Hong Kong J. Dermatol. Venereol. (2021) **29**, 75-79

Case Report

Co-existence of erythema elevatum diutinum and pyoderma gangrenosum: a case report

持久性隆起性紅斑和壞疽性膿皮病共病的病例報告

M Özaslan, B Erdoğan, M Yılmaz, A Kavak, D Sakız

Neutrophilic dermatoses (ND) are a group of diseases with similar clinicopathologies. However, the coexistence of erythema elevatum diutinum (EED) and pyoderma gangrenosum (PG) in the same patient is uncommon. In this paper, we present a patient who developed two types of ND, first EED and then PG. Also, we examine the coexistence of ND and its possible causes, atypical clinical features as well as possible concomitant disease development.

嗜中性球皮膚病是一組具有相似臨床病理的疾病。然而，同一患者同時出現持久性隆起性紅斑和壞疽性膿皮病的情況並不常見。在本文中，我們介紹了一位患有兩種嗜中性球皮膚病的患者，首先是持久性隆起性紅斑，繼而是壞疽性膿皮病。此外，我們檢查了嗜中性球皮膚病的共存及其可能的原因、非典型的臨床特徵以及可能的共病發展。

Keywords: Cutaneous, leukocytoclastic, pyoderma gangrenosum, skin diseases, vasculitis

關鍵詞：皮膚、白細胞破碎性、壞疽性膿皮病、皮膚病、血管炎

Introduction

Erythema elevatum diutinum (EED), pyoderma gangrenosum (PG), Sweet's syndrome (SS) and subcorneal pustular dermatosis are neutrophilic dermatoses (ND) with similar clinicopathologies. Although ND are well-known diseases in dermatology, the coexistence of EED and PG in the same patient is uncommon.[1-6] We present a patient with EED and PG and examine the coexistence of ND and its possible causes, atypical clinical features and long-term follow-up requirements as well as possible concomitant disease development.

Bakırköy Dr. Sadi Konuk Training and Research Hospital, Dermatology Clinic, Istanbul, Turkey

M Özaslan, MD
B Erdoğan, MD
M Yılmaz, MD
A Kavak, MD

Bakırköy Dr. Sadi Konuk Training and Research Hospital, Pathology Clinic, Istanbul, Turkey

D Sakız, MD

Correspondence to: Dr. M Özaslan
Beyhekim Training and Research Hospital, Dermatology
42060 Selçuklu, Konya, Turkey

Case report

A 39-year-old male patient, who was followed up for arthralgia in the rheumatology clinic, presented to us for skin lesions. The lesions started three years ago as painful papules on his inguinal regions, and similar lesions emerged over time on his extremities,

gluteal and abdominal region. In addition, the patient reported the development of a painful and ulcerated lesion on the anterior aspect of his right leg over the past 15 days.

On examination, there were multiple red, purplish papules and plaques on his abdominal and gluteal regions (Figure 1a) and the extensor surfaces of the extremities. Vesicles and pustules were observed in the periphery of the crusted plaques on the elbows (Figure 1b). A well-demarcated ulcerated lesion, 3x5 cm in size, with a solitary, painful, peripheral, violet-coloured halo was observed on the right pretibial area (Figure 2).

Histopathological examination of a purplish red plaque on the gluteal region and pustular lesions on the elbow revealed leukocytoclastic vasculitis (LCV) accompanied by dense dermal neutrophilic infiltration, erythrocyte extravasation, mild nuclear debris, vascular proliferation, oedema in the endothelial walls and fibrin accumulation (Figure 3a). The patient was diagnosed with early EED histopathologically and clinically. Histopathological examination of the ulcerated lesion on the right pretibial area revealed focal erosion on the epidermis, subepidermal fibrin accumulation, dermal necrosis accompanied by neutrophils, lymphocyte and histiocyte infiltration, vascular proliferation, mild nuclear debris and perivascular lymphocyte infiltration in the subcutaneous tissue (Figure 3b). In the last specimen, histopathological findings were not indicative of a specific disease and were evaluated as PG together with clinical findings.

Laboratory investigations including a complete blood count, hepatic and renal function, peripheral blood smear, anti-nuclear antibody, an anti-extractable nuclear antigens profile, antineutrophil cytoplasmic antibodies, rheumatoid factor, HLA-B27, serum protein electrophoresis, hepatitis markers and the anti-human immunodeficiency virus (HIV) antibody test were normal or negative. The wound swab culture from the ulcer on the pretibial area of right leg was negative. Chest radiography was normal. There were no signs of inflammatory bowel disease on colonoscopy. The eye examination was normal. Malignancy screening tests by age and gender were negative.

