SHORT REPORT

The efficacy of intensive granulocyte and monocyte adsorption apheresis in a patient with Crohn's disease complicated by extensive subcutaneous aseptic neutrophilic abscesses

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Abstract

Background and aims: Subcutaneous aseptic abscess is one phenotype of neutrophilic dermatitis. We were interested to see if a case of steroid refractory Crohn's disease (CD) complicated by subcutaneous aseptic neutrophilic abscesses responds to intensive granulocyte/monocyte adsorptive apheresis (GMA).

Methods: The patient was a 21-year-old male with worsening severe CD while on oral prednisolone (30 mg/day). His symptoms included fever, bloody diarrhoea and multiple painful subcutaneous nodules throughout his body. Skin biopsy showed chronic panniculitis with neutrophilic infiltrates. Further, colonoscopy showed oedematous sigmoid colon, while colonic biopsy showed non-caseous granuloma. Because biologics were feared to increase the risk of bacteraemia as the result of germ culture on his pus was not known at the time, we decided to treat this case with GMA. Five GMA sessions with the Adacolumn over 5 consecutive days (daily GMA) were initiated.

Results: On admission, his CD activity index (CDAI) was 355, C-reactive protein (CRP) 11.2 mg/dL. After 5 GMA sessions, CDAI decreased to 170, and CRP fell to 5.0 mg/dL, with no fever. GMA was restarted at 2 sessions/week (total 10 sessions). The patient's CDAI fell to <150, and the skin lesions re-epithelialized.

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Conclusions: In this CD case complicated by subcutaneous aseptic neutrophilic abscesses, GMA appeared to be effective. Our impression is that when biopsy reveals neutrophil infiltrate is a major feature of the lesions, GMA should be considered. As GMA appears to have no safety concerns, a frequent GMA protocol, like daily followed by 2 to 3 times/week should be preferred over the routine weekly GMA.

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1. Introduction

Neutrophilic dermatitis sometimes complicates inflammatory bowel diseases (IBD).\(^1,2\) Subcutaneous aseptic abscess is one phenotype of neutrophilic dermatitis.\(^2\) Further, patients with IBD present with elevated and activated myeloid lineage leucocytes (neutrophils, monocytes), which by releasing inflammatory cytokines are thought to be part of the immune pathology in IBD.\(^3\) Accordingly, selective depletion of granulocytes and monocytes by extracorporeal adsorption (GMA) with an Adacolumn (JIMRO, Takasaki, Japan) has been associated with significant efficacy in patients with immune disorders including IBD.\(^3-5\) Here we report on a case of Crohn’s disease (CD) complicated by extensive subcutaneous aseptic neutrophilic abscesses who responded well to a course of intensive GMA.

2. Case report

A 21-year-old male was admitted to our hospital complaining of fever, bloody diarrhoea and painful subcutaneous nodules. In the past, he had been diagnosed with ulcerative colitis (UC) and had received treatment with, up to 4000 mg/day 5-aminosalicylic acid (5-ASA) for one year. Painful swellings had appeared to his knees and footpads for the first time two months before admission to our hospital. Under our care, bloody stool and painful swellings worsened in spite of being on prednisolone (PSL, 30 mg/day, oral) for two months prior to arrival. The dose of PSL had been tapered to 15 mg/day two weeks before arrival. On admission, the patient had fever of 39.5 °C, cachexia, abdominal pain, bloody diarrhoea together with multiple painful subcutaneous nodules on his body including the plantar of his feet (Fig. 1). Inflammation markers were C-reactive protein (CRP) 11.2 mg/dL, erythrocyte sedimentation rate (ESR) 55 mm/h, and white blood cell (WBC) count 12.5×10\(^3\)/\(\mu\)L. Slight anaemia, haemoglobin (Hb) 11.0 g/dL was also noticed. Pus had started to ooze out from the subcutaneous nodules and circular ulcers (Fig. 1B and C). Five GMA sessions over 5 consecutive days were given to this patient instead of anti-tumour necrosis factor (TNF)-α biologics because biologics were feared to increase the risk of bacteraemia as the result of germ culture on the pus was not known at the time. Likewise, cyclosporin was considered

