Case Report: Mucous Membrane Pemphigoid

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Introduction

- "Mucous membrane pemphigoid (MMP) is a rare, chronic, autoimmune, subepithelial blistering and erosive disease that affects the mucosal surfaces of the mouth, eyes, nose, nasopharynx, hypopharynx, larynx, esophagus, genitals, and/or anus "[1].
- Bullous pemphigoid and mucous membrane pemphigoid (MMP) are autoimmune blistering diseases that most commonly arise in older adults. These disorders are characterized by subepithelial blister formation and the deposition of immunoglobulins and complement within the epidermal and/or mucosal basement membrane zone."[2].
- Primary goals of the treatment: halt the progression of the disease, improve symptoms, and prevent adverse sequelae of chronic tissue inflammation and scarring.
- "Treatment is largely guided by clinical experience and small uncontrolled studies. "[1] due to few high-quality trials
- Predominantly affect elderly female patients (60 to 80) [4], but potentially on the rise in multiple European studies, potentially due to population aging.
- The exact pathophysiological mechanism for bullous pemphigoid and mucous membrane pemphigoid has not been fully elucidated [5] however possibly due to damage to epithelial basement membrane from auto-antibody reactions. IL-17 producing immune cell implicated
- Autoantibodies against Bullous Pemphigoid Antigen 180, Bullous Pemphigoid Antigen 230, Alpha-6 beta-4 integrin, Type VII collagen, and Laminin 332 implicated in MMP [7] [8] [9][10] [11].
- Immunoglobulin G4 represents the most common antibody class implicated in basement membrane destruction in these disease processes [12].
- Triggered by autoantibody reactions vs basement membrane antigens → Inflammatory cytokines breakdown in the adhesions of the epidermis and dermis as well as the epithelium and subepithelial tissues [5].
- Other types of pemphigoid diseases include: pemphigoid gestationis*, Brunsting-Perry pemphigoid**and anti-p200 pemphigoid*** [14] [15][16].

*A subepidermal disease that develops peri-and postpartum involving bullae formation but generally is facial and mucosal sparing)
**A cicatricial pemphigoid disease that is male predominant localized to head and neck
***A pemphigoid disease that generally affects younger patients and involves autoantibody formation against the gamma-1 subunit of laminin 311 antigen)

Case report

- Case Information: (4/13/2023)
- 78y/o female with a history of blisters in the buccal area and temples diagnosed in August 2019
- Past treatment with prednisone 5mg PO, 3x(5-day courses) total and other prednisone-sparing treatments have failed (Methotrexate, Oral Cyclosporin A, Nicotine gum, Fluconazole, Cibinqo, Minocycline, and Tacrolimus)
- Path. Test & Results- Direct Immunofluorescent antibody studies (Pemphigoid diagnosis)
- Date of Biopsy- 08/14/2019
- Date Received- 08/16/2019
- Diagnosis- Benign Mucous Membrane Pemphigoid, for both sites at tooth #5 and tooth #21;staining positive at the point of the basement membrane (+3 of 4) for IgG and C3, and negative for fibrinogen, IgA and IgM.
- Physical Exam- Pink scaly papules of the temples. Erosion was noted.
- Treatment Plan - Hydroxychloroquine 200 mg PO BID. Follow-up in 1 month from 04/2023. Goals of tx. include reducing use of prednisone and improvement of symptoms and resolution of illness
- Result - Following the new treatment course, as of 7/19/2023, all old oral lesions were healed and no occurrences of new lesions as of 07/2023. However, prednisone could not be fully titrated away. Oral lesions would reappear when prednisone doses went below 5 mg, requiring an increase to at least 10 mg before the lesions would resolve.

References

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Discussion

- Clinical criteria for diagnosing includes chronic inflammation and blistering of the mucous membranes with/without irreversible cicatrix formation involve the oral (most common), ocular, nasal, nasopharyngeal, anogenital, skin, laryngeal and esophageal mucosa[18]
- Oral mucosal manifestations include erythematous patches, blistering, erosions and pseudomembrane-covered erosions. [18]
- Our patient's clinical picture presents classically with gingival (the most common oral region) involvement and blistering as well as with facial skin blistering on bilateral temples.
- Direct immunopathology criteria: detection of IgG, IgA and/ or C3 deposits in the basement membrane zone. [18]
- These findings do not rule out bullous pemphigoid, skin-dominated IgA bullous dermatosis or skin-dominated epidermolysis bullosa acquisita.[18]
- Our patient: benign MMP, for both sites at tooth #5 and tooth #21 coupled with the clinical picture confirmed the diagnosis of MMP.
- Treatment on MMP: difficult as it is often a treatment resistant disease and historically used treatments side effects can deter tolerance of a regimen, and location of oral mucosal lesion can impact methodology of treatment application.
- Low risk patients (only oral and temporal involvement): Typically started on topical corticosteroids either as a mouthwash or as a topical gel or ointment.[19]
- Oral inserts have been used in the past to maintain the treatment in place for adequate lesion exposure as maintaining treatment contact can prove difficult with oral mucosa involvement. [20]
- Refractory lesions are classically treated with intralesional glucocorticosteroid injections and systemic therapy such as dapsone or combined therapy using prednisone and azathioprine or mofetil. [19]
- Drawbacks with these treatments: side-effects of long-term topical steroid treatment (ex: oral candidiasis and mucosal atrophy) and complications associated with systemic steroid (ex: immunosuppression, sepsis, and osteoporosis)[21,22]
- This case was notable for the successful use of a combination therapy of hydroxychloroquine and prednisone for treating an MMP patient that was resistant to other conventional steroid-sparing treatments.
- Mechanism: Hydroxychloroquine interferes with MHC-peptide signaling downregulating CD4 immune cells through increasing intracellular vacuole PH that interferes with endosomal macromolecule assembly, lysosomal function, and posttranslational modification of proteins [23].

Conclusion

- Our patient was diagnosed with MPP presenting as a classical low risk clinical picture.
- Her lesions were successfully treated with a combination of hydroxychloroquine and low dose prednisone which could not be reduced to <5mg without lesions reappearing. An increased dose of 10mg was required before the lesions would resolve.
- The primary goal of treatment was achieved however, and her chances of acquiring long term sequelae due to long term steroid use has been minimized with the minimal effective dosage of prednisone used.
- We still do not fully understand the pathophysiology behind MPP which results in unknown variables pertaining to treatment plans.
- We do know the pathophysiology involves the autoantibody mediated destruction of basement membrane antigens as well as molecules such as IgG and C3.
- Research into future treatment aimed at immune complexes might shed light on how we may further aid in more effectively reducing symptoms of MPP. Especially regimens that can be effective without prednisone or glucocorticoids in general.