Reumatologia 2017; 55, 6: 323–327
DOI: https://doi.org/10.5114/reum.2017.72631

A child with subcorneal pustular dermatosis responded to IVIG treatment (Sneddon-Wilkinson disease)

Selcen Kundak, Özlem Bağ, Nesrin Gülez, Malik Ergin

Dr. Behcet Uz Children's Hospital, Izmır, Turkey

Abstract

Subcorneal pustular dermatosis (SPD) is a rare, chronic, recurrent dermatosis characterised by sterile pustules. It develops mainly in middle-aged or elder women, but is also rarely seen in children. The exact aetiology of the disease is unknown. In literature, cases associated with IgA gammopathy have been reported. In this article; we report a case of a five-year-old girl who was diagnosed as SPD by clinical features, histopathological characteristics, and direct immunofluorescence analysis results. IgA was high, and IgG-IgM and CD19+ B cell were low. We noticed that during IVIG treatment for immunodeficiency, dermatological symptoms were recovered rapidly. Clinical profile of SPD and its association with systemic diseases may provide early detection of immune dysfunction.

Key words: subcorneal pustular dermatosis, Sneddon-Wilkinson disease, subcorneal dermatosis.

Introduction

Subcorneal pustular dermatosis (SPD) is a rare eruption characterised by chronic, recurrent loose pustules with a large number of neutrophils histopathologically [1–3]. Pustules especially occur in the regions like the trunk and body folds whereas the face, palms, soles, and mouth mucosa are often protected. Loose pustules can develop in sizes ranging from 2–3 mm to 10 mm and tend to form groups as annular or serpiginous structures. They can easily become ruptured and result in hyperpigmentation. It rarely develops in childhood, although it often develops in middle-aged or older women [1–7].

Case report

A five-year-old girl was admitted to the dermatology unit with a complaint of eruption on various parts of the body. She had had recurring complaints for the last seven months, which occurred four or five times and last appeared two weeks previously. In her history, there was no particular feature except consanguineous marriage in her parents. The dermatological examination revealed erosion and pustules of 2 mm to 10 mm, which formed annular structures in the axillae, inguinal folds, upper and lower limbs, and pubis, and intensely in the neck, upper back, and upper body. The mouth and genital mucosa, palms, and soles were normal (Fig. 1). Moreover, decreased breathing sounds and rhonchi were noticed. The fever was 38.20°C and other vital findings were normal. We hospitalised the patient. In laboratory analysis her values were; Hb 9.8 g/dl, WBC 30,090×10³/µl, ESR 90 mm/h, CRP 18 mg/dl, IgA 625 mg/dl (57–282), IgG 545 mg/dl (745–1804), IgM 53 mg/dl (78–261) and C3 206 mg/dl (90–180), CD19+ B cells 3.9% (14–33%) in the lymphocyte panel. Anti-HBs antibodies (after vaccination or natural), anti-HIV, anti-CMV antibodies, anti-nuclear antibodies (ANA); ANCA (anti-neutrophil cytoplasmic antibodies), anti-dsDNA antibodies and celiac panel were negative. Blood and recurrent pustular cultures were negative. In chest radiography, pulmonary infiltration was on the right paracardiac area. Streptococcus pneumoniae was detected positively in the assay of respiratory polymerase chain reaction.

Histopathology showed pustules located immediately below the stratum corneum and contained mainly polymorphonuclear leukocytes with a few eosinophils, acantholytic cells in the cavity, and spongiosis in the epidermis. Indirect immunofluorescence analysis (DIF); IgG, IgM, IgA, and C3 were negative. Intermittent and linear fibrinogen was detected positive in the bulla cavity

Address for correspondence:
Selcen Kundak, Dr. Behcet Uz Children's Hospital, 35000 Izmır, Turkey, e-mail: drselcen@yahoo.com.tr
Submitted: 19.09.2017; Accepted: 27.11.2017

