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CASE REPORT

Multidisciplinary Management of Paraneoplastic Pemphigus Associated with B-Cell Lymphoma: A Case Report

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Background: Paraneoplastic pemphigus is a rare life-threatening blistering autoimmune mucocutaneous disease associated with various neoplasms. In contrast to the skin, mucosal lesions are refractory and requires considerable healing time, heals far more slowly. A multidisciplinary approach may provide a comprehensive management and a better prognosis.

Case Summary: A sixty-one-year-old male patient presented to the ER department in June 2020 complaining of severe inflammation of the left eye along with scaly erythematous skin eruptions affecting the hands, trunk, and feet. Subungual hematoma was also observed. Clinical examination revealed extensive oral ulceration involving the dorsum and ventral surface of the tongue, buccal mucosa, labial mucosa, and hematic crusts were noticed on the lips. The patient was admitted for panophthalmitis secondary to a perforated corneal ulcer. Dermatological investigations were requested in addition to extensive baseline studies to rule out malignancies. The patient had a retroperitoneal lesion and underwent CT guided biopsy. Result was suggestive of low-grade B cell non-Hodgkin's lymphoma. He was treated by the haematology-oncology, dermatology and oral medicine teams.

Conclusion: Paraneoplastic pemphigus (PP) is a fatal autoimmune blistering disease associated with underlying malignancy. A multidisciplinary approach to achieve early diagnosis and better management is essential to improve the quality of life of such patients despite their poor prognosis.

Clinical Significance: Paraneoplastic pemphigus is a rare disease associated with mucocutaneous ulcerations and various malignancies, including lymphoproliferative neoplasms. As demonstrated in the current case, multidisciplinary assessment and management have proven to be effective in managing the patient. Physicians and dentists should make their best effort to work collaboratively to manage patients and minimize patient distress and improve life quality and prognosis.

Keywords: paraneoplastic pemphigus, multidisciplinary, management, case report, oral medicine, dermatology

Introduction

Paraneoplastic syndrome encompasses diverse disorders that arise as a result of cancer. These conditions are characterized by systemic effects that do not stem directly from tumor invasion, size, or metastasis, but rather from the distant impacts of malignancy.[1] Such syndromes can affect multiple organ systems, including the endocrine, neurological, hematological, dermatological, rheumatological, musculoskeletal, gastrointestinal, renal, soft tissue, skeletal, and metabolic systems. The diagnosis of paraneoplastic syndrome can be particularly challenging, as its symptoms may resemble those of other medical conditions, highlighting the complex interplay between immune response and cancer development.[1] Mucocutaneous lesions showed variabilities and may appear as pemphigus vulgaris, pemphigus foliaceous, bullous pemphigoid, erythema multiforme and lichen planus.[2]

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Paraneoplastic pemphigus (PNP) is a rare life-threatening mucocutaneous autoimmune disease.[3] It is characterized by blistering, Intractable mucositis, and benign and malignant neoplasms.[3] Pathogenesis though not fully understood, however autoimmunity and cell mediated immunity have been proposed mainly against plakin family.[4] The development of paraneoplastic effects is closely tied to the interactions between tumors and the host immune system. Tumors can release onconeural antigens that provoke immune responses, inadvertently targeting nerve tissues due to shared epitopes. This can lead to paraneoplastic neurological syndromes (PNS), where neurological symptoms arise without direct tumor invasion. Research indicates that cytotoxic T lymphocytes (CTLs) are predominantly activated in response to these antigens, reflecting a strong immune mechanism aimed at tumor destruction that paradoxically damages the nervous system. Additionally, immune checkpoint inhibitors may reveal PNS, highlighting the breakdown of immune tolerance and suggesting potential therapeutic pathways. Overall, tumors orchestrate immune-mediated responses that result in PNS, illustrating the complex relationship between malignancy and neurological effects. The emergence of paraneoplastic effects is intricately linked to the interactions between tumors and the host's immune system. Tumors can secrete onconeural antigens that elicit immune responses, which may inadvertently target nerve tissues due to the presence of shared epitopes. This phenomenon can result in paraneoplastic neurological syndromes (PNS), characterized by neurological symptoms that occur without direct invasion by the tumor. Studies have shown that cytotoxic T lymphocytes (CTLs) are primarily activated in response to these antigens, indicating a robust immune response aimed at tumor elimination that, paradoxically, harms the nervous system. Furthermore, the use of immune checkpoint inhibitors may unmask PNS, underscoring the disruption of immune tolerance and suggesting new therapeutic avenues.[1,5,6] Clinical characteristics are very variable. The head and neck region, trunk and proximal extremities are most affected.[4] We report a case of PNP that was successfully treated using a multi-disciplinary approach.

