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Mini Review

Mucous Membrane Pemphigoid: A Review

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Abstract

Mucous membrane pemphigoid (MMP) belongs to the group of subepidermal blistering diseases and refers to a subgroup characterized by predominant mucosal involvement. Various target antigens are involved within the basement membrane zone.

INTRODUCTION

Mucous membrane pemphigoid (MMP) belongs to the group of sub epidermal blistering diseases and refers to a subgroup characterized by predominant mucosal involvement. Various target antigens are involved within the basement membrane zone. The average Annual incidence isestimated to be 1/500,000 to 1/770,000 in western countries and is regularly increasing. A slight male predominance is reported. In most cases, the treatment is based anti-inflammatory drugs (corticosteroids, dapsone or sulfasalazin) in association to immunosuppressants (ciclophosphamid, mycophenolatemofetil (MMF)). Rituximab and etanercept have also been proposed for resistant MMP but need further evaluations [1,2]. MMF is theoretically a treatment of choice due to its good long term tolerance and efficacy especially in the elderly patients.

CLINICAL DESCRIPTION

The averageage of onsetis 60-70 years. The median age at diagnosis in our center is 78 years The average time for diagnosisis 28 months [1].

The diseaseis rare in children. Mucous membrane pemphigoidis a chronic disease with periods of more rapid evolution. The disease manifests as fragile bullous lesions that give way to superficial erosions. The principle sites affected are the oral (80-90% of cases), ocular (50-70% of cases), pharyngolaryngeal (8-20% of cases), genital (15% of cases) and esophageal mucous membranes. Someforms affect only one mucosal membrane, in particular the buccal (erosive gingivitis) or ocular mucosae. An exclusively cutaneous form has also been observed in some cases. The ocular manifestations are initially inflammatory but then lead to retractile scarring of the conjunctive membrane, associated with corneal metaplasia resulting in vision loss.

PHYSIOPATHOLOGY AND DIAGNOSTIC TOOLS

The main antigens are the C term portion of collagen 17 and laminin 332 Whilst the etiology is unknown, several different antigens are implicated in the autoantibody response including BPAg1, BPAg2, integrin subunits alpha-6/beta-4, laminin 5 and 6, and type VII collagen.

Immunological Studies Reveal the presence of auto-antibodies against several antigens such as PB180, the alpha Laminin-5 subunit and the beta subunit of the integrin alpha-6 beta-4 complex. Histologically, the cutaneous or mucosal blisters are subepithelial, without evidence of acantholysis, and are indistinguishable from those of bullous pemphigoid. Diagnosis can be confirmed by direct (DIF) or indirect immunofluorescence analysis.unoelectronmicroscopycandifferentiatebullousfromcicatricialpemphigoid by the precise location of immune depositsalong the basement membrane. Immune deposits in MMP are located deeper than in bullous pemphigoid where they are restricted to the hemidesmosomal area [2].

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes the full range of autoimmune bullous disorders. Pemphigus vulgaris is differentiated by the DIF pattern with a labelling of the intercellular substance. Bullous pemphigoid is characterized by a predominant cutaneous involvement. Epidermolysis bullosa acquisita is a difficult to differentiate and relies on ELISA (enzyme-linked immunosorbent assay) anti collagene VII, a different localization of immune depositsalong the basement membrane zone as imaged by immunoelectron microscopy, or DIF on salt separated skin. Oral erosive lichen planus and recurrenta phtosis do not show any immune deposits on DIF.

MANAGEMENT AND TREATMENT

Management should be multidisciplinary with close follow-up in specialized center, in particular for the management of the ocular manifestations. The choice of therapeutic strategy (anti-inflammatorydrugs, immunosuppressive therapy, intravenous immunoglobulin or local treatments) depends in the severity of the oculardisease.

Dapsoneis the reference treatment for MMP with response rates of 50 to 80% in monotherapy [3] (Rogers 1988). The oral and inflammatory subypes of MMP are the best responder to dap-

sone [4].

There are 10-25% of adverse events and agranulocytosis can occur (1/400 at the beginning of treatment) sulfasalazine or cyclines car serve as alternative optoiions in patients intolerant to dapsone

Mycophénolatemofétil (MMF) is an inhibitor of purine synthesis and targets B and T Lymphocytes. MMF can be considered as the reference immunosuppressive drugs for the management of MMP and related disorders MMF is more efficient thancyclosprine and less toxic than cyclophosphamide. MMP score improvement ranges from 60 to 85% for inflammation andocular pain .A control of the disease can be obtained for up to 80 % of patients [5-7].

The optimization of MMF dose is efficient for refractory patients we have recently demonstrated in 8 patients with 15 adjustements that the the median AUC before Treatmentwas 36 mg.h/l whereas the therapeutic objective was 45-50 mg.h/l. In most patients the adjustement has led to a better control of the disease (unpublished results)

Rituximabhas been proposed for patients with refractory MMP. Most patients are now treated with the auto immune regimentwo cycles of 1000mg Two weeks apart. The clinical benefit of the treatment occurs within 12 weeks with 86% of controm of the disease [8]. Long term remissions seems more questionable and it seems that a maintenance treatment is necessary in decrease of 40% the relapse risk Oesophagal involvement should be carefully monitored in patients withsevere oral involvement and can be found in 10 to 40% of MMP patients whereas they present with clinical symptoms or not [9].

Ocular inflammation leading to corneal involvement with symblepharon and corneal opacification with a progressive risk of blindnessis one of the major goals for the treatment of ocular MMP. Manystudies have demonstrated that MMF allowed good control of ocular inflammation in 60 to70% of patients. We have treated 18 patients with ocular MMPwitha control of 81% of ocular inflammation. The combination of rituximab and intravenous immunoglobulin for recalcitrant ocular cicatricial pemphigoid may help to increases the control of inflammation [10].

Topical treatment plays a major role for MMP control.

Antisepsy and topical corticosteroids may help to control oral involvement.

Ocular inflammation control is also improved by artificial tears antiseptic eye drops vitamin B and regular ablation of entropion is eyelashes with the use of sclerallens.

Interferon or cyclosporine eye drops have been proposed to improve ocular MMP.

PROGNOSIS

The prognosis also revolves around the ocular manifestations, which may lead to blindness due to scarring of the conjunctive membrane and corneal metaplasia.

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