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LETTER TO THE EDITOR

Successful treatment of a refractory pyoderma gangrenosum with risankizumab

Dear Editors,

A 59-year-old female patient with pyoderma gangrenosum had been in our outpatient care for several years. Her medical history shows that 10 years ago, after a trauma, an ulceration of the left lower leg occurred for the first time, which healed under local therapy. Six years ago, very painful ulcerations occurred again. The first presentation took place in our dermatological wound centre. A skin biopsy showed an ulcerative suppurative inflammation; the PARACELSUS score[1] was 17 points, so that we made the diagnosis of a pyoderma gangrenosum. To exclude comorbidities, an extended serological and instrumental diagnosis was made, which was unremarkable.

Due to an insufficient clinical response to the initially initiated systemic therapy with prednisolone 1 mg/kg/day, we supplemented cyclosporine 2x 100 mg/day. Due to numerous side effects, the therapy with cyclosporine had to be discontinued after a few weeks. We then initiated a systemic therapy with infliximab 5 mg/kg body weight. Because the inflammatory ulcer was still progressive, methotrexate 7.5 mg/week was additionally given once a week. The pyoderma gangrenosum healed completely under this therapy. After 5 months, a recurrence occurred again. Since seronegative chronic polyarthritis was also diagnosed in the meantime, we decided, in consultation with our colleagues from the rheumatology department, on a therapy with prednisolone 0.5 mg/kg/day and adalimumab 40 mg every 2 weeks. Again, the response was insufficient, so we discontinued this therapy after 5 months and introduced azathioprine 100 mg/d additionally to prednisolone. Even under this therapy, the findings were progressive (Figure 1), so that we decided to try a therapy with risankizumab 150 mg. Risankizumab was administered after 4 weeks and then every 12 weeks. Azathioprine had to be discontinued due to side effects. The concomitant prednisolone dose was gradually reduced and finally discontinued. After four doses of risankizumab, there was a significant improvement in the clinical findings despite the discontinuation of the other immunosuppressants (Figure 2).

Pyoderma gangrenosum is a rare neutrophilic dermatosis clinically characterised by the appearance of very painful, clinically typical ulcerations. Today, diagnosis is made by summing up different, individually unspecific criteria with the help of corresponding evaluated scores.[1] The underlying aetiology has not yet been fully clarified. Among other things, genetic autoimmunological mechanisms leading to dysfunctions of neutrophilic granulocytes and increased inflammation are discussed. Associations with other inflammatory diseases such as rheumatoid arthritis and chronic inflammatory bowel diseases as well as neoplasia are increasingly known.[2,3]

The therapy of patients with pyoderma gangrenosum is often difficult and lengthy. Besides topical treatment options with highly potent glucocorticoids or tacrolimus, systemic immunosuppressive and immunomodulating therapies are usually used.[4] Currently, only prednisone and prednisolone are approved for systemic therapy.[5] Clinical studies that have shown efficacy for drugs in randomised clinical trials **(RCTs) have so far only been available for prednisolone, cyclosporine,[6] and infliximab.[5] The IL-23 inhibitor risankizumab[7,8] has been approved by the European Medicines Agency for the treatment of psoriasis vulgaris since February 2019. It blocks the p19 subunit of IL-23.[7] The centrally important role of IL-23 in neutrophil diseases has been described several times.[9] Histological examinations have also shown an overexpression of IL-23 in the pyoderma gangrenosum.[10] Since the aetiopathology of psoriasis vulgaris and pyoderma gangrenosum have some similarities[2,3] and various standard therapies had to be discontinued in the case presented by us because of side effects or insufficient response to therapy, we decided to conduct an individual healing approach with risankizumab in this patient.

