Pyoderma gangrenosum in the head location: a clinical study of three cases

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Post Dermatol Alergol 2011; XXVIII, 5: 412–417

Abstract

Pyoderma gangrenosum is a rare disorder whose aetiopathology is still unknown. The clinical manifestation of the disease is the presence of extensive ulcerations. Skin lesions can occur in several locations – on the trunk, on the limbs and also rarely in the skin of genitourinary organs. We present three cases of pyoderma gangrenosum in the rare head localization with diagnostic and therapeutic difficulties associated with this disorder.

Key words: pyoderma gangrenosum, diagnostic procedures, treatment.

Introduction

Pyoderma gangrenosum (gangrenous dermatitis, pyoderma gangrenosum – PG) is a rare skin disease with a not yet fully understood aetiology. It was first documented by Brunsting, Goeckerman and O'Leary in 1930 [1].

It is estimated that 3-10 patients per million per year will present with the disease. Most commonly it appears between the 20-50th year of life, with a predominance for female gender. The aetiopathogenesis is the subject of many studies. It is theorized that due to an unidentified stimulus an uncontrolled and abnormal acute inflammatory response occurs [2]. The clinical picture of this disease presents as difficult healing ulcers of different sizes and in varying locations. However, most reported cases of PG are located on the trunk and lower extremities [3]. Commonly, the first presenting skin change is a deep, painful nodule or a superficial bleeding pustule. Sometimes the skin change has a tendency to occur in areas having a disruption of the skin e.g., after surgical procedures, trauma, or even, as in the case of one of the described patients, after an insect bite. A characteristic feature of this disease, called pathergy, describes a reaction causing rapid spread of skin changes under the influence of minor abrasions, such as injection, surgical incision, etc. Presented below are 3 separate cases of pyoderma gangrenosum of atypical localization – skin of the head and neck.

Case reports

Case 1

A 60-year old man presented to the Clinic of Dermatology in Gdansk, because of skin changes characterized by 2 shallow ulcerations with the diameter of 10/18 cm and 12/20 cm localized in the region of the neck and occiput (Fig. 1). The first presenting skin change appeared in June 2009. The patient associated the skin pathology with a recent insect bite. The first medical contact was with the patient's primary physician, who made a referral to a surgeon. Oral and local antibiotics were prescribed. Due to lack of improvement and enlargement of skin lesions despite the antibiotics, the patient was admitted to the Dermatology Clinic at the Department of Dermatology, Venereology and Allergology, Medical University of Gdansk in March 2010.

During the physical examination, observation of the lesion demonstrated widespread yet shallow ulceration without signs of infection. In the region of the lesion, granulation tissue was observed. Skin biopsy was taken for histopathological examination (sample no. 7340/10). Results were as follows: epidermal hyperplasia with preserved maturation, a shallow erosion and infiltration of granulocytic cells in the circumference between healthy skin and lesion, and minute fibrosis under the area lacking epithelium. On the basis of the above examination, pyoderma gangrenosum cannot be excluded. The patient was referred to the Clinic for hospitalization, during which

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further tests were performed, including laboratory, microbiological, and radiological imaging. No significant aberrations were discovered. The patient does not suffer from any chronic illness. Also, on physical examination no significant anomalies were found. Treatment consisted of cyclosporine A 300 mg/day under the control of blood pressure and renal function. Local treatment consisted of octenidine dihydrochloride twice daily. After initiation of treatment, minor improvement of the lesion was observed. After approximately 4 weeks of monotherapy with inadequate results, methylprednisolone 32 mg/day orally was added. Also dexamethasone spray twice daily was used on the skin lesion. After 3 weeks of combination therapy, successful decrease in diameter of the ulcer was observed (Fig. 2). The patient was scheduled for regular control every 3 weeks.

Case 2

A 78-year old man was admitted to the Clinic because of deep ulceration of the occiput and temporal-parietal region as well as the oral mucosa. The first changes appeared in December 2009. Originally the clinical picture was an inflamed tumourous mass on the occiput, which after surgical incision progressed to ulceration (Fig. 3).

In addition, shortly after, a second tumour appeared on the temporal-parietal region with the diameter of 5 cm. Also, granular tissue changes appeared in the oral cavity accompanied by a shallow round erosion on the mucosa of the left cheek. The patient presented with dispersal of the skin lesions of the head soon after the surgical procedure. The oral cavity lesions appeared 1 week after tooth extraction performed by a dentist.

