Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that is characterized by painful and suppurating lesions. Herein, we report a case of severe HS that was refractory to multiple treatments but responded rapidly to anakinra injections.

Report of a Case

A 37-year-old woman with a 5-year history of severe HS, resistant to numerous topical and systemic agents, had inflammatory nodules, draining fistulas, and hypertrophic scars bilaterally in the axillary, perineal, pubic, and inguinofemoral regions (Figure 1). The regions were severely affected, corresponding to Hurley stage III (severe disease). The lesions caused considerable pain, marked suppuration, and malodor, resulting in severe discomfort and a substantial negative effect on quality of life.

The patient denied having a family history of HS. Her medical history included Crohn disease since age 16 years; however, the patient had reported low activity of Crohn disease for the past several years. She was a nonsmoker, weighing 119 kg with a body mass index of 40 (calculated as weight in kilograms divided by height in meters squared). Apart from HS, no signs of skin disease were noted, and the histopathologic findings were consistent with the clinical diagnosis of HS. She had been treated with several systemic agents, including oral antibiotics (including a combination of clindamycin and rifampin), azathioprine, cyclosporine, adalimumab, and infliximab, without significant improvement of the disease. Despite recent treatment with adalimumab (40 mg every week) and ongoing treatment with cyclosporine (150 mg twice daily), clindamycin (300 mg twice daily), and rifampin (300 mg twice daily) for the past 10 months, the patient continued to be severely affected by the disease and had a Dermatology Life Quality Index score of 24 (the score ranges from 0 [best quality of life] to 30 [worst quality of life]), indicating an extremely large effect on daily life.1 At no time during the past year had she been able to work full-time since she was either partially or fully absent from work due to HS.

Solution

Interleukin-1β (IL-1β) is substantially elevated in HS.4 Therefore, we started the patient on anakinra monotherapy (Kineret; Swedish Orphan Biovitrum AB), with 200 mg injected subcutaneously once daily (2 injections of 100 mg each) based on her weight. Before treatment, the patient underwent comprehensive laboratory investigations, including complete blood cell count; chemistry panel; tuberculosis (quantiFERON-TB Gold test; Cellestis Limited), human immunodeficiency virus, and hepatitis B and C screening; and chest x-ray. Except for anemia (hemoglobin 11.0 g/dL [to convert to grams per liter, multiply by 10.0]), a marginally elevated white blood cell count (11.2 × 10⁹/L) with neutrophil predominance, and an elevated C-reactive protein level (31 mg/L; normal range, 0-10 mg/L [to convert to nanomoles per liter, multiply by 9.524]), the results were normal.

Within 1 month, the patient experienced a considerable reduction in pain, suppuration, and malodor. During the following months, a continued reduction in disease activity was seen. Two months into treatment, the patient was able to resume full-time employment and an active social life. Consistent with our objective findings, a reduction in the Dermatology Life Quality Index score from 24 (an extremely large effect on quality of life) to 8 (a moderate effect on quality of life) was achieved over 3 months, indicating a marked improvement. During the following months, a reduction of both inflammation and suppuration was noted, and at the 1-year mark, the disease was in remission (Figure 2) with a Dermatology Life Quality Index score of 6. The C-reactive protein level was reduced (18 mg/L) but remained elevated. Throughout the therapy, the patient was closely monitored, including regular laboratory investigations. The patient experienced no injection site problems. Three episodes of pustular folliculitis due to Staphylococcus aureus, identified based on symptoms of stinging lesions, clinical folliculitis, and positive culture, were successfully treated with short-term oral antibiotics (amoxicillin and clavulanic acid). No other adverse effects were reported, and no other concomitant treatment was received by the patient. Now passing the 1-year mark, the treatment continues unchanged.
Discussion

Hidradenitis suppurativa is a chronic, recurrent, inflammatory skin disease of unknown cause. It presents clinically as painful inflamed nodules, draining fistulas, and abscesses. It is not a rare disease, with an estimated point prevalence up to 4% among young adults. The disease is associated with significant physical and psychological morbidity, including metabolic syndrome and depression. It substantially affects quality of life, more so than other chronic skin diseases, such as psoriasis and eczema. It can cause considerable pain, suppuration, and malodor, resulting in disruption of social life, difficulty retaining a job, and absence from work due to illness. The pathogenesis is most likely multifactorial, with a range of different factors implicated, including genetic predisposition, obesity, and smoking. It has been suggested that an immune response dysfunction leading to alterations in cytokine expression plays a key role in the pathogenesis. Since the benefit of TNF inhibitors on skin symptoms was first reported in patients with Crohn disease and concomitant HS, great attention has been paid to the role of cytokines and chemokines in the pathogenesis of HS. Analyses of the cytokine profile in HS lesions have shown elevated levels of proinflammatory cytokines, including IL-1β and TNF. A study comparing the cytokine levels in HS, psoriatic, and normal skin found a 31-fold increase in the level of IL-1β in lesional HS skin compared with normal skin. The detected levels of IL-1β in lesional HS skin were also higher than in psoriatic skin.

