Pyoderma gangrenosum with its subtype affecting oral mucosa pyostomatitis vegetans following skin melanoma surgical excision in a patient with ulcerative colitis: a case report

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Adv Dermatol Allergol 2018; XXXV (2): 212–216
DOI: https://doi.org/10.5114/ada.2018.75246

Pyoderma gangrenosum (PG) is a disease which aetiology has been described only partially. In the course of the disease damage to blood vessels occurs secondarily to neutrophils infiltration into the affected site. Skin lesions may be located throughout the body, but lower limbs are predominantly affected. The primary lesions include papule, nodule, pustule, vesicle which transform into peripherally growing skin ulcerations. Pyoderma gangrenosum may coexist with multiple conditions including haematologic disorders, inflammatory bowel disease, rheumatoid arthritis and other autoimmune diseases and malignancies [1–3].

Pyostomatitis vegetans (PSV) is classified by many authors as a subtype of PG, which affects oral mucosa. The majority of PSV cases coincide with inflammatory bowel disease [4].

This paper describes a case of a 69-year-old patient, with a history of ulcerative colitis (UC). Due to UC, the patient participated in a clinical trial of a biologic drug in 2009–2010, but no detailed data on the treatment were available. The disease was complicated with several episodes of gastrointestinal bleeding. The last reported bleeding occurred 3 months before the admission to the Clinic of Dermatology. It resulted in hypovolemic shock and it was associated with the occurrence of mucosal lesions. The patient was admitted to the Clinic of Dermatology in Bydgoszcz because of minor oral mucosa erosions observed for 3 months preceding hospitalization. During physical examination a pigmentary lesion sized 40 × 30 mm on the patient's back was observed. Clinical and dermoscopic characteristics of the lesion were typical of melanoma. Histopathological examination of the excised lesion confirmed melanoma pT1a (0.5 mm in Breslow scale) and complete excision. Clinical and dermoscopic presentation of melanoma diagnosed in our patient is presented in Figure 1.

Shortly after the skin lesion had been excised, a rapidly spreading ulceration on the patient's right lower limb appeared. The ulceration was 8 cm in diameter, with a necrotic crust in the middle of the lesion and an elevated dark red edge. Moreover, single pustules, which initially appeared on the patient's face, trunk and limbs began to transform into minor ulcerations. Erosions of oral mucosa progressed to deep ulcerations with inflammation in adjacent areas. Additionally, mucosal pustules within the oral cavity could be observed. Pathergy reaction within the post-surgical wound was present. Skin lesions were accompanied by systemic symptoms such as fever, malaise and pain. Skin and mucosal lesions observed in the course of the disease are presented in Figure 2.

Laboratory tests performed at admission revealed an increased C-reactive protein (CRP) plasma concentration (132 mg/l), increased erythrocyte sedimentation rate (85 mm/h), mild normocytic anaemia with haemoglobin concentration of 11.9 g/dl, and hypoalbuminaemia 3.28 g/dl. Microbiological examination of samples obtained from the surgical wound and thigh ulceration, as well as blood culture were negative. Additionally, only physiologic flora of the oral cavity was found in samples taken from oral mucosal ulcerations. Imaging examinations, including chest X-ray, abdominal ultrasound, peripheral lymph nodes ultrasound, paranasal sinuses computed tomography done during the hospitalization, revealed no significant abnormalities. A series of immunologic tests were performed, cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA) and perinuclear

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Received: 19.04.2017, **accepted:** 31.07.2017.

