Role of acantholytic food free diet in the management of patients with pemphigus

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ABSTRACT

Background: Pemphigus is an autoimmune blistering disease affecting skin and mucous membrane. The most characteristic histopathological feature is acantholysis. It may be provoked by external agents other than spontaneous autoimmune process. Those agents may be drugs or food.

Aim: To reduce steroid dose necessary for inducing remission in pemphigus patients by removing possible acantholytic agents from their daily diets.

Patients and methods: A total of twelve patients with established diagnosis of pemphigus were included in this study. Mean steroid dose was calculated for 14 months before and after application of dietary manipulation. Comparison of the doses was done based on paired T test for each patient separately and then for all patients collectively.

Results: The study included 7 males and 5 females with age ranged from 31 to 56 years (mean 41.58 ±7.9). The mean of previous total steroid doses given for all patients collectively before start of study was 749.1 ± 291.6 mg prednisone while it was reduced after application of food manipulation regimen to 324.5 ± 98.3 mg prednisone.

The difference of prednisone dose before and after regimen application was statistically significant for each patient separately (comparing 14 months before and after dietary restriction). It was also statistically significant when comparing all patients collectively.

Conclusion: Identification and removing acantholytic food stuff greatly reduced steroid doses necessary for pemphigus remission. The resulting remission was prolonged and the attacks of exacerbation became less frequent and much less severe.

KEYWORDS: Pemphigus, diet, acantholytic food

INTRODUCTION

The term pemphigus refers to a group of autoimmune blistering diseases of the skin and mucous membranes characterized histologically by intraepidermal blisters. The condition is debilitating and prior to advent of corticosteroid it was often fatal. Predisposition to pemphigus is linked to genetic factors. Certain MHC class II antigen are common in patients with pemphigus vulgaris. Individuals with a genetic predisposition to pemphigus will develop the disease only when one or more additional factors are present.

It has been established that exogenous factors, in particular thiol-containing drugs may play a role in the induction of pemphigus. Other chemical compounds within plants or food my also exert an acantholytic effect. The main compounds that were suggested to have an axantholytic effect include thiols, phenols and tannins groups.

Thiol groups are part of the molecular structure of certain plants that may have the same effects as thiol-containing drugs. Garlic belongs to the Allium group of plants, as do onion, shallot, chive, and leek, all of which contain a thiol group. Evidence for involvement of thiol-containing foods in autoimmunity is provided by case reports indi-
cating induction of pemphigus by garlic and leek. Elimination of these foods from the diet induced remission, and readministration caused exacerbation.5

It was found that certain allyl compounds (thiol group-related) such as allylmercaptan, allylmerhylsulfide, and allyl-sulfide which are found in plants belonging to the genus Allium (i.e. garlic, leek and onion) can provoke acantholysis in normal human skin cultured in vitro. The acantholytic effect is more prominent in samples taken from a donor with a pemphigus-prone antigen, i.e. DR4, in her human leukocyte antigen (HLA) phenotype.7

Tannins are naturally occurring plant polyphenolic compounds with considerable biologic activity. The astringency of many fruits during the early part of growth is due to high tannin content that declines as the fruit ripens. Certain woods, root materials, barks, leaves, and even hairs are also sources of tannin.5

It was found that tannic acid, when added to normal human skin cultured in vitro, at concentrations ranging from 0.1 to 2.mM, causes different cytotoxic effects, the most prominent of which are acantholytic changes. Interestingly, the concentrations needed to exert this effect varied remarkably among the subjects who provided explants, thus indicating a high interindividual variability in susceptibility to tannin acantholysis.8 Phenols also may be provocative factor evidenced by induction of pemphigus erythematosus following contact with tincture of benzoin.9 An example of such substances is Anacardiaceae family that includes the genus Toxicodendron (poison ivy, poison oak, and poison sumac), the most prominent genus in causing allergic skin reactions. There are many related cross-reacting species such as mango, pistachio, and cashew that belong to the same family.5

Artificial sweetener; aspartame as well as food additives such as food preservative, colorings, and flavorings all are considered to be phenol containing compounds. Sodium benzoate, tartrazine (yellow dye No. 5), vanillin, eugenol, caffeic acid, vitamins C and E, and cinnamic acid are all phenols. Cinnamic acid is present in apple, grape, orange, pineapple, and tomato juices.5

Other phenol related compound is Pinene which is used to flavor baked goods, beverages, candy, condiments, chewing gum, and ice cream. It is also found in tomatoes, potatoes, mangoes and bananas.5

AIM OF THE WORK
Trying to reduce steroid doses necessary for inducing remission in pemphigus patients through dietary manipulation. This manipulation was targeted toward exclusion of some food staff that containing acantholytic compounds. This may help in reducing possible steroid side effects.