The patient was admitted to the Clinic of Dermatology, Medical University of Gdansk, where based on the clinical picture and history of progression, pyoderma gangrenosum was diagnosed. During the physical examination two lesions were observed, characterized by a disintegrating tumourous mass. One was in the region of the occiput of a diameter of 9 cm with a small, deep ulceration in the central region. The other lesion was a smaller tumour of a similar description on the temporal-parietal region of diameter of 4 cm (Fig. 4). In the oral mucosa an infected ulceration was present.

Accompanying the lesions, the patient complained of severe pain and required treatment with non-steroid anti-inflammatory drug. On history taking it was noted that the patient was under the diagnosis of prostate cancer. Due to increased value of prostate-specific antigen, which was at the level of 19 ng/ml, prostate biopsies were carried out 4 times. This together with ultrasound and computed tomography did not confirm the presence of an expansive process. After recommendation from the urologist the patient received finasteride at a dose of 5 mg/day and tamsulosin 0.4 mg/day.

Additionally, in January 2010 the patient was diagnosed with depression and antidepressant therapy with sertraline 50 mg/day was initiated.

Recently, the patient had noticed a significant loss of body weight of approximately 10 pounds in a period of 2 months.

Laboratory, microbiological and imaging studies which were performed in the Clinic revealed no significant aberrations. After both urological and oncological consultation the patient was considered fit for immunosuppressive treatment. Pharmacological therapy included cyclosporine A 300 mg/day and prednisone 40 mg/day. On the skin lesions octenidine dihydrochloride was applied. The preparation contains proteo- and fibrolytic enzymes in a 0.5% solution of Argentum nitricum. After treatment a significant improvement of the skin changes was achieved (Figs. 5 and 6). In addition, the level of

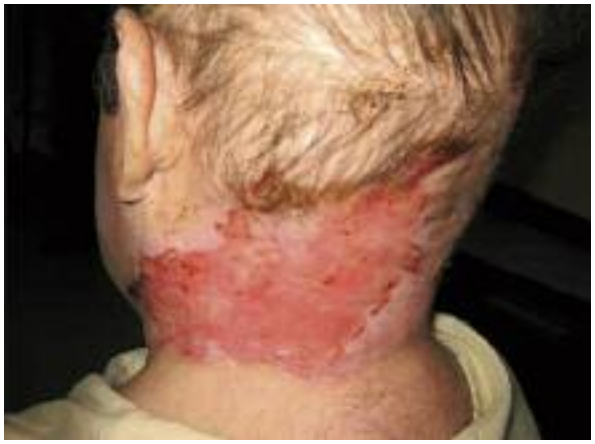

Fig. 1. Clinical picture of the skin lesions on the day of admission to the Clinic. Multiple widespread erosions visibly separated from the healthy skin

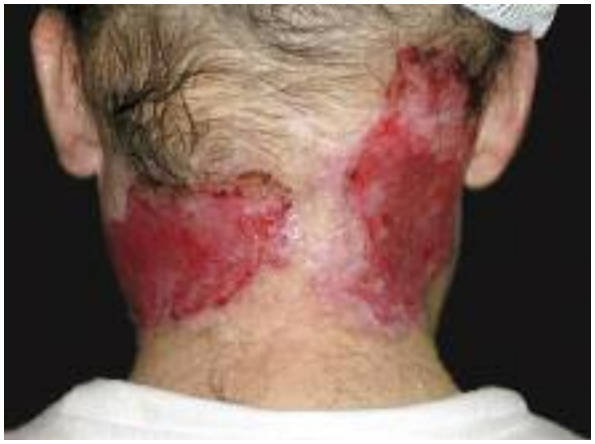

Fig. 2. Clinical picture of the skin lesions after 3 weeks of combined treatment with cyclosporine and methylprednisolone

