Biomedical Letters
2017 | Volume 3 | Issue 2|Pages 130-133

CASE REPORT OPEN ACCESS

Pyoderma Gangrenosum associated with type 1 Diabetes Mellitus: A Case Report

Muhammad Ahmed Javed[1], Muhammad Arif Anwar[2], Khawar Ali Shahzad[3], Santha Kumar Krishnagopalan[4], Eman Jasim Mohamed Saleh Alsaffar[1], Noor Sultan[5], Jin Hui[1*].

[1]Department of Endocrinology, Zhongda Hospital, Southeast University, Nanjing, China.
[2]Department of Cardiology, The Affiliated Zhongda Hospital of Southeast University, No. 87 Dingjiaqiao, Nanjing, China
[3]Department of Microbiology and Immunology, Medical School, Southeast University, Nanjing, China.
[4]Department of Dermatology, Gulou Hospital, Nanjing, China.
[5]Department of Public Health, Medical School, Southeast University, Nanjing, China.

Abstract
Pyoderma gangrenosum is a very rare non-infectious leukocytic dermatosis which is found to be associated with autoimmune disease process such as diabetes mellitus type I, resulting in compromised insulin production. The ulcers of pyoderma gangrenosum are mostly found at the surgical sites. Mostly, the oral and parenteral steroids (prednisolone and dexamethasone) and immunosuppressive agents such as cyclosporine are used as its first line of treatment. Herein, we report a case of pyoderma gangrenosum in a 24 years old Chinese (Han race) female who was presented with a skin infection that developed 10 days earlier and had a history of diabetes mellitus (type 1). The patient was already using insulin to control the hyperglycemia. Pyoderma is a very rare surgical complication that can only be treated successfully by corticosteroids and anti-bacterial agents. To the best of our knowledge, this is the first case report of pyoderma that has been associated with diabetes mellitus (type I).

Keywords: pyoderma gangrenosum, diabetes mellitus type I, dermatosis, corticosteroid, autoimmune disease.

Received September 11, 2017; **Revised** October 30, 2017; **Accepted** November 25, 2017
[*]**Correspondence:** Jin Hui **Email** jinhuison@126.com, **Contact**: +86-25-83262811

***To cite this manuscript*:** Javed MA, Anwar MA, Shahzad KA, Krishnagopalan SK, Alsaffar EJMS, Sultan N, Hui J. Pyoderma Gangrenosum associated with type 1 Diabetes Mellitus: A Case Report. Biomed Lett 2017; 3(2):130-133.

Introduction

Pyoderma gangrenosum (PG) is a rare neutrophilic inflammatory skin disease which is usually presented and categorized by persistent skin ulcers in almost 50% of cases [1]. It has also been associated with systemic autoimmune disorders, such as rheumatoid arthritis, type I diabetes mellitus (TIDM), inflammatory bowel disease, and hematological malignancies [2]. It was introduced and titled as pyoderma gangrenosum by Brunsting and colleagues in 1930 [3]. In this report, we presented a case of PG associated with a systemic disease known as diabetes mellitus (type I). Pyoderma gangrenosum has become a global epidemic, spreading from industrialized nations to the emerging economies of Asia and Africa [4]. Females are more prone to skin diseases such as pyoderma gangrenosum as compared to male individuals. The pathogenesis of PG is still unclear [5]. Corticosteroids and cyclosporine are the first-line treatment regime in adults and children. The most common symptoms of TIDM are polydipsia, polyuria, and polyphagia, which resulted in an increase of blood glucose values. The only treatment of TIDM is insulin therapy to control the hyperglycemia.

Case Report

A 24-year-old female with unknown comorbidities was received from the emergency to inpatient department at Southeast University affiliated Zhongda Hospital, Nanjing, China. The patient was presented with the history of fever from last 10 days and multiple painful lesions. At first, the lesions appeared as blisters, which later ruptured and resulted in raw areas and necrotic ulcerated lesions. The blood glucose of the patient was measured as 20.0 mmol/L and referred to the endocrinology department for addressing hyperglycemia. Definitive diagnostic tests such as serum creatinine, liver functions test (LFTs), complete blood count (CBC), hemoglobin A1c (HbA1c), immunoglobulin, etc. were performed for confirmation and determination of further treatment plan. The application of 12 U early /12 U middle/12 U late NovoMIX (insulin preparation) 12 U after 8 hrs and 20 U for subcutaneous injection of regular

insulin stat dose were given. Regular monitoring of pre- and post-prandial glucose was undertaken, and diet modification in the form of low salt and low-fat were adopted. A therapeutic regimen including ceftriaxone sodium injection, sodium chloride (normal saline) infusion 250ml, and levofloxacin sodium injection was administered. Moreover, she was advised to apply topical agents such as antibiotic based lotion, cover the lesions with pyodine dressing and change them regularly on daily basis.

