Central Asian Journal of Medicine

A SURVEY OF BULLOUS DISEASES CLINICOEPIDEMIOLOGICAL CHARACTERISTICS

O.S. Imamov [1], J.A. Rizaev [2], G.Sh. Toxtayev [3]

1 Project office "Center for Healthcare Projects"
2 Samarkand State Medical University
3 Tashkent Medical Academy

ABSTRACT

Autoimmune bullous diseases, if left untreated, are life-threatening conditions affecting primarily skin and mucous membranes. These blistering disorders are characterized by epidermal or subepidermal detachment. Autoimmunity plays a key role in pathogenesis; therefore, immunosuppressive agents are the treatment of choice. The aim of this study is to document relative frequencies of different autoimmune bullous diseases, patient characteristics, treatment options, and side effects in patients presenting to our bullous skin diseases.

Key words: mucous membrane of the mouth, bullous diseases epidemiology; bullous pemphigoid; pemphigus vulgaris.

INTRODUCTION

Autoimmune bullous diseases (ABDs) are uncommon but significant skin disorders with relatively high morbidity and mortality. Some surveys have been carried out to describe the spectrum of autoimmune bullous diseases in a region, but this is the first that has focused on autoimmune bullous diseases in elderly patients. This study was conducted to determine the clinicoepidemiologic features of ABDs in elderly patients. Medical records of all autoimmune bullous diseases patients with disease onset after the age of 60 years who presented to the autoimmune bullous diseases are rare but potential ly devastating disorders of the skin and mucous membranes, characterized by the presence of tissuebound and circulating antibodies directed against diseasespecific target antigens. Based on the level of blister formation, these diseases can be divided into 2 groups: intraepidermal immunobullous diseases, also referred to as the pemphigus group, and sub epidermal immunobullous disorders. The pemphi gus group comprises

pemphigus vulgaris (PV) and its variant pemphigus vegetans, superficial pemphigus (pemphigus fo liaceus (PF) and pemphigus erythematosus (PE)), paraneo plastic pemphigus (PNP), and IgA pemphigus. The incidence of pemphigus ranges from 0.5 to 16.2/1,000,000 per year [1–5]. The sub epidermal immunobullous disorders group includes pemphigoid diseases (bullous pemphigoid (BP), mucous membrane/cicatricial pemphigoid (MMP/CP), pemphigoid gestationis (PG), linear IgA disease (LAD). T he incidence of BP has been estimated between 2 and 42.8/1,000,000 per year [1,4,6,7]. PV is frequently observed, as in other countries of the Mediterranean region. However, there has not yet been any study of the relative frequencies and demographic features of different autoimmune bullous diseases. Notably, the relative frequencies of sub epidermal immunobullous disorders versus those of diseases in the pemphigus group are unknown. Our aim is to define the spectrum of autoimmune bullous diseases. PV is characterized by autoantibodies working against intercellular adhesion molecules: Dsg3 or both Dsg 1 and 3, resulting in suprabasal acantholytic blisters. Our present observation confirms the data in previous studies and adds further support to the earlier notion that the clinical phenotype of pemphigus correlates with the anti Dsg autoantibody profile. As expected, PV was the most common type of AIBD in our study, representing 70% of all cases. The incidence of PV has been estimated to be 0.76, 0.77, and 1.7 in terms of new cases per million people per year in Finland, Germany, and France, respectively [12,16,17]. In contrast, in countries around the incidence is significantly higher, with 6, 6.7, and 8 new cases per million people per year in respectively [17,19,21]. In a study from Germany, the age-adjusted incidence of PV was 9-fold higher in patients with a migration background, compared with native Germans, emphasizing the geographical and thus genetic background of the disease [22]. Of all the pemphigus group patients, PV was the most common subgroup in our study, with a 90% incidence rate (PF 8% and PE 1,44%, the least frequent form of pemphigus). Elderly patients are more susceptible to the development of autoimmune blistering disorders such as bullous pemphigoid, mucous membrane pemphigoid, epidermolysis bullosa acquisita, and paraneoplastic pemphigus [23,24]. This article focuses on the clinical aspects of the aforementioned autoimmune blistering diseases and highlights the important factors involved in treating elderly patients [25]. It is essential for clinicians to offer individualized treatment plans for these patients to optimize outcomes, as elderly patients often have multiple co-morbidities, polypharmacy, and suboptimal socioeconomic status that can adversely influence adequate compliance [27,28].