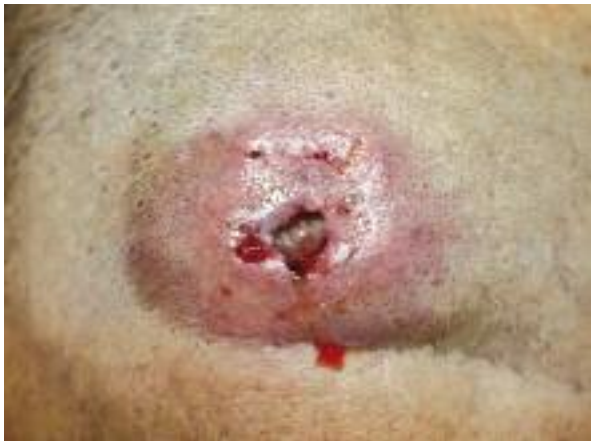

Fig. 3. Clinical picture of primary skin lesion before surgical intervention (picture thanks to kind permission of patient's family)

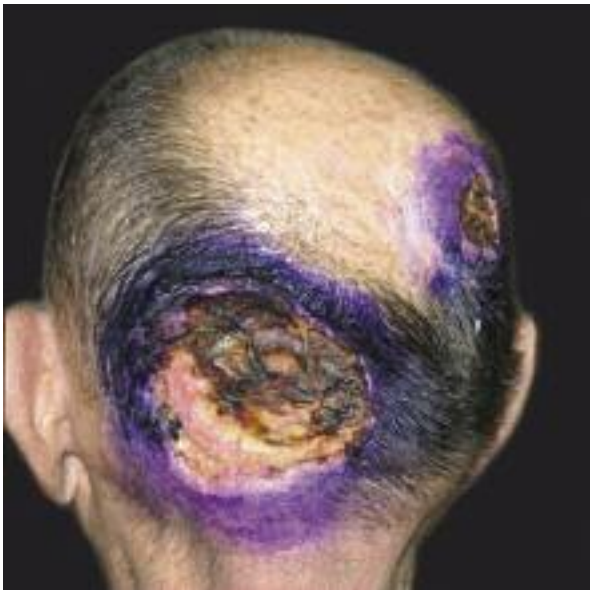

Fig. 4. Clinical picture of the skin lesions on the day of admission to the Clinic

prostate-specific antigen decreased substantially. Currently, the patient is under constant observation by the Department of Dermatology.

Case 3

A 68-year-old man was admitted to the Clinic in May 2010 due to extensive ulcerations of the skin of the head. 5-7 years ago, the patient suffered a fall from a height, in which the patient sustained significant head trauma. Intracranial bleeding was present and a craniotomy was performed; this was probably the initiation of the skin changes. The patient suffered from a number of systemic diseases: diabetes, insulin-dependent type 2, hypertension and renal failure. The patient was found several years earlier to have psycho-organic features and for this reason it was not possible to obtain an accurate history. The information gained from his daughter was that the patient for the past 4 years was under the care of a surgeon who performed surgical debridement of the wound, and was preparing to cover it with a graft. On the date of hospitalization, on the scalp a very large ulcer of size 15 cm/30 cm covering the entire parietal, frontal and occipital area was present. The skin lesion was deep, surrounded by a border of inflammation (Fig. 7). The laboratory, microbiological and imaging studies had shown evidence of urinary tract infection, chronic kidney disease and anaemia. The swab of the ulcer was colonized by a methicillin-resistant strain of *Staphylococcus aureus*. After the implementation of antibiotic therapy and stabilization of the patient at the Department of Nephrology, Medical University of Gdansk, azathioprine 100 mg/day and prednisone 40 mg/day was implemented. Locally

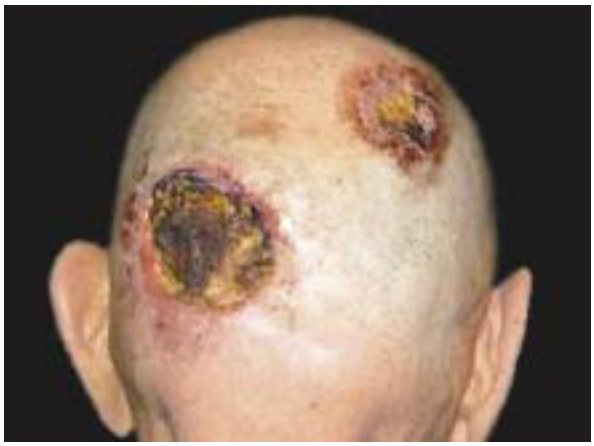

Fig. 5. Clinical picture of the skin lesions 3 weeks after combined treatment of cyclosporine and corticosteroids