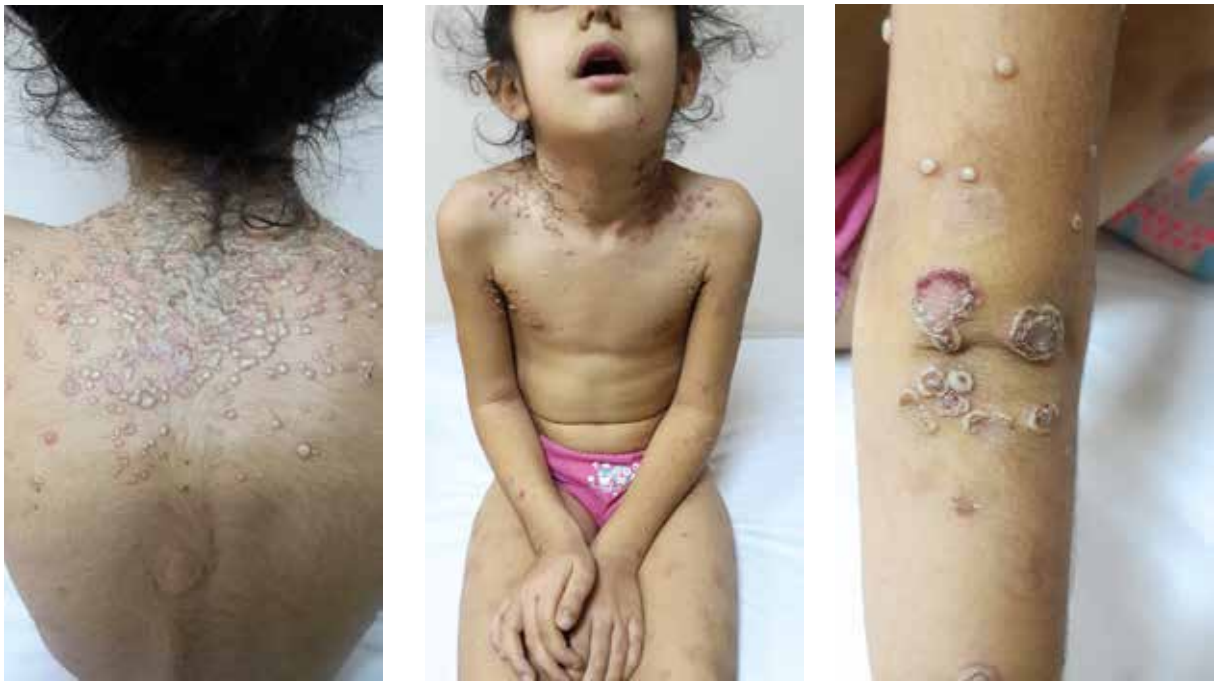

Fig. 1. Erosions and steril pustules formed an annular structure intensely on the neck, upper back and upper body.

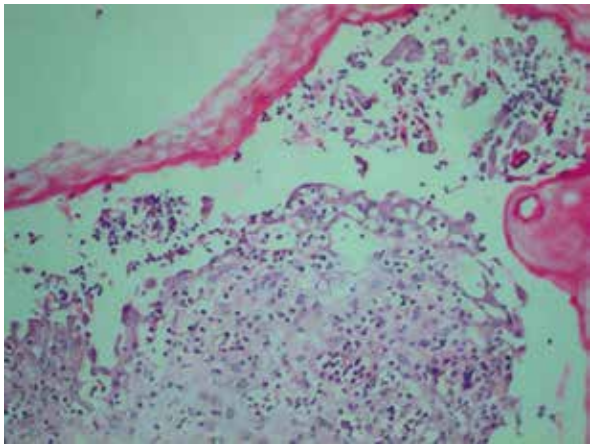

Fig. 2. The acantholytic cells in the cavity basement and inside and spongiotic focus (hemotoxylin-eosine staining, 200×).

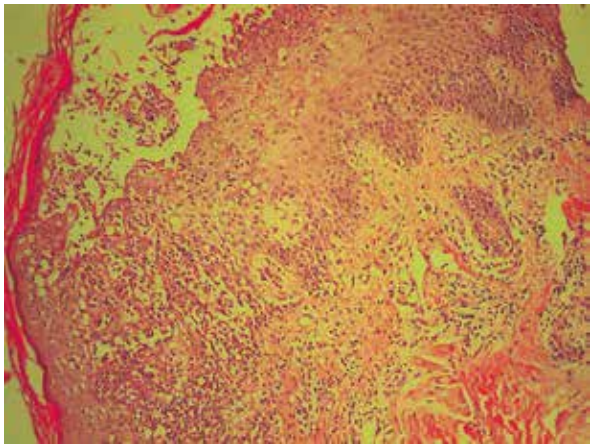

Fig. 3. Spongiosis with subcorneal bulla formation (hematoxylin-eosine staining, 100×).

and its periphery (Figs. 2, 3). Based on the findings, our patient was diagnosed SPD with IgA elevation without gammopathy but with CD19+ B cell deficiency in the lymphocyte panel, which resulted in the reduction of other immunoglobulins.

