BRIEF REPORT

BULLOUS PEMPHIGOID: A SERIES OF 50 CASES

Penfigoide bolhoso: série de 50 casos

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ABSTRACT

OBJECTIVES: This study aims to analyze data on the epidemiology, treatment and course of bullous pemphigoid in 50 patients and compare findings to the data already available in the literature. **METHODS:** Data were collected retrospectively through medical records and analyzed statistically. A review of the literature was conducted using articles indexed in the MEDLINE (via PubMed) database. **RESULTS:** The mean age at diagnosis was 71.1 years. Comorbidities were observed in almost all cases, and the association between bullous pemphigoid and neurological diseases was present in 18% of patients, in agreement with recent data in the literature. **CONCLUSION:** Care of comorbidities, especially neurological diseases, which increase the mortality of patients with bullous pemphigoid, is thus essential.

KEYWORDS: bullous pemphigoid; epidemiology; skin diseases; blister.

RESUMO

OBJETIVOS: Este estudo tem por objetivo analisar dados epidemiológicos, de tratamento e evolução de 50 pacientes com diagnóstico de penfigoide bolhoso e comparar aos dados já existentes na literatura. **MÉTODOS:** Os dados foram coletados retrospectivamente por meio de prontuários médicos e analisados estatisticamente. Foi realizada revisão da literatura mediante artigos indexados na base de dados MEDLINE (via PubMed). **RESULTADOS:** A média de idade ao diagnóstico foi de 71,1 anos. Comorbidades foram observadas em quase a totalidade dos casos, e a associação entre penfigoide bolhoso e doenças neurológicas esteve presente em 18% dos pacientes, em concordância com dados recentes da literatura. **CONCLUSÃO:** Ressaltamos a atenção às comorbidades, sobretudo doenças neurológicas, que aumentam a mortalidade dos pacientes com penfigóide bolhoso.

PALAVRAS-CHAVE: penfigoide bolhoso; epidemiologia; dermatopatias; bolhas.

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INTRODUCTION

Bullous pemphigoid (BP) is the most frequent autoimmune bullous dermatosis. It mainly affects the elderly, without predilection for gender or ethnicity, and causes great morbidity to these individuals. Clinically, it is characterized by scattered, pruritic blisters on an erythematous or urticated base, especially in flexural areas.[1]

PB results from the formation of autoantibodies — BP230 and BP180 — against hemidesmosome antigens in the basement membrane zone, which leads to the formation of subepidermal blisters, usually with an eosinophilic inflammatory infiltrate. Diagnosis is made through clinical features, anatomopathological examination (AP), and direct immunofluorescence (DIF). The main therapeutic strategy is immunosuppression with systemic and/or topical corticosteroids.[1]

Our objective is to describe clinical and epidemiological characteristics in a series of patients with BP and to compare these data with those already existing in the literature.

METHODS

This study retrospectively analyzed 50 patients diagnosed with BP who were followed up at an outpatient bullous dermatoses clinic from 1987 to 2016. Data were collected from medical charts, analyzed statistically, and compared to the existing literature, through a review of articles indexed in the MEDLINE database (accessed via PubMed).

RESULTS

There was a similar frequency between the genders, with 29 women (58%), and 21 men (42%). The mean age at diagnosis was 71.1 years (median 72.5 years, ranging from 22 to 99 years).

Diagnosis of BP was confirmed by clinical features and AP examination in 21 cases (42%), AP and DIF showing C3 and/or linear IgG in the basal membrane zone in 28 cases (56%), and DIF only in one case (2%).

Comorbidities were present in 47 of the 50 patients at the time of PB diagnosis. The most prevalent was hypertension (72%), followed by diabetes mellitus (20%), osteopenia/osteoporosis (20%), and neurological diseases, which were diagnosed in 18% of the patients (stroke, 55.5%; depression, 22.2%; epilepsy, 11.1% degenerative neuromuscular disease, 11.1%). Malignant neoplasms occurred in only four (8%) patients during the follow-up period, with one case each of non-Hodgkin lymphoma and prostate, uterine, and lung cancer.

Of the 50 patients, 49 were treated with systemic corticosteroids (0.5 to 0.75 mg/kg/day). Of these, 21 (42%) received prednisone alone, 17 (34%) were treated with prednisone plus tetracycline and nicotinamide, 6 (12%) required azathioprine, and 5 (10%) received other combination therapies, such as dapsone and methotrexate. One patient received only tetracycline and nicotinamide, and one particularly severe case required intravenous pulse therapy with methylprednisolone. A topical corticosteroid (clobetasol) was prescribed in combination with systemic treatment in all cases.

