Guest Editorial Recent Advances in the Treatment of Autoimmune Mucocutaneous Blistering Diseases

Autoimmune mucocutaneous blistering diseases (AMBDs) are rare, potentially fatal autoimmune disorders that manifest as blisters on the skin and in the mucous membranes. Examples include pemphigus vulgaris, bullous pemphigoid, cicatricial pemphigoid, linear IgA or bullous disease, and epidermolysis bullosa acquisita. The mucous membranes involved include those of the eye, nose, oral cavity, larynx, pharynx, esophagus, genitalia, and anus.[1]

In most patients with an AMBD, the oral cavity is the site of the earliest manifestations of the disease, and in almost all cases it is involved at some stage during the clinical course of the disease.[2] In many instances the patient first presents with a desquamative gingivitis or a limited gingivitis that is patchy and involves discrete areas in the anterior and posterior gingiva of both arches.[2] However, other areas of the oral cavity may be involved with equal frequency; therefore, it is very important for dental practitioners to be familiar not only with the diseases and their early diagnosis, but also with advances in their treatment and management.

Two dimensions in the advances of therapy for these diseases deserve attention. First and most important are the recent advances in drug therapy. Conventional therapy suggests that these diseases be treated with high-dose, long-term systemic corticosteroids, particularly prednisone. In addition, many immunosuppressive agents such as azathioprine, cyclosporine, mycophenolate mofetil, gold, cyclophosphamide, and methotrexate have been used. However, significant side effects are associated with long-term use of systemic corticosteroids, some of which can be catastrophic and occasionally fatal.[3] Moreover, the combination of corticosteroids and immunosuppressive agents produces prolonged immune suppression, which can often lead to opportunistic infections, the most common cause of death in patients with these diseases.[4] Another consideration, particularly in young individuals, is the high incidence of malignancies associated with prolonged immune suppression.[4,5]

Recently, several studies indicated that the use of intravenous immunoglobulin (IVIg) therapy results in long-term clinical remission of AMBDs and allows the discontinuation of systemic immunosuppressive therapy.[6] Hence, the use of IVIg therapy may have many benefits in patients for whom immunosuppressive therapy is not successful or produces significant side effects. Unlike conventional immunosuppressive therapy, IVIg therapy has very few side effects, providing a higher quality of life.[6] Moreover, pharmacoeconomic studies show that when the cost of the side effects directly resulting from the drug's use is taken into consideration, IVIg is more cost effective than conventional immunosuppressive therapy.[7] A protocol for the use of IVIg to treat AMBDs has been described in a consensus statement written by 36 international experts on blistering diseases.[8]

For patients in whom conventional immunosuppressive therapy is unsuccessful and IVIg therapy does not produce optimal results, the use of dapsone with or without methotrexate as an adjuvant has also been of significant benefit, resulting in sustained prolonged clinical remission (Ahmed A, unpublished data, 2007). When a patient with pemphigus vulgaris does not respond to any of these adjuvants, rituximab, a monoclonal antibody that selectively kills B cells, has been used in combination with the immunosuppressive agents, demonstrating significant clinical benefit, specifically by lowering the prednisone dose.[9] However, in many of these patients relapses have occurred. Some patients developed severe systemic infections and septicemia, causing morbidity and mortality.[9] In a recent study,[10] rituximab was used in association with IVIg (for immunoprophylaxis) to treat recalcitrant pemphigus vulgaris patients. This combination therapy resulted in rapid clearing of the disease and in sustained long-term remissions. The use of IVIg most likely also helped restore the immune regulation, an additional benefit of this combined therapy.

The second important and often neglected dimension of treatment is topical care.[2] Patients should be advised to use regular rinses in order to help produce local relief of symptoms, reduce inflammation, and avoid further spreading of lesions by trauma from hard foods (patients also should be advised to eat soft foods). In addition, frequent rinses with non–alcohol-containing

mouthwashes facilitate removal of residual food and debris and expedite healing. The application of topical steroid to localized areas is far better than using corticosteroid rinses, which can predispose to oral candidiasis. Injection of triamcinolone to affected areas that are sublesional, not intralesional, can expedite the healing process. Gentle dental hygiene procedures should be emphasized. Any procedure in the oral cavity should be done only if absolutely necessary and with significant caution to prevent trauma (ie, iatrogenic Nikolsky sign).

The majority of patients seek advice for erosive and bullous lesions in the oral cavity from their dental practitioner, particularly their periodontist. Therefore, it is imperative that practicing periodontists and other specialists in the field of dental medicine are aware of these recent advances and able to perform adequate biopsies from both normal and perilesional tissues to ensure a rapid diagnosis. Early diagnosis is associated with a better prognosis, more effective management, and desirable clinical outcomes. Since patients with such diseases require multiple specialists to provide optimal health care, centers that focus on treating blistering diseases with a multidimensional, all-inclusive approach should be created in every large metropolitan area to best serve the patients and act as a community resource.

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