***no patient handout*

Mucous membrane pemphigoid

Synopsis

Mucous membrane pemphigoid (MMP), also known as cicatricial pemphigoid, is a heterogeneous group of chronic autoimmune blistering diseases caused by autoimmunity to various components of the basement membrane. To date, autoantibodies to 3 different antigens in the basement membrane zone have been identified: laminin 332 (previously laminin 5), the β4 unit of α6β4 integrin, and BP180. Those patients with autoantibodies to α6β4 integrin present with predominantly ocular disease.

MMP is almost twice as common in females as it is in males, and it is seen most frequently in older individuals. MMP affects the mucous membranes and, less commonly, the skin. The mouth is involved most frequently (painful erosions and ulcers), followed by the conjunctiva (corneal injection, scarring that leads to symblepharon, and blindness). See **Ocular cicatricial pemphigoid**.

Nasal, anogenital, laryngeal, and esophageal mucosal surfaces can also be affected, leading to epistaxis, perianal erythema and scarring, phimosis or vaginal scarring, and hoarseness or dysphagia, respectively. Scarring is the endpoint for all sites of involvement except the oral mucosa.

Cutaneous disease, when present, most frequently accompanies mucous membrane disease. Occasionally, cutaneous blistering and scarring dominate the clinical picture (so-called Brunstig-Perry variant).

Codes

ICD10CM:
L12.1 – Cicatricial pemphigoid

SNOMEDCT:
34250006 – Cicatricial pemphigoid

Look For

In the oral cavity, look for bright red, eroded gingiva with scattered areas of necrosis and shallow ulceration. Ulcers may be present on nongingival mucosa. A pseudomembrane of necrotic epithelium or fibrin covers these ulcers. Desquamative gingivitis is another typical finding. Intact blisters are rarely seen in the oral cavity. There may be a positive Nikolsky sign (a blister can be induced on apparently normal oral mucosa by applying slight lateral pressure).

In the eye, look for conjunctivitis with fibrosis leading to symblepharon, entropion, and trichiasis.

Anogenital lesions consist of blisters and erosions. Scarring can cause phimosis and can lead to narrowing and stricture of the anus or vaginal introitus.

On the skin, look for erythematous plaques with superimposed blisters and erosions, with subsequent scarring and milia formation. The head, neck, and upper torso are sites of predilection. The Brunsting-Perry variant refers to the presence of these cutaneous findings with little or no mucous membrane involvement. Additionally, scarring alopecia can be seen.

Diagnostic Pearls

The disease is histologically identical to bullous pemphigoid. Diagnosis is made by the presence of blisters, erosions, and, most importantly, the scarring.

The ocular mucosa may be the sole affected site.

Cutaneous disease without mucous membrane disease is rare. Consider the diagnosis of cutaneous MMP if erythematous plaques, bullae, erosions, scarring, and milia involve the head (including the scalp where scarring alopecia eventuates), neck, and/or upper trunk.

Differential Diagnosis & Pitfalls

Oral lesions:

- **Lichen planus** – This may present as **desquamative gingivitis**, and Wickham striae may be present on the buccal mucosa.
- Hypersensitivity reactions such as plasma cell gingivitis may also present similarly.
- **Pemphigus vulgaris** – This is often (although not always) associated with skin lesions. The mouth ulcers are often the first manifestation and may precede skin lesions by months to years. Lesions of pemphigus are more likely to be ragged, superficial erosions.
- **Epidermolysis bullosa acquisita** – This almost invariably presents with typical skin lesions.
- **Linear IgA disease** – This may be indistinguishable, clinically.
- **Bullous pemphigoid** – This is almost always associated with skin lesions.
- Chronic (oral) **erythema multiforme**
- Severe **aphthous ulcerations** – They do not affect the keratinized attached mucosa of the gingiva.
- **Behçet disease**

Genital lesions:

- **Bullous pemphigoid** – Most frequently seen in the elderly; presents with nonfragile blisters that cause less scarring because they occur closer to the skin surface.
- **Pemphigus vulgaris** – Presents with flaccid, fragile blisters.
- The lesions of **erythema multiforme** are round, light-red spots with concentric zones and, at times, blisters and exudates.
- **Lichen sclerosus** lacks the vesicles and erosions seen in MMP.
- **Hailey-Hailey disease**
- Genital erosive **lichen planus**
- Genital **aphthous ulcers**
- **Behçet disease**
- Reactive nonsexually related acute genital ulceration (**RNSRAGU**)

Cutaneous lesions:

- **Bullous pemphigoid**
- **Epidermolysis bullosa acquisita**
- **Linear IgA bullous dermatosis**

Best Tests

The best tests are biopsies for histopathologic evaluation (lesional) and direct immunofluorescent (DIF) examination (perilesional). Repeat DIF evaluation may be needed before a positive result is obtained. A high index of suspicion should be maintained in a clinically concerning case with supportive histopathologic features.

Management Pearls

Topical pain control and anti-inflammatory therapy are essential to control the disease and symptoms.

Optimal oral hygiene will reduce the severity of gingival involvement. Patients should follow up regularly with a dentist.

If the genital area is involved, it is important to keep the perineal area clean using sitz baths or gentle flushing. Urologic or gynecologic evaluation may be needed.

Untreated ocular lesions can lead to blindness. Therefore, ensure that the patient follows up with an ophthalmologist.

Otorhinolaryngology and/or gastroenterology consultation may be needed. Esophageal strictures may require esophageal dilation.

Surgery to remove the skin adhesions and correct the scarring on any affected site may be needed if medical therapy has not been completely successful.

Therapy

MMP is a chronic disease that can be controlled but not cured. Topical high-potency steroids may be effective in controlling mild to moderate disease.

For cutaneous disease:

High-potency topical corticosteroids (class 1-2):

- Clobetasol cream, ointment – Apply every 12 hours (30, 45, 60 g), or
- Halobetasol cream, ointment – Apply every 12 hours (15, 50 g), or
- Betamethasone dipropionate cream, ointment – Apply every 12 hours (15, 45, 60 g), or
- Fluocinonide cream, ointment – Apply every 12 hours (15, 30, 60, 120 g), or
- Desoximetasone cream, ointment – Apply every 12 hours (15, 60, 120 g).

Potent corticosteroids should not be used on intertriginous areas due to skin atrophy and striae formation. Use for a maximum of 2 weeks on any given site.

For oral disease:

- Clobetasol and betamethasone (0.05% gel) may be applied to lesions 3 times daily. A customized bleaching tray (made by a dentist) may be very helpful, acting as a carrier for the steroid if there is extensive gingival disease.
- Topical tacrolimus 0.1% ointment may also be helpful.

For localized oral and cutaneous disease that is not responding to the above measures, intralesional steroid injections may be useful.

For nasopharyngeal involvement, corticosteroid inhalers can be helpful.

Additionally, dapsone is first-line oral therapy for mild to moderate oral and cutaneous disease and ocular disease that is not rapidly progressive:

- Dapsone 50-150 mg per day

For more severe disease, including rapidly progressive ocular disease:

- Cyclophosphamide 1-2 mg/kg/day is the treatment of choice
- It may be combined with oral corticosteroids, such as prednisone 60-80 mg/day

Other medications that have been used include azathioprine at a dose of 2 mg/kg/day and mycophenolate mofetil (2 g/day), methotrexate, and etanercept. Rituximab combined with other systemic immunosuppressive therapies was shown to cause earlier resolution without increased side effects.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
Alpha-adrenergic agonist	1
atenolol	1
Beta blockers	1
Chelating agents	1
clonidine	1
penicillamine	2