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Case report

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Jelica Tiodorovic
Viktor Lazarevic
Radmila Milenkovic
Danica Tiodorovic-Zivkovic

Clinic for Dermatovenerology, Clinical Centre Nis

PYODERMA GANGRENOSUM - CASE REPORT

SUMMARY

Pyoderma gangrenosum (PG) is a rare, inflammatory, non-infective, non-neoplastic skin disorder, which is often associated with systemic diseases (1). Etiology of PG is still unknown.

The paper presents the case of a 23 year-old male patient with skin lesions localized on the skin of the face, ear lobe, neck, chest and back. There were numerous pustules, papules, vesicles and blisters filled with hemorrhagic content, and shallow ulcers covered with dark yellow crusts.

The patient had been treated from ulcerative colitis for year and a half prior to skin lesions.

After starting the therapy with Cyclosporine accompanied with low doses of corticosteroids, the overall condition of our patient improved, the number of stools was reduced, and the ulcers on the skin began to epithelize. There have not been new lesions in our patient during these 11 months of follow-up.

Key words: **pyoderma gangrenosum, ulcerative colitis, cyclosporine**

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare, inflammatory, non-infective, non-neoplastic skin disorder, which is often associated with systemic diseases (1).

PG was first recognized as a disease entity in 1930, when Brunsting and two of his colleagues described five patients who had painful, enlarging necrotic ulcers and ulcerative colitis, and initially the cutaneous changes were regarded as a manifestation of inflammatory bowel disease (IBD) (2).

PG mainly affects adults between the ages of 25 and 54; it can also occur in children, usually in association with systemic disease (1). The four main clinical types of PG are ulcerative, pustular, bullous, and vegetative, each with distinctive clinical and histopathological features, varying rates of progression, different disease association, and often requiring different types of treatment (1).

Etiology of PG is still unknown. Although a variety of gram-positive and gram-negative microorganisms have been cultured from ulcers, the early lesions are always sterile.

Overall, approximately 50% of patients with PG have an associated systemic disease. It has been shown that the majority of patients (>70%) with ulcerative PG will have an associated disease such as IBD, arthritis, monoclonal gamapathy, and internal malignancy (1).

Paraneoplastic PG was first described in 1993 by Duguid et al. in four patients with myeloprolifrative malignancy and PG (1).

Case report

The paper presents the case of a 23 year-old male patient, who came to the Clinic for

Corresponding author: Jelica Tiodorovic • Phone: +381 18 232 837 • E-mail: btio@bankerinter.net

Dermatology in February 2006, with few pustules on the face, diagnosed as acne, and an adequate treatment was prescribed. Two or three days later, the patient came to the Clinic for the second time, with new pustules on the skin of the neck and back. This new condition was comprehended as pyoderma, and a smear of the pustules was taken. General condition of the patient was aggravating, and skin lesions were spreading, so the patient was admitted for clinical treatment. On admission, the patient was conscious, highly febrile (40 C), weak and exhausted, with extremely pale skin and visible mucosa, hardly mobile. His blood pressure was 85/50, pulse 105. Anamnestic data were taken from the patient's mother. There was no family history of inflammatory bowel disease.

On the skin of the face, ear lobe, neck, chest and back there were numerous pustules and papules filled with unclear content, and shallow ulcers covered with dark yellow crusts. On the lower extremities there were rare lesions with central umbilicus surrounded by erytematous hallo *(Figures 1, 2 and 3)*.