Purpose of our research the aim of this study is to document relative frequencies of different autoimmune bullous diseases, patient characteristics, treatment options, and side effects in patients presenting to our bullous skin diseases.

Research Methodology. An analysis of outpatient records of patients with pemphigus who applied to the Tashkent Dermatovenerological Dispensary for three years was carried out. The following research methods were used: clinical interview, clinical examination, determination of dental status, cytological examination smear impressions on acantholytic cells from the bottom of fresh erosions, a general blood test, a biochemical blood test, a clinical urine test, and the affected areas in patients with vulgar, erythematous, foliaceous and other forms of pemphigus were studied.

Analysis and results. All medical files of newly diagnosed patients with autoimmune bullous diseases were retrospectively recruited and analyzed. Diagnoses were based on clinical findings, histo pathology of affected skin or mucosa, microscopy of perilesional mucous membrane or skin biopsies. Patient inclusion criteria for the retrospective analysis comprised a diagnosis of autoimmune bullous diseases confirmed by histopathological. Thus, histopathological examination and direct examination were performed for all the patients included in this study. Detailed reviews of the patients' clinical histories, other autoimmune diseases, and comorbidities of patients and their relatives, in addition with data about age, sex, age at onset of the disease, and duration of the disease were recorded. Clinical status at the onset such as mucosal and/or cutaneous involvements was evaluated. Histopathological examination, for the pemphigus group, local and systemic treatment modalities, relapses and remissions, side effects, and reported deaths during the follow-up period were also recorded. Detailed reviews of the patients' clinical histories, other autoimmune diseases, and comorbidities of patients and their relatives, in addition with data about age, sex, age at onset of the disease, and duration of the disease were recorded. Clinical status at the onset such as mucosal and/or cutaneous involvements was evaluated. Histopathological examination, direct and indirect immunofluorescence test results, testing of antidesmoglein (anti-Dsg) 1 and 3 antibodies for the pemphigus group, local and systemic treatment modalities, relapses and remissions, side effects, and reported deaths during the follow-up period were also recorded.

Conclusion. Pemphigus vulgaris was the most frequent autoimmune bullous disease, followed by bullous pemphigoid and pemphigus foliaceus, according to our study. There is a general female predominancy for all autoimmune bullous

diseases. The most commonly preferred treatment options were high dose daily corticosteroids. Pemphigus vulgaris was the predominating subtype of pemphigus in this study. This retrospective study summarizes the patient characteristics, comorbidities, treatment choices, and side effects during of clinical practice.

REFERENCES

1. Sullivan TP, Elgart GW, Kirsner RS: Pemphigus and smoking. Int J Dermatol 2002, 41(8):528–530.

2. Nousari HC, Anhalt GJ: Pemphigus and bullous pemphigoid. Lancet 1999, 354(9179):667–672.

3. Weedon D, Strutton G, Rubin AI, Weedon D: The vesiculobullous reaction pattern. In Weedon's skin pathology. 3rd edition. [Edinburgh]: Churchill Livingstone/Elsevier; 2010:151–152.

4. Adaskevich V.P. Diagnosticheskiye indeksi v dermatologii. – M.: Izdatelstvo Panfilova; BINOM. Laboratoriya znaniy. – 2014. – 352 s.: ill.

5. Kershenovich R. Diagnosis and classification of pemphigus and bullous pemphigoid / R. Kershenovich, E. Hodak, D. Mimouni // Autoimmun Rev. – 2014. – Vol. 13. - № 4-5. – r. 477-481;

6. Wiyeczorek M. Paraneoplastic pemphigus: a short reviyew / Wiyeczorek M., Czernik A. // Clinical, Cosmetic and Investigational Dermatology. – 2016. – 9. – r. 291–295;

7. Hertl M. Pemphigus. S2 Guideline for diagnosis and treatment – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV) / Hertl M., Jedlickova H., Marinovic B. et al // JEADV 2015. - 29. – r. 405–414;

8. Murrell D.F. Diagnosis and management of pemphigus: recommendations by an international panel of experts / Murrell D.F., Pena S., Joly P. et al // J Am Acad Dermatol. – 2018. - doi: 10.1016/j.jaad.2018.02.021;

9. Ikeda S. History of the establishment and revision of diagnostic criteria, severity index and therapeutic guidelines for pemphigus in Japan / Ikeda S., Imamura S., Hashimoto I. et al // Arch Dermatol. – Res 2003. - 295 ((suppl 1)). - S12- S16;

