

A Possible Case of Drug-induced Familial Pemphigus

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Two sisters developed pemphigus vulgaris and pemphigus erythematosus within 3 years. The diagnosis was confirmed by clinical, histologic and immunofluorescent antibody studies. One of the sisters experienced a common cold before the pemphigus developed and displayed a positive macrophage migration inhibition (MIF) test to a combination drug compounded of paracetamol, caffeine, chlorpheniramine maleate and phenylephrine HCl, which she had received 2 weeks prior to the appearance of the cutaneous lesions. It is suggested that her pemphigus was triggered by the drug. Although the patient had a strong genetic and familial predisposition to pemphigus, her clinical symptoms did not become evident until they were activated through an exogenous factor, namely, the causative drug. This case offers an example of a possible interaction between endogenous, genetic factors, and exogenous, triggering factors in the development of full-blown disease. Key words: Endogenous, exogenous factors inducing pemphigus.

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Familial pemphigus has been rarely chronicled since its original description, by Morris (1). Subsequently, there have been reports of pemphigus vulgaris, erythematosus, foliaceus and vegetans (2, 3). An association with HLA A26, B38 and DR4 has been reported in some cases (4, 5). A case of a familial occurrence of pemphigus vulgaris probably triggered by a drug is described here and the interaction of endogenous (genetic) and exogenous (inducing) factors discussed.

CASE REPORTS

Case 1

A 56-year-old Jewish woman of Ashkenazi origin was admitted for evaluation of an erosive eruption of 3 months' duration. Initially, the lesions involved the upper abdomen and anterior part of the chest, progressing later to involve

the upper back and scalp. Two weeks prior to the onset of the disease a history of common cold and an outbreak of herpes simplex labialis were documented. The patient used a combination drug composed of paracetamol, caffeine, chlorpheniramine maleate and phenylephrine HCl. Examination revealed erosions on the upper back, chest and abdomen. The remainder of the physical examination was unremarkable.

Histopathologic examination of a biopsy specimen from the chest revealed a suprabasilar acantholytic cleft within the epidermis. Direct immunofluorescent microscopic studies of perilesional tissue and uninvolved skin showed intercellular deposition of IgG and C3, as well as IgA traces. Indirect immunofluorescence demonstrated an anti-intercellular substance antibody titre of 1:40. Thus, the diagnosis of pemphigus vulgaris was confirmed.

The laboratory results were within normal limits. HLA typing displayed HLA A24, A26, B35, B38 and DR4,6. Since the possibility of a drug-induced pemphigus was considered, a macrophage migration inhibition (MIF) test was performed. This test has been used for many years in a laboratory collaborating with us in the detection of drug allergies, producing reliable results and a very low rate of false-positive results (6–8). The test produced positive results with the combination drug used by the patient.

Case 2

A 60-year-old patient, sister of the previous case, has had pemphigus erythematosus for the past four years. Her past history included hypertension and duodenal ulcer. The lesions were reported on sun-exposed areas, lower back and abdomen. Histopathologic findings were consistent with the diagnosis. Direct immunofluorescent microscopic studies revealed an intercellular deposition of IgG and C3, C4. Indirect immunofluorescence was positive and showed anti-intercellular antibody in a titre of 1:80. HLA typing showed A3;26, B38, DR3;5.

DISCUSSION

In a series of 117 cases of pemphigus reported by Beutner & Chorzelski (9) only one patient had a family history of the disease. Occasional reports in the literature suggest familial pemphigus as being an unusual presentation. The first report of familial pemphigus vulgaris and pemphigus foliaceus with histologic and immunopathologic evidence was made by Voelter (10).

Genetic factors are involved in the susceptibility

to pemphigus. The association of certain HLA antigens has been demonstrated by several investigators. Hashimoto et al. (11) found HLA A10 concentrations to be significantly increased in a group of non-related Japanese pemphigus subjects. A significant association between HLA A10 and Jewish patients with pemphigus was reported by Krain et al. (4). David et al. (12) and Park et al. (5) produced evidence of HLA A26 and DRw4, respectively, being associated with the disease. Other investigators have also implicated Bw 38 in pemphigus.

This report documents two sisters with histological and immunopathological evidence of pemphigus. HLA A26 and DR4 were also noted, in accordance with previous findings (13). The pemphigus in our patient was probably triggered by the drug that she had been taking before the onset of the skin lesions. The causal relationship between the drug and the eruption is based mainly on circumstantial evidence and further strengthened by the positive MIF test results.

In the cases presented, the clinical and immunological signs of the disease developed and persisted even after withdrawal of the drug, indicating that it did not represent a pure form of induced pemphigus. We believe that this case depicts a so-called "triggered pemphigus" according to the classification of Ruocco & Pisani (14). This form of pemphigus is biologically similar to the idiopathic pemphigus, the only feature distinguishing it from the latter being the existence of a suspected inducing factor.

Our patient had a strong genetic familial predisposition for pemphigus. However, the endogenous genetic autoimmune factors did not become evident until they were activated by an exogenous initiating stimulus, namely the suspected drug. Although the role of the endogenous factors in our patient was decisive, the inducing factors should certainly not be overlooked. The fact that both sisters developed

their pemphigus at the same age is worthy of note. This report presents an example of a possible interaction of endogenous genetic factors and exogenous factors in the development of pemphigus.

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