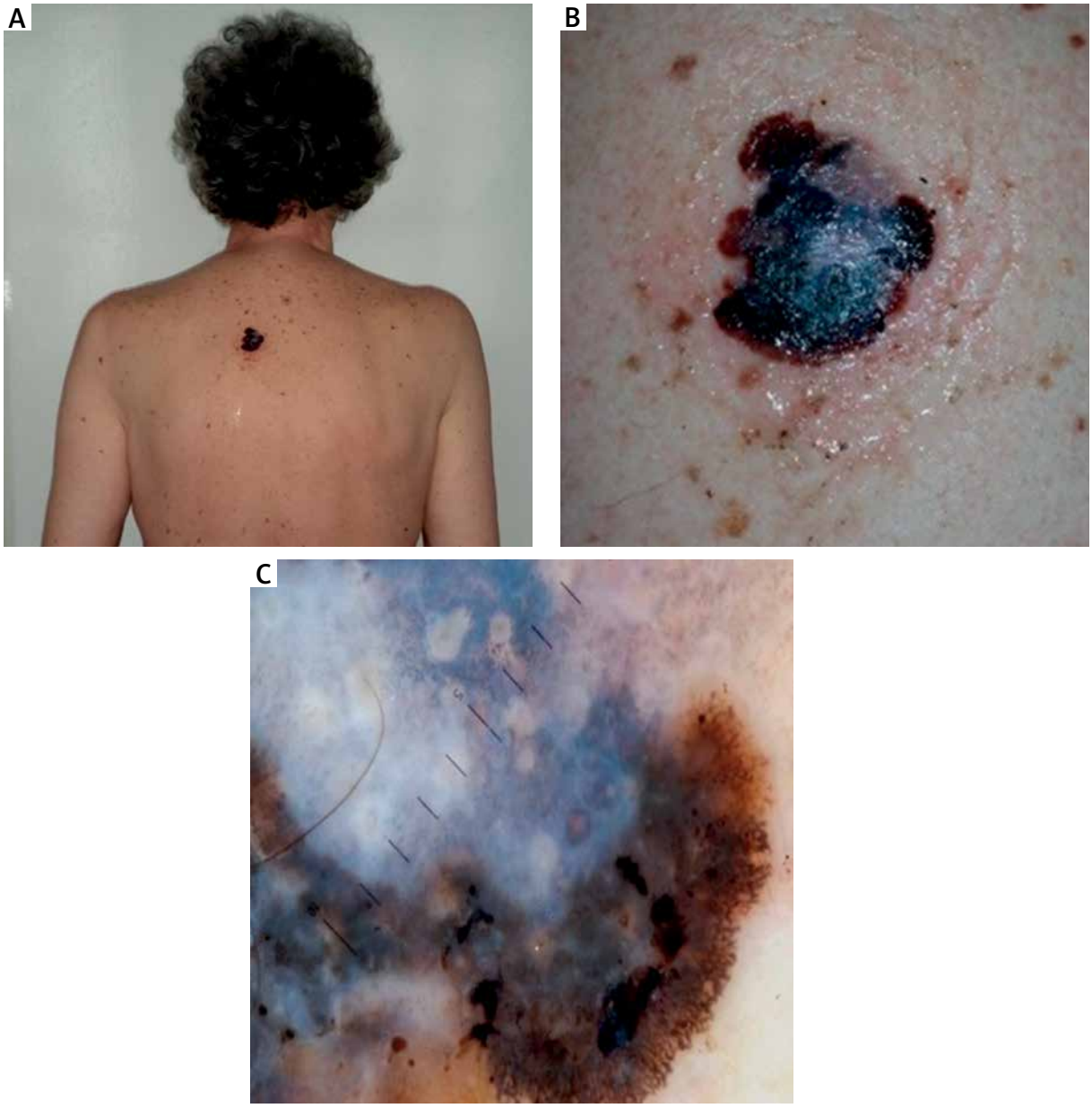

Figure 1. Clinical and dermoscopic presentation of melanoma

anti-neutrophil cytoplasmic antibodies (p-ANCA) were negative, squamous epithelium-specific antibodies (SESANA), pemphigus and pemphigoid associated antibodies were negative. Oral mucosa direct immunofluorescence assay was negative. Anti-nuclear antibodies (ANA) of a homogenous and speckled pattern in titre 1 : 640 were found, whereas ANA EUROLINE profile 3 was negative. Ophthalmologic examination did not reveal traits of choroiditis or retinitis.

Initially, histopathological examination of oral mucosa revealed features of discreet keratosis, intraepithelial abscesses, reactive vascular proliferation within subepithelial connective tissue, erythrocyte extravasation with diffuse mononuclear cells influx (Figure 3 A). When oral mucosal ulcerations appeared, the histopathological evaluation revealed massive eosinophilic, neutrophilic and lymphocytic infiltrate, acanthosis and eosinophil intravascular mobilization (Figure 3 B). Histopathological findings of the biopsy obtained from the edge of skin ulcerations included abundant suppurative infiltrate, necrosis with abscess formation and features of leukocytoclastic vasculitis (Figure 3 C).

