of $^{125\text{i}}$-arginine vasopressin. She was given corticosteroids and vinblastine for histiocytosis X along with an intranasal dose of 10 µg of DDAVP. The next morning she developed a raised erythematous rash over the anterior and lateral aspects of the both thighs, the buttocks and the front of the chest and in the axillae and the chin, which was quite similar to that previously seen after the injection of vasopressin tannate in oil, but disappeared completely within 72 hours. Meanwhile the patient remained alert and blood pressure was not changed. Despite these untoward reactions she required DDAVP treatment because of a marked improvement in polydipsia and polyuria. In addition to hydrochlorothiazide and clofibrate, 1 µg of DDAVP twice daily was therefore started 2 weeks later. This was continued for one week without any allergic reaction (Fig. 1). The next week she was on 2 µg of DDAVP twice daily without any reaction. When 4 µg of DDAVP was administered twice daily in the third week (Fig. 1), she developed a faintly erythematous rash after the second dose. This dose was, therefore, continued for an additional two weeks in combination with antihista-

Discussion

The feature of interest in this case is the development of a quite similar rash associated with both natural and synthetic preparations of vasopressin. To our knowledge there has been no report of a rash associated with DDAVP treatment although several cases of hypersensitivity to commercially available animal vasopressin preparations have been reported in patients with diabetes insipidus (Roth et al., 1966; Lawrence et al., 1972). Allergic reactions following the natural preparations are considered to be due to extraneous protein components contained in the preparations, being unrelated to vasopressin-specific antibody (Roth et al., 1966; Lawrence et al., 1972). DDAVP, the pure synthetic derivative of
arginine-vasopressin, is hardly expected to cause allergy as an inciting antigen. Very recently, however, chlorobutanol, which is included as a preservative in both DDAVP (Itabashi et al., 1980) and heparin preparations (Dux et al., 1981), has been shown to be a causative agent in the allergic reactions to these drugs since the chlorobutanol-free preparations produced no response (Itabashi et al., 1980; Dux et al., 1981) while chlorobutanol alone induced positive skin reactions and the patient's lymphocytes gave positive macrophage inhibition test (Dux et al., 1981). Since chlorobutanol is also added to the natural vasopressin preparations it might cause the rash associated with both natural and synthetic preparations as observed in this case. Whatever the mechanism of DDAVP allergy is, it is noteworthy that the continuous use of gradually increasing doses of DDAVP made the patient so insensitive to the drug, probably through the desensitization process, which immunosuppressive agents given simultaneously may partly help to facilitate, that the conventional doses could be safely used.

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References