Cefotaxime and clindamycin treatment was started with the diagnosis of pneumonia. Bone marrow biopsy and myeloma cell screening using flow cytometry were performed, and no gammopathy or myeloproliferative condition was found. We treated the patient with intravenous immunoglobulin (IVIG) at 600 mg/kg because of immunodeficiency. All pustular lesions improved by leaving post-inflammatory hyperpigmentation within one week of IVIG treatment (Fig. 4). Due to regression of infiltration on control chest radiography and no exacerbation of skin lesions, the patient was discharged from hospital with the maintenance of IVIG treatment for four weeks. In order to avoid recurrent exacerbations, the patient received 1 mg/kg dapsone and she was registered for follow up.

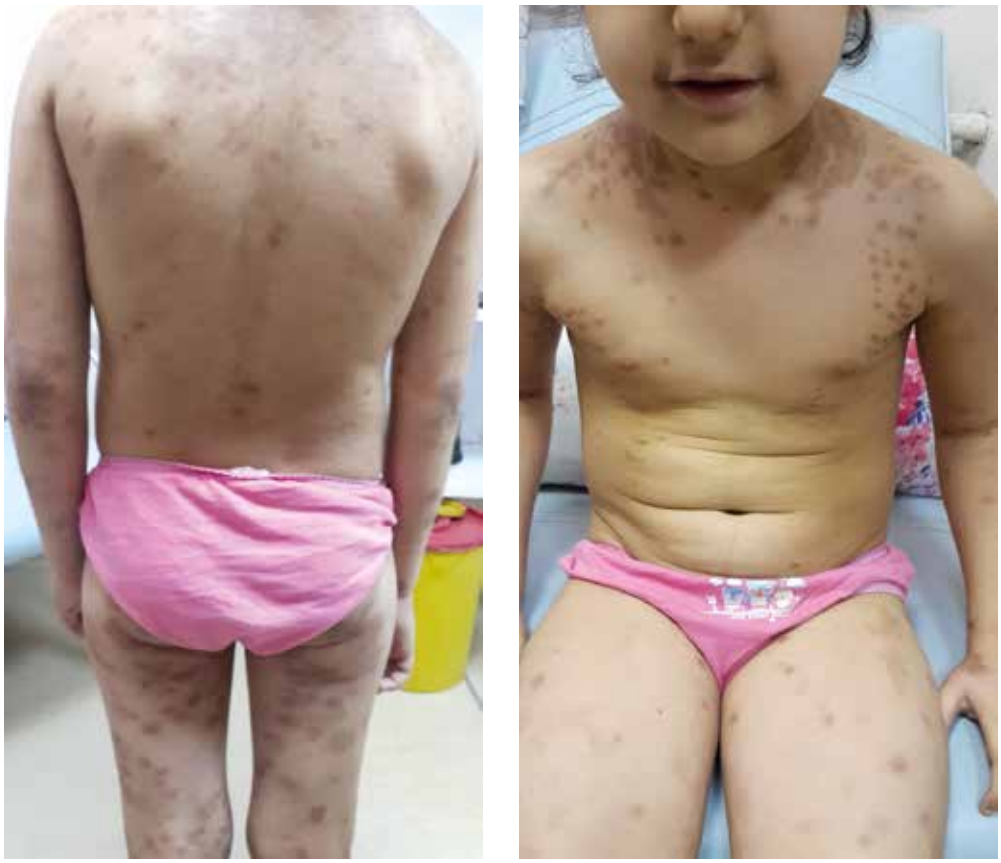

Fig. 4. Hyperpigmented macules in place of pustules after 1 week of single dose IVIG treatment.