On her recent visit to the hospital, she was suffering from polyuria, polyphagia, and fever. She disagreed with the history of vomiting and nausea, cardiac, GIT or urinary tract diseases. There was no previous history of known allergy. During the physical examination, big necrotic ulcers with pus were found on lower extremities of her right thigh (**Figure 1A**) and the upper portion of the shoulder (Figure 1B and C). After the biopsy, pyoderma gangrenosum associated with T1DM was diagnosed.

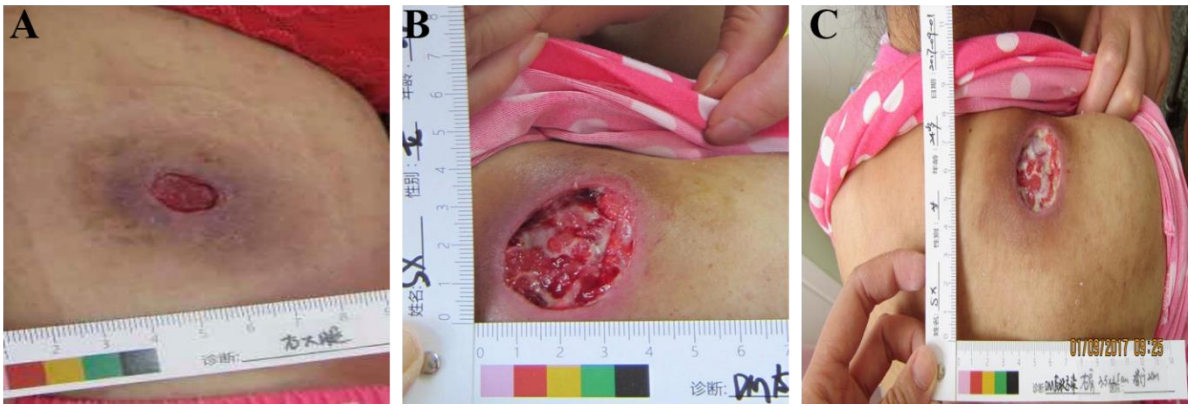

Figure 1: Ulcers having a purulent base, asymmetrical borders on the right thigh (**A**) and the back of the shoulder (**B** and **C**).

Her treatment commenced with blood glucose monitoring for first 24 hours before and after the meal along with broad-spectrum antibacterial agents such as ceftriaxone, levofloxacin sodium, potassium chloride tablets, hydrochloride tablets (2 × 0.5g), sodium chloride infusion, protamine recombinant, and human insulin injection (twice a day). An extensive serological evaluation that included coagulation profile, liver function tests (LFTs), complete blood test (CBC), antinuclear antibody, anti-double-antibody (DS) and deoxyribonucleic (DNA) were performed (**Table 1**). Laboratory test results showed a decrease in hematocrit and inflammatory reactions. The white blood cell count was normal, whereas platelets count was elevated because of deficiency in antithrombin (**Table 2**). Electrolytes evaluation demonstrated a decrease in sodium, urea, and hemoglobin (**Table 3**).

The blood glucose level of the patient was found significantly increased before treatment, and chest x-ray of posterior anteriorly (PA) was normal. The complete blood test (CBC) was repeated after two days which showed an increase in WBC count and hemoglobin A1c (hbA1c) that indicated a skin infection. The case was then referred to hepatitis panel, as it has an association with pyoderma gangrenosum, but it was unremarkable. Protein and enzymes estimation tests and coagulation profile of the patient are given in **Table 4, 5 and 6**.

