

## Case Report

# Unusual case of extracutaneous pyoderma gangrenosum with myelodysplastic syndrome

Lei-Lei Zhang<sup>1\*</sup>, Hua-Xiong Pan<sup>2\*</sup>, Song Tong<sup>3</sup>, Lin Liu<sup>1</sup>

Departments of <sup>1</sup>Haematology, <sup>2</sup>Pathology, <sup>3</sup>Thoracic Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, P. R. China. \*Equal contributors.

Received April 20, 2019; Accepted July 25, 2019; Epub September 1, 2019; Published September 15, 2019

**Abstract:** Pyoderma gangrenosum (PG) is a rare, noninfectious, inflammatory disease characterized by neutrophilic infiltration and destruction of tissue. Extracutaneous involvement in PG is unusual. Myelodysplastic syndrome (MDS) is the most frequent hematologic disease associated with PG. We present a case diagnosed with MDS-EB-I. He had a large ulcer in his buttocks. Tissue culture and microscopy showed no evidence of fungi, bacteria, or mycobacteria. Histology showed granulation tissue, inflammatory infiltrate, abscess formation, and focal necrotizing vasculitis. Dermatology opinion confirmed PG. The skin lesions responded well to corticosteroid treatment at first, but it relapsed quickly with involvement of skin and lungs. In the meantime, MDS progressed to acute myeloid leukemia. The patient received chemotherapy and immunosuppressive therapy at the same time. After achievement of complete remission (CR), he had allogeneic hematopoietic stem cell transplantation. Two years later, the patient is still in CR status with no sign of PG relapse.

**Keywords:** Pyoderma gangrenosum, myelodysplastic syndrome, PG, MDS

### Introduction

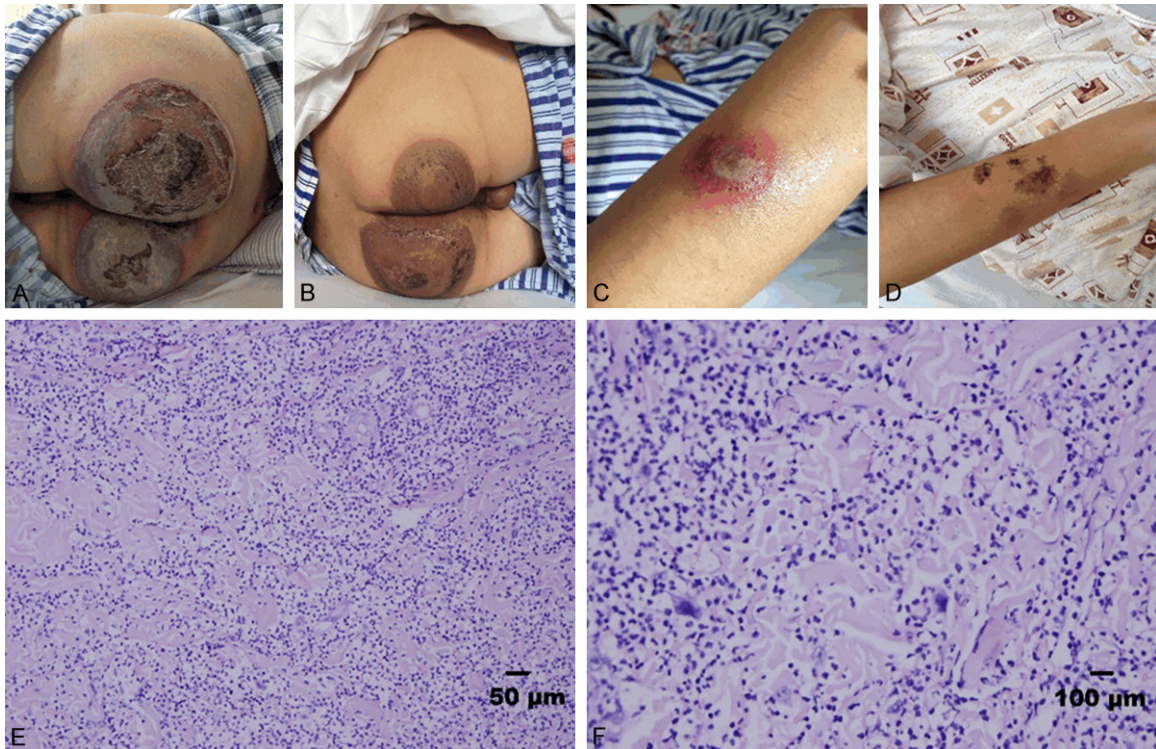
Pyoderma gangrenosum (PG) is a rare inflammatory ulcerative skin disease associated with systemic disease. PG is associated with inflammatory bowel disease, polyarthritis, and hematologic disorders in up to 50% of cases [1]. Myelodysplastic syndrome (MDS) is the most frequent hematological disorder associated with PG. MDS is a heterogeneous group of stem cell malignancies characterized by morphologic abnormalities. The major hallmark of this disorder is ineffective hematopoiesis with a variable risk of transformation to acute leukemia. We report a patient suffering from progressive cutaneous and extracutaneous lesions with underlying MDS. Treatment with allogeneic hematopoietic stem cell transplantation achieved long-term complete relief.