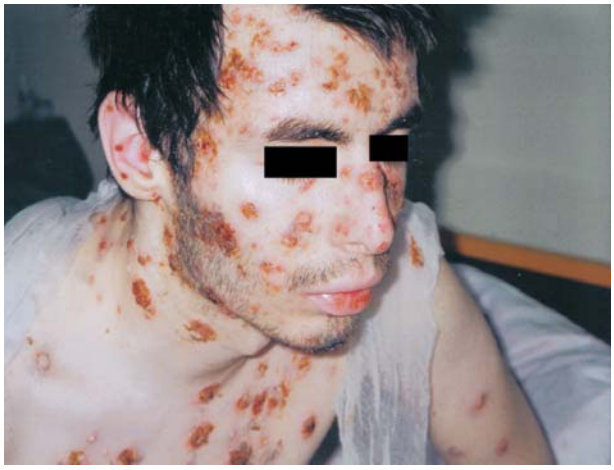

Figure 1. Lesions on the face

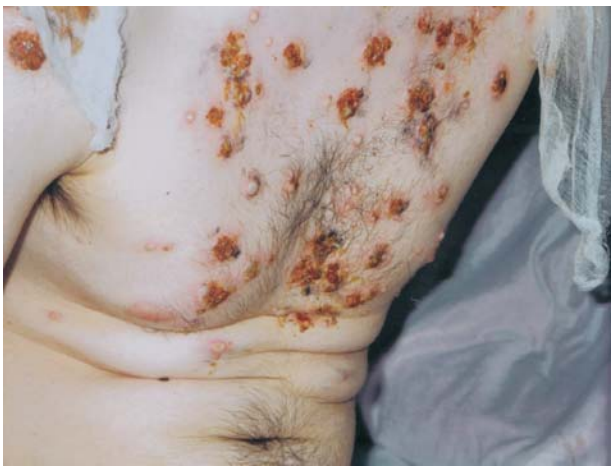

Figure 2. Skin changes on the chest

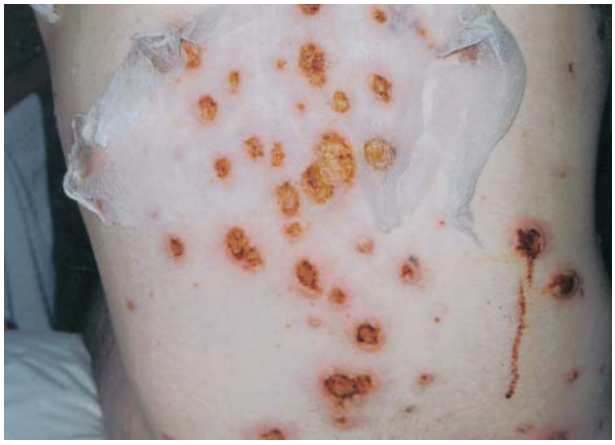

Figure 3. Lesions on the back

Patient had been treated for ulcerative colitis with systemic corticosteroids (initial dose was 40mg and was reduced to 5 mg of prednisolone) and 5-ASA (5-aminosalicylates) for year and a half. In December 2005, he was hospitalized because of blood in the stool and diarrhea, and the dose of prednisolone was increased to 30 mg.

Laboratory studies included sedimentation rate 105 mm/h, leukocyte count 23,0x 10^9/l, erythrocytes 3,12x10^{12}/l, hemoglobin 78 g/l. Levels of glucose, sodium, potassium, chlorides, urea, creatinin in serum and urine, osmotic pressure, and total proteins were normal. Calcium 2,08 mEq/l, albumin 21mg/l, cholesterol 1,91 mmol/l, magnesium 0,62 mEq/, serum iron 4 mol/l, AST 43 U/l, C-reactive protein 214 mg/l. ALT, LDH, and GTA were normal. IgG 16, 70 g/l, levels of IgA, IgM, C3, C4 were normal. Complete work-up for infection including hemoculture, human immunodeficiency serology, hepatitis B and C serology, was negative. VDRL, TPHA, ASTO, Waaler Rose, Latex RF were negative. ANA, c-ANCA and LE cells were not found. Abdominal ultrasound, renal ultrasound and X-ray of lungs and heart were normal.

Smear of the lesion of the skin showed Enterobacter, and Staphylococcus negative to coagulasa in repeated smear. Tissue culture for fungi was negative.

Biopsy was taken from an edge of ulceration: intense mixed inflammatory infiltrate consisting of neutrophiles, plasmocytes and some eosinophils.

The gastroenterologist and specialist for infectious diseases were consulted. The patient was treated with multiple systemic and therapies (Prednisolone, Vancomycin, Metronidazole, Rifampicin, Tienam (imipenem and cilastatin sodium), Acyclovir, Fluconazole, 5-ASA, Endobulin (intravenous immunoglobulin)), and substitution therapy (albumin, plasma, washed erythrocytes). The local therapy included diluted potassium permanganate

solution, corticosteroids, and silver sulphadiazine cream applied twice per day to the ulcers, hydrocolloid dressings.

In spite of this therapy, diarrhea and blood in the stool persisted, and the skin lesions were getting worse. Because of the arising of bullas, the patient was sent to another institution in Belgrade *(Figure 4)*.

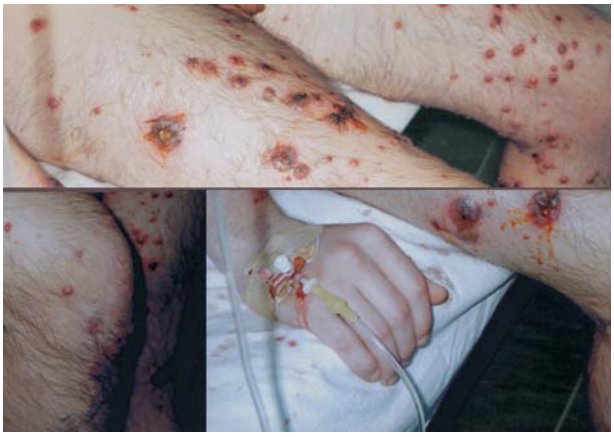

Figure.4. Skin lesions on the lower extremities

Biopsy of the skin lesion was repeated: subcorneal pustules, large amount of neutrophiles in the upper dermis, fibrinoid necrosis in the capillary walls. Blood vessels of dermis were edematous.