Case Presentation

Chief Complaints

Sixty-one years old male patient presented to the ER department with severe inflammation of the left eye and scaly erythematous skin eruptions affecting the hands, trunk, and feet.

History of Present Illness

The patient lesions started to develop a month before presentation to ER.

History of Past Illness, Personal and Family History

The patient history was insignificant.

Physical Examination

Twenty nail dystrophies with multiple violaceous to brownish edematous plaques and hemorrhagic crusts over the proximal nail folds were observed (Figure 1). Multiple superficial skin erosions with erythematous bases over the trunk (Figure 2). He also had extensive oral ulceration involving the dorsum and ventral surfaces of the tongue, buccal mucosa, labial mucosa, erythematous bleeding areas and encrustation of the lips (Figure 3). These lesions were associated with significant unintentional weight loss and loss of appetite. The patient was admitted to the hospital for a full workup including screening for malignancy.

Laboratory Examinations

Histopathological examination of the skin lesions confirmed a diagnosis of paraneoplastic pemphigus (Figure 4).[7] After screening for malignancy, the patient was found to have a large retroperitoneal mass. CT tomography-guided biopsy of the tumor confirmed the diagnosis of low-grade B cell non-Hodgkin.

Final Diagnosis

This patient was diagnosed with paraneoplastic pemphigus associated with B-Cell lymphoma.

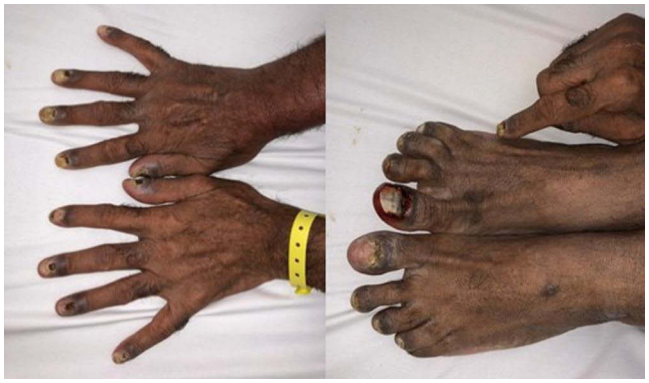

Figure 1 Oral ulceration in the dorsum surface of the tongue, erythematous papules on the lip.

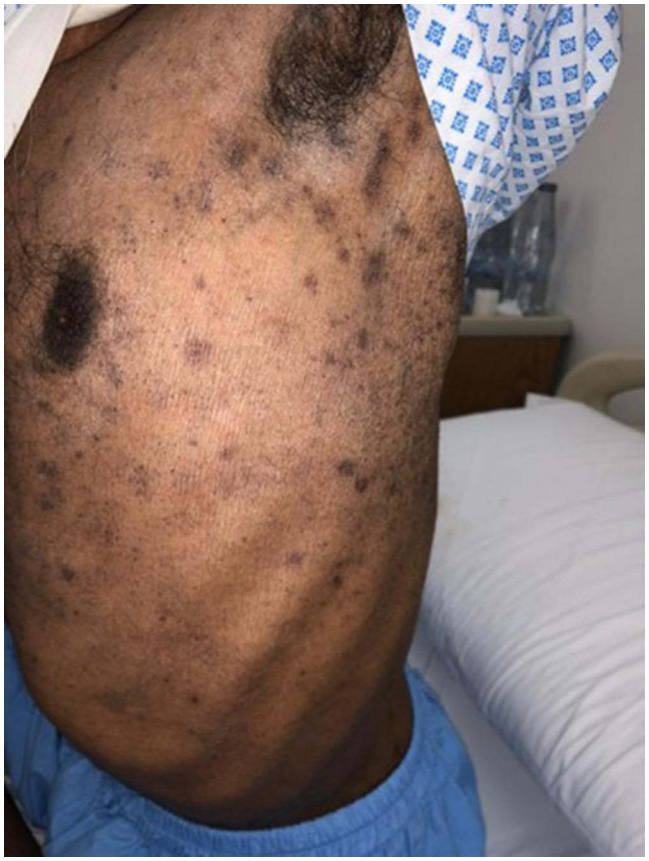

Figure 2 Onychodystrophy with multiple violaceous to brownish edematous plaques and hemorrhagic crusts over the proximal nail folds.

