# Superficial granulomatous pyoderma with IgA monoclonal gammopathy: A case report.

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ABSTRACT:

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Superficial granulomatous pyoderma (SGP), also known as vegetative pyoderma gangrenosum, is a rare variant of pyoderma gangrenosum (PG), which is commonly characterized by well-defined erythematous or violaceous, clean-base ulcer with superficial vegetative plaque at border, predominantly located on the trunk. Diagnosis is mostly confirmed by clinical and histopathological findings while exclusion of the other cutaneous conditions such as infection, autoimmune disease, cutaneous malignancy and cutaneous metastasis should be considered. SGP is not usually related to systemic conditions and it tends to response well to less aggressive treatment as compared to the other variants of PG. We present an unusual case of a male patient with a 3-year history of SGP on several sites of the body with subsequent diagnosis of IgA monoclonal gammopathy.

**Key words:** IgA monoclonal gammopathy, superficial granulomatous pyoderma, vegetative pyoderma gangrenosum

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**บทคัดย่อ:**

**ปิยะรัตน์ ธัญนิพัทธ์ เพ็ญวดี พัฒนปรีชากุล สุขุม เจียมตน รายงานผู้ป่วยโรคผิวหนังอักเสบ SUPERFICIAL GRANULOMATOUS PYODERMA ในผู้ป่วย IgA MONOCLONAL GAMMOPATHY**

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โรคผิวหนังอักเสบ superficial granulomatous pyoderma (SGP) หรือ vegetative pyoderma gangrenosum จัดอยู่ในโรคผิวหนังอักเสบชนิดหนึ่งของ pyoderma gangrenosum (PG) ซึ่งลักษณะของ SGP มักจะมาด้วยผื่น แดง ม่วง แตกเป็นแผลลุกลามที่มีขอบลักษณะ vagetative border ตำแหน่งที่พบได้บ่อยคือ ลำตัว โดยที่ต้องแยกจากภาวะติดเชื้อที่ผิวหนัง โรคทาง autoimmune และโรคมะเร็งผิวหนัง การวินิจฉัยโรคนี้อาศัยอาการและอาการแสดงทางคลินิก และลักษณะทางพยาธิวิทยาเพื่อช่วยในการวินิจฉัยแยกโรค เนื่องจาก SGP เป็น PG ชนิดที่มักไม่สัมพันธ์กับโรคทางระบบอื่นๆ ของร่างกาย รายงานนี้นำเสนอกรณีศึกษาผู้ป่วย SGP ที่มีแผลกระจายหลายตำแหน่งของร่างกาย ร่วมกับมีภาวะ IgA monoclonal gammopathy ซึ่งพบรายงานน้อยมากที่จะสัมพันธ์กับภาวะดังกล่าว

**คำสำคัญ:** อิมมูโนโกลบุลินเอ โมโนโคลนอล แกมโมพาที, แผลไพโอเดอร์มา แกงกรีโนซุ่ม ชนิดตื้น, แผลไพโอเดอร์มา แกงกรีโนซุ่ม ชนิดเวเจเตชั่น

## Introduction

Superficial granulomatous pyoderma (SGP) is a rare variant of pyoderma gangrenosum (PG) characterized by slowly progressive, superficial vegetative, painless, clean-based ulcer without undermined edge at periphery. The lesions typically located on trunk, but face, extremities or intertriginous sites had been reported. SGP is less frequently associated with systemic diseases. We present a case of extensive SGP with IgA monoclonal gammopathy. The patient has responded well to systemic isotretinoin, corticosteroid and dapsone. Then, we discuss the subtypes of PG along with therapeutic consideration and prognosis.

## Case report

A 50-year-old Thai male presented with a 3-year duration of multiple chronic ulcers which initially developed as vesiculo-pustules on extremities and progressed to chronic painful erythematous vegetative plaques on the face, trunk, axillary regions and extremities. In the previous hospital, multiple skin biopsies had been performed and histological findings demonstrated mixed inflammatory cell infiltrate with granulomatous formation with negative results on tissue cultures for bacteria, mycobacteria and fungus. The patient had never experienced any episode of fever or other systemic constitutional symptoms and had no

known underlying diseases, comorbidities, or concurrent medication. After several courses of oral antibiotics and local wound care for one year with no significant response, the patient was transferred to our hospital, a tertiary care hospital, for further investigation and management.

