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Original Article

The frequency of autoimmune thyroid disorders in patients of pemphigus vulgaris

Farheen Hassan, Sadia Jabeen, Shehla Shaukat, Ghazala Butt, Raffad*, Arsilah Erum, Ijaz Hussain

Department of Dermatology, King Edward Medical University, Mayo Hospital, Lahore.
* Department of Medicine, Khawaja Muhammad Safdar Medical college, Sialkot.

Abstract

Objective To determine the frequency of autoimmune thyroid disorders in patients of pemphigus vulgaris.

Methods It was cross sectional study conducted at department of dermatology, Mayo hospital, Lahore. A total of 164 patients of pemphigus vulgaris satisfying the inclusion and exclusion criteria were enrolled. The diagnosis of pemphigus vulgaris was made clinically and confirmed on biopsy while autoimmune thyroid disease was confirmed by the presence of anti-thyroid antibodies and abnormalities in thyroid function tests. Reports were assessed and autoimmune thyroid disorder was labeled.

Results Out of 164 patients with pemphigus vulgaris, 114(69.5%) were males, while 50(30.5%) were females. Age range was between 20 to 70 years with mean age of 43.2±16.0 years. Among 164 patients, 9(5.5%) had auto-immune thyroid disorder, 3(33.3%) had Hashimoto thyroiditis and 6 (66.7%) had Graves' diseas.

Conclusion Pemphigus vulgaris may exist together with autoimmune thyroid diseases especially Hashimoto thyroiditis and Graves' disease.

Key words
Pemphigus vulgaris, autoimmune thyroid disorders.

Introduction

Pemphigus is an autoimmune blistering disease, characterized by formation of blisters and erosions on body. Pemphigus vulgaris (PV) is the most common variant of this group of diseases that causes painful blisters and erosions on skin and mucosal surfaces.[1] The usual onset of disease is in fifth decade of life and females are affected predominantly.[2] It is characterized by auto antibodies to the desmosomal adhesion protein, mainly desmoglein 3.[3]

Address for correspondence
Dr. Farheen Hassan
Department of Dermatology,
Mayo Hospital, Lahore.
Email: farheen.hassan77@gmail.com

PV is associated with other autoimmune disorders like rheumatoid arthritis, type 1 diabetes mellitus, systemic lupus erythematosus, including thyroid disorders.[4] A recent study has showed increase likelihood to the development of autoimmune diseases in the family members of patients with PV.[5]

Incidence of hypothyroidism and other autoimmune disorders is higher in patients of pemphigus as compared with the general population.[5,6]

Mukaddes Kavla et al. performed a study in 80 diagnosed patients of PV that showed primary thyroid disease was found in 13(16%) of the patients and out of these 7 (9%) were having

characteristics of Hashimoto thyroiditis (HT).[5]

Significant changes in thyroid biochemical profile including thyroid stimulating hormone (TSH), serum free triiodothyronine (fT3), free thyroxine (fT4), as well as, positive titers for anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies were found.[5]

In Canada, frequency of Hashimoto thyroiditis in PV patients was reported to be 12.8% by Heelan et al.[6] while Lesham et al. studying autoimmune diseases in PV patients and their relatives reported autoimmune thyroid disease in 4% PV patients.[7]

The association of pemphigus with autoimmune thyroid diseases, namely Hashimoto thyroiditis and Graves' disease, is well known.[8] However, controlled studies evaluating thyroidal autoimmunity in pemphigus patients are limited. Anti-TPO and anti-Tg are sensitive tests for assessing thyroidal autoimmunity.[8] So it is suggested that as part of pemphigus investigations and surveillance, investigating for these conditions should be considered.[1,6]

Methods

This cross-sectional study was conducted at department of dermatology, Mayo Hospital, Lahore, from June 17, 2017 to December 17, 2017 in collaboration with medical department at Lahore General Hospital, Lahore. A total of 164 patients of age 20-70 years of either gender with pemphigus vulgaris were included in the study. Those patients who had history of thyroid surgery or receiving thyroid medication, steroids, immunosupressants and any drug which interfere with thyroid functions like lithium, octreotide, beta-blockers and barbiturates in last 6 months were excluded. After approval from hospital ethical committee, patients were enrolled in the study after taking informed consent. Basic demographic information of each patient like age and gender were noted. Detailed history and clinical examination were carried out and tissue biopsy from lesion was taken and sent to pathology department. Each specimen was examined after haematoxylin and eosin stained sections from paraffin embedded 10% buffered formalin fixed tissue blocks. Tzanck smear for acantholytic cells was used to reach the provisional diagnosis of PV. Then biopsy proven patients with pemphigus vulgaris were analyzed using serum-free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH), anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies by electro-chemiluminescence assay. A patient clinically with symptoms of heat intolerance, palpitation, diarrhea, weight loss, increased appetite, and biochemically with serum T4 more than