Regarding disease progression, 12 patients were discharged due to disease control, having received an average of 3.1 years of corticosteroid therapy (range, 1 to 8 years). To the best of our knowledge, two patients died (of non-BP-related causes) during the follow-up period.

However, progression could not be evaluated reliably in this study because 32 patients were lost to follow-up: 20 with active BP and 12 with no lesions or mild activity. Currently, five patients are still being followed: four with no disease activity on low-dose prednisone (mean 2.2 years of treatment) and one with active disease 2 years after diagnosis.

DISCUSSION

In this series of patients with BP, there was a predominance of older adults. This is consistent with the literature, in which onset of BP is usually reported after age 60 years.[1]

The primary risk factor for BP is advanced age, and the relative risk for patients over 90 years of age appears to be approximately 300 times greater than in patients aged 60 or younger.[2] Other risk factors include the presence of neurological diseases and use of some medications, such as diuretics (furosemide and spironolactone) and neuroleptics.[1,3] The mechanisms by which these drugs may facilitate development of BP remain unclear. There is no conclusive evidence for an association with malignancies or other autoimmune diseases.[1]

The spectrum of clinical presentation is very broad; initially, it may be restricted to mild to severe itching, associated with excoriated, eczematous, papular and/or urticariform lesions. The bullous phase is characterized by tense vesicles and blisters on an erythematous or urticated base, distributed symmetrically and especially in flexural areas, which may be localized or generalized. Despite the widely varying clinical spectrum, the clinical features of BP appear to be similar in both the elderly and younger adults.[2]

Regarding comorbidities, the high prevalence of neurological diseases (18% of cases) is worthy of attention, in agreement with recent evidence of association between BP and neuropathies.[1,4,5] The potential underlying mechanisms of this association are not fully understood. It is possible that patients with BP produce antibodies against other antigens by

the phenomenon of epitope spreading.[4,5] In addition, BP230 autoantibodies have been found in the cerebrospinal fluid of patients with multiple sclerosis.[6] Alternatively, it is hypothesized that some medications used to treat these diseases could trigger BP.[7] The mean age of patients with neurological disease and BP was 67.4 years, lower than the overall mean of this study. This contradicts the possible bias of the association between advanced age and neurological disease.

Regarding malignant neoplasms, an association still controversial in the literature,[5] the prevalence in this study was low (4%).

BP is a chronic disease, with a relapsing-remitting course that may last months to years, but most patients progress to with clinical remission with treatment. The goal of treatment should be symptom control with the least possible side effects.[2]

Systemic corticosteroid therapy is the recommended standard treatment for BP, and the current guidance is to use doses between 0.5 and 0.75 mg/kg for a non-prolonged time due to the risks of complications and adverse events when using high doses of systemic corticosteroids.[1] Adjunctive use of tetracyclines has been an accepted therapeutic strategy for several years, despite the lack of controlled studies to ratify this recommendation. A recent clinical trial compared doxycycline with prednisolone in the initial treatment of BP and suggested that this antibiotic at a dose of 200 mg/day was not inferior to corticosteroid therapy, with fewer long-term side effects.[8] Some authors who have recommended whole-body, high-potency topical corticosteroid therapy (clobetasol) for mild to moderate cases, suggesting good efficacy and greater safety when compared to high doses of systemic corticosteroids.[9]

Patients with active BP have twice the mortality rate of the general population of the same gender and age.[1,7] A meta-analysis was recently conducted to define the factors of poor prognosis in BP, and concluded that advanced age, comorbid dementia and stroke, and presence of circulating autoantibodies confer an increased risk of death in these patients. There was no significant association of gender, clinical extent of disease, or mucosal involvement with survival time in this meta-analysis.[10]

CONCLUSION

In this study, mean age at BP diagnosis was 71.1 years, confirming the predominance of this disease in the elderly. Comorbidities were present in 94% of patients at the time of diagnosis, and the rate of comorbid neurological diseases was relatively high, corresponding to 18% of cases, an association that has been reported in several studies. The vast majority of patients received systemic corticosteroids (98%), in combination with tetracycline in 34% of cases. Among patients who achieved disease remission, the mean duration of treatment was 3.1 years. All patients also received high-potency topical corticosteroids, a tendency that has been observed in the literature and has even been recommended as monotherapy in mild cases, a practice also observed in this sample. There were no deaths attributable to BP in this sample.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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