

A case of chronic ulcer due to subcutaneous arteriolosclerosis in an obese patient mimicking pyoderma gangrenosum

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Abstract

The differential diagnosis of chronic ulcers covers a wide range of diseases and poses a diagnostic challenge. Subcutaneous ischemic arteriolosclerosis can lead to local ischaemia and ulceration as a result of arteriolar narrowing and reduction of tissue perfusion. This pathophysiological feature can be seen in eutrophication (nonuremic calciphylaxis) in morbid obesity, hypertensive ischemic leg ulcer (Martorell ulcer) and calciphylaxis in chronic renal insufficiency. All of the ulcers happened in this way can be wrongly diagnosed as pyoderma gangrenosum because of clinical similarity and inadequate biopsies. We report a case of chronic ulcer due to subcutaneous arteriolosclerosis in morbid obesity, wrongly diagnosed as pyoderma gangrenosum. It can be detrimental to misdiagnose the ulcers due to subcutaneous arteriolosclerosis as pyoderma gangrenosum since they need a diametrically different approach.

Introduction

The differential diagnosis of chronic ulcers covers a wide range of diseases and poses a diagnostic challenge.^{1,2} The clinical presentations, underlying etiology, and pathological manifestations of the ulcers are major clues to make the diagnosis.

Hafner reviewed four diseases: i) calciphylaxis (distal pattern); ii) calciphylaxis (proximal pattern); iii) Martorell hypertensive ischemic leg ulcer; iv) calciphylaxis with normal renal and parathyroid function (eutrophication) all having the same clinical features as necrotizing livedo, skin infarctions and ulcerations at typical locations. Hafner stated that these four diseases largely share the same risk factors including arterial hypertension, diabetes mellitus (types 1 and 2), secondary or tertiary hyperparathyroidism (in end-stage kidney disease) and oral anticoagulation with vitamin K

antagonists.³ Also a shared histopathology has been stated in these diseases: subcutaneous ischemic arteriolosclerosis characterized by a medial calcinosis and stenosis due to thickening of the vessel wall (hyperplasia of the smooth muscle layer) and/or intimal hyperplasia.²⁻⁴ Hafner *et al.*⁵ suggested the term *uremic small artery disease with medial calcification and intimal hyperplasia* instead of the customary denomination *calciphylaxis*. In 1992 Ramsey-Stewart reported a case of progressive dermatoliponecrosis in a morbidly obese patient and suggested the term *eutrophication* for. Even though he did not investigate the existence of subcutaneous arteriolosclerosis he claimed that in obese people inadequate peripheral tissue perfusion affects the apex of grossly dependent adipose folds and leads patchy gangrenous changes and skin infarctions.⁶

Case Report

A 44-year-old man who had Nissen fundoplication and incisional hernia repair operation one year and three months ago respectively, referred to our hospital for a linear necrotic ulcer 15 cm in length 5 cm in width at the anterior abdomen, on incision line. He had type 2 diabetes mellitus for five years, no hypertension or renal insufficiency and he was obese as his body mass index was 31.1 kg/m². The ulcer first appeared after removing the sutures of incisional hernia repair and rapidly enlarged. After surgical debridement of necrotic tissues and three sessions of negative pressure wound therapy with vacuum dressings, a prominent effect was not observed. The ulcer kept on growing, reached 15×10 cm dimensions with raised and rolled undermining margins (Figure 1A). By the way the incisional biopsy taken from the edge of the ulcer concluded as pyoderma gangrenosum. After taking 80 mg/day methylprednisolone for one week the ulcer got worse, enlarged and deepened (Figure 1B). Systemic steroid treatment stopped and a second biopsy was taken in a large elliptical shape starting from healthy skin at the ulcer edge extending into the fascia. Histological examination revealed subcutaneous arteriolosclerosis with thickened arteriole walls and narrowed lumens and Von Kossa staining also displayed the calcification in the vessel walls (Figure 2). Serum concentration of urea was 14 mg/dL [normal range (nr): 19-50], creatinine was 0.73 mg/dL (nr: 0.72-1.25), parathyroid hormone was 32.5 pg/mL (nr: 11-88), calcium was 10.1 mg/mL (nr: 8.8-10.6) and phosphate was 3.3 mg/mL (nr:

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2.5-4.5), alanine aminotransferase was 5 U/L (nr: 0-50), aspartate aminotransferase was 15 U/L (nr: 0-50), gamma-glutamyl transferase was 27 U/L (nr: 0-55), total bilirubin was 0.2 mg/dL (nr: 0.3-1.2), direct bilirubin was 0.1 mg/dL (nr: 0-0.2). His other liver function parameters including prothrombin time test, serum protein electrophoresis and abdominal ultrasonography were in normal limits. Also he had no history of weight loss, pain, fever, fatigue, persistent cough or hoarseness, no change in bowel habits and no finding of lymphadenopathy in physical examination. With these clinical and laboratory findings we ruled out uremic calciphylaxis, liver failure, neoplasia and made the diagnosis of eutrophication (nonuremic calciphylaxis). After six more sessions of negative pressure wound therapy with vacuum dressings, split thickness skin grafting was done successfully.

Discussion

Eutrophication or nonuremic calciphylaxis or calciphylaxis in normal renal function affects morbidly obese people who has also arterial hypertension and type 2 diabe-

tes mellitus. It is characterized by rapid appearance of progressive skin infarctions in places where fatty tissue is particularly thick such as inner thigh, fatty abdominal apron, breasts or outer upper arms.^{3,4} The skin infarction begins with a painful livedoid area and becomes necrotic with progressive livid margins. Histologically arterioles show massive thickening of the vessel wall (hyperplasia of the smooth muscle layer) leaving a narrow lumen which is often thrombosed. This subcutaneous ischemic arteriolosclerosis is a common pathophysiological feature also in Martorell hypertensive ischemic leg ulcer, calciphylaxis in chronic renal insufficiency. All of them can lead to local ischaemia and ulceration as a result of arteriolar narrowing and reduction of tissue perfusion.^{2,3,7}

On the other hand, pyoderma gangrenosum (PG) is a rare neutrophilic inflammatory skin disease presenting with painful sterile ulcerations. Its etiology remains unknown however it is commonly associated with inflammatory bowel disease, rheumatoid arthritis, hematologic malignancies and disorders.^{8,9} Also it may occur in areas of trauma or surgery; a phenomenon called pathergy.¹⁰ Jockenhöfer *et al.*¹¹ also suggested an association of obesity and PG.

Our patient was a confusing case as he did not have a disorder like inflammatory bowel disease, rheumatoid arthritis or hematologic malignancy but he was obese, had a surgery before the ulceration, his ulcer with livid margins and undermining edges enlarged progressively directing us to the diagnosis of PG. After the pathological confirmation of pyoderma gangrenosum we decided to start systemic steroids which are often the first choice drugs for PG along with other immunosuppressive treatments. But he did not benefit from steroid treatment and even it aggravated the ulcer.

The ulcers mentioned above whose shared histopathology was subcutaneous ischemic arteriolosclerosis can be wrongly diagnosed as pyoderma gangrenosum because of clinical similarity and inadequate biopsies.^{3,4,12} Moreover, superficial biopsy samples taken from many types of chronic wound base can be misdiagnosed as pyoderma gangrenosum because necrotic dermis with sheets of neutrophil granulocytes can be found. In a study by Hafner *et al.*⁴ 50% of 31 cases of Martorell ulcers were misdiagnosed as pyoderma gangrenosum and 20% as necrotizing vasculitis. So in the suspicion of eutrophication and other ulcers caused by subcutaneous arteriolosclerosis, biopsies should be of sufficient depth extending into the subcutis. Our case's not the first but the second biopsy which was taken in a large elliptical shape starting from

healthy skin at the ulcer edge extending into the fascia yielded the subcutaneous arterioles with hyperplasia of the smooth muscle layer and narrowing of the lumen. Our patient's ulcer did not begin spontaneously but occurred after the surgery on the incision line but it is not contradictory to the eutrophication (nonuremic calciphylaxis) theory as the subcutaneous arteriolosclerosis and decreased tissue perfusion did not allow the cutt to heal and enlarged the ulcer.