Taking into consideration the overall clinical presentation as well as the results of laboratory tests and histo-

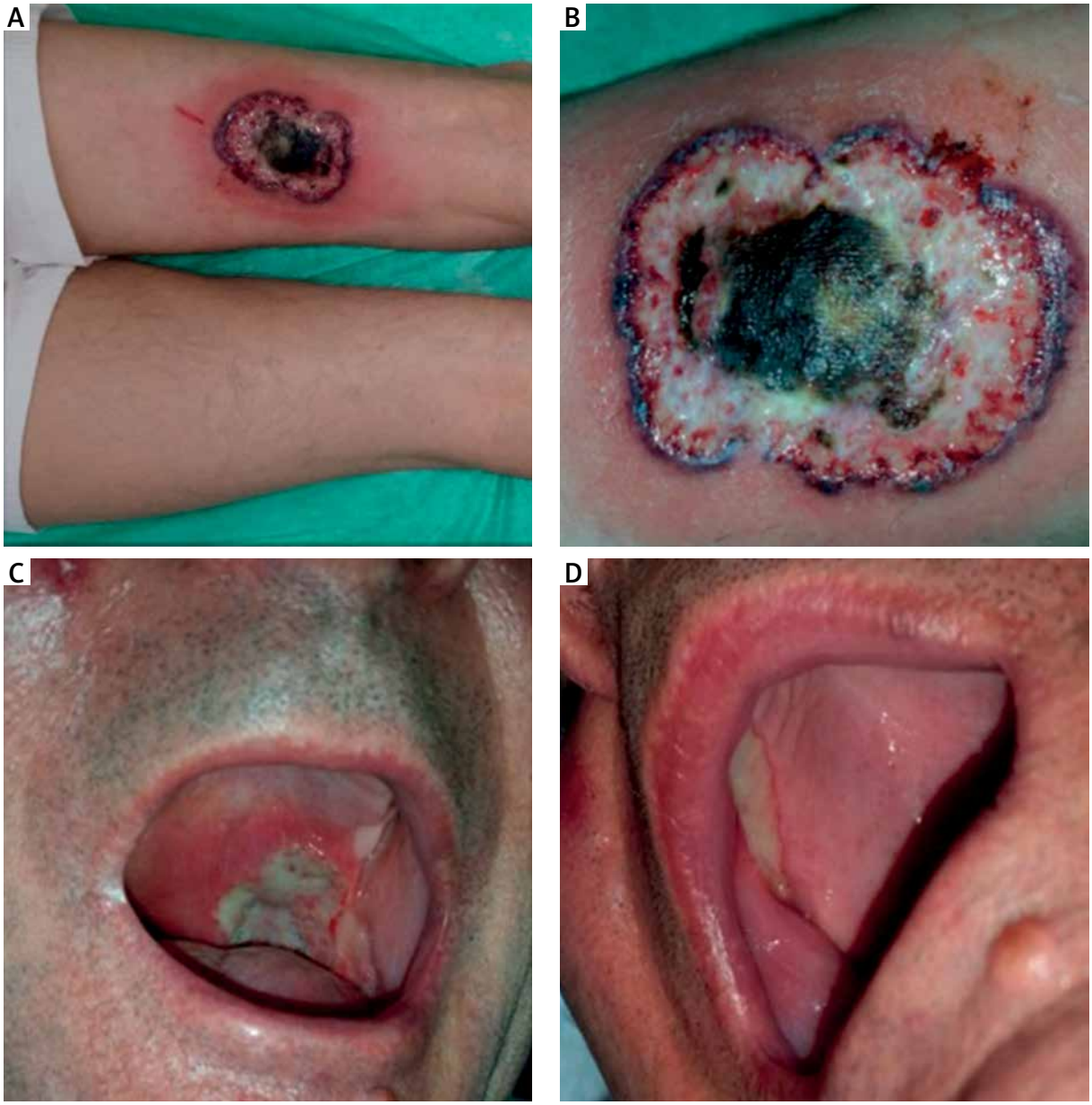

Figure 2. Skin and mucosal lesions observed in advanced phase of the disease

pathological examinations, the most probable diagnosis of PG and its subtype PSV was made.

