Successful treatment of oral pemphigus vulgaris using intralesional corticosteroids and levamisole immunomodulation: A case report

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Abstract
Oral manifestations of dermatologic and immune-mediated disease are not so uncommon. These include the blistering diseases such as pemphigus, mucous membrane pemphigoid, and bullous pemphigoid. Out of these, pemphigus vulgaris occurs with a higher frequency than others. Management of oral pemphigus is a tedious task as the lesions take a long time to heal and new lesions crop up often. A case of pemphigus vulgaris in a 53-years-old female patient, successfully managed with intralesional steroids and immunomodulation using levamisole is being reported.

Keywords: Autoimmune blistering, Ig G, levamisole, oral ulcer, pemphigus vulgaris

Introduction
Pemphigus vulgaris is one of the painful autoimmune mucocutaneous disorders that affect the oral cavity. The terminology, pemphi means a blister and vulgaris means common, and hence it is considered as the most common variety of oral blistering disease.[1,2] Wichman is credited with first describing and reporting this entity as early as 1791.[1] It generally shows six different types of clinical presentations, namely, pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceus, paraneoplastic variant, and the Ig A type. Out of these, vulgaris is most common to have oral lesions, and the foliaceus is almost never seen in the oral cavity.[1-3]

Case Report
A 53-year-old female patient visited with a complaint of oral ulcers of 3 months duration. To start with, the patient had noticed fluid filled blisters on her buccal mucosa, 3 months ago, which ruptured within a day to form ulcers. The patient noticed that the initial lesion had not healed, but new and similar lesions started to occur all over her oral cavity leading to extreme pain, burning sensation, inability to eat, and swallow. She had initially consulted a medical practitioner who had prescribed her a mouth wash, with which she found no relief. Later, on the advice of the medical practitioner, she sought help from a dental practitioner, who prescribed her systemic B-complex capsules and a topical anesthetic gel, which gave her only temporary relief. Her medical, surgical, and dental histories were insignificant. On enquiry, she denied any scalp, skin, or genital lesions, in association with the oral lesions. On examination, the maxillary and mandibular labial vestibules showed multiple, flaccid bullae, ulceration, and surrounding mucosa showed extreme erythema [Figure 1 and 2]. The ventral tongue, buccal mucosae also showed similar lesions. On examination, the maxillary and mandibular labial vestibules showed multiple, flaccid bullae, ulceration, and surrounding mucosa showed extreme erythema [Figure 1 and 2]. The ventral tongue, buccal mucosae also showed similar lesions. Occasional lesions were also noted on the hard palate and oropharynx [Figure 3 and 4]. Excessive debris was noted on the teeth and gingival margins. Pressure was applied over the uninvolved posterior buccal mucosa which showed positive Nikolsky’s sign. With a presumptive diagnosis of pemphigus vulgaris, the patient was started on dexamethazone 0.5 mg tablet as a mouth rinse, thrice daily; (tablet to be dissolved in 1 cup of water and use it as swish and spit) followed by topical application of triamcinalone 0.1% oral paste, 4 times a day; both for 1 week. 1 week later,
Figure 1: Intraoral photograph showing flaccid vesicles and ulcerations over the maxillary labial vestibule and gingiva

Figure 2: Intraoral photograph showing flaccid vesicles and ulcerations over the mandibular labial vestibule and gingiva

Figure 3: Lesions on the posterior palate on the right side

Figure 4: Extensive lesions noted on the left lateral aspect of the tongue

Figure 5: 2-week post-treatment view of the maxillary vestibule

Figure 6: 2-week post-treatment view of the mandibular vestibule

dexamethasone, 4 mg/ml; over the labial and buccal mucosae, twice a week; along with systemic immunomodulation using tablet levamisole; 150 mg; once daily, for three consecutive
days, for the next 8 weeks. The patient was continued on “swish and spit” dexamethosone 0.5 mg and triamcinolone 0.1% oral paste. The patient was reviewed after 3 days of the second injection, and there was about 50% improvement in the lesions, and the patient also felt better. After two more injections and 2 weeks of immunomodulation, the lesions had improved by 80% [Figure 5 and 6]. The patient was continued with the same medications, along with topical antifungal agent, Clotrimazole 1% and by the end of 8 injections, about 90% lesional improvement was noted. Intralesional injections were stopped at this stage, but maintenance of topical steroids was continued for 4 more weeks. After 8 weeks, 100% improvement was noted. The patient was followed up for 8 months and no new lesions were noted.

