Case Report

Pyoderma gangrenosum and spinal epidural abscess after subcutaneous administration of recombinant human erythropoietin


Department of Internal Medicine, Catholic University Medical College, Seoul, Korea

Key words: erythropoietin; diabetes mellitus; end-stage renal failure; pyoderma gangrenosum; spinal epidural abscess

Introduction

Pyoderma gangrenosum is an uncommon non-contagious condition of unknown aetiology resembling a Shwartzman-like hypersensitivity reaction. It typically begins as a pustule and presents as solitary or multiple sterile ulcerated nodules or plaques. The pustules may progress to large necrotic ulcerative lesions with painful undermined dusky margins [1]. Pyoderma gangrenosum may appear spontaneously or after trauma to the skin. It may be associated with systemic diseases, e.g. Crohn’s disease, ulcerative colitis, polyarteritis, or a variety of haematological disorders [2]. Recently pyoderma gangrenosum has been reported after administration of haematopoietic colony-stimulating factors [3,4]. Although the exact mechanism involved remains uncertain, many findings point to abnormal or depressed immune responses in patients with pyoderma gangrenosum [5,6].

Although infections and bacteraemia are common in haemodialysis patients, spinal epidural abscess formation is rare. Infection of the epidural space is most frequently the result of haematogenous dissemination from a distant focus [7], e.g. bacteraemia secondary to infected arteriovenous graft or haemodialysis catheter. Staphylococcus aureus was found in about 60% of the cases. Early recognition and prompt treatment with antibiotics and decompressive laminectomy improve the otherwise poor outcome [7,8].

We report a case of spinal epidural abscess formation subsequent to pyoderma gangrenosum which had developed after subcutaneous administration of recombinant human erythropoietin (rHuEpo).

Case report

A 41-year-old Korean woman with end-stage renal failure secondary to diabetic nephropathy had been on maintenance haemodialysis for 12 years. She was admitted with high fever, and multiple erythematous ulcerated pustules of the skin on the lateral aspect of the right upper arm, lower back, left thigh, and both ankles. Five days earlier rHuEpo has been administered by s.c. injection on the lateral aspect of the right upper arm. One day after injection, high fever and multiple erythematous macules and papules appeared at the site of injection and at other areas of the skin. On admission, the patient was alert, had a temperature of 30.2°C, regular pulse (96/min), a blood pressure of 100/60 mmHg, and a respiration rate of 20/min. Cardiopulmonary examination was unremarkable. There was no lymphadenopathy, hepatosplenomegaly, or arthralgia. The neurological examination was unremarkable. Laboratory investigations revealed WBC 14 000/mm$^3$ (segment 88%), haemoglobin 7.4 g/dl, haematocrit 23%, and platelets 50 000/mm$^3$. Other findings included BUN 25.8 mg/dl, creatinine 3.5 mg/dl, total protein 4.7 g/dl, albumin 3.0 g/dl. Fibrin degradation products and fibrinogen were within the normal range. Repeated blood cultures and swabs taken from the lesions remained negative. Septicaemia was suspected and cephalosporin and gentamicin were administered. On the 3rd day, the patient was afebrile and a skin biopsy was taken from the site of injection (Figure 1). It revealed acute necrotizing inflammation with perivasculitis in the subcutaneous tissue (Figure 2). The finding was consistent with pyoderma gangrenosum. Sigmoidoscopy, barium enema examination, antinuclear antibodies (ANA), anti-dsDNA, antineutrophil cytoplasm antibody, C3, C4, rheumatoid factor, serum protein electrophoresis, and immunoelectrophoresis were all normal. On the 12th day, the patient was started on steroids and antiseptic wound dressings were administered. Thereafter the wounds began to heal and the general condition improved. On the 19th day the patient developed back pain in the dermatomes T$_9$ to T$_{12}$ without focal neurological deficit. Persistent erythema...
Fig. 1. The lesion of pyoderma gangrenosum arise on the upper arm over recombinant human erythropoietin injection site. This lesion is centrally ulcerated and crusted, with a raised peripheral margin.