### Case report

A 39-year-old male patient was admitted under general medicine with a huge painful ulcer in his buttocks. He reported a scratch in his but-

tocks 4 months earlier that worsened over time into an ulcer, in spite of antibiotic treatment. Since 2014, he was diagnosed with myelodysplastic syndrome (MDS) refractory anemia (MDS-RA) at another hospital. He was referred to our hematological institute for further treatment in 2016.

On admission, the patient was afebrile, bearing a sharply demarcated ulcer with purple undermined borders in his buttocks (**Figure 1A**). The cutaneous lesions were cultured for bacteria, Mycobacterium tuberculosis, and fungi. Empiric therapy was started with meropenem with teicoplanin. A dermatology opinion was sought and a working diagnosis of pyoderma gangrenosum (PG) was made. A skin biopsy was performed. A week later, the lesions showed no improvement after the antibiotic treatment. Further cultures were negative. Anti-neutrophil cytoplasmic antibody and other autoantibodies suggestive of connective tissue disorders were also negative. Histologic analysis of skin biopsy revealed epidermal ulceration with predominant infiltration of neutrophils (**Figure 1E** and

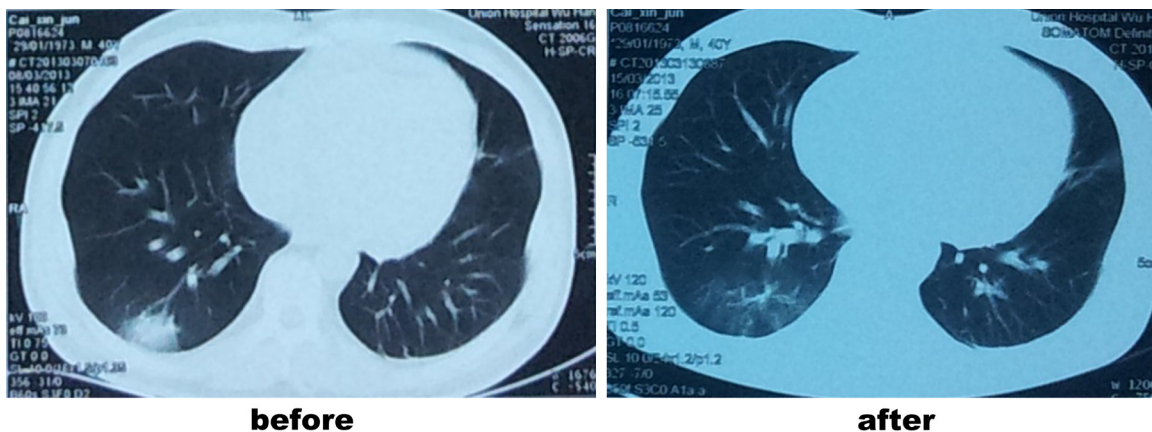


**Figure 1.** Skin lesion of patient before and after treatment. A. Ulcers with a necrotic center in patient's buttocks; B. Skin lesions in patient's buttocks after the treatment in two weeks; C. Pustular lesions on the extremities; D. Skin lesions on the extremities after the immuno-suppressive therapy; E. Histopathology of skin lesions, scale bar = 50  $\mu\text{m}$ ; F. Histopathology of skin lesions, scale bar = 100  $\mu\text{m}$ .