Dapsone (50 mg daily) and systemic methylprednisolone (0.5 mg/kg/day) were initiated concurrently. Dapsone was discontinued on the third day of treatment due to abdominal pain and diarrhoea. Topical clobetasol 17-propionate was started for the ulcerated lesion on the leg. The dose of systemic methylprednisolone was gradually reduced within one month, and a significant clinical response was observed in both the EED and PG lesions at the end of the first month of treatment.

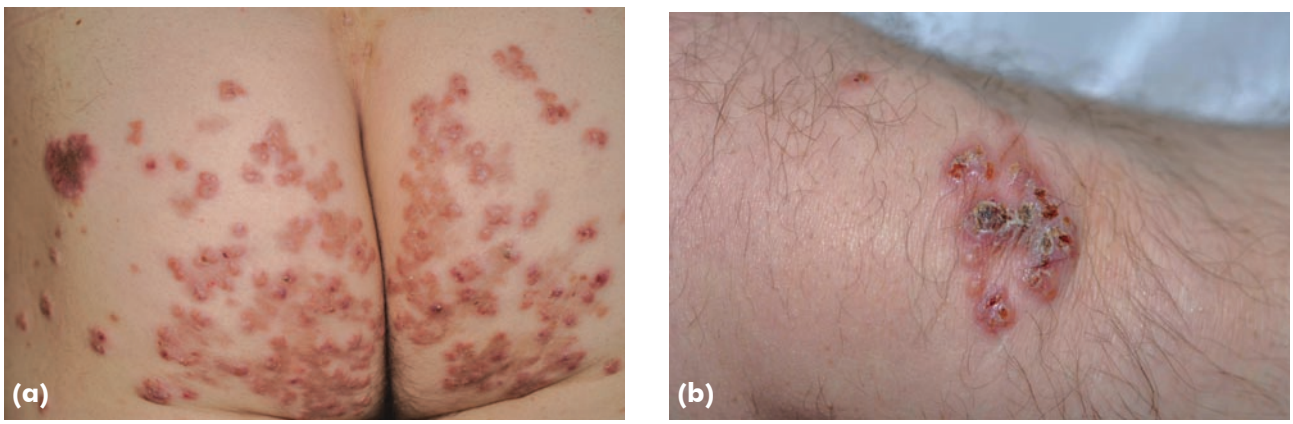

Figure 1. (a) Multiple red, purplish papules and plaques on his gluteal region. (b) Vesicles and pustules in the periphery of the crusted plaques on the elbow.

Discussion

The co-existence of LCV and PG has been reported in the literature, but detailed information about the clinical type of LCV has not been provided in case report by Thompson et al.[7] In addition, there were a total of seven cases of the concurrent EED and PG (Table 1).[1-6] Similar to our case, in the reported cases, EED occurred first. PG emerged before EED in only one case.[6]

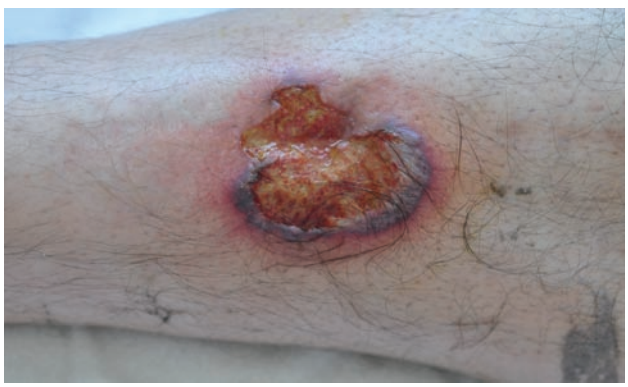

Figure 2. A well-demarcated ulcerated lesion, 3x5 cm in size, with a solitary, painful, peripheral, violet-colored halo on the right pretibial area.

It is known that chronic antigenic stimulation triggers immune complex formation and causes vasculitis in the pathogenesis of EED.[8] It is not clear whether the arthralgia in our case resulted from this antigenic stimulus or directly from the disease. Interestingly, EED occurs before other ND in the reported cases. Although the role of auto-inflammation and dysregulation in the innate immune system in the pathogenesis of ND is emphasised,[9] there is no hypothesis on the order of in which diseases in this spectrum occur. The role of complement activation in the pathogenesis of LCV is critical.[10] Unlike other ND, EED, which is one of the subtypes of LCV, a disease in which immune complexes play an important role, may trigger other ND by causing systemic chronic inflammation with systemic complement activation.