Fig. 2. Photomicrograph of a skin biopsy specimen from pyoderma gangrenosum demonstrates a moderate perivascular neutrophil and lymphocyte infiltration with endothelial swelling. Epidermal changes include mild intercellular oedema and exocytosis (H&E × 200).

and sloughing (6 × 5 cm) of the skin at the site of past rHuEpo injection were noted. The WBC was 10 400/mm³. The plain X-ray films of the thoracolumbosacral spine and a bone scan were unremarkable. On the 24th day the patient complained of severe back pain. Tenderness over the lumbar spine, weakness of the right leg, and fever were noted. Magnetic resonance imaging showed an extradural mass extending from the inferior portion of T₁₂ through the superior portion of L₂ (Figure 3) and right lateral indentation of the L₁ disc with displacement of the anteromedial aspect of the canal (Figure 4). The echocardiogram failed to show valvular vegetations. The WBC was 12 000/mm³. Sonographically guided epidural abscess biopsy showed a mixed acute and chronic inflammatory reaction with granulation tissue. The aspirates yielded no bacterial growth. A combination of vancomycin, metronidazole, and ciprofloxacin was given and immediate neurosurgical intervention was recommended. The patient and her family refused surgical interven-

Fig. 3. An ovoid high signal intensity is noted at the level of T₁₂ and extended paraspinal back muscles and interlaminar soft tissue from T₁₁–₁₂ to L₂ (arrows, sagittal section, T₂ W1).

Discussion

Pyoderma gangrenosum may be a purely cutaneous disorder. More commonly it presents as a systemic Shwartzman-like reaction. It may be linked to conditions with depressed and abnormal immunological status, e.g. diabetes mellitus, chronic ulcerative colitis, regional ileitis, rheumatoid arthritis, dysproteinuria, and occasionally leukaemia or lymphoma [1,2]. Recently pyoderma gangrenosum was also observed after administration of haematopoietic colony-stimulating factors (CSF) [3,4]. These cutaneous side-effects of CSF have been linked to upregulation of neutrophilic function and release of cytokines [4].

The administration of recombinant human erythropoietin (rHuEpo) in renal patients has been associated with several adverse effects, i.e. hypertension, seizures, increased clotting of vascular access or dialysers, reduced dialysis efficiency, and influenza-like syndrome. Pyoderma gangrenosum has so far not been described in association with injection of rHuEpo [9]. In our patient, the eruption occurred in temporal association with the s.c. injection of rHuEpo, similar to what had been reported for CSF [3]. Pyoderma gangrenosum began the day after injection of rHuEpo at the site of subcutaneous injection, and a skin ulcer persisted as long as the patient was hospitalized. Further inflammatory nodules and pustules occurred in multiple skin areas.
We cannot exclude the chance association between pyoderma gangrenosum and the administration of rHuEpo. If there is a link, it is curious why this should only occur in the occasional patient. Whether this is related to some predisposing immune abnormality is uncertain [10–12].

Spinal epidural abscess is rare. The incidence is approximately 0.5 to 1.2 cases per 10,000 hospital admissions in the United States. Only 12 cases have been reported in haemodialysis patients [7]. It consists of bacterial infection of the epidural fat. In haemodialysed patients the source of the bacteria are usually endovascular prosthetic grafts and skin infections. Half of the patients have diabetes mellitus. Our patient was diabetic and presented with the classical syndrome of fever, backache, local spinal tenderness, and weakness of lower extremities. The source of the bacteria was presumably haematogenous dissemination from the superinfected skin ulcers. In 70% of the patients cultures from blood and abscess are positive, mostly yielding Staphylococcus aureus [7]. Cultures were negative in our patient, presumably because of previous administration of antibiotics.

The diagnosis of spinal epidural abscess formation requires imaging procedures, myelography, or magnetic resonance imaging (MRI) with gadolinium enhancement, which has become increasingly popular. It is non-invasive and its sensitivity is comparable to that of CT myelogram [13]. The most common site of spinal epidural abscess formation is the thoracic spine and the average number of spinal segments involved is 3.1. The prognosis is poor [7] and immediate decompression and prolonged antibiotic therapy are the procedures of choice [7,8,14].

The present case is of interest because of the potential, but not definitely proven, link of pyoderma gangrenosum to subcutaneous administration of rHuEpo and further illustrates the possibility of development of spinal epidural abscesses from superinfected skin lesions of pyoderma gangrenosum.

**Acknowledgements.** The authors thank the St Vincent Hospital and Dialysis Unit nurses for kind assistance.

**References**


**Received for publication: 26.11.96**

*Accepted in revised form: 5.3.97*