**1F)**, consistent with the diagnosis of PG. Complete blood count demonstrated pancytopenia. Bone marrow examination showed multilineage dysplasia with 7.5% blasts, expressing CD13, CD15, CD33, CD38, CD117. No chromosomal abnormality was found by G-banded karyotype analysis or fluorescence in situ hybridization. A diagnosis of MDS-EB-I was made.

Systemic administration of methylprednisolone 60 mg once daily plus ciclosporin 150 mg twice daily was given. The skin lesions responded dramatically to the treatment in two weeks (**Figure 1B**). The patient showed aggravated pancytopenia with gradual tapering of the steroids. A month later, bone marrow examinations were checked again with 25% blasts, indicating evolution to acute myeloid leukemia (AML). In the meantime, he reported a non-productive cough without dyspnea, fever, or chest pain. A chest CT examination revealed a nodular lesion in the right lobe (**Figure 2**). Broad-spectrum antibiotics plus anti-fungal treatment was given. Meanwhile, he presented with dis-

seminated pustular lesions on the trunk and extremities (**Figure 1C**). Blood cultures and cultures after bronchoalveolar lavage were both negative. The respiratory symptoms did not respond to antibiotics. Pulmonary involvement by PG was suspected. CT-guided core biopsy was performed. Histopathologic staining revealed infiltration of neutrophils and lymphocytes. Therapy of methylprednisolone and ciclosporin was started again. Both the cutaneous and pulmonary symptoms responded well to the immunosuppressive therapy (**Figure 1D**). Two weeks later, with cutaneous lesions almost healed, methylprednisolone was stopped and ciclosporin was reduced to 75 mg twice a day. The patient was started on induction chemotherapy with decitabine (20 mg/m<sup>2</sup> once daily for 5 days). Two weeks later, a follow-up chest CT scan showed that thin-walled cavity and inflammatory changes were resolved (**Figure 2**). Ciclosporin was tapered. The patient had a good hematologic response to the hypomethylation therapy with the decrease of blasts to 11% in the bone marrow. For the second cycle, he received decitabine combined with low dose



**Figure 2.** Computer tomography of pulmonary lesions before and after treatment.

chemotherapy. He achieved complete remission with no blasts detected in the bone marrow and the PG lesions were almost completely healed with no recurrence elsewhere. He had a human leukocyte antigen (HLA)-matched sibling donor and underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT). At 6 months after HSCT, the patient discontinued all immunosuppressive agents. At 24 months after HSCT, he was still in complete remission of AML with no symptoms of PG.

### Discussion

PG, first described in 1930s, is a rare, ulcerating, neutrophilic dermatoses (ND). PG typically involves the lower extremities, buttocks and perineal region, as well as the head and neck. Extracutaneous manifestations of PG is an even rare occurrence. It may involve sites such as the eyes, the lungs, the spleen, and the musculoskeletal system. Most cases have a history suggestive of PG [2, 3]. Our patient had lung lesions, when the cutaneous lesions relapsed. A chest CT scan showed a nodular lesion. Core biopsy showed neutrophil infiltration, consistent with PG. Both pulmonary and cutaneous lesions responded markedly to immunosuppressive therapy. In a recent report, the author systematically reviewed 41 PG cases with pulmonary involvement [4]. Approximately half of the patients presented with PG skin lesions before the onset of pulmonary disease. Clinical presentation was non-specific and most displayed cavitating lesions, infiltrates, and nodules. As expected, neutrophil infiltration was usually found on histopathology. In isolated PG, it is most common for PG patients to have underlying IBD and rheumatoid arthritis [5]. In

contrast, for PG with pulmonary involvement, the majority were associated with underlying hematologic disease. The most common hematologic disease was MDS.