PATIENTS AND METHODS
Twelve patients with settled diagnosis of pemphigus (vulgaris, foliaceous and vegetans) were included in this study. No cases of para-neoplastic pemphigus were included in this study. All patients were chronic patients under steroid as well as adjuvant steroid sparing drugs (azathioprin or dapsone). The dose of steroid sparing drugs was almost fixed or limitedly changed for long time so the manipulation was targeted toward steroid doses only.

The previous total monthly dose of prednisone was calculated using patient’s file. Strict instruction given to the patients and his companions regarding avoidance of acantholytic food staff (garlic, onion, strawberry, tea, cabbage, cauliflower etc.). The patients were counseled for the potentially hazardous effects of acantholytic foods and hence advised to refrain from such food. All patients were adjusted to the dose which in-
duced complete remission. They also were instructed to attain the dermatology clinic whenever there is any recurrence or start of oral soreness for proper dose adjustment.

Patients were followed up for 14 months with recording total monthly doses of prednisone. At each visit, patients were asked for proper following the dietary instruction in addition to monitoring the clinical improvement and the general progress. Comparison of doses before and after application of dietary restriction regimen was done for each patient separately and then for all patients collectively. Paired sample T-test was applied.

RESULTS
All of the twelve patients (seven males & five females) completed the study. Their age ranged between 56 and 31 years old (mean 41.58 ± 7.9). The mean of previous total steroid doses given for all patients collectively before start of study was 749.1 ± 291.6 mg prednisone while it was reduced after application of food manipulation regimen to 324.5 ± 98.3 mg prednisone.

Table 1 Showing mean monthly prednisone dose before and after dietary manipulation

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<th>Case number</th>
<th>Paired Samples Statistics</th>
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<tr>
<td></td>
<td>Mean</td>
<td>Std. Deviation</td>
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<tr>
<td></td>
<td>Before</td>
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</tr>
<tr>
<td>Case 1</td>
<td>1114.29</td>
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<td>Case 11</td>
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Table 2 Comparing mean prednisone doses for all patients before and after dietary restrictions

<table>
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<tr>
<td></td>
<td>Mean</td>
<td>Std. Deviation</td>
<td>Std. Error Mean</td>
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<tr>
<td>Pair before</td>
<td>424.583</td>
<td>248.469</td>
<td>71.726</td>
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The difference of prednisone dose before and after regimen application was statistically significant for each patient separately when comparing 14 months before and after dietary restriction (Table-1). Also, there was statistical significant difference regarding mean collective doses for all patients before and after dietary restriction (Table-2). The changes of total monthly prednisone doses before and after food regimen application in each patient was illustrated in Fig. 1.

**Fig. 1** The changes of total monthly prednisone doses before and after food regimen application in each patient. Blue line represent steroid doses before dietary regimen while violet line represent the steroid doses after the regimen


DISCUSSION

Pemphigus is a group of mucocutaneous autoimmune diseases mediated by IgG autoantibodies directed against keratinocyte adhesion molecules. Pemphigus Vulgaris is a potentially life-threatening disease with a mortality rate of approximately 5-15%. Systemic corticosteroids remain the mainstay of therapy for pemphigus vulgaris. Complications secondary to the use of high-dose corticosteroids contribute to the mortality rate. Morbidity and mortality are related to the extent of disease, the maximum dose of systemic steroids required to induce remission and the presence of other diseases. Prognosis is worse in patients with extensive disease and in older patients.

The cause of the disease remains unknown, but the great variations of incidence rates, clinical features and demographic characteristics among countries lead to a suspicion of different risk factors. In many diseases, it appears that autoimmunity is preceded by some environmental insult. Tissue damage may be the key event that either allows for release of sequestered antigens from immunologically privileged sites or causes local inflammation resulting in lymphokine release and subsequent expression of antigens, or both. Depending on previous information regarding the acantholytic effect of some chemicals within food, this study evaluated such dietary restriction which gave promising results. Most of the patients showed marked dose reduction in the same time with satisfactory remission.

Different mechanisms of action have been postulated for such acantholytic food stuff for example, tannins that react with structures on or in the red blood cell membrane, frequently used as a cross-linking agent, and similar cross-linkage in the epidermis may possibly be the mechanism through which these compounds induce pemphigus. Similarly, the first step in drug-induced acantholysis involves binding of the drug to the cell membrane.

Tannins exert affinity toward keratinocyte evidenced by electron microscope study which revealed staining of cell surface and intercellular material in squamous epithelium and the desmosomes with tannin. Evidence for involvement of thiol-containing foods in autoimmunity is provided by case reports indicating induction of pemphigus by garlic and leek. Elimination of these foods from the diet usually induce remission while re-administration may cause exacerbation. Relapse was occurred in 3 patients and it was related to junk-food intake or inability to continue the recommended regimen.

CONCLUSION

Removing possible pemphigus provocative factors in the food resulted in marked steroid dose reduction associated at the same time with satisfactory remission. Additionally, relapses frequency and severity became much more less than before.

REFERENCES