C A S E R E P O R T

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Atypical *pyoderma gangrenosum* in a patient with osteomyelofibrosis

Atipična *pyoderma gangrenosum* kod bolesnika sa osteomijelofibrozom

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Abstract

Background. Atypical forms of *pyoderma gangrenosum* generally appear on the upper extremities; most frequently they are associated with myeloproliferative disorders, including *osteomyelofibrosis*. A response to systemic steroids is more pronounced than in classical form. Sometimes it may be the first sign of an underlying malignancy. **Case report.** We reported a patient with atypical *pyoderma gangrenosum* developed during the course of a myeloid malignancy – *osteomyelofibrosis*. The lesions occurred after a minor trauma. Painful blistering plaques, with an elevated, bluish-gray border were located on the dorsal aspect of hands. No skin malignancy was found. The lesions resolved rapidly to systemic steroids. **Conclusion.** Considering the unusual clinical presentation which makes the diagnosis difficult, as well as the fact that atypical forms of *pyoderma gangrenosum* can be the first sign of malignancies, especially myeloproliferative ones, recognizing this entity enables timely guiding future investigations toward their prompt detection.

Key words:
pyoderma gangrenosum; myeloproliferative disorders; diagnosis; drug therapy; adrenal cortex hormones; treatment outcome.

Apstrakt

Uvod. Atipične forme *pyoderma gangrenosum* obično se javljaju na gornjim ekstremitetima. Najčešće su udružene sa mijeloproliferativnim oboljenjima uključujući i osteomijelofibrozu. Odgovor na opštu kortikosteroidnu terapiju mnogo je brži nego kod klasične forme. Ponekad mogu biti prvi znak postojećeg maligniteta. **Prikaz bolesnika.** Prikazali smo bolesnika sa atipičnom formom *pyoderma gangrenosum* koja se razvila tokom osnovne bolesti – osteomijelofibroze. Lezije na šakama javile su se nakon manje traume. Na dorzumu šaka nalazili su se bolni plakovi sa bulama i uzdignutim, plavosivim, lividnim ivicama. Evaluacijom promena na koži nisu otkriveni znaci kutanog maligniteta. Primenom opšte kortikosteroidne terapije postignuta je brza klinička regresija kutanih lezija. **Zaključak.** S obzirom na neuobičajenu kliničku sliku koja otežava dijagnostiku, kao i činjenicu da atipične forme *pyoderma gangrenosum* mogu biti prvi znak prisustva maligniteta, naročito mijeloproliferativnih maligniteta, poznavanje ovog entiteta omogućava pravovremeno usmeravanje daljih ispitivanja u pravcu njihovog promptnog otkrivanja.

Ključne reči:
pioderma gangrenozum; mijeloproliferativni poremećaji; dijagnoza; lečenje lekovima; kortikosteroidni hormoni; lečenje, ishod.

Introduction

The diagnosis of *pyoderma gangrenosum* (PG) is mostly based on the appearance of typical lesions – raised plaques with progressive central necrosis and a bluish-red necrotising border [1, 2]. Histopathological features are variable and not specific; the presence of vasculitis is thought by some authors to exclude the diagnosis [1].

In 50% of the cases, PG is associated with bowel diseases, although atypical forms are mostly reported with haematologic diseases [3, 4].

Diagnostic difficulties may arise in the absence of systemic disease or with uncommon associations such as myeliod malignancies [1, 2]. Patients with myeloproliferative disorders often have an atypical clinical presentation of PG, with blisters, and relatively superficial involvement, obscuring the correct clinical diagnosis [1, 2, 5, 6].

Myelofibrosis with myeloid metaplasia (chronic myelofibrosis, osteomyelofibrosis) is a primary, Philadelphia negative, myeloproliferative disorder arising from the level of the haematopoetic stem cell. It is characterized with hepato/splenomegaly, anemia and the tear drop erythrocytes with leukoerythroblastic changes in typical cases. The hallmark is bone marrow fibrosis and myeloid metaplasia in the spleen and liver [1, 7]. It is a rare disease of adults and the elderly. Generally, the disorder is progressive, after several

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years, insufficiency of hematopoesis and spleen enlargement becomes the hallmark of the disease [1, 7].

