® Postepy Hig Med Dosw (online), 2016; 70: 210-218
e-ISSN 1732-2693

www.phmd.pl
Original Article

Received: 2014.08.04
Accepted: 2016.01.15
Published: 2016.03.16

Wegener's granulomatosis and pyoderma gangrenosum – rare causes of facial ulcerations*

Rzadkie przyczyny owrzodzeń twarzy na przykładzie ziarniniaka Wegenera i piodermii zgorzelinowej

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Karolina Kędzierska[1,A B D E], Krzysztof Sindrewicz[2,B D E F], Tomasz Smektała[2,D E], Magda Wiśniewska[1,A D], Marek Masiuk[3,D E], Ewelina Staniszewska[2,D E], Katarzyna Sporniak- Tutak[2,A D], Edyta Gołembiewska[1,A D], Kazimierz Ciechanowski[1,A D]

[1]Department of Nephrology, Transplantology and Internal Medicine, Pomeranian Medical University, Szczecin, Poland
[2]Department of Maxillofacial Surgery, Pomeranian Medical University, Szczecin, Poland
[3]Department of Pathomorphology, Pomeranian Medical University, Pomeranian Medical University, Szczecin, Poland

Summary

Background: Pyoderma gangrenosum (PG) is caused by immune system dysfunction, and particularly improper functioning of neutrophils. At least half of all PG patients also suffer from autoimmunological diseases, one of which is Wegener granulomatosis (WG). The purpose of this article was to compare cases of patients with WG and PG in terms of their clinical course, histopathology, and applied treatment. In both, histopathological features are not fully distinct. Data from microbiological and immunological evaluation and clinical presentation are required to establish the diagnosis. We also present the case of a patient with WG and deep facial skin lesions not responding to standard treatment.

Methods: Systematic review of the literature in PubMed using the search terms "Wegener granulomatosis AND Pyoderma gangrenosum" and case report.

Results: The finding of 22 reports in the literature (PubMed) suggests that it is a rare phenomenon. This study revealed a similar rate of comorbidity of WG and PG in both genders and an increased incidence of both diseases after the age of 50. Among skin lesions there was a dominance of ulceration, most often deep and painful, covering a large area with the presence of advanced necrosis and destruction of the surrounding tissue. The most common location proved to be the cervical-cephalic area. The most popular treatment included steroids with cyclophosphamide.

Discussion: The rarity of the coexistence of these two diseases results in a lack of effective therapy. In such cases sulfone derivatives are still effective and provide an alternative to standard immunosuppression methods. Hyperbaric therapy and plasmapheresis can also play an important complementary role.

Keywords: **skin ulcer • pyoderma gangrenosum • Wegener granulomatosis • dapsone • hyperbaric oxygenation.**

* Work funded by the statutory budget of the Pomeranian Medical University.

Full-text PDF: http://www.phmd.pl/fulltxt.php?ICID=1197372

Word count: 2982
Tables: 1
Figures: 7
References: 30

Author's address: Karolina Kędzierska, MD, PhD, Department of Nephrology, Transplantology and Internal Medicine, Powstańców Wlkp. 72, 70-111 Szczecin, Pomeranian Medical University, Poland; e-mail: karolina.kedzierska@gmail.com

Introduction

Wegener's granulomatosis (WG) is a systemic disease of unknown etiology which is characterized by the presence of granulomas and necrotizing vasculitis of small and medium-sized blood vessels with a predilection for the respiratory system, kidneys and skin. Skin lesions can occur in up to 50% of cases of this disease [25]. Cutaneous manifestations described in WG include palpable purpura, pyoderma-like ulcerations, subcutaneous nodules, pustules, gingival hyperplasia, small ulcers or panniculitis [5,9]. There are no pathognomonic lesions for WG in the histopathological presentation, which in the case of purely cutaneous manifestations of the disease can be difficult to diagnose and must be differentiated from various disease entities with different etiologies. One, described as slow-healing skin lesions in the course of WG, is pyoderma-like ulcerations. On the other hand, at least half of all pyoderma gangrenosum patients also suffer from systemic illnesses, and one of them is Wegener granulomatosis. Pyoderma gangrenosum is a condition that leads to skin necrosis and development of deep ulcers that usually occur on the legs (the 'typical' ulcerative form). An 'atypical' form of PG is more superficial and occurs in the hands and other parts of the body; both forms lead to chronic wounds. Though the etiology of PG is not well understood, the disease is thought to be due to immune system dysfunction, and particularly improper functioning of neutrophils [8]. The purpose of this article was to compare cases of WG described in the literature with features of pyoderma gangrenosum in terms of its clinical course, histopathology, and applied treatment. In addition, we present the case of a young patient with WG with facial skin lesions not responding to standard treatment. The process leading to the final diagnosis of PG and the application of effective therapy is then discussed.

Case report

Patient's medical history

A 20-year-old patient was admitted to the Rheumatology Department because of swelling and gingival overgrowth. The first symptoms occurred when the patient was 19 years of age and increased significantly during pregnancy. After giving birth, hemorrhagic-purulent nasal discharge, conjunctival hyperemia, and uveitis of the right eye were apparent. The typical clinical picture and necro-inflammatory lesions of the nasal mucosa found at a histopathological examination, despite the absence of antineutrophil cytoplasmic antibodies (ANCA) and no changes seen in chest X-ray, led to a diagnosis of Wegener's granulomatosis. Initially, the patient was effectively treated with methylprednisolone pulse therapy (3x500 mg), as well as maintenance therapy with Prednisone (dose of 40 mg), and cyclophosphamide (6 pulses of 1 g). For half a year the patient did not appear for routine visits.