The patient was initially treated with a combination of prednisone 40 mg daily (0.6 mg/kg body weight) and cyclosporine A 250 mg daily (4.3 mg/kg body weight). Significant improvement was observed after 3 weeks of treatment. Complete remission of mucosal and skin lesions was achieved after a 6-month therapy.

According to available literature, a strong correlation between PSV and inflammatory bowel disease can be confirmed. Results of the retrospective analysis of all cases of PSV described in Mayo Clinic between 1995 and 2014 showed that PSV coexisted with inflammatory bowel disease (either Crohn's disease or UC) in all patients [5]. Moreover, PSV can be considered a marker of inflammatory bowel disease activity [6]. These findings are consistent with the case of our patient where mucosal lesions and UC exacerbation occurred concurrently. Pyostomatitis vegetans may affect patients at any age, but it is most commonly observed in ones between 20 and 59 years. Males show a considerable predominance over females with an incidence ratio of 2 : 1–3 : 1, respectively [7, 8]. Characteristic features of PSV clinical presentation include mucosal ulcerative lesions, pustules

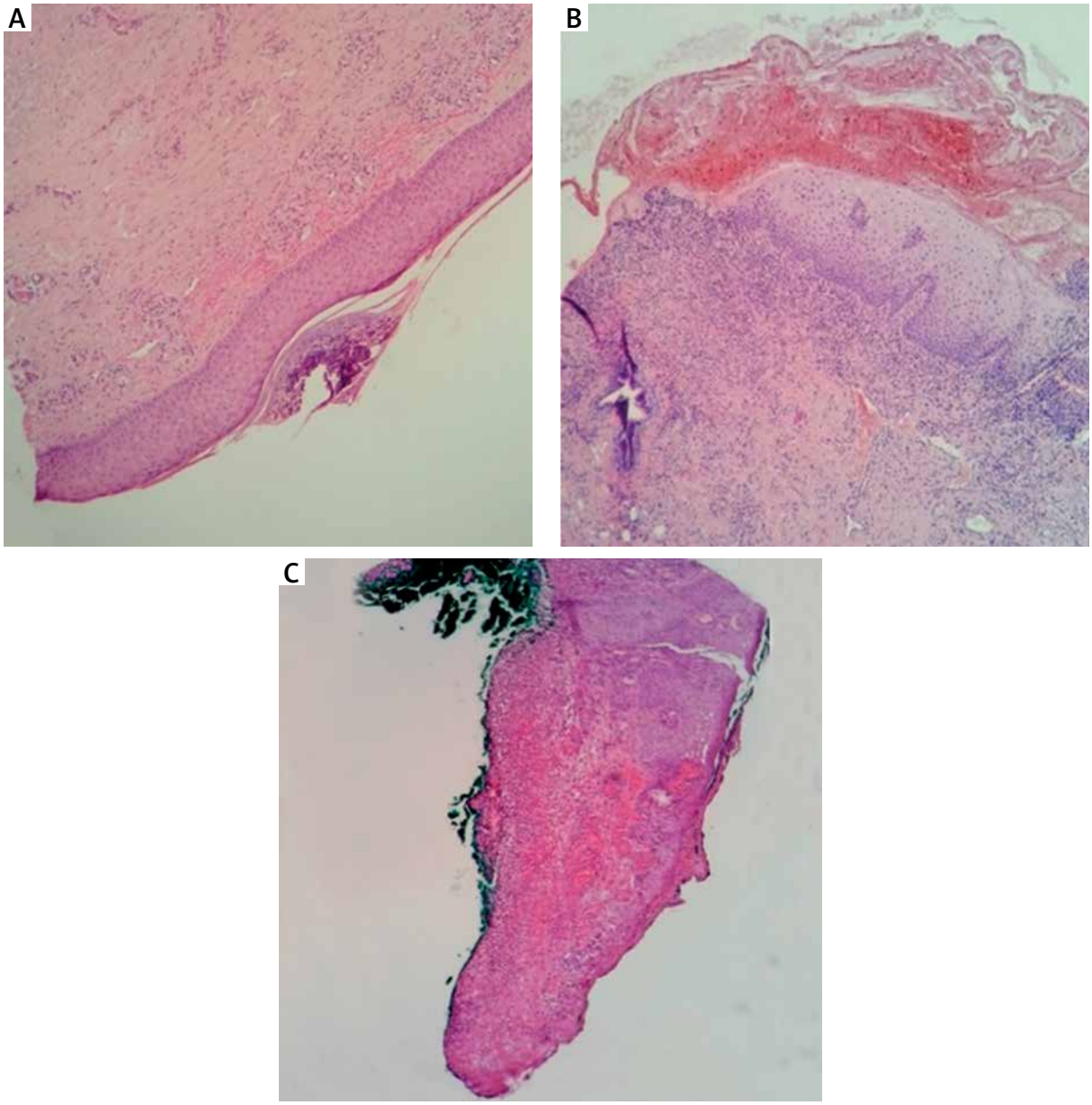

Figure 3. Histopathological features of initial phase mucosal lesions – mucosal pustules and erosions (**A**), advanced phase mucosal lesions – mucosal ulcerations (**B**), skin ulceration (**C**)

with mucosal erythema and oedema at the base. Major histopathological microscopic features of PSV comprise formation of intra-epithelial or sub-epithelial micro-abscesses as well as neutrophilic and eosinophilic infiltration. Additionally, hyperkeratosis and acanthosis can be found [9, 10]. These abnormalities could be observed in our patient's case before the mucosal ulcerations appeared. Direct immunofluorescence for IgA, IgG and C3 deposits is negative in PSV, which allows to distinguish PSV from blistering autoimmune diseases [11]. Peripheral blood eosinophilia is a common but not mandatory abnormality described in PSV. In the aforementioned research by Clark *et al.*, eosinophilia was present in 3 out of 7 patients with PSV [5], whereas other authors indicate that the rate of eosinophilia in the course of PSV can be much higher, even up to 90% [12]. There was no eosinophilia in the presented case.