On his arrival, clinical examination revealed multiple discrete painful papules, pustules and well-circumscribed ulcerative plaques of variable size with vegetative border, central cribriform scars and purulent discharge on both cheeks, neck, chest wall, left buttock and extremities (Fig 1 A and C). Superficial lymphadenopathy was not palpable and other systematic examinations showed unremarkable findings.

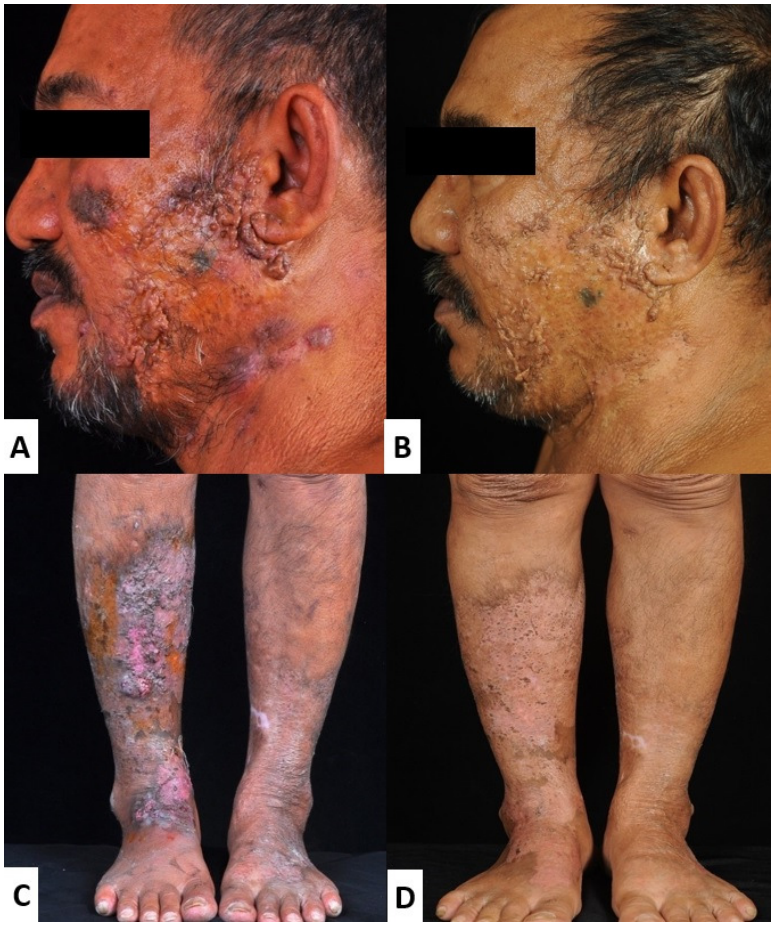


**Figure 1**

A, C) Multiple vegetative, ulcerated plaques on the face and legs.

B, D) After 6 weeks of treatment, healing with residual vegetative plaques and cribriform scarring in the center of the lesions and post-inflammatory hyperpigmentation were observed.