Figure 1  Patient’s skin appearance. Aseptic abscesses, notably painful subcutaneous nodules on the footpad (A), oozing pus from the neck (B) and round-shaped ulcers on the foot (C), were recognized before granulocyte and monocyte adsorptive apheresis (GMA) treatment. Round-shaped ulcers on the neck (D) and foot (E) were healed after GMA treatments.
unfavourable in this case. GMA was initiated and PSL (15 mg) was allowed to continue. After 5 GMA sessions, fever disappeared and the CRP titer decreased to 5.0 mg/dL. Pus ceased at the end of the second twice a week GMA therapy (Fig. 2). GMA was restarted at two sessions per week. After 10 GMA sessions, the patient asked to be spared from azathiopurine for the fear of developing alopecia. Then we opted for tacrolimus for extended medication. Tacrolimus was given because prior to the diagnosis of CD in our hospital, the patient’s IBD was assumed to be UC-like indeterminate colitis (before colonoscopy). Fig. 3 shows colonoscopic images before and after GMA treatment. Before GMA, endoscopic images showed oedematous sigmoid colon, and UC-like indeterminate colitis (Fig. 3A). However, After GMA treatment longitudinal ulcers and cobblestone appearance were clearly recognizable as mucosal swellings had receded following GMA (Fig. 3B). Colonic biopsy specimens showed non-caseous granuloma. Skin biopsy showed chronic panniculitis and neutrophilic infiltrates. He had multiple skin abscesses that had not merged. His skin lesions were different from either erythema nodosum or pyoderma gangrenosum. Finally he was diagnosed as having CD complicated by subcutaneous aseptic neutrophilic abscesses (not UC). The CDAI score decreased from the initial value of 355 to 170, and then to below the clinical remission level of 150 at the final GMA session (Fig. 2). The skin lesions re-epithelialized after GMA therapy (Fig. 1E, F).

3. Discussion

To our knowledge, this is the first report on a case in whom CD was complicated by subcutaneous aseptic neutrophilic abscesses that responded well to GMA. Daily followed by twice a week GMA therapy appeared very effective and well tolerated in this case. GMA is a natural intervention, which has been associated with a striking down-modulation of inflammatory cytokines including TNF-α.5 It is noteworthy to mention here that a previous study reported a similar effect for GMA in a case with very severe pyoderma gangrenosum (PG) lesions.6 Aseptic abscesses are characterized by deep, sterile, circular lesions containing large numbers of neutrophils and do not respond to antibiotics. The main clinical manifestations of aseptic abscesses are fever (90%), abdominal pain (67%), and cachexia (50%).2 Aseptic abscesses usually have visceral involvement like abdominal lymph nodes, liver, lungs, pancreas, and brain. Aseptic abscesses are also encountered in patients with IBD. PG is another major form of neutrophilic dermatosis, but no more than 2% of patients with IBD will have PG.6,7 Further, PG usually consists of merged large skin ulcers. In contrast, the present case had sterile circular ulcers in the lower and upper limbs, hips, neck and head. However, most subcutaneous abscesses have been reported in patients with UC.2 Cutaneous aseptic neutrophilic abscess that had deep round-shaped ulcers have also been reported in a CD patient infected with Yersinia enterocolitica.1 This case responded well to PSL,1 while the present case was refractory to PSL.

As described above, the main action of GMA is to selectively adsorb and deplete the activated neutrophils and monocytes, which are elevated with activation behaviour and increased survival time in patients with IBD.3,5 Since its introduction in 2000 for the treatment of patients with UC, GMA has routinely been given at one session per week with often inadequate efficacy.8–10 This was replaced by 2 sessions per week by Sakuraba and colleagues, calling it intensive GMA therapy.11 We also found12 that GMA at 2 sessions per week had better efficacy for CD as compared with the routine weekly GMA therapy.8,9 More recently, GMA was administered to patients with active UC at one session per day with no safety concerns.13 Further, the Adacolumn...
has CE mark, which allows its clinical application in the European countries. With this background in mind, the present case was treated with daily followed by twice a week GMA. To our knowledge, hitherto, one case of neutrophilic dermatitis has been reported in association with GMA. Infliximab (IFX) is another intervention for the treatment of neutrophilic dermatitis like PG. However, as stated above, IFX was not selected because biologics were feared to increase the risk of bacteraemia.

In conclusion, this case of CD complicated by subcutaneous aseptic neutrophilic abscesses responded well to GMA. Our impression is that when biopsy reveals neutrophil infiltrate is a major feature of the lesions, then GMA should be considered. As GMA appears to have no safety concerns, a frequent GMA protocol, like daily followed by 2 to 3 times per week GMA should be preferred over the routine weekly GMA.

Conflicts of interest

None.

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