AUTOIMMUNE BULLOUS DISEASES

THE RELATIONSHIP OF P-GLYCOPROTEIN WITH CORTICOSTEROID DOSING AND DISEASE CHARACTERISTICS IN PEMPHIGUS VULGARIS

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Background: P-glycoprotein (Pgp) is a transporter that excretes intracellular metabolites as a mechanism of cellular protection, but its overfunction may reduce the intracellular concentration of multiple drugs, including prednisone. The expression of Pgp can be induced by cytokines and the prolonged use of corticosteroids (CS).

Objective: To explore the relationship of Pgp activity with CS and disease characteristics in PV.

Materials and methods: We included PV patients from two centers in Mexico City. Daunorubicin (DNR) is a fluorescent substrate of Pgp and we determined the uptake and efflux of DNR as a measure of Pgp activity. Results are expressed as the percentage of DNR-effluxing lymphocytes (DEL). Pgp overfunction was defined as a value greater than the 99 percentile of 30 healthy controls (i.e., 6.7). We used Spearman´s Rho for correlations.

Results: We enrolled 41 patients, 30 (73.2%) were women. The median age of patients was 49.9 years (22 – 75). The median percentage of DEL was 5.9% (1.4 – 82), 18 patients (44%) presented an elevated percentage. In the group of patients with elevated DEL we found correlation of DEL and time of disease onset (r=-0.66; p=0.003), and the score of oral activity (r=0.58; p=0.01); we found no correlation among DEL and CS dosing.

Conclusions: We confirmed the lack of correlation of CS dosing and Pgp activity in PV. A novel finding was the inverse correlation of Pgp activity and time of disease onset. PV presents a TH2 response and IL-4 increases the expression of Pgp, therefore the elevated initial activity of Pgp may alter the response to treatment in some patients. Pgp can be antagonized by numerous drugs, including common medications as verapamil, cyclosporine A or tacrolimus. Targeting Pgp at the time of disease onset could represent an additional

strategy to induce an early disease response.