Skin changes in osteomyelofibrosis are infrequent. Dermatitis resembling Sweet's syndrome or PG has already been described [1–3].

Case report

A 66-year-old Caucasian man was admitted to our Institute in November 2006, with lesions on the dorsa al sides of hands, which occurred about a month earlier, after a minor trauma (working on the farm). Lesions enlarged symmetrically and were accompanied by painful sensations.

Family history was unremarkable. In personal history he had osteomyelofibrosis with myeloid metaplasia since 2003. The patient was treated with hydroxyurea (1–1.5 g daily). Because of severe anemia and almost transfusion dependence, the treatment with danazole started (400 mg daily) in the beginning of September 2006. During the episodes of severe anaemia, he also suffered from pneumonia.

A physical examination revealed dark erythematous plaques, of 4 × 6 up to 8 × 10 cm in diameter, with a pronounced, bluish-gray border, hemorrhagic blisters in the dorsal sides of both hands (Figures 1A, 1B), more pronounced in the right one. Vesicles and pustules were noticed on the surface of the lesions (Figure 1A). In the hospital, the lesions enlarged quite rapidly, approximately 0.5 cm weekly, reaching up to 12–14 cm in diameter.

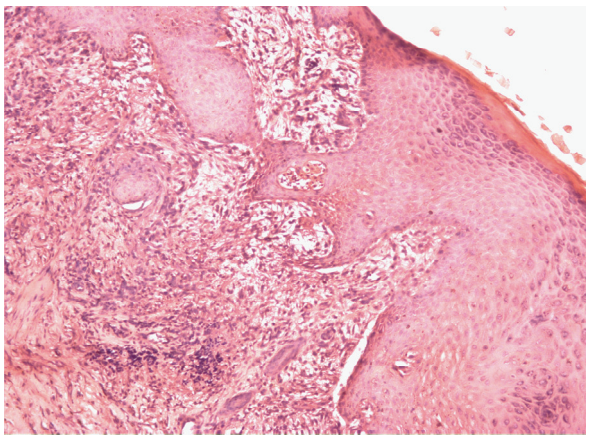

Fig. 2 – Acanthosis and focal spongiosis in the epidermis; dense mixed infiltrate in the dermis (H&E, 40 ×)

Immunological findings of antinuclear antibodies (ANA), and antineutrophil cytoplasmic antibodies (ANCA) were negative. Chest radiography was in physiological limits. Protein electrophoresis was normal. There was a pronounced leukocytosis, up to 34 × 10^9/l, with anemia – read blood cell (RBC) count 2.74 × 10^{12}/l, hemoglobin (Hgb) 80 g/l and thrombocytopenia – platelet (Plt) 49 × 10^9/l. The sedimentation rate was increased – 80 mm in the first hour.

Routine biochemistry, including glucose level, total and direct bilirubine, urea and creatinine, serum electrolytes, liver enzymes was normal, except the raised level of lactate

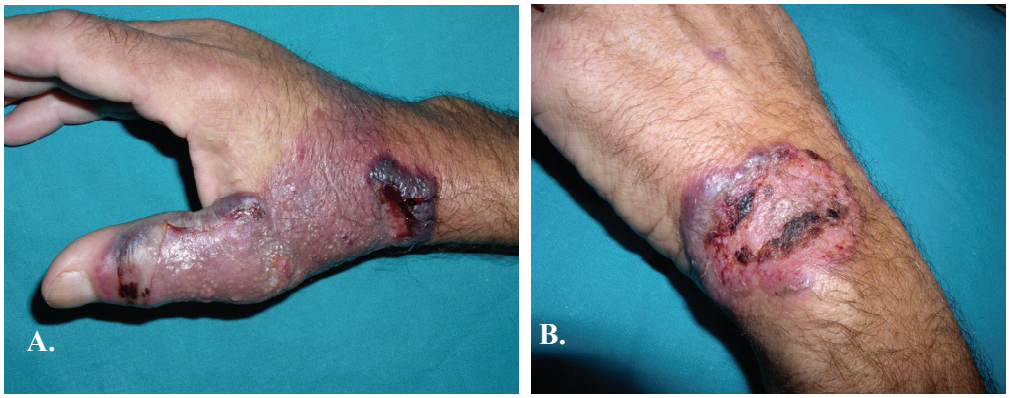

Fig. 1 – A) right hand – dark erythematous plaque with vesicles and hemorrhagic blisters, B) left hand – erythematous blistering plaque with pronounced bluish-gray border

No fever or other symptoms, except for lesional pain, were found.