The patient was treated in the Gastroenterology Clinic in Belgrade, where biopsy of the colon and rectum were taken. Biopsy showed active ulcerative colitis. After corticosteroids, the number of stools was reduced.

Neoral (Cyclosporine) was induced in the therapy with initial dose of 6mg/kg, with reducing to 4mg/kg, with the low dose of corticoids. Serum levels of cyclosporine were 209 mg/ml at the beginning of therapy and 124mg/ml when reduced.

There were atrophic scars on the places of prior skin lesions.

DISCUSSION

In adults, PG may arise in healthy population, or in the subjects with systemic disease (1). In our patient, ulcerative colitis was diagnosed a year and a half prior to the skin lesions.

PG occurs in 0.5–5.0% of the patients with ulcerative colitis (3).

The four main clinical types of PG are ulcerative, pustular, bullous, and vegetative (1). There are unusual presentations of PG: pathergic, peristomal, PG of the head and neck, PG of the dorsum of the hand, PG with multisystemic involvement, paraneoplastic PG (1). It should be recognized, however, that more than one morphological variant may be seen in individual patient, so this classification is based on the predominant feature presenting to the clinician of that patient. In our patient, the skin lesions presented simultaneously in a form or pustules and shallow ulceration.

Typical lesions (95%) arise on the trunk and limbs, while atypical variants develop in the head and neck (4). The first lesions in our patient arose on the skin of his face, spreading to the skin of the entire body.

Diagnosis of PG is made on the basis of clinicopathologic findings and exclusion of conditions that can mimic PG. These include entities such as: infectious, vasculitic, neoplastic, and connective-tissue disorders (5). Laboratory and other investigations excluded infectious, vasculitic, neoplastic disorders, or disorders of connective tissue in our patient.

Histology of PG is not specific. Lesions may reveal a neutrophilic vascular reaction early on, whereas fully developed ulcerations may exhibit marked tissue necrosis with a surrounding infiltrate of mononuclear cells (6). In our case, the biopsy pointed to the diagnosis of PG.

Specific treatment for the cutaneous lesions may be local or systemic, and often a combination of both is required depending on the type of PG lesions being treated. Also, the age, mobility, and compliance of the individual patient should be considered. In addition, because of the persistent and recurrent nature of PG, a long-term maintenance therapy may be required in some patients. As a general measure, bed rest, pain relief, correction of anemia, nutrition, and management of associated disease are important (1).

Several agents are commonly used in systemic therapy used for PG: Corticosteroids, Minocycline, Dapsone, Cyclosporine, Tacrolimus, Mycophenolate mofetil, Clofazamine, Infliximab, Azathioprine, Methotrexate, Cyclophosphamide, Interferon-α, Thalidomide, and Colchicine (7-11). Systemic steroid therapy (1 to 2 mg/kg/day given in divided doses) remains the treatment of choice and will lead to rapid relief of pain and initiation of healing in most patients (2). Many immunosuppressive agents have been reported to be successful in individual or small series of patients, but with the possible exceptions of cyclosporine and tacrolimus they have not offered an improved risk/benefit ratio in terms of positive outcome when compared with systemic steroid therapy (2). In 1994, Lichtiger *et al*. first reported cyclosporine A (CYA), another immunosuppressant, to be highly effective against severe corticosteroid-resistant ulcerative colitis (3).

Locally effective agents that have been found to be helpful in reported cases of PG are: corticosteroids-topical or intralesional, Tacrolimus, intralesional cyclosporine, hyperbaric oxygen, disodium chromoglycate, macrophage colony–stimulating

factor intralesional, human platelet-derived growth factor, skin grafts (12, 13, 14).

After starting the therapy with Cyclosporine accompanied with low doses of corticosteroids, the overall condition of our patient improved, the number of stools was reduced, and the ulcers on the skin begun to epithelize *(Figures 5 and 6)*.