One year later at the time of admission to the Department of Nephrology the patient was found to have: a nodular lesion within the right cheek below the zygomatic bone with a massively revised buccal mucosa, the presence of a fistula between the right cheek and the oral cavity and external auditory meatus, an ulceration of a diameter of around 0.5 cm with purulent leakage below the right ear, early stage lockjaw and finally strawberry gingival hyperplasia (Fig. 1). The patient still did not present any other clinical signs or symptoms.

Laboratory parameters: hemoglobin – 6.14 mmol/l (normal range: 7.7-10); hematocrit 0.32 (0.37-0.47); leukocytes 12.32 x 10^9/l (4-10); eosinophil count 0.85 x 10^9/l (0- 0.85), monocyte count 0.65 x 10^9/l (0.1- 0.9); creatinine level 0.82 mg/dl (0.5- 1.0). Electrolyte levels, liver enzymes levels and urine examination were all normal.

Antibody analysis: ANCA were negative (indirect immunofluorescence)

Ultrasound examination of the kidneys: normal.

Computed tomography (CT):

- Paranasal sinuses CT showed a thickening of the mucous membrane of the alveolar recesses of both the maxillary sinuses and the presence of a pathological mass in individual posterior ethmoid cells on the right side without evidence of bone destruction.

- Chest CT showed a subpleural nodule measuring 3.5 x 3 mm in segment IX of the right lung, and a subpleural nodule measuring 2.5 mm in segment VI of the left lung.

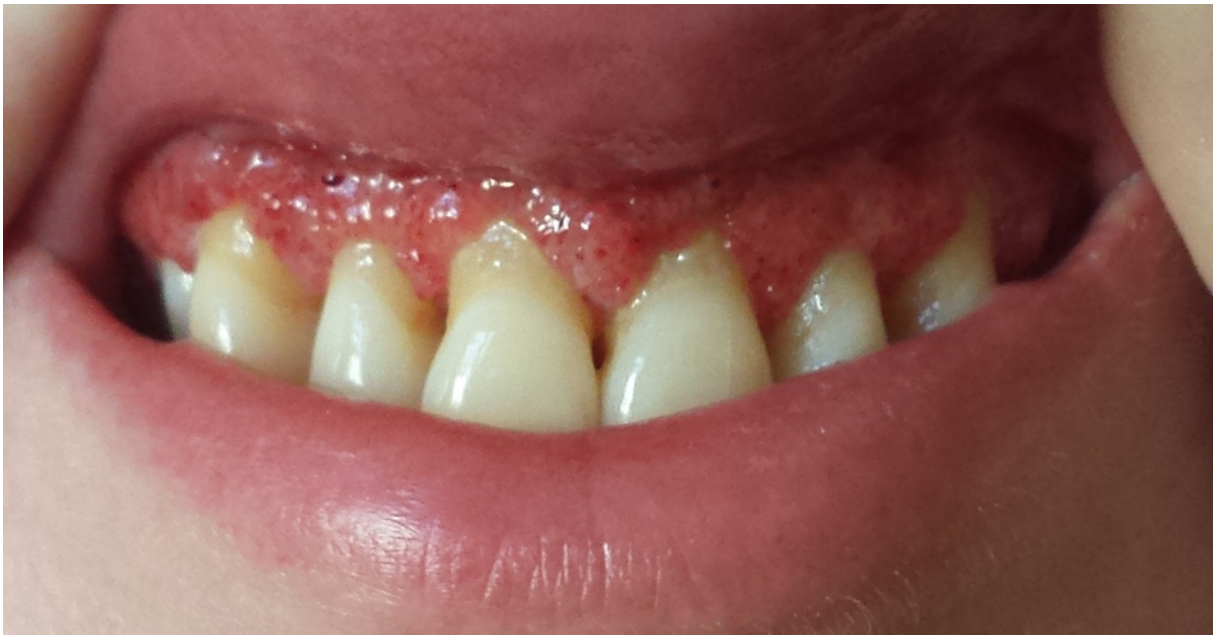

Fig. 1. Strawberry gingival hyperplasia

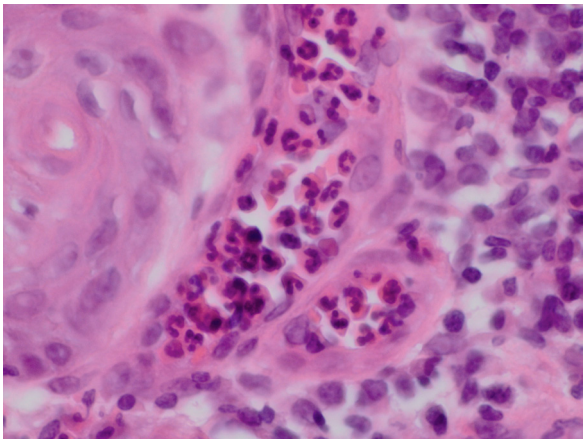

Fig. 2. Cross sections of small vessels with polymorphonuclear leukocytes within their walls can be seen in inflammatory infiltrate