Differential diagnosis of PSV should include blistering autoimmune diseases (pemphigus vulgaris, pemphigus paraneoplasticus, bullous pemphigoid, acquired epidermolysis bullosa), bullous drug eruptions, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal

Table 1. Differential diagnosis of pyostomatitis vegetans

Disease	Major typical features
Blistering autoimmune diseases	Positive direct immunofluorescence test ± indirect immunofluorescence test
Chronic ulcerative stomatitis	Chronic condition, SES-ANA present in direct and/or indirect immunofluorescence test
Behçet's disease	International Study Group Criteria for Behçet's disease (recurrent oral ulcerations + 2 of the following: recurrent genital ulcerations, eye lesions, skin lesions, positive pathergy reaction)
Erosive lichen planus	Histopathological features typical of lichen planus Skin and nails lesions typical of lichen planus
Systemic lupus erythematosus	Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus [13]
Herpetic stomatitis	Early age at onset, short course, spontaneous recovery, positive herpes testing
Aphthae	Recurrent episodes, spontaneous recovery
Systemic Vasculitis –Wegener's granulomatosis	Typical histopathological presentation, organ disorders (especially lungs, kidneys), positive ANCA test
Malignant neoplasms	Typical histopathological features, medical history and physical examination findings

necrolysis, chronic ulcerative stomatitis, Behçet's disease, erosive lichen planus, systemic lupus erythematosus, herpetic stomatitis, Wegener's granulomatosis and malignant neoplasms. Typical features of these diseases are presented in Table 1 [13].

In our patient's case, shortly after the excision of previously diagnosed melanoma, skin and mucosal lesions typical of PG appeared. Pyoderma gangrenosum most often coexists with PSV as its vegetating presentation (pyodermatitis vegetans). However, our patient presented with typical PG lesions. It remains unknown whether the procedure of melanoma excision or the melanoma itself should be considered as a triggering factor of PG appearance.

Conflict of interest

The authors declare no conflict of interest.

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