Treatment

The patient was referred to a hematology-oncology team. During his hospital admission, he was treated with cyclophosphamide 600 mg for six cycles and 60 mg/day prednisone orally for five days, but the oral lesions were resistant. Therefore, an oral medicine team was consulted for further management. Oral lesions were managed with: Prednisolone 10 mg tablets use fresh mixture twice daily morning and before bedtime dissolve in 10 mL of water, gargle and hold in the mouth for 5 to 10 minutes, do not swallow. Tetracycline 250-mg mouthwash four times daily was used to hold the fresh solution and spit out. A thin film of betamethasone dipropionate topical ointment 0.05% bid and fucidic acid cream

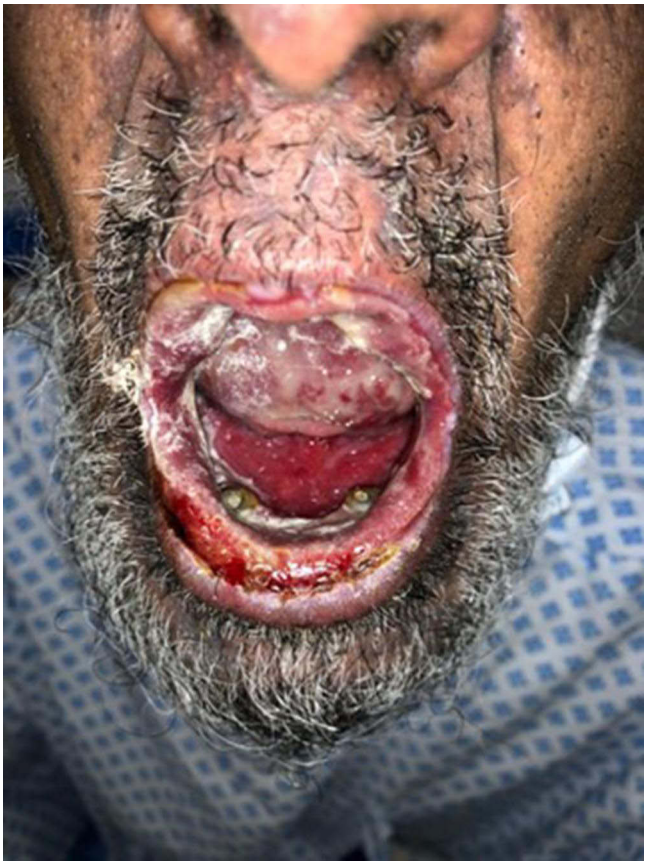

Figure 3 Multiple superficial skin erosion with erythematous bases over the trunk.

2% qid were applied to the lips. This resulted in a better lesion response and improved oral intake by the patient (Figure 5), which has a significant positive impact on patient's satisfaction and quality of life. Consent was obtained from the patient for the publication of the case report including pictures.

Outcome and Follow-Up

Follow-up for 2 years, the patient has fully recovered.

Discussion

Paraneoplastic pemphigus (PNP) is a rare autoimmune skin condition classified among blistering diseases and is consistently linked to neoplasms.[8] The concept of paraneoplastic autoimmune multiorgan syndrome (PAMS) was introduced by Nguyen et al in 2011, emphasizing on the systemic nature of PNP[9] which is seen as multiorgan involvement in these patients a variety of subsets of auto-antibodies to several tissues.[3,10,11]