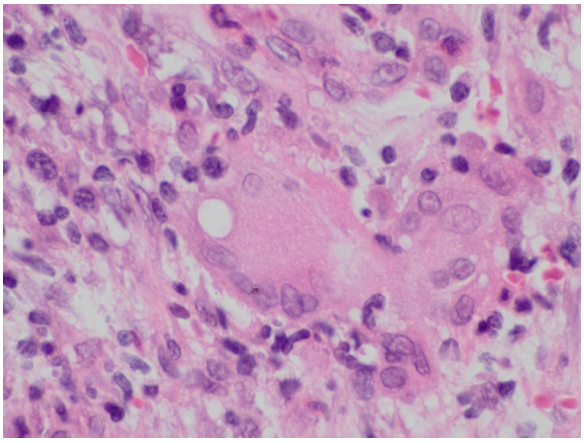

Fig. 3. Inflammatory infiltrate with giant cells

Histopathological analysis:

Biopsy of oral cavity mucosa.

Histopathologic diagnosis: necrotic debris with polymorphonuclear leukocytes and a fragment of skin with ulceration and abundant inflammatory infiltrate consisting of plasma cells, lymphocytes and several polymorphonuclear leukocytes. Small epithelioid granulomas with giant cells are also seen. Cross sections of small vessels with polymorphonuclear leukocytes within their walls can be seen in inflammatory infiltrate. The histological picture is not unequivocal but it does not exclude Wegener's granulomatosis. Immunohistochemical reactions: V-9, CD31, CD34, CD20, CD3, CD56, Ki-67, CD68, CD138 (Fig. 2 and 3).

The abscess of the right parotid gland was evacuated with antibiotic prophylaxis at the Department of Maxillofacial Surgery. The patient was treated with repeated doses of immunoglobulin (at the dose of 1g/kg Kiovig iv), Solu-Medrol pulses (at a dose of 500 mg in 500 ml of 0.9% NaCl) and Endoxan (500 mg). This resulted in regression and stabilization of mucosal necrotic lesions and reduced the infiltration around the right parotid gland. An ANCA control test gave a negative result.

After 6 months subcutaneous infiltration was observed in the left cheek (Fig. 4), which after the reapplication of immunoglobulin (Kiovig dose of 0.5 g/kg iv), methylprednisolone pulses (at a dose of 500 mg in 500 ml of 0.9% NaCl) and 5 plasmapheresis procedures was completely resolved. The treatment included Prednisone at

a maintenance dose (10 mg), which led to one-year stabilization of the disease.

After a period of remission, there was significant progression. A weeping ulceration appeared around the right gland with a diameter of about 10 cm covering the auricle (Fig. 5), with massive granulomatous infiltration of the mucosa of the mouth and the left cheek. ANCA antibodies were still found to be negative. It was then decided to treat with a plasmapheresis procedure, supplemented with administration of immunoglobulin (Kiovig at a dose of 0.5 g/kg iv), which gave a very good response. The total reduction in infiltration of the left side and a significant regression of the right side resulted in permanent catheterization and the performance of repetitive plasmapheresis treatment (total of 10 treatments).

After about 2 months, there was a deteriorating response to plasmapheresis, with severity of skin lesions and several episodes of bacterial superinfection, which required multiple surgical decompression and antibiotic therapy according to the antibiogram made. Due to the severe course of the disease the patient was consulted repeatedly at a Dermatology and Rheumatology Clinic; finally pyoderma gangrenosum was diagnosed. Once again infiltration of the left cheek was revealed, accompanied by lesions in the right subscapular area. The lesions unfortunately did not respond to treatment with plasmapheresis procedures. Mucosa and ulceration sections around the right gland were taken, which were compared to sections taken during testing for Wegener's granulomatosis, Tuberculosis of the skin was excluded (typical and atypical mycobacteria) and finally a cutaneous form of pyoderma gangrenosum through Wegener's granulomatosis was diagnosed. Finally, the patient began treatment with dapsone at an initial 100 mg, gradually increasing to control the level of methemoglobin to a maximum dose of 300 mg per day and 40 mg of Prednisone. The treatment resulted in almost immediate regression of the lesions. This meant that the patient could be then referred to a Burn Treatment Center in order to treat the skin defects. After plastic surgeon consultation it was decided that in the present condition of the patient, surgery was not feasible. Due to the impossibility of skin transplantation it was decided to implement treatment in a hyperbaric chamber, which resulted in complete healing of the wounds (Fig. 6 and 7). The patient was further referred to maxillofacial surgeons for the performance of scar revision.