Table 1: Liver Function Test

Tests	Results	Values	Ref. range
Total protein	57	g/l	65-85
Albumin	28.3	g/l	40-55
Globin	28.7	g/l	20-40
White blood ratio	0.99		1.2-2.4
Parvalbumin	0.05	µmol/L	0.20-0.40
Total bile acid	13.7	µmol/L	0.0-10
Total bilirubin	4.8	µmol/L	2.0-20
Direct bilirubin	2.0	µmol/L	0.0-6
Indirect bilirubin	2.8	IU/L	2-18
Glutamic pyruvic transaminase	7	IU/L	7-40
AST	12	IU/L	13-35
Alkaline phosphate	84	IU/L	35-100
Y-glutamyl peptide	12	IU/L	7-45
Lactate dehydrogenase	127	IU/L	120-220
Cholinesterase	3210	IU/L	5000-12000
Creatine kinase	18	IU/L	0-145
Glucose	19.71	µmol/L	4.20-6.40
Urea nitrogen	2.1	µmol/L	2.6-7.5
Creatinine	61	µmol/L	41-73
Uric acid	195	µmol/L	155-357

The patient's overall hygienic condition was poor. She also complained about insomnia due to the pain of her wounds which made her irritable. Cardiac examination showed no critical stenosis. A deep elliptical biopsy including subcutaneous tissue of the skin from the right leg was obtained under local

anesthesia and sent for histopathological examination. During a biopsy, the patient was administered with normal saline (i.v) along with the local application of pyodine solution and tropical antibacterial agents.

Table 2: Complete Blood Count

Tests	Results	Values	Ref. range
White blood cell	3.81	10^9/L	3.5-9.5
Red cell count	2.84	10^{12}/L	3.8-5.1
Haemoglobin	90	g/L	115-150
Platelet count	127	10^9/L	125-350
Neutrophil ratio	48.1	%	40-75
Lymphocyte ratio	37.4	%	20-50
Monocyte ratio	14.1	%	3-10
Eosinophils	0.2	%	0.4-8
Basophils	0.2	%	0-1
Neutrophil count	1.83	10^9/L	1.8-6.3
Lymphocyte count	1.42	10^9/L	1.1-3.2
monocyte count	0.54	10^9/L	0.1-0.6
Value of eosinophil	0.01	10^9/L	0.02-0.52
Value of mu basophil	0.01	10^9/L	0-0.06
MCV	95.3	fL	82-100
Haematocrit	0.27	L/L	0.35-0.45
MCHb content	31.7	pg	27-34
MCHb concentration	332	g/L	316-354
RBC distribution width	12.2	%	11.6-14.8
Rbc distribution	42.7	fL	36-48
Mean platelet volume	8.6	fL	7.4-11
Platelet aggregation	0.109	%	0.158-0.452
Platelet distribution width	16.1	fL	12-16.5
Large platelet ratio	16.3	%	12-45

Table 3: Electrolytes Estimation Tests

Tests	Results	Value	Ref. range
Pco2	31.5	mmhg	35-45
SO_2	98.3	%	95-98
Hct	27	%	38-46
Hb	9.0	g/dL	10-14
HCO3	21.2	mmol/L	22-27
Na	131.4	mmol/L	135-145
Glu	21.40	mmol/L	3.6-6.1
Urea	2.4	mmol/L	2.5-6.4
Pco2Tc	31.5	mmhg	35-45

Based on history, biopsy, physical examinations, and lab test results pyoderma gangrenosum associated with systemic disease T1DM was diagnosed. Insulin intake for diabetes and tropical antibacterial agents such as corticosteroids (tacrolimus and hydrocortisone), methotrexate and immunosuppressive agents were prescribed for the treatment of skin infections. She was discharged from the hospital and advised for follow up with regular outpatients' visits.

Table 4: Proteins Estimation Test

Tests	Results	Values	Ref. range
Ati-TG	<10	IU/mL	0-115
aTPO	12.60	IU/mL	0-34
Thyrotropin	<0.300	IU/L	0-1.75

Table 5: Enzymes Tests

Tests	Results	Values	Ref. range
Erythropoietin	63.39	mIU/ml	2.59-18.5
Vitamin B12	1456	pg/ml	180-914
Folic acid	6.79	ng/ml	3.1-19.9

Table 6: Coagulation profile

Tests	Results	Values	Ref. range
Antithrombin	76	%	77-123
Fibrinogen degradation products	6.07	mg/L	0-5
Fibrinogen	4.13	g/l	2-4