Mucosal involvement is considered a characteristic of PNP. In the case presented, the entire oral cavity, including the tongue and lips, was affected. The lesions presented as painful ulcers, erosions, and crusting of the lips, which showed minimal response to treatment. Early mucosal involvement is recognized as a key indicator of PNP, affecting the entire oral cavity, tongue, lips, or other mucosal areas.[12] These lesions typically manifest as painful erosions that do not respond well to treatment.[12] Conversely, skin lesions exhibit a broader and more diverse range of appearances, primarily located on the torso, head, and proximal extremities.[12]

As Regard to the diagnosis and management of such a case, include a high clinical suspicion, early diagnosis, complete tumor resection, and intravenous immunoglobulin (IVIG) administration.[12] As in the current case, one of the associated tumors with PNP includes non-Hodgkin's lymphoma.[3,13] Additionally, as observed in this instance, the most

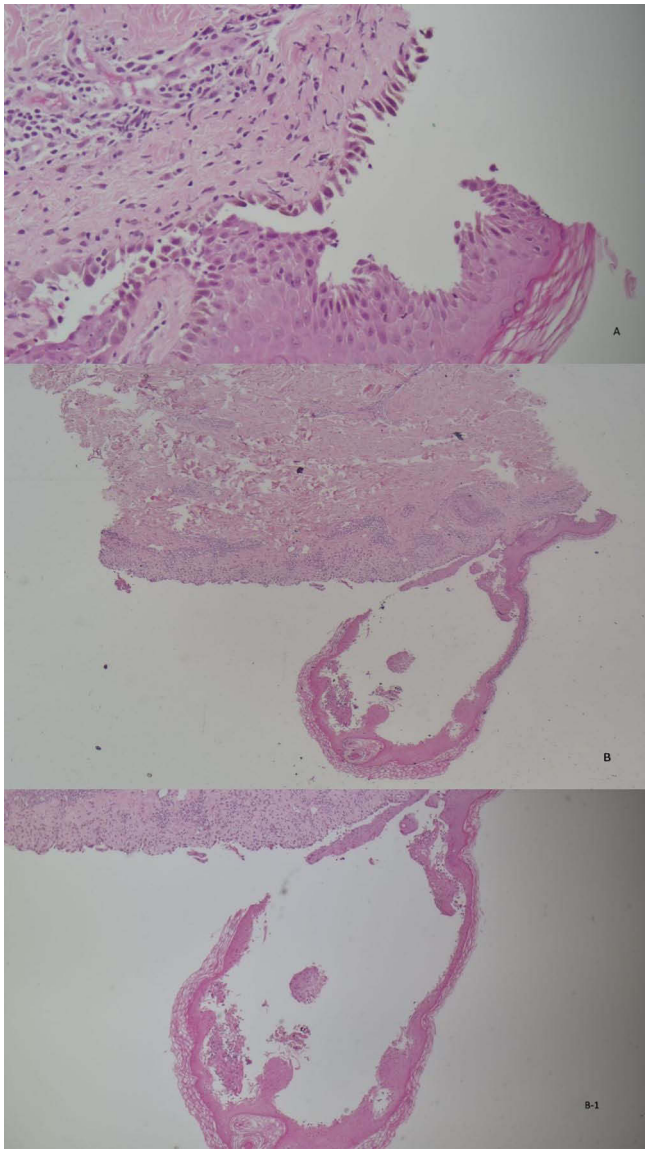

Figure 4 Histopathological examination of skin lesions was consistent with paraneoplastic pemphigus showing (**A**) suprabasilar acantholysis with "tombstoning" of the basilar keratinocytes and (**B, B**-1) band-like lymphocytic infiltrate in the dermis with some eosinophils, and full thickness epidermal necrosis. (hematoxylin and eosin stain, x 40) (hematoxylin and eosin stain, x 10).

consistent clinical manifestation is the persistent stomatitis, which is recognized as an early indicator due to its intensity and resistance to treatment.[14]

Erosions and ulcerations can impact all areas of the oropharynx, with a significant extension onto the vermillion border of the lip.[14] Mucosal lesions often persist, and recovery may take several months.[12] A single patient may exhibit various types of lesions, which can transition from one form to another.[15,16] This variability may be attributed to the dominance of either cell-mediated or humoral-mediated pathogenic mechanisms.[17] Diagnosing such cases is complex and should adhere to the diagnostic criteria initially established by Anhalt et al, which have recently been updated by Mimouni et al.[18] Differential diagnosis, may include Pemphigus vulgaris, Bullous pemphigoid and Erythema multiforme.[19]