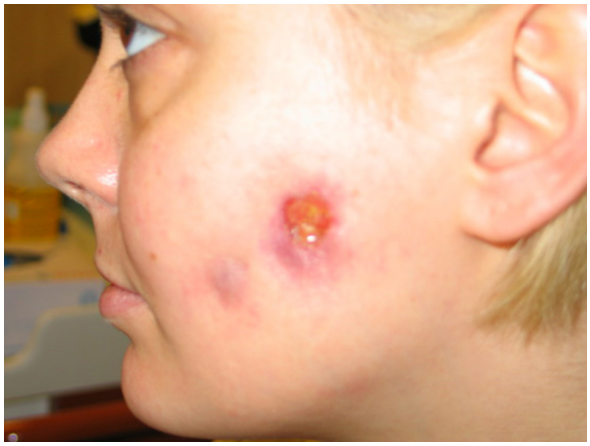

Fig. 4. Relapse 1- infiltration in the left cheek

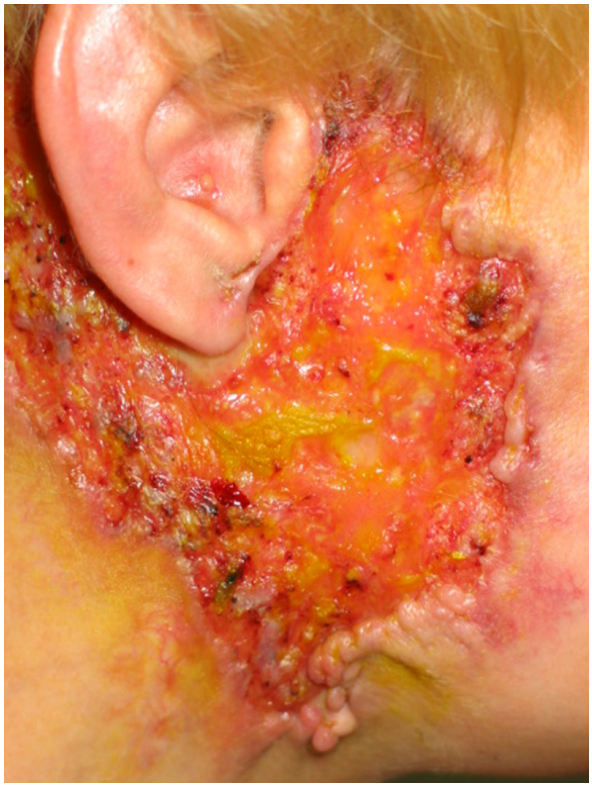

Fig. 5. Relapse 2- weeping ulceration around the right gland

Discussion

Table 1 gives an overview of the cases described in the literature as variations of pyoderma gangrenosum in the course of WG. Criteria for WG by the American College of Rheumatology (ACR), which include the presence of inflammatory lesions in the nose or mouth, radiological changes in a lung image, a pathological image of urinary sediment and a histopathological picture, were the basis of our comparison. The presence of 2 of 4 ACR criteria according to Leavitt has a sensitivity of approximately 88% and a specificity of approximately 92% in recognizing WG [16]. In 1992 Chapel Hill Consensus Conference unified criteria for the diagnosis of the disease to the presence of granulomatous inflammation of the respiratory tract and inflammation of small and medium-sized blood vessels [11]. One of the criteria adopted in this case was a comparison of the presence of cytoplasmic ANCA (cANCA) antibodies, which is a specific marker of WG [23].

The number of reports in the literature on the coexistence of these two disease entities (22 results in PubMed

