Necrotizing fasciitis with slow progression in a patient with rheumatoid arthritis receiving tocilizumab

Necrotizing fasciitis (NF) is a rapidly progressive, life-threatening infection involving the skin, soft tissue and deep fascia [1]. The pathogenesis of NF with group A Streptococcus pyogenes (GAS) infection is thought to involve interleukin-6 (IL-6), tissue-damaging enzymes released by activated host neutrophils, and uncontrolled T-cell responses to superantigens [2]. Tocilizumab, an anti-IL-6 receptor monoclonal antibody, reduces the disease activity of rheumatoid arthritis (RA) by the blockade of IL-6 [3]. In RA patients, tocilizumab treatment increases the risk of severe infection and masks its symptoms by suppressing C-reactive protein (CRP) production [4]. Herein, we report a case of NF with slow progression in a patient receiving tocilizumab to treat RA.

A 68-year-old woman noticed acute development of pain, swelling, erythema, and purpura over the right lower leg without fever, and visited our emergency department three days later (figure 1A). The patient had been treated with methotrexate (4 mg/week) and tocilizumab (8 mg/kg once every four weeks) for RA. The last administration of tocilizumab was given 25 days before the first visit. Physical examination revealed swelling, erythema, and purpura from the right lower leg to the dorsum of the foot without septic shock. Laboratory tests showed leukocytosis (19,300/µL [normal range: 3,200–9,400/µL]) and an elevated CRP level (2.4 mg/dL [normal range: 0–0.2 mg/dL]) with otherwise normal findings. Blood culture test results were negative. Computed tomography showed no abscesses or gas spaces. Hence, she was diagnosed with cellulitis of the right leg. The patient was hospitalized and treated with cefazolin intravenously. Her condition did not improve, and the cefazolin was switched to piperacillin-tazobactam on Day 4. Clinical findings revealed no recovery despite four days of treatment, therefore the patient was transferred to our dermatology department and vancomycin was added on Day 5. A blood blister larger than 10 cm in diameter developed in the lesion on Day 6, suggesting epidermal necrosis (figure 1B). Laboratory tests showed a white blood cell count of 9,890/µL, and a CRP level of 2.4 mg/dL. The creatine kinase level was not elevated (20 U/L [normal range: 43–157 U/L]). A surgical incision and a finger test in the lesion led to the diagnosis of NF. Radical debridement was subsequently performed with additional clindamycin administration. GAS was detected from the microbial culture of the excised tissues and was susceptible to antibiotics including penicillin and cephem. Thus, we switched piperacillin-tazobactam to ceftriaxone on Day 11. Skin grafting using negative pressure wound therapy was applied to the wound, and she was discharged on Day 82 when most of the lesion was epithelialized.

In this case, the patient was diagnosed with NF 10 days after onset, due to slow progression without severe symptoms. Similar RA cases treated with tocilizumab were reported to exhibit the delayed manifestations of NF [5-7]. Only one (14%) out of seven reported cases, including our current case, died of NF; whereas the mortality rate in general NF cases is about 33% [1]. The precise mechanism of NF with GAS remains elusive, although superantigens are assumed to trigger a cytokine storm involving IL-6, leading to shock and multiple organ failure [2, 8]. In addition, an elevated frequency of IL-6-producing cells was found in the circulation in cases with severe GAS infection including NF [9]. These findings suggest that the cytokine storm stimulated by GAS was suppressed by tocilizumab, resulting in better prognosis in our case. Tocilizumab is reported to reduce the severity of other diseases with cytokine storms relating to IL-6, such as coronavirus disease 2019 (COVID-19). Consistently, early treatment with tocilizumab decreases the mortality in COVID-19 patients [10]. We assume that tocilizumab might be a potential therapeutic option for decreasing mortality in NF.

Regarding the limitations of this report, it is firstly a single-case, descriptive study, and secondly, the potential efficacy of tocilizumab on NF was based on our speculation. In conclusion, we experienced a case of NF with relatively slow progression under tocilizumab treatment. It was challenging to make an early diagnosis of NF due to its slow progression and milder symptoms, compared to those of general NF. Urgent surgical intervention resulted in a favourable outcome in our current case; therefore, continuous attention should be paid to the condition of patients who are treated with tocilizumab since the clinical course can be extensively modified.

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Blaschkoid expansive eccrine nevus with a trace of hyperhidrosis confirmed by a sensitivity-reduced iodine–starch test

Eccrine nevus (EN) is a very rare entity of cutaneous lesions accompanied by increases in eccrine gland number or size [1] without vascular proliferation around eccrine glands. Here, we report a case of EN without clinical hyperhidrosis successfully confirmed by the subtle hyperfunction of sweat glands in the lesion, as determined by our optimized sensitivity-reduced iodine-starch test.

A 16-year-old male with plaques on the lower body was referred to our hospital. At the age of six months, rough-textured plaques with thin hairs had been recognized on the left abdomen, hip and thigh. The lesions gradually hardened and became hairier with the patient’s growth, but they showed no erythema, discoulouration or hyperhidrosis. The patient had shown healthy growth, other than the skin manifestations, which followed the Blaschko lines (figure 1A, C). The characteristic dermoscopic findings, including perifollicular hyperpigmentation, that were seen in a previous reported case [1], were not observed in the present case [2]. A punch biopsy was taken from a lesion, and another was taken from an adjacent normal area on the abdomen. Histopathologically, the lesional biopsy showed larger, more numerous eccrine glands than the adjacent normal biopsy (figure 1E, F). However, neither the proliferation of vessels nor mucin deposition was seen in the lesion (figure 1G). The amounts of basal pigmentation and smooth muscle fibre were not increased. Mild dermal fibrosis was seen, as in a previous report [3]. Becker’s melanosis shows hyperpigmentation and hypertrichosis clinically, and the amounts of basal pigmentation and smooth muscle fibre are increased. But eccrine glands are not increased. Connective tissue nevus is a hamartoma in which the amount of collagen is increased, but that of the other appendages is not increased. Morphea would have shown thickened and hyalinized collagen bundles and atrophic eccrine glands. Thus, we ruled out those entities.

To assess sweat gland function, we performed a starch-iodine test using the Wada-Takagaki method, which differs from the Minor’s test in that a mixture of starch powder and...