The fact that pustular and bullous types have been reported for both EED and PG means that it can be difficult to differentiate between the two diseases.[11,12] There were three different clinical types of lesions in our patient. Although EED lesions on the gluteal region and PG lesions on the right leg (Figures 1b and 2) were clinically typical, various diseases could be considered in the

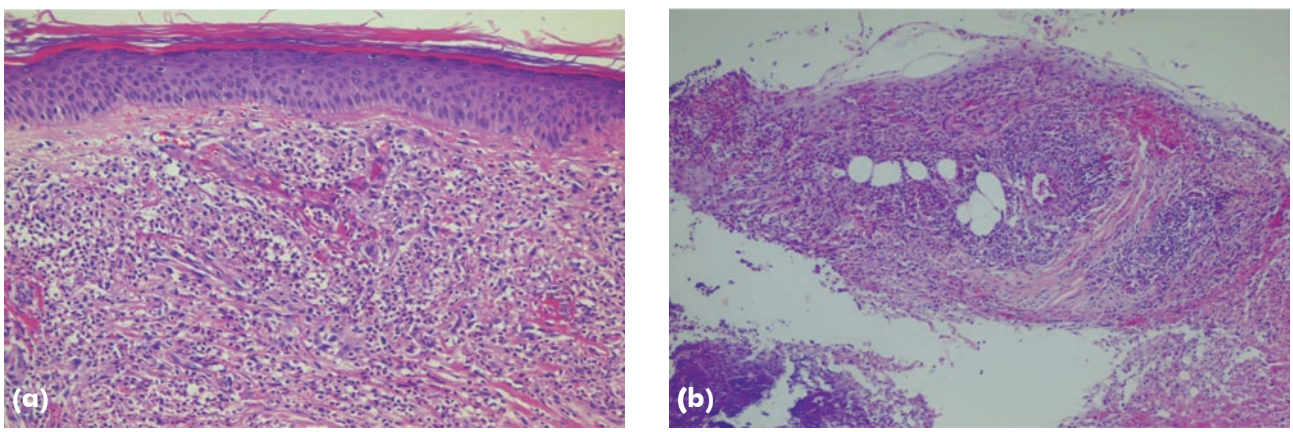

Figure 3. (a) Histopathological examination of EED shows leukocytoclastic vasculitis accompanied by dense dermal neutrophilic infiltration, erythrocyte extravasation, mild nuclear debris, vascular proliferation, edema in the endothelial walls and fibrin accumulation (H & E x40). (b) Histopathological examination of PG shows focal erosion on the epidermis, subepidermal fibrin accumulation, dermal necrosis accompanied by neutrophil, lymphocyte and histiocyte infiltration, vascular proliferation, mild nuclear debris and perivascular lymphocyte infiltration in the subcutaneous tissue (H & E x10).

differential diagnosis for vesiculopustular plaques on the knee and elbow. A histopathological examination of the pustules was found to be consistent with EED. The age of the lesion is important in the histopathology of EED. It is thought that epidermal necrosis observed secondary to the formation of LCV in early lesions may cause vesicle formation.[8] In our case, the presence of typical nodular lesions as well as vesicular lesions may be a different sign of the disease.

EED and PG produce similar histopathological findings. LCV is seen during the early stages of EED, as in our case. In PG, on the other hand, vasculitis is not a typical finding and is observed as a secondary change at the base of the ulcer and its surroundings. Since there is no specific histopathological marker for the diagnosis of PG, this diagnosis should be made by excluding other diseases based on clinical findings.

It is noteworthy that cases of EED and PG with concurrent IgA monoclonal gammopathy, SS, HIV or myelodysplastic syndrome have been reported.[2-4,6] In addition, IgA gammopathy developed during the follow-up of a case with concurrent LCV and PG.[7] The mean follow-up period of the cases is five years (Table 1), and there is no relationship between the follow-up periods and the duration of comorbidity. In the two-year follow-up of our case, no comorbidity was detected except arthralgia. Nevertheless, considering the low number of patients reported, it will be appropriate to perform long-term follow-up in these patients to assess the possibility of serious systemic involvement (kidney, bone, eye or cardiac disease)[3] due to extracutaneous neutrophilic infiltrates and other accompanying diseases.