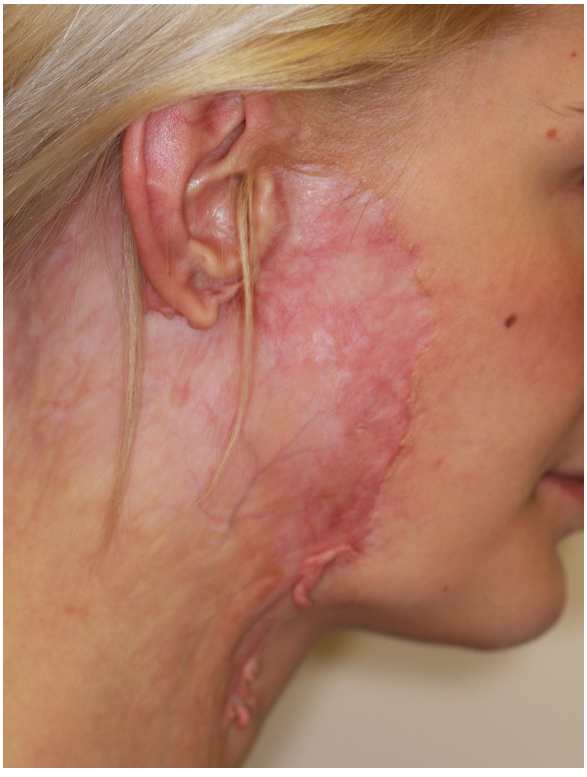

Fig. 6. Effects of treatment- right parotid area

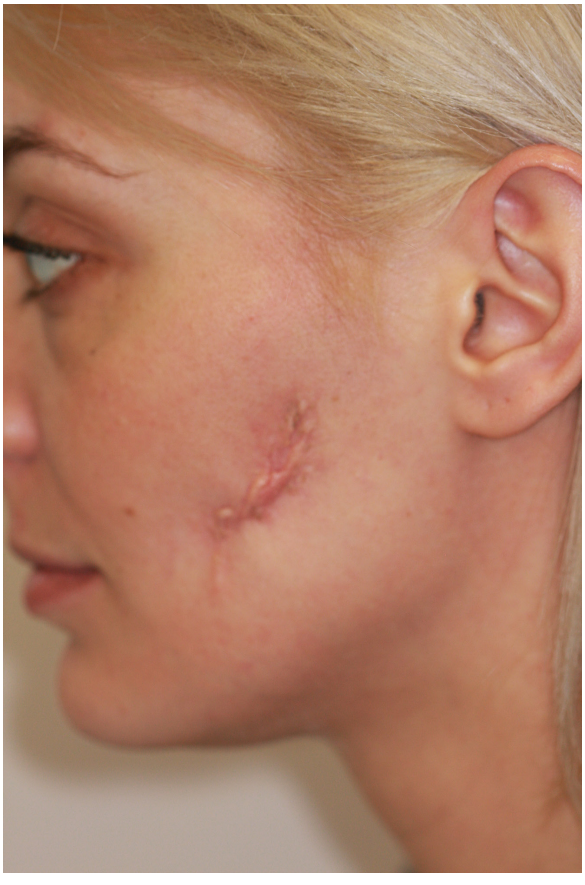

Fig. 7. Effects of treatment- left cheek

using the search terms "Wegener granulomatosis AND Pyoderma gangrenosum") suggests that it is a rare phenomenon. This study revealed a similar incidence of WG and PG comorbidity in both sexes and an increased incidence of both diseases after the age of 50, in contrast to our patient, in whom the disease began at 19 years of age. When the clinical picture of these two entities becomes coupled, there is a plurality problem which is both diagnostic and therapeutic. The information presented in Table 1, and the example of our patient, led us to conclude that the course of WG can be very different. This can concern mainly manifestations where the most typical symptoms such as respiratory or kidney involvement may not be present. Among the presented cases with skin symptoms, as in our case, there was a dominance of ulceration, most often deep and painful, covering a large area with the presence of advanced necrosis and destruction of the surrounding tissue. The most common location proved to be the cervical-cephalic area (4 cases). Skin lesions in the course of WG are not characteristic symptoms, but may be present in as many as 15% to 50% of cases of the disease and suggest cutaneous Wegener's granulomatosis as in the case described [15]. What is more, they can be initial symptoms in up to 10% of WG cases and indicate an active, systemic disease process [5,13,15,30]. The lesions may be of a very different nature from the most common palpable purpura through ulceration pyoderma-like, subcutaneous nodules, pustules, gingival hyperplasia, ulceration and panniculitis [5,9]. The etiology and pathogenesis of PG are not fully understood. This disease is often associated with other diseases such as inflammatory bowel diseases, rheumatic diseases and hematological malignancies. Concomitant systemic disease represents up to 50% of cases [2]. The variety of causes of PG and multiple forms of skin WG explain the difficulty in establishing a diagnosis in both our patient and other cases cited. In addition, the literature distinguishes a malignant variant form of pyoderma, which according to some authors is a cutaneous form of Wegener's granulomatosis, and differentiation is under consideration [9,14]. Malignant pyoderma is rare and is a chronic, ulcerative, destructive skin disease more often affecting men and young people. Lesions are most often located on the head and neck [21]. Both in the course of WG and in PG, sections from the lesions do not exhibit pathognomonic features for these disease entities. The presence of necrosis, hemorrhagic infiltration and massive neutrophilic infiltrates, often resembling an abscess or cellulitis, although not specific to PG, allows for the exclusion of other causes of skin ulcers [2,28]. As shown in our case, and in the review of the literature, there is a dominance of necrosis and infiltration of multinucleated cells as a main manifestation, which suggest that these ulcers are PG and can develop just on the basis of WG, but as seen in the attached expert opinion, identifying a definitive diagnosis can be difficult. The diagnosis of PG in the present case required long-term observation of clinical presentation, comparison of obtained histopathological pictures, and microbiological and immunological