PNP therapy presents significant challenges due to the infrequency of the condition.[19] To address this, it may be beneficial to adhere to the six steps outlined by Frew et al, which encompass the stabilization of vital signs, assessment for any underlying malignancies, precise diagnosis of PNP, removal and medical management of the triggering tumor,

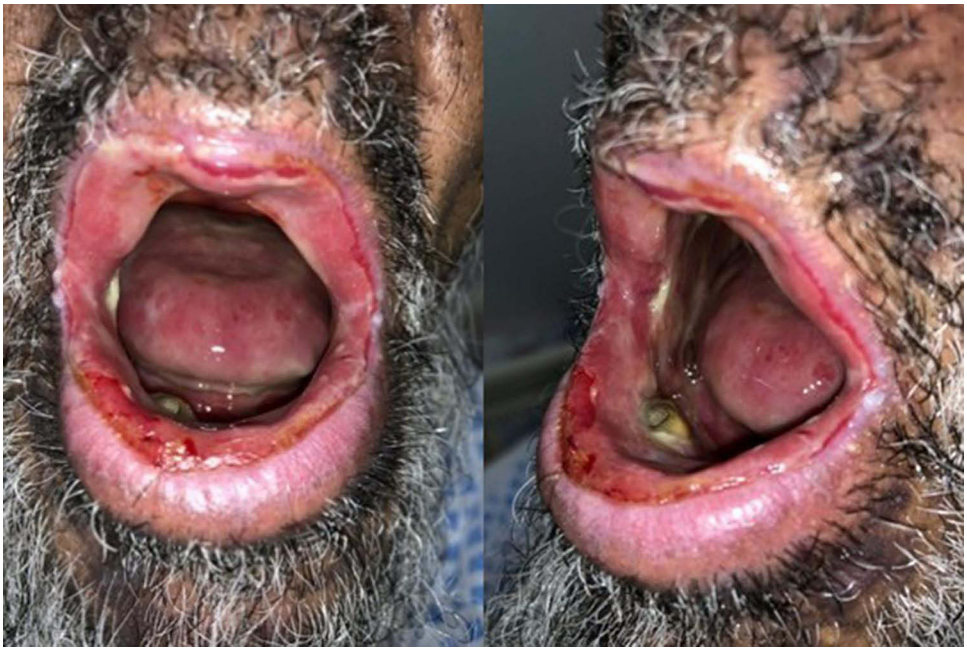

Figure 5 Oral ulceration on the 5th day post therapy.

and the treatment of PNP through immunosuppression, immunomodulation, or plasmapheresis.[20] Moreover, High-dose corticosteroids can be used as first line therapy such as high-dose prednisolone.[20–22] Additionally, high-dose corticosteroids, such as high-dose prednisolone, can serve as a primary treatment option. Mucosal lesions tend to respond poorly to treatment, thus multidisciplinary approach may facilitate healing and improve overall prognosis.[16]

Conclusion

Paraneoplastic pemphigus (PP) is a rare and fatal autoimmune disease associated with an underlying malignancy. Management of PNP is challenging and involves several therapeutic modalities. This report highlights the importance of a collaborative holistic approach, especially for serious conditions that affect well-being. A multidisciplinary approach to achieve early diagnosis, prevention and better management is essential to improve the quality of life of such patients despite the possible poor prognosis.

Institutional Review Board Statement

Ethical review and approval were not required for this case study due to the specific policies of King Saud University. The institution does not provide an institutional review board (IRB) for case reports, as these typically involve the retrospective analysis of a single patient's medical history. Such reports are generally considered to have a lower level of ethical concern compared to other research methodologies that involve multiple participants or interventional procedures. This approach is based on the understanding that case reports primarily focus on documenting and sharing unique or noteworthy clinical observations, which can contribute to medical knowledge without posing significant ethical risks. However, it is important to note that patient confidentiality, agreement and privacy were still maintained throughout the reporting process, adhering to standard ethical practices in medical publishing.

Disclosure

The authors report no conflicts of interest in this work.

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