Discussion

Subcorneal pustular dermatosis (SPD), described by Sneddon and Wilkinson in 1956, is a recurrent, chronic dermatosis characterised by highly superficial, easily erupting, sterile pustules [1–3]. Although the disease is observed in middle-aged and older women, it is rarely seen in childhood. Scalvenzi et al. [4] reported that there were 15 similar paediatric cases in literature and described a seven-year-old male case in 2013. We examined the literature again and found that some of the cases were from Turkey. Koçak reported a 13-year-old girl in 2003, Yaylı described juvenile SPD in 2006, Ağladıoğlu described a nine-year-old girl with SPD in 2008, and Afşar also described a 2.5-year-old boy in 2010 [4, 6, 7]. Our case was a five-year-old girl.

Although the exact aetiology of the disease is unknown, many theories including infectious and autoimmune etiology have been suggested. There are well-documented SPDs associated with benign IgA gammopathy [1–7]. However, IgA elevation without gammopathy has also been reported [1–7]. It has been suggested that IgA proteins interacting with the normal epidermis play a role in the pathogenesis of SPD. However, immunological disturbance resulting from the abnormal cytokine profile has been generally accepted as the underlying cause. The isolation of neutrophil chemoattractants in pustule contents of SPD cases supports this opinion [5, 7]. Over-activation of neutrophils is thought to cause neutrophil accumulation and destruction in the tissue. However, an infectious agent or an immunological trigger have not yet been identified in SPD cases [1–8]. SPD may be accompanied with pyoderma gangrenosum, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, familial Mediterranean fever, hyperthyroidism, and apudoma [6, 9, 10]. Additionally, IgA myeloma and marginal zone lymphoma have also been reported [8]. However, it is still unknown whether disease-related gammopathies play a primary role in the pathogenesis of the disease or occur secondarily during the course of the disease.

Ratnarathorn and Newman [8] reported a rapid response to SPD with marginal zone lymphoma after rituximab treatment for lymphoma, but radiological response in the lymphoma was limited. Rituximab (RTX) is an anti-CD20+ B lymphocyte monoclonal antibody, which targets CD20 antigen of B lymphocytes. CD20 an-

tigen is expressed in all stages of B cell lymphocyte as much as in B cell lymphoma. The lymphotoxic effect of the RTX inhibits the conversion of B cells into plasma cells and thus the production of other antibodies, including IgA. In this case, the response of SPD to RTX supports the idea that IgA has a role in the aetiopathogenesis of the disease [8]. In our case, IgG, IgM, and CD19+ B cells were low, and significantly high levels of IgA were detected. Myeloproliferative diseases and myeloma are excluded from the results of bone marrow biopsy and skull radiography.

In SPD histopathology, subcorneally localised pustules filled with polymorphonuclear leukocytes are seen. Acantholytic cells and eosinophils may be seen in the pustule. Minimal spongiosis or in some cases acantholysis may occur [1–5]. Direct immunofluorescence analysis is negative. Although intercellular, intrapustular, or subcorneal IgA accumulation is reported in some cases in literature, nowadays it is widely accepted that this finding should be evaluated as SPD type IgA pemphigus [1–5]. IgA pemphigus represents a newly defined group of autoimmune intraepidermal bullous diseases characterised by circulating IgA autoantibodies. Two different types of IgA pemphigus are defined as SPD type IgA and intraepidermal neutrophilic type. Because SPD type IgA pemphigus is not different from classical SPD clinically and histopathologically, immunological evaluation is considered necessary to distinguish these two diseases from each other [2, 3].

In the histopathological examination of our case; subcorneal bulla formation with intense polymorphonuclear leukocytes and sporadic eosinophilic leukocyte infiltration and the acantholytic cells were observed in the cavity basement and inside. Direct immunofluorescence analysis for IgG, IgA, IgM, and C3 was negative, but intermittent and linear fibrinogen had positive staining around the bulla cavity.

SPD is a chronic dermatosis with variable relapses and remissions. Treatment options are very limited. Topical retinoids and topical corticoids may be useful for a limited number of lesions [1–5]. However, in SPD, dapsone is accepted as the first option. The research has shown that dapsone inhibits the neutrophil myeloperoxidase [9]. In some cases resistant to dapsone, retinoid derivatives such as acitretin or isotrexin, and PUVA and colchicine have been used successfully [7, 9, 11]. As mentioned earlier, we would like to re-emphasise the positive effect of rituximab treatment, which was initiated due to lymphoma with SPD, incidentally on SPD lesions [8].