evaluations. The lack of fibrinoid necrosis and the presence of neutrophil infiltration in the walls of vessels located near ulcerations led finally to the diagnosis of PG. We believe that long-term immunosuppressive treatment led to the remission of Wegener's granulomatosis. This, in turn, modified the clinical and histopathological presentation, revealing features of pyoderma gangrenosum. PG started to be a vicious circle. This hypothesis can be confirmed by the fact that immunosuppressive treatment taken by the patient during exacerbations of the disease did not bring the expected effect. Eventually, the treatment with a sulfone derivative (dapsone) and hyperbaric therapy was the most effective. Currently, the existing treatment regimen of Wegener's granulomatosis is based primarily on the use of steroids and cyclophosphamide [1]. The most frequently described PG treatment regime includes administering steroids together with cyclosporin A. In cases of non-response it is recommended to associate steroids with mycophenolate mofetil, cyclosporine with mycophenolate mofetil and with treatment with tacrolimus, or infliximab or a plasmapheresis procedure [22]. However, as shown in Table 1, the summary demonstrates that there is no single treatment regimen when a poorly healing skin ulcer with PG develops on the base of WG. In practically every case, PG treatment was based on the use of steroids with another immunosuppressive drug. The choice of a second drug was problematic and was often found after a lack of treatment effectiveness. The most frequently chosen effective regimen included steroids with cyclophosphamide, which may imply the dominance of WG in the clinical picture of the disease. The case described here is unique, because the effective solution turned out to be a different strategy. The initial stages of a typical treatment involving steroids, immunoglobulins and cyclophosphamide meant a short temporary remission of skin symptoms. We therefore decided to use plasmapheresis treatment, which is considered a controversial treatment for patients with WG. Subsequent studies have shown that they cause a significant improvement, especially in patients with severe renal impairment (creatinine> 5.7 mg/dl at the start of treatment) [10]. A study conducted by Szprit et al. showed that plasmapheresis gives beneficial effects especially in the induction treatment even in patients with a creatinine level of> 2.85 mg/dl. [26]. Moreover, there is evidence that therapeutic plasma exchange should be performed on any patient with pulmonary hemorrhage [7]. Plasmapheresis treatments are therefore used increasingly in patients with vasculitis and the presence of ANCA. Our case shows that they can mean a positive outcome even in patients with severe skin lesions, without significant changes in the kidneys or lungs. The first plasmapheresis treatments caused a regression of skin lesions, but in spite of continued treatment a relapse meant the return of skin lesions and severe reoccurrence of the disease, which may emphasize the function of plasmapheresis at the initiation of treatment. Due to the deteriorating condition of the patient it was decided to change the treatment. Dapsone attached to steroids, a medicament from the sulfones group, is one of the fundamental medicaments along with steroids and sulfonamides for patients with a rapid and severe course of PG who do not respond to local treatment. It can be used as monotherapy or as in the present case in combination with steroids [2]. After four weeks of this treatment a regression of skin lesions was noted. More noteworthy was the extremely good response to treatment in the hyperbaric chamber, which meant complete healing of the wounds. It is well known that hyperbaric oxygen therapy (HBOT) is supportive care for the healing of difficult wounds, such as gas gangrene or other severe infections of the skin, as well as tissue damage after radiotherapy, necrotizing fasciitis, burns, ulcers or bedsores [27]. Animal studies and clinical trials have confirmed the benefits of HBOT in an environment with a reduced oxygen concentration in areas with a reduced amount of vessels and cells, when a wound does not respond to standard therapy. An additional advantage of hyperbaric oxygen is to enhance the action of many drugs, including antibiotics and sulfonamides, as well as causing metabolic disorder of bacterial cells (g+ and g-) and finally the stimulation of phagocytosis [18, 27]. In standard atmospheric pressure, the amount of oxygen that is diffused into the damaged tissue is low and often insufficient for metabolic needs and the healing process. Hyperbaric pressure, with increased oxygen tension, allows for greater diffusion even with the obstructing tissue swelling or reduced blood flow from damaged vessels, and leads to the therapeutic effect [18]. The presence of cANCA antibodies is a highly sensitive and specific marker in the diagnosis of Wegener's granulomatosis [23]. The specificity of antibodies against proteinase-3 is estimated to be about 98-99%, whereas the sensitivity depends on the extent and activity of the disease and can range from 60-67% in the case of active and limited lesions up to 93-96% in the case of active and generalized forms [19]. Research conducted by Daoud suggests that patients with a cutaneous manifestation of WG have antibodies in 81% of cases [4]. This is reflected in our comparison, where each case, excluding those described by the authors, revealed the presence of cANCA antibodies. It must not be forgotten that there are cases in the literature of pyoderma gangrenosum with cANCA antibodies, despite the absence of other symptoms of WG [6].

Conclusion

Hard to heal skin ulcerations can pose many problems for diagnosis and treatment. One should be aware that one of the reasons may be a disease of autoimmune etiology such as WG. Sometimes it is very hard to differentiate PG-like ulceration from PG. PG may be idiopathic or complicate the course of other diseases, including WG. The destruction of the surrounding tissues, the large area of skin affected, the vast depth of infiltration, lack of fibrinoid necrosis with the presence of vascular wall changes in vessels close to the ulceration in histopathological examination and the unresponsiveness to treat-

Table 1. Comparison of the cases described in the literature with the presence of lesions characteristic for PG in the course WG

Gender/age years	Skin lesions	cANCA	Nasal or oral inflammation	Abnormal chest radiograph
Male /59	Several skin ulcers on the back and on both legs of 0,5-10 cm size with hemorrhagic borders	+	+ (hemorrhagic- purulent discharge from the nose)	+
Female/68	10x11cm superficial ulcer with red, undetermined borders and a dirty-yellow ulcer bed on the lower left shin	+	-	-
Female/27	6,5x4 deep peri- auricular ulcer with with a raised purplish undermined border, the base of which was covered with a purulent haemorrhagic exudates, 1cm infra-auricular nodule was noted on the contralateral side	+	+ (nasal congestion, rhinorrhoea, serosanguinous nasal crusting, sinus radiology(-))	-
Female/69	Ulcer with blue undermined edges along the whole lenght of thoracotomy wound	first-recurrence+	?	+
Female/78	5,5x3 cm granulating ulcer with exposed underlying facial muscle on the ipsilateral side, peri- wound erythema, bilateral retroauricular ulcers measuring 2,2x0,8 on the left and 5,5x 3,0 on the right	+	+	-
Male /56	Deep cutaneous ulceration without livid rim or pus discharge, at the preauricular cheek,overlying the angle of the mandible, with smaller, similar lesions at the umbilicus, left wrist and peri-anal area	+	? history of recurrent sinusitis	-
Male /41	Multiple, painful, deep necrotic ulcers 1-3cm covering the trunk and neck	+	+? (sinusitis)	+
Male /54	Skin lesions resembling PG?	+	+ haemoptysis	+
Female/54	Painful violet- edged ulcers 1-5 cm on the legs	?	+dry cough, bloody sputum	+
Male /47	15x8 cm ulcer with irregular, raised, congestive, violet coloured erythematous edges along with abundant granulation tissue in the right arm	Diagnosed WG	Diagnosed WG	Diagnosed WG