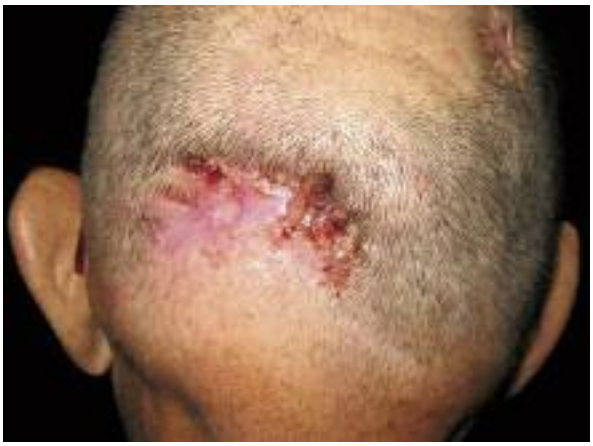

Fig. 6. Clinical picture of skin lesions 4 months after therapy. Almost complete healing of the ulceration

applied dressings of octenidine dihydrochloride were performed twice daily. After treatment, gradual decrease of inflammation around the ulcer was observed. The skin lesion has been steadily declining in depth and diameter. Currently, the patient is under the care of an Outpatient Clinic and in good condition. During follow-up visits to the clinic a significant improvement of the local skin is observed. Treatment is kept unchanged.

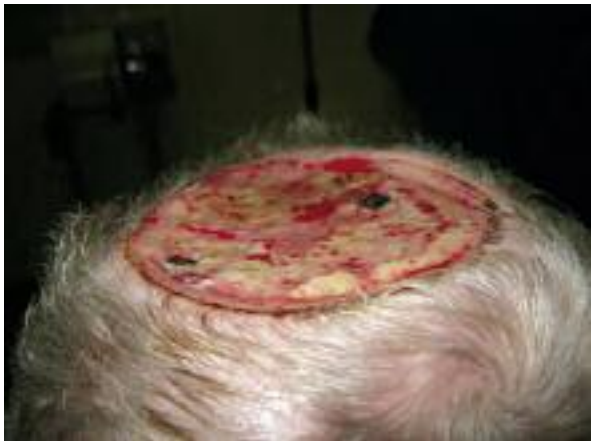

Fig. 7. Deep ulceration on the head skin with visibly separated heaped-up edge

Discussion

Gangrenous dermatitis is often one of the first signs of an existing tumour or a chronic inflammatory systemic disease. In about 50% of cases PG is associated with systemic disease. The most common disorders seen in patients with PG are the inflammatory bowel diseases such as ulcerative colitis or Crohn's disease. The PG also occurs in patients with monoclonal gammopathy and proliferative haematological disorders [4, 5]. In the course of PG, apart from skin changes, neutrophil infiltrations of the lungs, heart, nervous system and gastrointestinal tract can be found [6]. In case 2 abnormal PSA levels were observed, and therefore, consultation of the patient excluded the presence of urological and prostate cancer. However, all patients with this severe dermatosis should undergo vigilant oncological observations.

One of the major problems encountered in clinical practice is that the condition is not recognized by doctors in other specialties. This was the case as described above, in 2 patients (patients 2 and 3). In the second description the patient was diagnosed with bacterial skin infection, furunculosis. Incision of the skin lesions was performed, which gave rise to pathergy and rapid spread of the ulcer. In the third patient there were several attempts at surgical intervention involving the transplantation of skin. The skin lesion was diagnosed as a classic post-traumatic ulcer.

Treatment of PG is very difficult and longstanding. So far there is no universal treatment regimen of severe dermatosis. General immunosuppressive drugs used alone or in combination play the most important role in the treatment of PG. Choosing the right agent depends on many factors. First of all, one must take into account the size and depth of the lesion and the rate of spread of the outbreak of the disease. Moreover, the choice of therapy depends on the condition of the patient and accompanying diseases. In the case of topical treatment, the degree of purity of the lesion should be assessed, and measures to protect the wound from bacterial colonization should be taken. One should not forget that during the general immunosuppressive therapy, open skin lesions are particularly vulnerable to superinfection by pathogens. In the literature there are few reports on the effectiveness of drugs used only topically to change the course of cutaneous PG. The most beneficial treatment is topical treatment with triamcinolone acetate along the edges of ulcers twice a week. For small changes, this method can be used as a monotherapy, but in most cases it is part of a combination therapy with general agents. As previously reported, efficacy has been seen in the use of topical formulations of tacrolimus, strong steroids under occlusion or injection of cyclosporine [7-10]. In single cases an improvement of the skin after application of topical nitrogen mustard, sodium cromoglycate, or 5-aminosalicylic acid has been reported [8, 11]. However, by choosing to apply topical formulation to the skin changes in the course of PG, one must keep in mind the rate of absorption into the body of the drug from the skin and the side effects associated with it. Therefore, in the above-described clinical cases, the primary method of treatment was topical disinfectant containing alcohol dihydrochloride octenidine and phenoxyethanol. Only in one case of a shallow ulcer, where the local absorption is limited, was it decided to include the preparation of steroid spray.