Discussion

The etiology of this entity was initially not clear, but extensive research in this field has clarified it. The primary cause is the production of antibodies against the intercellular adhesion molecules, the desmosomes, which are present on the keratinocytes of the mucosa or skin epithelium, leading to severance of the desmosomes, further leading to loss of cell-to-cell adhesion resulting in accumulation of intercellular fluid and formation of vesicles or bullae. The circulating antibodies are generally Ig G and Ig M type, but rarely Ig A also could be found. Loss of cell to cell adhesion is known as acantholysis.

A genetic predisposition has been identified for the development of pemphigus. HLA class I and II genes may influence for the development of this lesion. Furthermore, certain triggering factors have been identified for the development of these lesions, including some food items, drugs, infections, and neoplasms.

The intracellular mechanism of acantholysis has been much studied and is available in the literature. Incidence of this lesion is quite low with cases occurring at the rate of 0.5 per 1 lack population per year. This disease entity is commonly found in some ethnic groups such as the Ashkenazi Jews, people of Mediterranean and Asian descent, especially Indians and Chinese. It is a disease of the middle-aged, occurring in the 4-6th decades while a few cases have also been described in the young participants. In the present case, the patient was aged 53 years. Although a female preponderance for this disease has been found, some studies have shown equal gender distribution. Nevertheless, obeying the general rule of autoimmunity, the patient in the present case was a female.

Although it is a mucocutaneous disorder, it predominantly almost always begins on the oral mucosa. It is said that in about 50% of the cases, oral cavity presentation is seen as an initial manifestations and in some it may even be as high as 90%.

Clinically, the lesions tend to occur as vesicles and bullae of fragile walls which tend to rupture very early in the course of the disease, leaving irregular, shallow ulcerations, and erosions. These eruptions rupture due to occlusal forces and due to continuous movement of the oral mucosa. The lesions will be extremely painful and will make the routine oral activities difficult. Individual lesions of pemphigus do no heal and Nikolsky’s sign will generally be positive. Some studies have found palate to be the most common followed by buccal mucosa, gingiva, and labial mucosa. Another study found that gingiva to be the most common location.

On an average, oral lesions are present for about 5 months before the skin lesions appear and oral lesions will be present for about 5-10 months before diagnosed and treated. Tzanck test is considered as a rapid test to diagnose pemphigus as it shows acantholytic cells. Furthermore, a biopsy of the lesion with H and E stains will show the presence of a supraepithelial split with inflammatory infiltrate, and some studies state that H and E stain is sufficient to diagnose cases of pemphigus in about 90% of cases.

Direct or indirect immunofluorescence has been utilized to diagnose autoimmune mucocutaneous disorders. In pemphigus, there will be deposition of Ig G in the intercellular spaces. An ELISA test to detect the circulating antibodies has also been devised. Management of pemphigus vulgaris is critical and needs to be started at the earliest to minimize patient’s suffering. Corticosteroids, till date, remain the mainstay of management of pemphigus, although certain other steroid-sparing agents have also been utilized in whom steroids are contraindicated. Corticosteroids, either systemic, topical, or even intralesional, have been used successfully. Steroid-sparing agents utilized include methotrexate, cyclophosphamide, mycofenolate, dapsone, and azathioprine.

Even with the advent of steroids and early administration, the mortality rate of pemphigus remains at 6% as compared to 30% in the pre-steroid era. One study found that the average remission time was 32 months. It is said that longer remissions are possible if the initial disease presentation was mild and if treatment was instituted early. A case series describing the use of levamisole, successfully in oral pemphigus, in combination with oral prednisolone, is available in the literature.

Conclusion

A case of oral pemphigus vulgaris, which was resistant to conventional corticosteroid therapy, successfully treated with a combination of intralesional and topical corticosteroids along with immunomodulation using levamisole, for 8 weeks, is presented. Clinicians can make use of such combination therapy to achieve remission of the disease and to provide comfort to the patient.

References