	Urinary sediment	Granulomatous inflammation on biopsy	Effective treatment	Ref.
	+ (microscopic hematuria)	Necrosis, acute and chronic infiltration with lymphocytes, plasma cells, macrophages and eosinophil granulocytes, fibrinoid deposition	Methylprednisone (1 mg/kg,day) Cyclophosphamide (2 mg/kg/day) Antibiotics	[25]
	+ (microhematuria)	Mildly hyperplastic epidermis, infiltrate of neutrophilic granulocytes, eosinophilic granulcytes and histiocytes involved the entire dermis and existed to subcutaneous fat, leukocytoclastic vasculitis in and around the vessel walls, perivascular fibrin deposits, erythrocyte extravasates, granulomas consisting of histiocytes arranged around a centrally located area of necrosis	Cyclophosphamide (10 mg/kg i.v. every 4 weeks) Prednisolone (1 mg/kg/day) Cotrimoxazole (160 mg/800 mg, 2x weekly)	[1]
	-	Previously- ruptured epidermoid cyst, showed pseudoepitheliomatous hyperplasia with abscess formation in the deep dermis and subcutis, necrosis at the centre of the abscess, surrounded by palisading histiocytes and scattered multinucleated giant cells. At the time of attempted skin grafting- large foci of serpiginous necrosis surrounded by palisades of histiocytes and scattered multinucleated giant cells	Prednisone- 30 mg daily Methotrexate *p.os*- 15 mg weekly	[24]
	?	Focal absecess with an infiltrate of neutrophil polymorphs	Steroids (topical and oral) Cyclosporin	[29]
	?	Suppurative inflamation and granulation tissue	Solu-Medrol Cyclosporine Antibiotics	[9]
	-	Fibrinoid degeneration of the walls associated with neutrophil- predominant, mixed perivascular infiltrates disrupting blood vessel architecture, palisaded granulomatous infiltrate surrounding this areas,scaterred multinucleated giant cells, neutrophils and nuclear debris	Methylprednisone (1 mg/kg,day) Cyclophosphamide (750 mg/m^2)	[14]
	?	Inflamatory suppurative dermal infiltrate harbouring neutrophils, lumphocytes and histiocytes	Mycophenolate mofetil (2 g/day orally) Corticosteroids (1 mg/kg/day)	[17]
	-	Epithelial cell necrosis and acute inflammatory changes with no evidence of vasculitis or granulomas	Methylprednisolone Cyclophosphamide in *i.v.* pulses	[20]
	-	Dense inflammatory infiltrate in the dermis with neutrophils and fibrin deposits in the vessels	Cyclophosphamide bolus of 15 mg/kg every 2 weeks(3 pulses) followed by 15 mg/kg every 3 weeks (6 pulses)	[12]
	Diagnosed WG	Inflamatory infiltration, consisting of neutrophil accumulation, abscess formation, disintegration of the matrix and areas of necrosis, prence of necrotizing perivasculitis and leukocytoclastic vasculitis of the peripheral tissue, lymphocytes and macrophages around the microvascularization	Betamethasone Valerate with Gentamicin (saline solution and topical application)	[3]

ment should guide one towards an alternative diagnosis of PG. Due to the rarity of the coexistence of the two entities and the lack of an established, effective treatment regimen, often therapy is selected empirically. In such cases sulfone derivatives are still an effective alternative to standard immunosuppression methods. Hyperbaric therapy can also play an important complementary role.

References

[1] Boudny C., Nievergelt H., Braathen L.R., Simon D.: Wegener's granulomatosis presenting as pyoderma gangrenosum. J. Dtsch. Dermatol. Ges., 2008; 6: 477-479

[2] Callen J.P.: Pyoderma gangrenosum. Lancet, 1998; 351: 581-585

[3] Castillo R.F., Cañadas-De la Fuente G.A., Husein-Elahmed H., Cantero-Hinojosa J.: Pyoderma gangrenosum developing over an arteriovenous fistula scar. Intern. Med. J., 2011; 41: 436-437

[4] Daoud M.S., Gibson L.E., DeRemee R.A., Specks U., el-Azhary R.A., Su W.P.: Cutaneous Wegener's granulomatosis: clinical, histopathologic, and immunopathologic features of thirty patients. J. Am. Acad. Dermatol., 1994; 31: 605-612

[5] Francès C., Du L.T., Piette J.C., Saada V., Boisnic S., Wechsler B., Blétry O., Godeau P.: Wegener's granulomatosis. Dermatological manifestations in 75cases with clinicopathologic correlation. Arch. Dermatol., 1994; 130: 861-867

[6] Hoffman M.D.: Pyoderma gangrenosum associated with c-ANCA (h-lamp-2). Int. J. Dermatol., 2001; 40: 135-137

[7] Iwatani H., Uzu T., Kakihara M., Nakayama Y., Kanasaki K., Yamato M., Hirai Y., Umimoto K., Yamauchi A.: A case of Wegener's granulomatosis with pulmonary bleeding successfully treated with double filtration plasmapheresis (DFPP). Clin. Exp. Nephrol., 2004; 8: 369-374

[8] Jackson J.M., Callen J.P.: Pyoderma Gangrenosum. Emedicine. http://emedicine.medscape.com/article/1123821-overview (28.01.2016)