Skin involvement in MDS is not common, but it is being recognized to have prognostic and therapeutic significance [6, 7]. The specific lesions are characterized by the presence of neoplastic hematopoietic cells in the skin and are associated with poor prognosis. Non-specific cutaneous manifestations include ND, cutaneous vasculitis, and Behcet disease. Most common non-specific cutaneous lesion is ND, such as Sweet syndrome, and PG. In early studies, skin lesions were taken as paraneoplastic autoimmune phenomena in patients with myelodysplastic syndromes [8]. In Farah's study, 15 cases in 157 MDS patients (9.55%) had skin lesions. Among them, most common (4.46%) was PG. The survival analysis showed that the risk of transformation into AML was slightly but not significantly increased in patients with skin lesions compared with patients without skin lesions [6]. Our patient had a history of MDS-RA for 2 years and suffered relapsed cutaneous and pulmonary lesions, while MDS transformed into AML. The prognostic value of skin lesions in MDS patients is still controversial [9]. Because of the rarity of cutaneous lesions in MDS, the only evidence from case reports and small series studies indicates that skin lesions, especially Sweet syndrome and PG, are associated with poor prognosis and with transformation into AML.

It is well-known that PG cases generally respond well to immunosuppressive therapy. Corticosteroids and cyclosporine are consid-

ered as first-line systemic agents. Many patients remain dependent on corticosteroids, because PG cases have a characteristic course of remissions and relapses. Some patients with MDS respond well to immunosuppressive agents, including corticosteroids, cyclosporine, and antithymocyte globulin. However, long-term immunosuppressive therapy may deteriorate the immune system of PG patients and increase the risk of infection. The primary curative therapy for MDS is stem cell transplantation, especially for MDS-EB cases. In this case, his cutaneous and extracutaneous lesions responded dramatically to immunosuppressive therapy, while his MDS progressed to AML. He received induction chemotherapy and tapered ciclosporin at the same time. He achieved long-term survival free from PG and AML after allo-HSCT.

### Conclusion

We reported an MDS case with a rare coexistence of cutaneous and extracutaneous lesions. His cutaneous and extracutaneous lesions responded dramatically to immunosuppressive therapy, while MDS progressed to AML. He achieved long-term disease-free survival for PG and AML after transplantation.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Lin Liu, Department of Haematology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1,277 Jiefang Avenue, Wuhan 430022, Hubei, P. R. China. Tel: +86-27-85726387; Fax: +86-27-85726387; E-mail: doctorliulin@hotmail.com

### 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] Marzano AV, Borghi A, Wallach D, Cugno M. A Comprehensive review of neutrophilic diseases. *Clin Rev Allergy Immunol* 2018; 54: 114-130.
- [3] Wallach D, Vignon-Pennamen MD. Pyoderma gangrenosum and sweet syndrome: the prototypic neutrophilic dermatoses. *Br J Dermatol* 2018; 178: 595-602.
- [4] Gupta AS, Greiling TM, Ortega-Loayza AG. A systematic review of pyoderma gangrenosum with pulmonary involvement: clinical presentation, diagnosis and management. *J Eur Acad Dermatol Venereol* 2018; 32: e295-e297.
- [5] Kaffenberger BH, Hinton A, Krishna SG. The impact of underlying disease state on outcomes in patients with pyoderma gangrenosum: a national survey. *J Am Acad Dermatol* 2018; 79: 659-663, e2.
- [6] Farah C, Bulai Livideanu C, Jegu J, Paul C, Viraben R, Lamant L, Delavigne K, Adoue D, Laurent G, Beyne Rauzy O. Prevalence and prognostic value of cutaneous manifestations in patients with myelodysplastic syndrome. *J Eur Acad Dermatol Venereol* 2010; 24: 1171-5.
- [7] Hamada T, Matsuura H, Oono T, Morizane S, Yamasaki O, Asagoe K, Yamamoto T, Tsuji K, Iwatsuki K. Karyotypic analysis of bone marrow cells in pyodermic lesions associated with myelodysplastic syndrome. *Arch Dermatol* 2008; 144: 643-8.
- [8] Enright H, Jacob HS, Vercellotti G, Howe R, Belzer M, Miller W. Paraneoplastic autoimmune phenomena in patients with myelodysplastic syndromes: response to immunosuppressive therapy. *Br J Haematol* 1995; 91: 403-8.
- [9] Saif MW, Hopkins JL, Gore SD. Autoimmune phenomena in patients with myelodysplastic syndromes and chronic myelomonocytic leukemia. *Leuk Lymphoma* 2002; 43: 2083-92.