A histopathological examination of an incisional biopsy of the lesion from the dorsal side of the left hand revealed a dense mixed infiltrate in the papillary and reticular dermis, consisting of lymphocytes, with no obvious malignant transformation and neutrophils. The infiltrate is more pronounced and dense in the reticular dermis, consisting mostly of lymphocytes with rare neutrophils. There were no signs of vasculitic lesions. In the epidermis some irregular acanthosis and focal spongiosis were observed (Figure 2).

Immunohistochemical staining did not reveal any malignancy of the skin lesions (staining for CD34, CD3, c- kit, CD79, CD 68 and myeloperoxidase (MPO) were negative).

dehydrogenase (LDH) (1 700 U/l) and low iron level (5.6 µmol/l).

Echosonography of the abdomen revealed an enlargement of the liver and spleen.

The patient was treated with oral prednisolone, 40 mg/day, and doxycycline, 200 mg/day. After only four days of the initiating therapy, the lesions stopped to enlarge, the inflammatory border was less pronounced. After a week of the therapy the lesions started to regress. Oral prednisolone was gradually tapered after two weeks of the treatment. A month later, only hyperpigmented patches on the dorsal hands were observed, no new lesions occurred (Figure 3). The therapy was completely discontinued two months after the initiation.

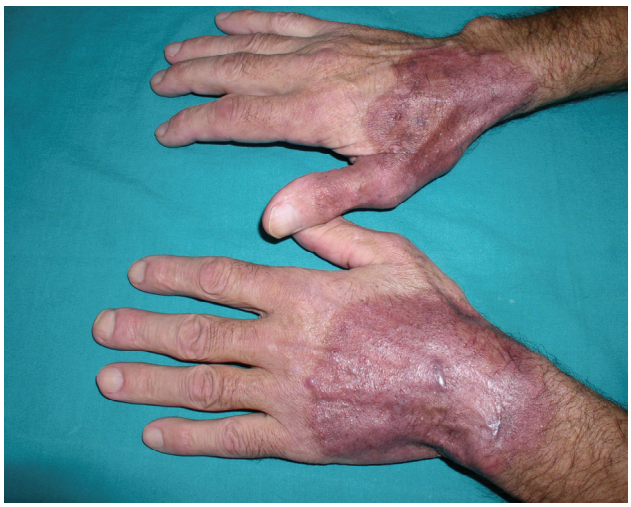

Fig. 3 – Complete regression with hyperpigmented patches

rect diagnosis [3, 5]. With classical PG, the predilection sites are the legs, approximately in 78% of cases. On the contrary, the lesions of atypical forms are frequently located in the upper extremities [4, 6]. Lesions often occur at the sites of minor trauma [4], as in our case, and are more superficial [1–9].

Because of atypical appearance of PG, usually with hemorrhagic blisters, pustules and crusting, especially in the absence of systemic disease, or in the less obvious myeloproliferative disorders, a correct diagnosis may be delayed or missed in such patients [1, 5, 10].

Once the diagnosis has been achieved, the response to steroids is rapid, faster than in classical PG [4]. This rapid response lends further supports to the diagnosis and is thought by some authors to be an essential diagnostic criterion [4, 5, 11].

The development of PG is possible in patients with myeloid malignancy at any stage of the disease, even as the presenting sign; the prognosis of these patients is particularly poor [1, 7].

Discussion

The uncommon association between myeloproliferative disorders and PG is now well documented [1–8]. The lesions are almost usually of an atypical appearance, with a bluish-grey border instead of red violaceus border seen in classical forms of PG and often accompanied by blisters [1, 2]. The distribution of the lesions may be helpful in establishing a cor-

Conclusion

Considering the unusual clinical presentation which makes the diagnosis difficult, as well as the fact that atypical forms of *pyoderma gangrenosum* can be the first sign of malignancies, especially myeloproliferative ones, recognizing this entity enables timely guiding future investigations toward their prompt detection.

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