Before initiation the appropriate formulation for the treatment of general PG, one must remember to screen for inflammatory or malignant systemic diseases. The basis of treating dermatosis is glucocorticosteroids. The most commonly used drug in monotherapy and in combination is prednisone at a dosage of 1-2 mg/kg body weight/daily [2, 9, 12]. The introduction of corticosteroids causes a very rapid initiation of healing. An equally common immunosuppressive drug used in PG is cyclosporin A [13-17]. This medicine should not be used in patients suffering from renal failure or hypertension, or in patients with haematological disorders. In gangrenous dermatitis the most commonly used dose of cyclosporine A is 2-3 mg/kg b.w./daily. During long-term treatment with this drug, both kidney function and blood pressure should be closely monitored.

Another drug for the treatment of PG is dapsone. The drug is part of the sulfones group and is used either alone or in combination with corticosteroids. In medium and

severe cases, the recommended dose is 100-400 mg/daily. In severe forms of PG the immunosuppressive drug azathioprine can be used. It is cytotoxic and causes abnormal DNA synthesis [8, 14]. For the third patient described, it was decided to include this agent due to the underlying diseases that did not allow for treatment with cyclosporine A. Also, the skin lesion was very extensive and that contributed to the decision to treat with azathioprine.

Methotrexate, tacrolimus and cyclophosphamide are other drugs also used in the treatment of dermatoses. However, they are most commonly used as second-line agents and rarely at the beginning of treatment [18, 19].

Immunoglobulins are an alternative to immunosuppressive treatment for PG. The literature describes cases of complete remission of skin lesions after an intravenous dose of 2 g/kg body weight per month divided into three-per-day infusions [20].

Due to the pathergy effect seen in patients with pyoderma gangrenosum, invasive treatment should be avoided, including skin biopsies and frequent deep injections. However, in very severe forms of the disease, in which despite aggressive treatment with combined therapy there is no overall reduction in skin lesions, one should take into consideration auto-or allo-transplantation of keratinocytes. According to reports, Phillips *et al.* [21] after about 6 weeks after transplantation there was a decrease in ulcer diameter of about 2 cm, while the associated pain almost completely disappeared. The transplantation of epidermal cells in this case initiated the healing of ulcers, which could not be achieved using general high-dose therapy [21]. A very promising method, not only in skin diseases, employs fibroblast cell cultures. Fibroblast cultures are the best source of cellular material harvested for autologous transplantation. However, these treatments are difficult to obtain and expensive.

Increasingly popular drugs in dermatology are biological agents. Recent studies have demonstrated their effectiveness in treating PG, especially in cases where the skin changes are accompanied by changes in inflammatory bowel disease or rheumatoid arthritis. Most data in the literature concern the effectiveness of infliximab and etanercept in the treatment of PG [22, 23]. There have also been increasing reports of the use of other biologics such as etanercept, adalimumab, and alefacept in the treatment of skin diseases [24-26]. The advantage of using biological agents compared to classical formulations is that the remission of skin lesions is very rapid. Unfortunately, this therapy is expensive and not fully explored in terms of long-term side-effects.

Conclusions

Gangrenous dermatitis is a dermatosis increasingly encountered in clinical practice by dermatologists and doctors in other specialties. Early diagnosis and selection of proper treatment can be difficult. It is essential to have knowledge about the disease and the factors contributing to its rapid progression.

In selecting agents for the treatment of dermatoses, patients with underlying diseases should always be taken into consideration. A thorough diagnosis must always be performed to confirm PG. It is extremely important to maintain photographic documentation of skin lesions, which allows one to monitor the effectiveness of the induced therapy.

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