

Oral Paraneoplastic Pemphigus and Pharyngeal Squamous Cell Carcinoma: A Rare Case Report and Review of Literature

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Abstract- Paraneoplastic pemphigus (PNP) is an autoimmune vesiculobullous disease of the skin and mucous membrane associated with benign and malignant neoplasm. The most common malignancies associated with PNP are hematologic and lymphomatoid. Association of oral PNP with squamous cell carcinoma of the pharynx is very scarce, very few cases are reported, and also the cases of PNP are usually refractory to the treatment mainly those associated with hematologic. Here, we reported a case of oral paraneoplastic pemphigus with squamous cell carcinoma of the pharynx that resolved on its own after completion of treatment of pharyngeal squamous cell carcinoma.

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Introduction

Paraneoplastic pemphigus (PNP) is an autoimmune vesiculobullous disease of the skin and mucous membrane associated with benign and malignant neoplasm. The most common malignancies associated with PNP are hematologic and lymphomatoid (1). Anhalt *et al.*, (1990) first described five cases of pemphigus in association with lymphoproliferative diseases (2). The pathogenesis of PNP seems to be the interaction between immunity and concomitant neoplasm, with the formation of autoantibodies against desmosomal and hemidesmosomal antigens. PNP associated with benign neoplasm has a good prognosis after excision of neoplasm; however, PNP associated with malignancy can be quite severe and doesn't respond to the treatment (1). Recently Lee *et al.*, in a review from 1990-2008, reported four cases of paraneoplastic pemphigus associated with squamous cell carcinoma (SCC), reflecting the scarcity of literature available on the association between paraneoplastic pemphigus and squamous cell carcinoma (3). It is, therefore, important to add such kind of rare reports to the literature for a better understanding of the association and its treatment. An unusual case of PNP that was associated with SCC of the pharynx is reported, interestingly, after treatment of malignancy, PNP lesion resolved spontaneously.

Case Report

A 60-year-old patient came to the outpatient department with the complaint of the replacement of missing teeth. He was diagnosed with squamous cell carcinoma of the posterior pharyngeal wall with T3N2c M0 staging two years ago. The patient had recently completed two cycles of neoadjuvant (NACT) chemotherapy with paclitaxel 240 mg and cisplatin 50 mg and radiotherapy with 66 grays, 30 fractions. The patient also had a habit of tobacco chewing for 15 years. The patient was recently detected diabetic. Intraoral examination revealed an edentulous mandibular ridge. Right buccal mucosa had vesicles that were filled with blood color fluid that were frequently hemorrhagic (Figure 1).



Figure 1. Blood filled vesicle seen on the right buccal mucosa

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Oral PNP and pharyngeal SCC

On the application of lateral digital pressure, there was the development of new vesicles, indicating positive Nickolsky sign. No cutaneous lesion was present. On the basis of the above findings provisionally, the lesion was diagnosed as the vesiculobullous lesion. The biopsy was taken from the right buccal mucosa. Hematoxyline and Eosin (H and E) stained slide shows, stratified squamous epithelium and underlying connective tissue, focal areas of suprabasal acantholysis, focal areas of suprabasal and sub-basal clefts noted, separation of epithelium from connective tissue, patchy inflammatory cell infiltrate, extravasated RBCs and normal submucosal structures (Figure 2). The clinicopathological correlation confirmed the diagnosis of PNP. After one month without any institution of treatment, the patient was recalled for follow up; there was no active lesion in the oral cavity (Figure 3). The patient is kept on regular follow up; there was no recurrence after two years.

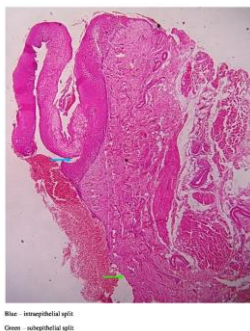


Figure 2. Hematoxyline and Eosin (H and E) stained slide shows, stratified squamous epithelium and underlying connective tissue, focal areas of suprabasal acantholysis, focal areas of suprabasal and sub-basal clefts



Figure 3. Post biopsy photograph reveals no active lesion

Discussion

A search was conducted on PubMed by using keywords (paraneoplastic pemphigus AND squamous cell carcinoma) until June 2018. A total of 12 articles

were found; of them, we found 5 case reports of PNP and squamous cell carcinoma involving various organs (one each of tongue, esophagus, uterus, and two pulmonary). Out of these five case reports, no report was found of oral PNP with pharyngeal SCC. It was, therefore, important to report this case.

Kaplan *et al.*, reported a review of PNP of 163 cases, 84% of these cases were associated with hematologic related neoplasm (4). Other PNP cases are comprised of carcinoma or sarcoma (2). Wong *et al.*, reported the first case of SCC of the tongue with pemphigus with pemphigoid like features (5).

The present case report is a unique case of oral PNP associated with SCC of the pharynx. Clinically PNP presents with variable features, however painful and intractable mucositis are a constant feature. Mucositis presents as ulceration and erosions affecting the involved surfaces. The mucosal involvement of PNP is more extensive, necrotic, and resistant to treatment. Contrastingly a case of focal mucosal involvement is also reported. Interestingly in our case report, only right buccal mucosa was involved with erosions and with positive Nickolsky sign. Histopathological features of PNP varies according to varied morphology of clinical lesion. It shares features of subepithelial clefting as that of pemphigoid and suprabasal or intraepidermal clefting, as seen in pemphigus. These findings were consistent with the findings of the reported case.

It is still unclear why PNP lesions are associated with underlying malignancy; two hypotheses have been proposed for this causation (6). Firstly an antitumor immune response may cross-react with normal epithelial protein. Our patient had pharyngeal SCC that produced desmoplakin and desmosomes. Skin and mucosa contain similar proteins. Because, human body produces antibodies against these common proteins in tumoral tissues, which could cross-react with the normal mucosa proteins. However, most patients with PNP have lymphomas and chronic leukemias of B-cell origin, which do not naturally produce desmosomes or express desmoplakins. Secondly, dysregulated cytokine production by tumor cells may induce autoimmunity.

Most of the cases of PNP associated with malignancies are refractory to treatment, but our patient showed resolution of the lesion after completion of the treatment of pharyngeal SCC (1).

Usually, the cases of PNP are refractory to the treatment. Although it was a case of PNP associated with pharyngeal SCC, the lesion of PNP resolve after the treatment of pharyngeal SCC.

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