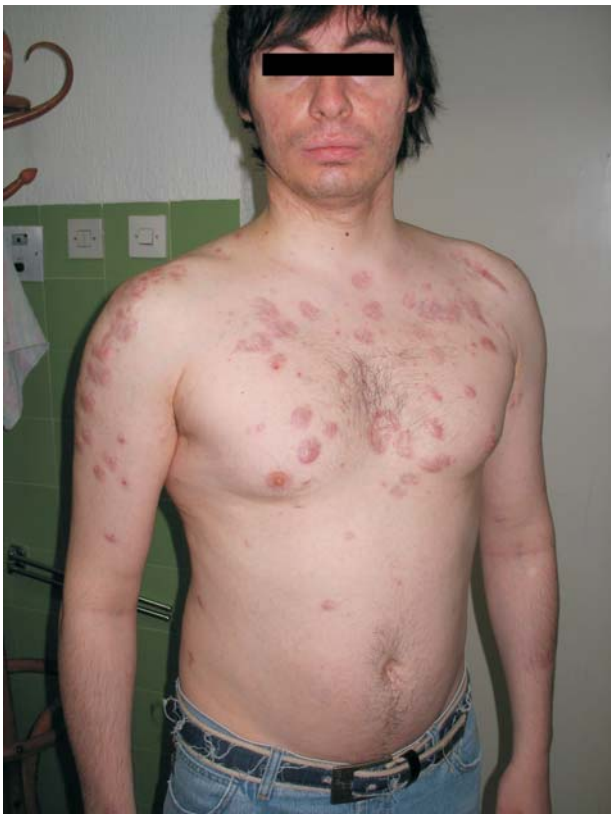

Figure 5. Scars on the sites of prior lesions on the chest

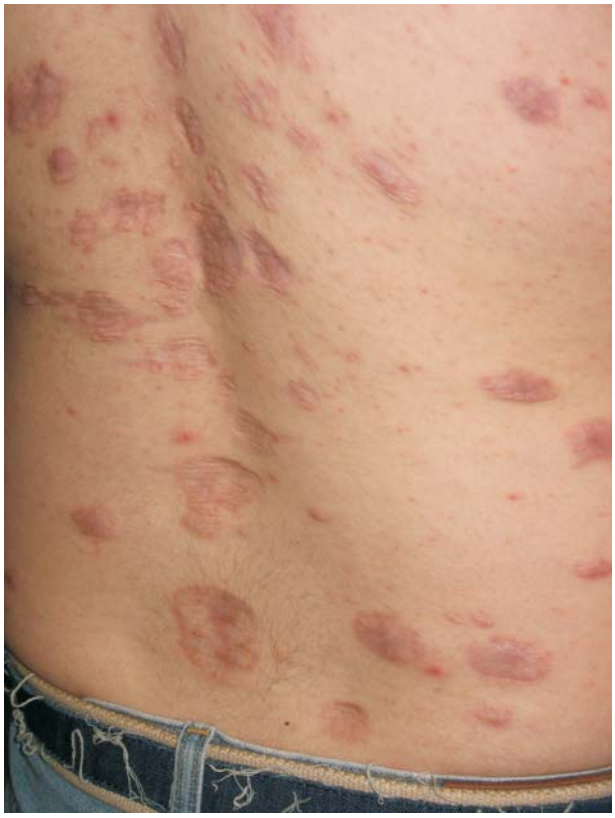

Figure 6. Scars on the sites of prior lesions on the back

There have been no new lesions in our patient during these 11 months of follow- up.

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PYODERMA GANGRENOSUM - PRIKAZ SLUČAJA

Jelica Tiodorović, Viktor Lazarević, Radmila Milenković i Danica Tiodorović-Živković

Klinika za dermatovenerologiju, Klinički centar Niš

SAŽETAK

Pioderma gangrenosum (PG) je retka, inflamatorna, neinfektivna, neneoplastična kožna bolest, koja je često povezana sa sistemskim bolestima (1). Etiologija PG je nepoznata.

Prikazujemo 23-godišnjeg bolesnika sa promenama lokalizovanim na koži lica, ušnih školjki, vrata, leđa i grudnog koša, u vidu brojnih pustula, vezikula i bule ispunjene hemoragičnim sadržajem, kao i plitke ulceracije prekrivene krustom.

Godinu i po dana pre prijema bolesnik se leči od ulceroznog kolitisa.

Nakon terapije Cyclosporinom i niskim dozama kortikosteroida, opšte stanje bolesnika se poboljšalo, broj stolica se smanjio, ulceracije počele da epitelizuju. Nema novih promena tokom 11 meseci praćenja.

Ključne reči: **pioderma gangrenosum, ulcerozni kolitis, cyclosporin**

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Chapters:

4. Rycroft RJG, Calnan CD. Facial rashes among visual display unit (VDU) operations. In: Pearce BG (ed), Health hazards of VDUs. Willey, London, 1984: 13-15.

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Associate Professor
E-mail: anagorni@bankerinter.net

Faculty of Medicine
81 Dr Zoran Djindjic Blvd.
18000 Nis, Serbia
Phone: +381 18 226 712
Fax: +381 18 238 770
ana@medfak.ni.ac.yu
bojana@medfak.ni.ac.yu

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