To the best of our knowledge, this is the first case report of a successful therapy of a patient with pyoderma gangrenosum with risankizumab. From our point of view, the newly

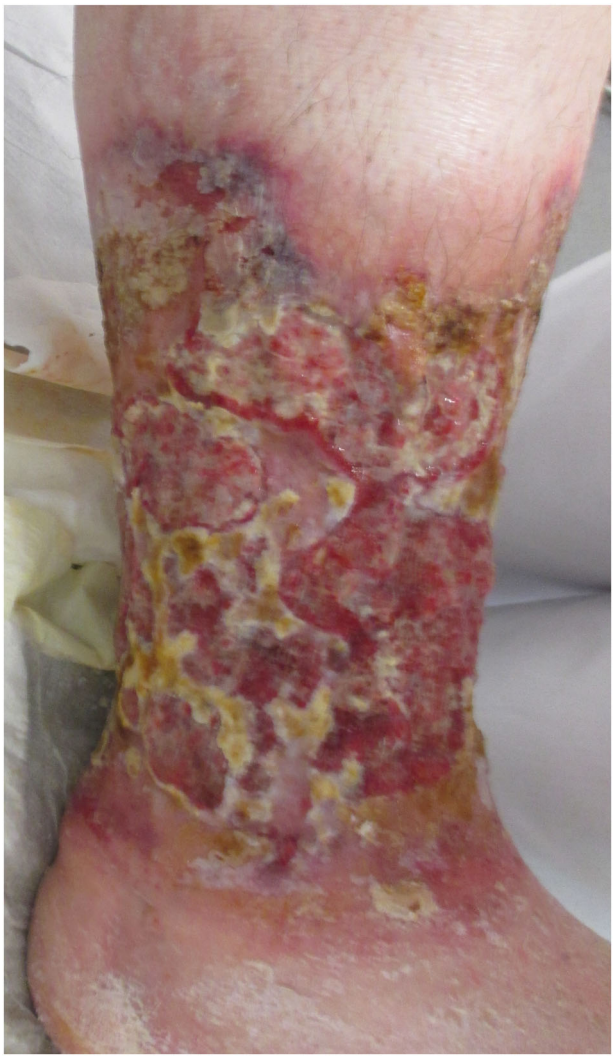

FIGURE 1 Pyoderma gangrenosum before treatment with risankizumab using complex systemic immunosuppressive therapy with glucocorticoids and azathioprine

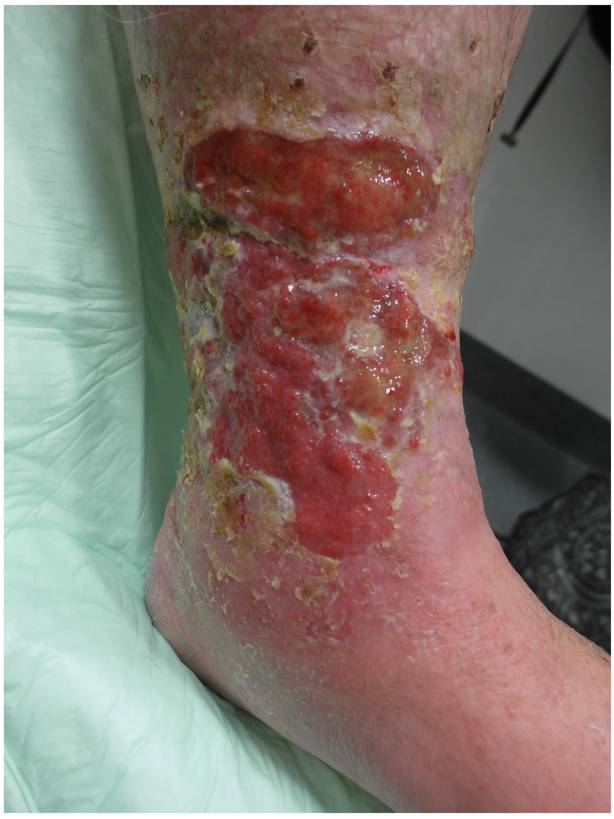

FIGURE 2 Pyoderma gangrenosum after 7 months of immunomodulating treatment with risankizumab solely

available IL-23 inhibitors in off-label use extend the treatment options and help to save other immunosuppressive drugs. Therefore, the use of these IL-23 inhibitors should be considered especially in otherwise refractory courses of patients with pyoderma gangrenosum.

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