23pmol/ L, serum T3 more than 5.8pmol/ L and serum TSH less than 0.30mIU/ L was labeled as hyperthyroid. A patient clinically with symptoms of cold intolerance, constipation, weight gain, poor appetite and biochemically with serum T4 less than 11.5pmol/ L, serum T3 less than 2.5 pmol/ L and serum TSH more than 5.0 mIU/ L was labeled as hypothyroid. Antibodies against Thyroid Peroxidase (TPO) positive in a patient of hypothyroidism was labeled as having Hashimoto thyroiditis. While anti-thyroglobulin antibodies positive in a patient of hyperthyroidism was labeled as having Graves' disease. All study findings were recorded in detail in a pre-designed proforma and results were evaluated. All patients were managed as per standard protocol. The collected data was analyzed through SPSS v23.0. Quantitative variable like age was presented in the form of Mean±S.D. Qualitative variables like gender, autoimmune thyroid disorder and type of disorder were presented in the form of frequency and percentage. Data was stratified

for age and gender. Stratified groups were compared by using chi-square test. A p-value <0.05 was considered as statistically significant

Results

In this study, 164 patients with pemphigus vulgaris were enrolled. Among these patients, 114(69.5%) were males and 50 (30.5%) were females. Age range was from 20 to 70 years with mean age of 43.2±16.0 years. Majority of the patients 63(38.4%) were between 20 to 35 years of age. In biochemical profile status, Most of the patients 101(61.6%) were euthyroid, while 48(29.3%) and 15(9.1%) were hypothyroid and hyperthyroid respectively.

In anti-thyroid anti-bodies status, most of the patients 69(42.1%) had anti-Tg, while 68(41.5%) and 27(16.5%) had anti-TPO and No anti-bodies status respectively **(Table 1)**.

Among patients, 9(5.5%) had auto-immune thyroid disorder and who had auto-immune thyroid disorder, 3(33.3%) had hashimoto thyroiditis and 6(66.7%) had grave's disease.

Table1 Frequency distribution of Anti-thyroid anti-bodies

Anti-thyroid Anti-bodies	*Frequency*	*Percent*
Anti-TPO	68	41.5
Anti-Tg	69	42.1
No Anti-body	27	16.5
Total	164	100.0

Discussion

Autoimmune disorders may accompany each other and coexistence of PV with autoimmune disorders such as myasthenia gravis, systemic lupus erythematosus, rheumatoidarthritis and Graves' disease has been reported.[9] In addition, autoimmune thyroid disorders have been reported in association with PV.[10]

In our study we found alterations in thyroid function tests and thyroid auto-antibodies in 5.5% of PV patients. Our findings were similar to the findings of Pitoia et al. who screened 15 PV patients with respect to thyroid diseases and found abnormalities in serum thyroid profiles in 7% of PV patients.[11]

The authors found anti-TPO auto-antibodies in 40% of PV patients and 7% of the controls; only one of the patients with anti-thyroid antibodies had Hashimoto thyroiditis. Ansar et al. found anti-TPO antibodies in 23% of 22 PV patients and in 6% of the controls, they found no thyroid diseases in none of the patients with positive anti-thyroid antibodies.[12]

Similar to the recent studies, we found higher prevalence of anti-thyroid antibodies (anti-TPO and anti-Tg) in PV patients (5.5% of PV patients). But we found subclinical Hashimoto thyroiditis in all of the PV patients with positive anti-thyroid antibodies.

Former studies reported only presence of anti-thyroid antibodies but they found no abnormalities in thyroid function tests.[12] We found thyroid function abnormalities in a higher number of patients in PV group than the control group and we observed that average fT3 levels were significantly lower and average fT4 levels were significantly higher in PV patients than the control group.

Our study differed from the other two studies because we found primary thyroid disease (PTD) in all of the patients who were found to have serum thyroid profile alteration and PV patients were found to have higher prevalence of PTD when compared to placebo.[12]

In addition, PV and Hashimoto thyroiditis were found to have a significant association and Hashimoto thyroiditis was more common in the mucosal form of PV even though this finding was not statistically significant.

Pitoia et al. found subclinical hypothyroidism in 7% of PV patients, while Ansar et al. did not find any thyroid disease which is associated with abnormalities of thyroid functions.[11,12] We found subclinical hypothyroidism in 29.3%, subclinical hyperthyroidism in 9.1% and euthyroid syndrome in 61.6% of PV patients and all of these patients had alterations in thyroid function tests. We did not find any association between PTD and clinical phenotype of PV and gender of the patients.

Conclusion

Even though the exact causes remain unidentified, the results of our study showed that PV could accompany thyroid autoimmunity and primary thyroid diseases especially Hashimoto thyroiditis. We recommend laboratory testing for thyroid auto-antibodies and thyroid function tests in patients with PV even if they do not have a clinical indication of thyroid disease.

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