In our case, IVIG treatment was recommended because of immunodeficiency. Significant improvement in SPD lesions was noted after the first IVIG treatment (Fig. 4). In literature, Rash et al. [12] performed an IVIG treatment in an 83-year-old man with SPD accompanied with combined deficiency of IgG and IgM in 2009 and reported complete regression in lesions. The action mechanism of IVIG is not fully understood. However, immunomodulatory effects such as functional blockage of Fc receptors, inhibition of complement-related damage, alteration of cytokine structures, and neutralisation of toxins which trigger autoantibody production, are mentioned [2, 3]. Case presentations and some uncontrolled studies indicate that it may be useful in some dermatoses. In our case, rapid improvement with IVIG was observed in acute exacerbation of SPD, and thus IVIG may be chosen as an alternative treatment option during acute exacerbations and in severe cases and in cases of resistance to other treatments.

Conclusions

In SPD, there are many things that need to be clarified in terms of aetiopathogenesis, classification, and treatment alternatives. It is particularly a matter of debate whether gammopathies play a primary role or if dermatosis emerges as an autoimmune paraneoplastic syndrome. The understanding of the clinical profile of SPD and its association with systemic diseases may provide early detection of immune dysfunction and myeloproliferative disorders.

The authors declare no conflict of interest.

References

1. Braun-Falco O, Plewig G, Wolf HH, Burgdof WHC. Pustular Disease. In: Dermatology, 2nd ed. Springer Verlag, Berlin 2000; 1575-1576.
2. Trautinger F, Hönigmann H. Subcorneal pustular dermatosis (Sneddon-Wilkinson Disease). In: Fitzpatrick's Dermatology in General Medicine 8th ed, Goldsmith LA, Katz SI, Gılchrest BA, Paller AS, Leffell DJ, Wolf K (eds.). McGraw-Hill USA 2012; 383-385.
3. Kasha EE Jr, Epinette WW. Subcorneal pustular dermatosis (Sneddon-Wilkinson disease) in association with a monoclonal IgA gammopathy: a report and review of the literature. J Am Acad Dermatol 1988; 19: 854-858.
4. Scalvenzi M, Palmisano F, Annunziata MC, et al. Subcorneal pustular dermatosis in childhood: a case report and review of the literature. Case Rep Dermatol Med 2013; 2013: 424797.
5. Tajiri K, Nakajima T, Kawai K, et al. Sneddon-Wilkinson disease induced by sorafenib in a patient with advanced hepatocellular carcinoma. Intern Med 2015; 54: 597-600.
6. Ağladıoğlu SY, Bozkaya D, Fidan K, et al. Juvenile Subcorneal Pustular Dermatosis In A Case Of Familial Mediterranean Fever And Sacroiliitis. Gazi Medical Journal 2008; 19: 50-52.

7. Afsar FŞ, Ortac R, Diniz G. A Juvenile subcorneal pustular dermatosis case with a course of mild exacerbations after acitretin treatment. Turk J Dermatol 2010; 4: 84-87.
8. Ratnarathorn M, Newman J. Subcorneal pustular dermatosis (Sneddon-Wilkinson disease) occurring in association with nodal marginal zone lymphoma: a case report. Dermatol Online J 2008; 14: 6. 3.
9. Khachemoune A, Blyumin ML. Sneddon-Wilkinson disease resistant to dapsone and colchicine successfully controlled with PUVA. Dermatol Online J 2003; 9: 24. 7.
10. Puechguiral-Renaud I, Carpentier O, Piette F, Delaporte E. Subcorneal pustulosis and pyoderma gangrenosum associated with a biclonal gammopathy. Eur J Dermatol 2006; 16: 687-690.
11. Marliere V, Beylot-Barry M, Beylot C, et al. Successful treatment of subcorneal pustular dermatosis (Sneddon-wilkinson disease) by acitretin: report of a case. Dermatology 1999; 199: 153-155.
12. Rasch A, Schimmer M, Sander CA. Subcorneal pustulosis with combined lack of IgG/IgM and monoclonal gammopathy type IgA/Kappa. J Dtsch Dermatol Ges 2009; 7: 693-696.