Discussion

PG is a very rare idiopathic neutrophilic dermatosis with an occurrence rate of 6 patients per million annually and poses very tough challenges indefinite diagnosis [6, 7]. It is mostly found in adults, and only 4-5% of patients are children or infants [8]. In children, the most common comorbidity associated with pyoderma gangrenosum is inflammatory bowel disease (IBD), in addition to arthritis and leukemia and diabetes mellitus [9]. PG is categorized as bullous, pustular, vegetative, ulcerative, vesiculopustular, and personal disease [10]. It has been found that the increased occurrence of metabolic disorder is because of chronic systematic Th1 mediated inflammatory reaction. However the etiology of PG is still unknown [11]. It is considered that the possible association of metabolic syndrome can be the potential cause of pyoderma gangrenosum occurrence. Additionally, one major and two minor criteria must be met for a definitive diagnosis. The major criteria include progressive ulcerated necrotic lesions, while the minor criteria include rapid response to corticosteroids and pathergy [12, 13]. Histopathological analysis showed neutrophilic infiltration, also with or without lymphocytic vasculitis.

Conclusion

PG is a very rare chronic disease with many non-specific symptoms that sometimes overlooked by clinicians. A multidisciplinary approach must be required for better treatment involving an endocrinologist, dermatologist, and a general surgeon. Misdiagnosis of this disease can result in devastating effects hence it is required to refer the patient to a dermatologist. The prognosis of the patient in present report was good after treatment with corticosteroids and antibacterial agents.

References

[1] DeFilippis EM, Feldman SR, Huang WW. The genetics of pyoderma gangrenosum and implications for treatment: a systematic review. Br J Dermatol. 2015; 172:1487-1497.

[2] Gonzalez-Moreno J, Ruiz-Ruigomez M, Callejas RJ, Rios FR, Ortego CN. Pyoderma gangrenosum and systemic lupus erythematosus: a report of five cases and review of the literature. Lupus. 2015; 24:130-137.
[3] Brunsting L, Goeckerman W, O'leary P. Pyoderma (echthyma) gangrenosum: clinical and experimental observations in five cases occurring in adults. Arch Derm Syphilol. 1930; 22:655-680.
[4] Unnikrishnan R, Pradeepa R, Joshi SR, Mohan V. Type 2 diabetes: demystifying the global epidemic. Diabetes. 2017; 66(6):1432–1442.
[5] Berger N, Ebenhoch M, Salzmann M. Postoperative pyoderma gangrenosum in children: the case report of a 13-year-old boy with pyoderma gangrenosum after hip reconstruction surgery and a review of the literature. J Pediatr Orthop. 2017; 37(6): e379-e383.
[6] Brunsting LA, Goeckerman WH, O'Leary PA. Pyoderma (echthyma)gangrenosum: clinical and experimental observations in five cases occurring in adults. Arch DermSyphilol. 1930; 22:655–680.
[7] Langan SM, Groves RW, Card TR, Gulliford MC. Incidence, mortality, and disease associations of pyoderma gangrenosum in the United Kingdom: a retrospective cohort study. J Invest Dermatol. 2012; 132(9):2166-2170.
[8] Bennett ML, Jackson JM, Jorizzo JL, Fleischer AB Jr, White WL, Callen JP. Pyoderma gangrenosum. A comparison of typical and atypical forms with an emphasis on time to remission. Case review of 86 patients from 2 institutions. Med. 2000; 79(1):37-46.
[9] Braswell SF, Kostopoulos TC, Ortega-Loayza AG. Pathophysiology of pyoderma gangrenosum (PG): an updated review. J Am Acad Dermatol. 2015; 73(4):691-698.
[10] Crowson AN, Mihm MC Jr, Magro C. Pyoderma gangrenosum: a review. J Cutan Pathol. 2003; 30(2):97-107.
[11] Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities, and therapy in 103 patients. Br J Dermatol. 2011;165(6):1244–1250.
[12] Al Ghazal P, Körber A, Klode J, Dissemond J. Investigation of new-cofactors in 49 patients with pyoderma gangrenosum. J Dtsch Dermatol Ges. 2012;10(4):251–257.
[13] Yasin F, Assad S, Zahid M, Malik SA. Extensive pyoderma gangrenosum: a challenging diagnosis and literature review of management. Cureus. 9(7): e1486.