

ADRENAL CORTICAL FUNCTIONS IN PEMPHIGUS

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Summary

Urinary excretion of 17-Hydroxy-corticosteroids was measured in 23 adult patients with various types of Pemphigus and compared with 21 normal adult controls. The values were found to be significantly lower in patients with Pemphigus. The possible relationship to disease and therapy are discussed.

Pemphigus, a dreaded fatal dermatosis, is characterised by vesiculo-bullous lesions on the skin and mucous membranes. Biochemical abnormalities in blood and urine that could be attributed to adrenal cortical deficiency, were seen to exist by Talbot, Lever and Consalazio (1940). Goldzeiher (1945) on autopsy of 6 patients afflicted with pemphigus, demonstrated in the adrenal cortex, a spectrum of changes varying from acute degeneration to fibrotic lesions. The present study was undertaken to assess, in patients with pemphigus, changes in adrenal cortical functions as measured by daily urinary excretion of 17-Hydroxy-corticosteroids.

Subjects and Methods

Twenty three adult patients with pemphigus (Pemphigus vulgaris-19; pemphigus erythematosis-3; pemphigus foliaceus-1) of both sexes formed the subjects for this study. All patients were on systemic corticosteroid therapy which was briefly withdrawn for 24-72 hours in 15 patients, before the estimation of 17 hydroxycorticosteroids was undertaken. The severity of the disease

was arbitrarily graded into following 4 categories:

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| Grade I | Less than 10 vesiculo-bullous lesions. |
| Grade II | Patients with 11-30 vesiculo-bullous lesions. |
| Grade III | Patients with 11-30 cutaneous lesions and involvement of mucous membranes. |
| Grade IV | More than 30 cutaneous lesions and or severe mucous membrane involvement. |

17-Hydroxy-corticosteroid estimation in 24 hour urine samples was made using modification of Birke et al (1958) on the original method of Appleby et al (1955).

Twenty-one healthy adults of comparable ages of both sexes were used as controls for estimation of daily 17-Hydroxy-corticosteroid excretion in the urine.

In 4 patients, 17-Hydroxy-corticosteroid estimation was made before and 24 hours after injection of 20 units of A.C.T.H. given intra-muscularly.

Results and observations

Twelve of these patients were males and eleven females with ages varying between 18-87 years. The duration of disease varied between 4 months and 9 years; with six of them having disease

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Received for Publication on 3-7-1972

for less than a year; 5 having it for 1-2 years; 2 between 2 - 3 years; and 5 with disease of 3 - 4 years' duration. Rest 5 patients had it for more than 4 years.

Severity of disease was graded as of grade I in 12 patients; grade II in 3; grade III in 6 and grade IV in 2 patients. Patients were more or less evenly distributed as far as duration and grading of disease were concerned, though patients with disease of more than 5 years' duration belonged to grade I.

The mean values for 17-Hydroxy-corticosteroids for patients with pemphigus were 8.24 mgm/24 hours in the males and 8.37 mgm/24 hours in females.

Corresponding values for controls were 10.70 mgm/24 hours for males and 10.12 mgm/24 hours for females.

Following A.C.T.H. administration in 4 patients there was an elevation in the excretion of 17-Hydroxy-corticosteroids in all patients, but in only one this could be regarded as significant (over 50% increase).

Discussion

From the above mentioned results it will be seen that the mean values for 17-Hydroxy-corticosteroids in Pemphigus are statically significantly lower (for males $P \leq 0.01$) and for females $P \leq 0.06$) than in the normal controls. And since excretion values of 17-Hydroxy-corticosteroids is an indirect way of assessing the adrenal cortical activity, it may be logical to deduce that the adrenal cortex is working at a sub-normal level. Many workers in the past had also pointed to a deficiency of adrenal cortical activity (Talbot, Lever and Consalazio 1940) using various laboratory procedures as well as autopsy studies (Lever and Talbot 1944; Goldzieher 1945). Quiroga and Cort (1955) went to the extent of saying that estimation of 17 Ketosteroids is helpful in the

diagnosis of Pemphigus. Such conclusions, in our opinion, do not seem warranted since no diagnostic specificity can be attached to lowered 17-Hydroxy-corticosteroid excretion values. Whether or not this depression of adrenal cortical activity is caused by a permanent or absolute structural damage, is difficult to assess since only in one patient a significant elevation (over 50%) of 17 Hydroxycorticosteroids was observed following A.C.T.H. therapy.

The cause and significance of adrenal cortical depression are by no means settled. Recent work (Beutner) has demonstrated fairly conclusively an auto immune aetiology of the disease process in pemphigus which would tend to discount the earlier hypothesis of adrenal cortical deficiency playing a causative role as alleged by Cassat and Micheleau (1906). Goldzieher (1945) pointed out that pemphigus is by no means a primary adrenal disease and that the causative agent of pemphigus produces damage to the adrenals as a complication of cutaneous disease.

Kuhn and Iverson (1948) and Lever (1953) also believed that adrenal deficiency is secondary in pemphigus. In the present series it is difficult to ascribe even a secondary role to poor adrenal cortical functions because of an additional complicating factor, that these patients had been on systemic corticosteroid therapy for variable, though sufficiently long periods of time, before being subjected to the present investigations. And because of dependence of the disease on systemic corticosteroids, it was not possible for therapy to be discontinued for long periods, without endangering the patient's life. An attempt at correlating the values of 17-Hydroxy-corticosteroids and the severity of disease showed that a strict relationship was not possible, though the values for 17-Hydroxy-corticosteroids tended to be low if the disease process was severe and the duration of the disease short.

Values of 17-Hydroxy-corticosteroids as estimated in 24 hours urine specimens expressed as mgm, per 24 hours.

PEMPHIGUS		CONTROLS	
Males	Females	Males	Females
7.67	9.00	11.00	9.83
9.17	13.38	8.53	7.31
6.79	6.81	13.33	11.25
6.5	7.79	7.11	10.14
8.28	6.07	13.16	9.61
7.67	9.04	11.75	10.79
14.27	9.24	10.98	11.96
8.66	10.64	8.44	
7.18	9.70	7.46	
7.13	5.01	13.70	
8.18	6.41	12.99	
7.32		10.00	
Mean Values	Mean Values	Mean Values	Mean Values
8.24	8.37	10.76	9.7

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False

Histologically, Koplik's spots show giant cells which on electron microscopy shows aggregates of microtubules within the nuclei and the cytoplasm. The presence of these structures characteristic of paramyxovirus indicate that the lesion result from direct invasion of the epithelia by the virus. The skin lesions of Measels show identical histological features.

Reference : New England J Med 283 : 1139, 1970.