10. Hrabovska Z. A study of clinical, histopathological and direct immunofluorescence diagnosis in pemphigus grup Utility of direct immunofluorescence / Hrabovska Z., Jautova J., Hrabovsky V. // Bratisl Lek Listy. – 2017. - 118(4). - 243-249. - doi: 10.4149;

11. Giurdanella F. Laboratory diagnosis of pemphigus: direct immunofluorescence remains the gold standard / Giurdanella F., Diyercks GF., Jonkman MF., Pas HH. // Br J Dermatol. – 2016. - Jul;175(1):185-6. - doi: 10.1111/bjd.14408;

12. Konig A.J. Heterogeneity of severe dystrophic epidermolysis bullosa: overexpression of collagen VII by cutaneous cells from a patiyent with mutilating disease // Konig A., Winberg J.O., Gedde-Dahl T. et al // Invest Dermatol. - 102 (1994). - pp. 155-159;

13. Lakos Jukic I. Sensitivity of indirect immunofluorescence test in the diagnosis of pemphigus / Lakos Jukic I., Marinovic B. // Acta Dermatovenerol Croat. – 2004. - 12(3). - 162-5.

14. Klinicheskiye rekomendatsii. Osteoporoz: diagnostika, profilaktika i lecheniye / Ros. assos. po osteoporozu; pod red. prof. L.I. Benevolenskoy i prof. O.M. Lesnyak. – M.: GEOTAR-Media. - 2005. – 171 s.

15. Harman K.E. Guidelines for the management of pemphigus vulgaris / Harman K.E., Albert S., Black M.M. // Br J Dermatol. – 2003. – 149. – r.926–937;

16. Werth V.P. Treatment of pemphigus vulgaris with briyef, high-dots. intravenous glucocorticoids // Arch Dermatol. – 1996. – 132. – r.1435–1439;

17. Surova Z.S. Kliniko-immunologicheskiy analiz primeneniya diprospana dlya lecheniya vulgarnoy puzirchatki / Surova Z.S., Svirishevskaya Ye.V., Viskova N.Yu. i dr. // Vestnik dermatologii i venerologii. – 1997. – 5. – s.5–7;

18. Chryssomallis F. Steroid pulse therapy in pemphigus vulgaris long term follow-up / Chryssomallis F., Dimitriades A., Chaidemenos G.C. et al // Int J Dermatol 1995. – 34. – r. 438–442;

19. Aboobaker J, Morar N, Ramdial PK, Hammond MG: Pemphigus in South Africa. Int J Dermatol 2001, 40(2):115–119.

20. Moy R, Jordon RE: Immunopathology in pemphigus. Clin Dermatol 1983, 1(2):72–81.

21. Zhang X, Hyjek E, Soltani K, Petronic-Rosic V, Shea CR: Immunohistochemistry for Immunoglobulin G4 on Paraffin Sections for the Diagnosis of Pemphigus. Arch Pathol Lab Med 2012, 136(11):1402–1407.

22. Kordofani YM, Shah IM, El-Agraa B, Shalayel MH: Pemphigus in Khartoum Skin Teaching Hospital. Sudan Medical Monitor 2008, 3(2):58–60.

23. Suliman NM, Astrom AN, Ali RW, Salman H, Johannessen AC: Oral mucosal lesions in skin diseased patients attending a dermatologic clinic: a cross-sectional study in Sudan. BMC Oral Health 2011, 11(1):24

24. Cirillo N, Cozzani E, Carrozzo M, Grando S: Urban legends: pemphigus vulgaris. Oral Dis 2012, 18(5):442–458.

25. Sagi L, Baum S, Agmon-Levin N, Sherer Y, Katz BS, Barzilai O, Ram M, Bizzaro N, SanMarco M, Trau H, et al: Autoimmune bullous diseases the spectrum of infectious agent antibodies and review of the literature. Autoimmunity reviews 2011, 10(9):527–535.

26. Ruocco V, Ruocco E: Pemphigus and environmental factors. Gital Dermatol Venereol 2003, 138:299–309.

27. Bastuji-Garin S, Turki H, Mokhtar I, Nouira R, Fazaa B, Jomaa B, Zahaf A, Osman AB, Souissi R, Hemon D, et al: Possible relation of Tunisian pemphigus with traditional cosmetics: a multicenter case–control study.Am J Epidemiol 2002, 155(3):249–256.

28. Valikhani M, Kavusi S, Chams-Davatchi C, Daneshpazhooh M, Barzegari M, Ghiasi M, Abedini R: Pemphigus and associated environmental factors: a case–control study. Clin Exp Dermatol 2007, 32(3):256–260.