[9] Jacob S.E., Martin L.K., Kerdel F.A.: Cutaneous Wegener's granulomatosis (malignant pyoderma) in a patient with Crohn's disease. Int. J. Dermatol., 2003; 42: 896-898

[10] Jayne D.R., Gaskin G., Rasmussen N., Abramowicz D., Ferrario F.,Guillevin L., Mirapeix E., Savage C.O., Sinico R.A., Stegeman C.A., Westman K.W., van der Woude F.J., de Lind van Wijngaarden R.A., Pusey C.D.: European Vasculitis Study Group: Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J. Am. Soc. Nephrol., 2007; 18: 2180-2188

[11] Jennette J.C., Falk R.J., Andrassy K., Bacon P.A., Churg J., Gross W.L., Hagen E.C., Hoffman G.S., Hunder G.G., Kallenberg C.G., et al.: Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum., 1994; 37: 187-192

[12] Jiménez-Gallo D., Albarrán-Planelles C., Linares-Barrios M., Rodríguez-Hernández C., Martínez-Rodríguez A., García-Moreno E., Bravo-Monge R.: Pyoderma gangrenosum and Wegener granulomatosis-like syndrome induced by cocaine. Clin. Exp. Dermatol., 2013; 38: 878-882

[13] Kawakami T., Obara W., Soma Y., Mizoguchi M.: Palisading neutrophilic granulomatous dermatitis in a Japanese patient with Wegener's granulomatosis. J. Dermatol., 2005; 32: 487-492

[14] Kouba D.J., Mimouni D., Ha C.T., Nousari C.H.: Limited Wegener's granulomatosis manifesting as malignant pyoderma with corneal melt. Int. J. Dermatol., 2003; 42: 902-904

[15] Kuchel J., Lee S.: Cutaneous Wegener's granulomatosis: a variant or atypical localized form? Australas. J. Dermatol., 2003; 44: 129-135

[16] Leavitt R.Y., Fauci A.S., Bloch D.A., Michel B.A., Hunder G.G., Arend W.P., Calabrese L.H., Fries J.F., Lie J.T., Lightfoot R.W. Jr., et al.: The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum., 1990; 33: 1101-1107

[17] Le Hello C., Bonte I., Mora J.J., Verneuil L., Noël L.H., Guillevin L.: Pyoderma gangrenosum associated with Wegener's granulomatosis: partial response to mycophenolate mofetil. Rheumatology, 2002; 41: 236-237

[18] Mills B.J.: Wound healing: the evidence for hyperbaric oxygen therapy. Br. J. Nurs., 2012; 21 (Suppl. 20): S28-S34

[19] Nölle B., Specks U., Lüdemann J., Rohrbach M.S., DeRemee R.A., Gross W.L.: Anticytoplasmic autoantibodies: their immunodiagnostic value in Wegener granulomatosis. Ann. Intern. Med., 1989; 111: 28-40

[20] Perkins G.D., Moudgil H., Jones R.: Pyoderma gangrenosum. Thorax, 2000; 55: 347

[21] Powell F.C., Winkelmann R.K.: Malignant pyoderma. Br. J. Dermatol., 1983; 109: 597-603

[22] Reichrath J., Bens G., Bonowitz A., Tilgen W.: Treatment recommendations for pyoderma gangrenosum: an evidence-based review of the literature based on more than 350 patients. J. Am. Acad. Dermatol., 2005; 53: 273-283

[23] Schönermarck U., Lamprecht P., Csernok E., Gross W.L.: Prevalence and spectrum of rheumatic diseases associated with proteinase 3-antineutrophil cytoplasmic antibodies (ANCA) and myeloperoxidase-ANCA. Rheumatology, 2001; 40: 178-184

[24] Sinovich V., Snow J.: Protracted superficial Wegener's granulomatosis. Australas. J. Dermatol., 2003; 44: 207-214

[25] Szõcs H.I., Torma K., Petrovicz E., Hársing J., Fekete G., Kárpáti S., Horváth A.: Wegener's granulomatosis presenting as pyoderma gangrenosum. Int. J. Dermatol., 2003; 42: 898-902

[26] Szpirt W.M., Heaf J.G., Petersen J.: Plasma exchange for induction and cyclosporine A for maintenance of remission in Wegener's granulomatosis - a clinical randomized controlled trial. Nephrol. Dial. Transplant., 2011; 26: 206-213

[27] Szymańska B., Kawecki M., Knefel G.: Kliniczne aspekty hiperbarii tlenowej. Wiad. Lek., 2006; 59: 105-109

[28] Wollina U.: Clinical management of pyoderma gangrenosum. Am. J. Clin. Dermatol., 2002; 3: 149-158

[29] Wong Y.W., Lyon C.C., Benbow E.W., Bradley B.L., Beck M.H.: Pyoderma gangrenosum in a thoracotomy wound associated with a pulmonary cavitating lesion. Clin. Exp. Dermatol., 2003; 28: 274-276

[30] Zycinska K., Wardyn K., Zielonka T.M., Nitsch-Osuch A., Smolarczyk R.: Cutaneous changes: an initial manifestation of pulmonary Wegener's granulomatosis. Adv. Exp. Med. Biol., 2013; 755: 307-310

The authors have no potential conflicts of interest to declare.