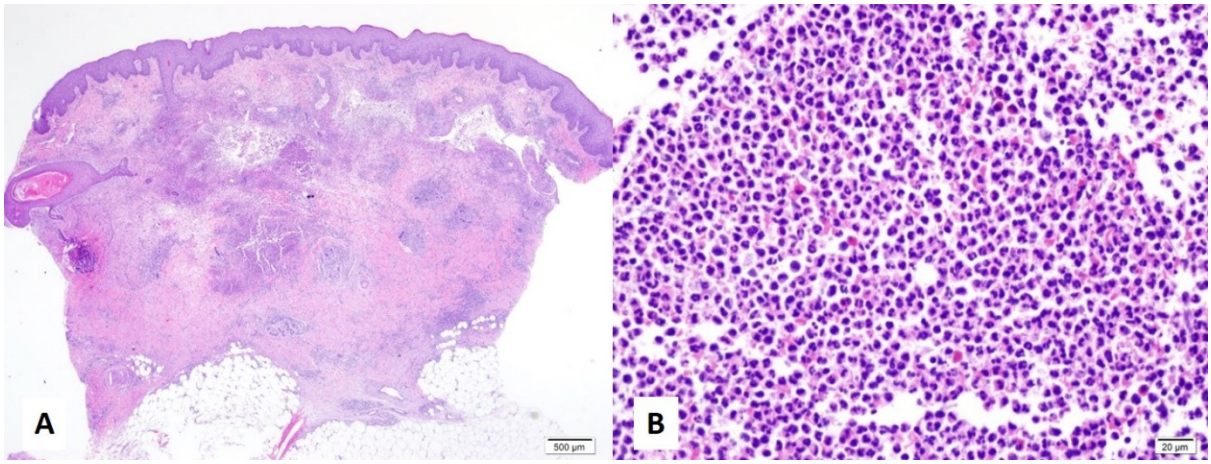


**Figure 2**

A) Pseudoepitheliomatous hyperplasia, sinus tract formation with nodular and diffuse dermal infiltrate with neutrophils. (Hematoxylin-Eosin stain, Magnification x40)

B) Diffuse infiltrate predominantly of neutrophils with few eosinophils and plasma cell. (Hematoxylin-Eosin, Magnification x400)

Skin biopsy obtained from each vegetative ulcer from both arms revealed similar histopathological findings which demonstrated an ulcerated epidermis with presence of pseudoepitheliomatous hyperplasia and dense acute inflammatory cell infiltrate in dermis without dermal papillary edema or granulomatous inflammation (Fig 2). Stains for acid-fast bacilli and fungus in biopsy section was negative. Potassium hydroxide preparation, Gram stain, and Wright stain from pus were repeatedly negative. Tissue and pus culture also revealed negative results for bacteria, mycobacteria or fungi. Direct PCR for mycobacterium tuberculosis complex in tissue specimen was negative.

Hematological and biochemical investigations were within normal range. Serology for anti-nuclear antibody, anti-HIV antibody, hepatitis B antigen, anti-hepatitis C antibody, anti-interferon gamma autoantibody and rheumatoid factor were all negative. Chest x-ray showed no evidence of pulmonary tuberculosis. Additional investigation for serum protein electrophoresis and immunofixation showed abnormality of monoclonal alpha heavy chain, however, bone marrow aspiration and biopsy were normal.

Based on clinical and histological features, repeated negative tissue cultures and abnormal increased level of serum alpha heavy chain, the patient was finally diagnosed with SGP with IgA monoclonal gammopathy. The patient was initially treated with oral prednisolone 0.5

mg/kg/day, then with tapering dose in 10 months. Dapsone 100 mg/day and isotretinoin 25 mg/day orally were added later on for steroid sparing purpose and the maintenance of treatment. After treatment for 6 weeks, all lesions showed gradual improvement and substantial decreasing in diameter and depth (Fig 1 B and D). However, during combination therapy with low-dose prednisolone (2.5-5 mg/day), dapsone 100 mg/day and isotretinoin 25 mg/day, recurrence of lesions occurred on the face and extremities at 4-month follow-up visit. Increasing dose of oral prednisolone was intermittently given to control cutaneous lesions. Regular follow up with hematologist for underlying monoclonal gammopathy of undetermined significance (MGUS) had been scheduled.

**Discussion**

We present a case of SGP showing aggressive clinical feature of cutaneous manifestation with uncommon alpha heavy chain monoclonal gammopathy. The case demonstrated generalized and extensive ulcerative lesions on several body sites. This clinical feature was contrast to previous reports of SGP which usually had limited and less aggressive clinical presentation.[1,2] Despite the typical cutaneous lesions, definite diagnosis had been made one year later due to atypical clinical presentation. Presence of granulomatous reaction in previous skin biopsies with negative tissue culture supports the diagnosis of SGP. Furthermore, histological finding of diffuse dermal infiltrate of neutrophils without presence of microorganism in biopsy section and tissue culture, is even more supportive for the diagnosis of neutrophilic dermatosis.

