

A rare association of squamous cell carcinoma with paraneoplastic pemphigus

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Abstract Pemphigus vulgaris is an auto-immune blistering disorder associated with splitting at the dermo-epidermal junction. It targets the desmoglein structural protein of skin thus causing formation of blisters. It is seen to be associated with esophageal and laryngeal malignancies. Here in this case report, we try to highlight the unusual presentation of squamous cell carcinoma of buccal mucosa with pemphigus vulgaris.

Key words

Pemphigus vulgaris, squamous cell carcinoma, desmogleins.

Introduction

Pemphigus is a chronic disease with formation of blisters over skin and mucosal membranes.¹ Antibodies IgG are targeted at desmoglein 1 and 3 which disturbs intra-epidermal adhesion leading to acantholysis which presents clinically as blisters, vesicles and erosions.² Various associations are seen with pemphigus vulgaris as insomnia, hidradenitis, myasthenia gravis and haematological neoplasia.² Associations with lung carcinoma were also observed.² Squamous cell carcinoma associated pemphigus vulgaris was noticed in a patient who was on long term immunosuppressive drugs for pemphigus vulgaris.³

We report here a rare case report of a patient who presented with nodular growth over his cheek followed by fluid filled lesions over his trunk.

Case Report

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A 40 year old male patient presented to our department with painless nodular growth over his right mandibular region extending to the maxillary region for 5 months. Nodular growth was with hemorrhagic and necrotic areas. Since it was not associated with any complaints, the patient kept ignoring it until it increased to a large size of approximately 3x3 cm, disfiguring his face. On palpation, right mandibular lymphadenopathy was noticed. Simultaneously he also complained of fluid filled lesions over his chest, abdomen and trunk for 1 month. No other associated complaints were given by the patient.

Blood investigations including complete blood count, kidney and liver function tests, blood sugar tests, thyroid tests were done and were within normal limits. Patient was advised biopsy for nodular growth and for fluid filled lesions. Intraoral buccal biopsy was done and it was suggestive of squamous cell carcinoma. Punch biopsy from fluid lesions over abdomen suggested pemphigus vulgaris. Direct immunofluorescence showed positivity for Dsg1 and Dsg2 with fishnet pattern. He was also advised CT head and neck to look for involvement of any neighbouring structures; it



Figure 1 displaying nodular lesion on right mandibular area.



Figure 2 Displaying fluid filled blisters on chest.

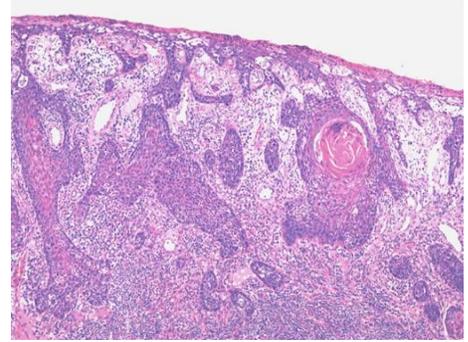


Figure 3 Intraoral biopsy which is suggestive of squamous cell carcinoma.

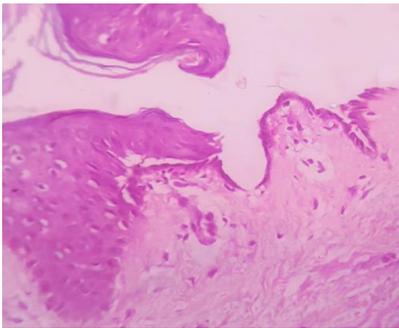


Figure 4 Punch biopsy of fluid filled lesion showing acantholysis.

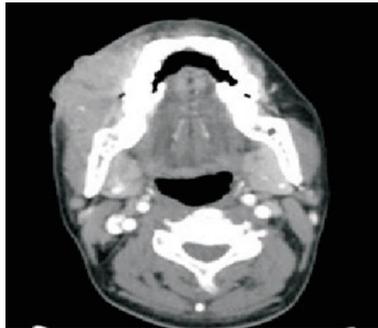


Figure 5 CT head and neck suggestive of heterogeneously enhancing mass in lower right gingival sulcus with submandibular and submental lymph node metastases.

revealed heterogeneously enhancing lesions in lower right gingival sulcus with multiple submental and submandibular node metastases.

Discussion

Pemphigus being an autoimmune disorder, the antibodies IgG (specifically IgG4)⁴ are targeted against desmoglein proteins Dsg1 and Dsg3.^{5,6} These auto-antibodies bind to the intercellular adhesion proteins causing their destruction, which results in bullae formation.⁷ It is a type 2 hypersensitivity reaction causing destruction of these cells.⁴ It is the most common clinically found type of pemphigus group of disorders.⁵ Nikolsky sign is positive in patients of pemphigus vulgaris which creates erosions due to sideward shearing friction of normal appearing epidermis.⁸

Exacerbation or induction of pemphigus disorder can be due to malignancies.⁹ Hence it is

suggested that with removal of tumor, pemphigus may regress.⁹ Sinha *et al.* proposed the 'super compensation hypothesis' where steric hindrance causes functional loss of adhesion molecules and various other mechanisms have been suggested for antibody induced acantholysis.⁸ Associations of pemphigus with malignancies such as lung cancer, post treatment with certain drugs as also with radiation therapy is observed.¹⁰ According to a study conducted by Germans, most commonly associated malignancies were oropharyngeal, gastro-intestinal and colon cancer.¹¹

In the above case report, the patient presented simultaneously with both the complaints. It is assumed that the malignant tumor destroys the tissue altering the morphology of epithelial surface antigens. This releases the hidden antigens which when exposed generates an

immune response, also known as epitope spreading.¹¹ This above proposed mechanism is suggested as the cause of association of pemphigus vulgaris with squamous cell carcinoma in the above case report.

Contrary to this, another theory mentions that long standing irritation of tissues in pemphigus vulgaris leads to development of malignancies due to pro-neoplastic mutations, stimulation to angiogenesis and resistance to apoptosis.¹¹

Pemphigus thus might be caused due to malignancy or may be induced by malignancy.

Conclusion

Here the association of squamous cell carcinoma induced pemphigus vulgaris is highlighted which is a rare association. It also suggests us to look for any warning/clinical signs of malignancy which will help us in prompt diagnosis and better management.

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