In conclusion, the coexistence of EED and PG is rare. Similar clinical subtypes, such as vesicular and pustular types, may exist in both dermatoses. In such cases, differential diagnosis and coexistence should be interpreted together with clinical and histopathological findings. Clinicians

Table 1. Characteristics of EED + PG patients reported in the literature[1-6]

	Age	Gender	Cutaneous lesion morphology	Associated conditions	Time to onset of PG (months)
Planagumà et al.[1]					
Patient 1	53	M	Papule, plaque, pustule, haemorrhagic vesicle	–	24
Patient 2	44	F	Papulovesicle	–	108
Wayte et al.[2]	27	M	Plaque	IgA gammopathy[a]	18
Caucanas et al.[3]	50	F	Papule, nodule, plaque	SS	120
Maksimovic et al.[4]	53	M	Nodule	HIV	9
Hügel et al.[5]	37	F	Nodule, plaque, ulcer	–	15
Vide et al.[6]*	24	M	Nodule, plaque	Arthritis[c], MDS[d]	120
Thompson et al.[7]**	51	F	Urticaria, papule, plaque, vesicle, bullae	IgA gammopathy[b]	48
Our case	39	M	Papule, plaque, pustule, vesicle	–	36

SS: Sweet syndrome

[a]Diagnosed at admission; [d]Diagnosed 7 years after admission; [c]Diagnosed 3 years after admission; [d]Diagnosed 8 years after admission

* First PG, then EED emerged; ** LCV case

should look out for the possible development of systemic comorbidities in the presence of two different ND.

References

1. Planagumà M, Puig L, Alomar A, Matias-Guiu X, de Moragas JM. Pyoderma gangrenosum in association with erythema elevatum diutinum: report of two cases. Cutis 1992;49:201-6.
2. Wayte JA, Rogers S, Powell FC. Pyoderma gangrenosum, erythema elevatum diutinum and IgA monoclonal gammopathy. Australas J Dermatol 1995; 36:21-3.
3. Caucanas M, Heylen A, Rolland F, Müller G, Olemans C, Sass U, et al. Associated pyoderma gangrenosum, erythema elevatum diutinum, and Sweet's syndrome: the concept of neutrophilic disease. Int J Dermatol 2013;52:1185-8.
4. Maksimovic L, Duriez P, Lascaux-Cametz AS, Andre C, Bagot M, Revuz J, et al. Erythema elevatum diutinum associated with pyoderma gangrenosum in an HIV-positive patient. Ann Dermatol Venereol 2010;137: 386-90.
5. Hügel R, Brasch J, Yordanova I, Schröder JO, Fazel A, Gläser R, et al. Erythema elevatum diutinum associated with severe oropharyngeal ulceration and pyoderma gangrenosum. J Dtsch Dermatol Ges 2018;16:617-20.
6. Vide J, Brás G, Guimarães JE, Mota A. Pyoderma gangrenosum and erythema elevatum diutinum associated with a high-risk myelodysplastic syndrome: case report. Hematol Transfus Cell Ther 2018;40: 192-5.
7. Thompson DM, Main RA, Beck JS, Albert-Recht F. Studies on a patient leucocytoclastic vasculitis 'pyoderma gangrenosum' and paraproteinaemia. Br J Dermatol 1973;88:117-25.
8. Prat L, Bouaziz JD, Wallach D, Vignon-Pennamen MD, Bagot M. Neutrophilic dermatoses as systemic diseases. Clin Dermatol 2014;32:376-88.
9. Grabbe J, Haas N, Möller A, Henz BM. Erythema elevatum diutinum-evidence for disease-dependent leucocyte alterations and response to dapsone. Br J Dermatol 2000;143:415-20.
10. Giang J, Seelen MAJ, van Doorn MBA, Rissmann R, Prens EP, Damman J. Complement Activation in Inflammatory Skin Diseases. Front Immunol 2018;9:639.
11. Smitha P, Sathish P, Mohan K, Sripathi H, Sachi G. A case of extensive erosive and bullous erythema elevatum diutinum in a patient diagnosed with human immunodeficiency virus. Int J Dermatol 2011;50:989-91.
12. Tomasini C, Seia Z, Dapavo P, Pippione M. Infantile erythema elevatum diutinum: report of a vesiculo-bullous case. Eur J Dermatol 2006;16:683-6.