To date, pathogenesis of PG is poorly understood. Multifactorial pathophysiology including neutrophilic dysfunction, abnormal inflammatory mediators or genetic predisposing have been proposed.[3] Four major clinical and histopathological variants have been noted: as ulcerative, pustular, bullous and vegetative (Table 1).[1,2,4,5] Some reports added peristomal PG for the fifth variant.[4] For diagnosis of SGP, clinical and histopathological findings were the mainstay after excluding other causes such as infections, autoimmune diseases or cutaneous malignancies. Histopathological findings of 3-layered central zone of neutrophils surrounding with granuloma and outer layer of numerous plasma cells and eosinophils, with sinus tract formation usually found in SGP.[1]

**Table 1.** Subtypes of pyoderma gangrenosum.[1,2,4,5]

| Subtype | Clinical features | | | Histologic features | Associated systemic conditions |
|---|---|---|---|---|---|
| | Characteristic of lesion | Painful | Location | | |
| Ulcerative (Classic) | Single or few violaceous ulcer(s) with undermined borders<br>Necrotic base<br>Some small pustules<br>Rapidly progression | + | Traumatic area<br>Lower extremities | Subcorneal neutrophilic collections<br>Fibrin deposition in blood vessels wall with endothelial swelling<br>Thrombosis | IBD<br>Arthritis and RA<br>Monoclonal gammopathy<br>Malignancy |
| Bullous | Superficial bullae<br>Blue-gray border of ulcer(s)<br>Less invasive<br>Rapidly progression | + | Face<br>Extremities | Subepidermal bullae<br>Intra-epidermal and dermal neutrophilic infiltrate | Myeloproliferative disorder: leukemia, myelodysplasia<br>IBD |
| Pustular | Rare<br>Pustules<br>Red halo<br>Often symmetric | + | Lower extremities<br>Upper trunk | Subcorneal pustules<br>Perifollicular neutrophilic infiltrate | IBD<br>Jejunoileal bypass<br>PCV<br>Hepatobilliary disease |
| Vegetative (SGP) | Rare<br>Single or few superficial and vegetative ulcer(s)<br>Lack of violaceous raised border<br>Clean base<br>Sinus tracts<br>Slowly progression<br>Less aggressive | - (painless) | Trunk<br>Face | Pseudoepitheliomatous hyperplasia<br>Sinus tracts<br>Granuloma formation<br>Dermal neutrophilic infiltrate | Uncommon (report: Behcet's disease, multiple sclerosis) |
| Peristomal | Erythematous to violaceous papules<br>Undermined border(s)<br>Same as classic PG | + | Adjacent to stoma | Granulation tissue<br>Neutrophilic collection<br>Mixed inflammatory cell infiltrate in dermis | IBD<br>GI malignancy<br>Monoclonal gammopathy<br>CNT disease |

+ painful

- painless

CNT = connective tissue, GI = gastrointestinal; IBD = inflammatory bowel disease; PG = pyoderma gangrenosum; PCT = polycythemia vera; RA = rheumatoid arthritis; SGP = superficial granulomatous pyoderma.

The data from reports and reviews of PG management determines lack of gold standard of therapy, however there are suggestions for treatment of underlying disease such as IgA monoclonal gammopathy, inflammatory bowel disease, hematologic malignancies, Behcet's disease, Sweet syndrome, hepatitis, HIV, acne conglobata, chronic psoriasis, rheumatoid arthritis, systemic lupus erythematosus, pregnancy, and Takayasu arteritis.[2,3,6,7]

SGP is not frequently associated with systemic disease, however Behcet's disease and multiple sclerosis were reported.[8,9] SGP usually has better therapeutic response than classic PG. Complete responded with topical corticosteroid, topical tacrolimus, systemic methylprednisolone therapy, tetracyclines, dapsone, cyclosporin, intravenous immunoglobulin (IVIg), and biologic agents such as infliximab have also been reported.[1,5,10,11,12,13] Facial SGP tends to be recalcitrant for treatment.[11] Surgical procedure of SPG is not recommended due to frequently positive pathergy. SGP shows good prognosis, although recurrence is common.[1,10]

In summary, our case should raise awareness in clinical practice to consider SPG as a possible cause of chronic non-healing superficial or vegetative ulcers, especially in the patient who experiences failure of treatment with antibiotics and adequate wound care. Clinical findings, histopathology and repeated negative culture of causative infectious organisms could be useful for making diagnosis. Although uncommonly related with systemic diseases, prompt investigation for monoclonal gammopathy or systemic involvement may be essential in these population. Although SGP has a better prognosis than the classic form, the patient should be advised for a long-term monitoring and maintain regular checkup schedule on both cutaneous lesions and underlying monoclonal gammopathy.

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