It can be detrimental to misdiagnose eutrophication (nonuremic calciphylaxis) and other subcutaneous arteriolosclerotic ulcers as pyoderma gangrenosum since they need a diametrically different approach. Pyoderma gangrenosum needs systemic steroid treatment and surgical approaches are

not recommended.^{3,4,9} However treatment of skin infarctions from subcutaneous ischemic arteriolosclerosis includes surgical debridement, negative pressure wound therapy and split thickness skin grafting and systemic medication for analgesia and infection.^{1,3,7} Systemic steroids can cause exacerbation as in our case, sepsis and even death in subcutaneous arteriolosclerosis.

Conclusions

According to Hafner³, eutrophication (nonuremic calciphylaxis) and other entities showing subcutaneous ischemic arteriolosclerosis are not known very well and familia-

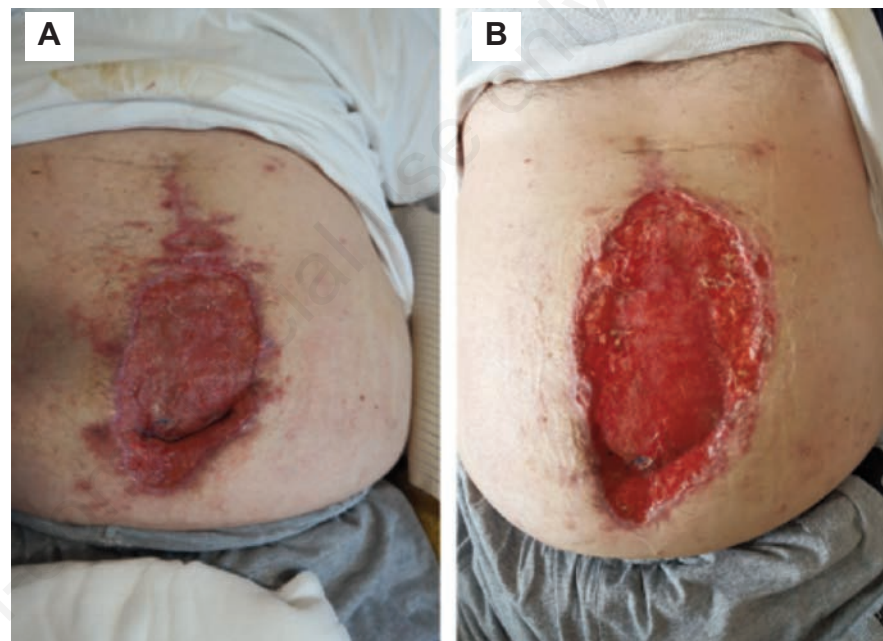


Figure 1. The ulcer on the incision line at the anterior abdomen had livid undermined margins resembling pyoderma gangrenosum, before steroid treatment (A) and after taking 80 mg/day methylprednisolone for one week the ulcer enlarged and deepened (B).

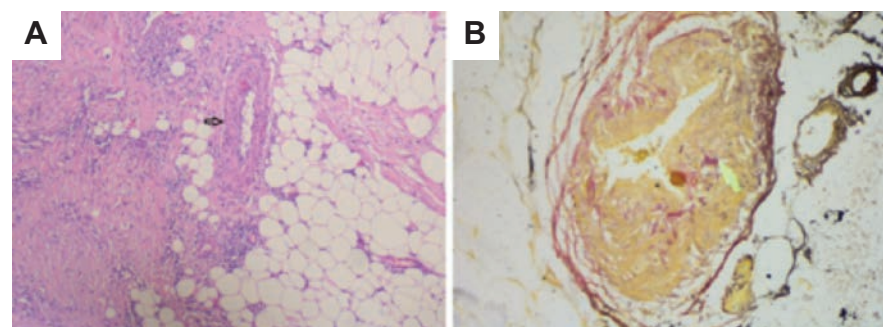


Figure 2. A) Subcutaneous arteriole (black arrow) shows hyperplasia of smooth muscle layer, narrowing of the lumen and increased wall-to-lumen ratio resulting in skin infarction leading to ulceration (hematoxylin-eosin, original magnification $\times 10$). B) Von Kossa staining ($\times 20$) shows vessel calcification (yellow arrow) in addition to narrowing of the lumen.

rity with these disorders should be improved especially because of the risk of confusion with pyoderma gangrenosum. And our case demonstrates that he is wright.

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