Interleukin 1 is a proinflammatory cytokine that plays an important role in the regulation of inflammation and immune response. The 11 members of the IL-1 gene family include genes encoding IL-1α, IL-1β, and IL-1 receptor antagonist (IL-1Ra). Interleukin-1α and IL-1β induce inflammatory responses, such as fever, anorexia, tissue damage, and remodeling, whereas IL-1Ra is a naturally occurring antagonist that competes with IL-1α and IL-1β for the IL-1 receptor. The relative amounts of IL-1α, IL-1β, and IL-1Ra influence the severity of inflammation. Anakinra is a recombinant nonglycosylated form of the human IL-1Ra competitively inhibiting the biologic activity of IL-1α and IL-1β.

The US Food and Drug Administration and the European Medical Agency have approved the use of anakinra for the treatment of moderate to severe rheumatoid arthritis. Similarly to several other biologic agents, a systematic review based on randomized placebo-controlled clinical trials of anakinra in patients with rheumatoid arthritis found a higher incidence of serious infections in patients receiving anakinra than in placebo-treated patients (1.8% in the group receiving anakinra, 50-150 mg/d vs 0.6% in the placebo group). Our patient experienced episodes of bacterial folliculitis that were manageable using standard treatment. The most commonly reported infections associated with anakinra in other studies were pneumonia and cellulitis. Injection site reactions, the most frequently reported adverse events, were experienced by a considerable portion of patients (71% in the anakinra group vs 28% in the placebo group). Nevertheless, a Cochrane review conducting an indirect comparison among various biologic agents reported that anakinra was associated with a significant lower risk of serious adverse events compared with most other biologic agents.

Successful off-label use of anakinra has been reported in various autoinflammatory conditions. Among those, 3 patients with overlapping pyoderma gangrenosum and HS, 1 of whom was diagnosed with PASH (pyoderma gangrenosum, acne, and HS) syndrome, have been described. Substantial but not complete resolution of inflammation in the patient with PASH syndrome, 75% improvement in the size and depth of pyoderma gangrenosum ulcers in 1 patient, and minimal improvement in the other patient with overlapping pyoderma gangrenosum and HS were reported. The PASH syndrome implies a pathogenic association between the constituent diseases and a role for autoinflammatory conditions.
reactions. In our case, however, the diagnosis was exclusively HS, and the treatment efficacy was assessed based solely on improvement of HS lesions. This is, to our knowledge, the first report of a patient with isolated severe HS successfully treated with anakinra. Given the premise that IL-1β plays an important role in the pathogenesis of HS, anakinra may, therefore, represent a logical therapeutic option for select cases of severe HS.

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NOTABLE NOTES
Bartholomew the Apostle: The Saint of Dermatology
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Bartholomew the apostle has long been associated with skin diseases and may be considered the patron saint of dermatology. This distinction is attributed to one theory regarding his proposed manner of death. After Bartholomew cured the daughter of King Polymios of Armenia, the King converted to Christianity. As a result, Astyages, the King’s brother, sentenced St Bartholomew to be flayed and skinned alive, after which he was scourged upside down. In the Sistine Chapel, he is depicted in Michelangelo’s “Last Judgment” as flayed and holding his own skin in his left hand. In Marco d’Agrate’s statue of St Bartholomew, found in the Basilica of Santa Maria della Steccata in Parma, Italy, he is depicted carrying his skin across his body similar to a coat or blanket. Because of this gruesome history, he has been recognized as the saint of dermatology. This association has also earned him the designation of patron saint of tanning, in which animal skin is removed and processed to create functional goods.

Little is known about St Bartholomew’s life, other than that he was born in Galilee in the first century and served as one of Jesus’s 12 apostles. Even his true name is unclear, as his name can mean “son of Tolmay” or “son of the furrows.” As such, he is often thought to be synonymous with Nathanael of Galilee, who was introduced to Jesus through his apostle Philip. Each time Bartholomew’s name is mentioned in the Synoptic Gospels (Matthew 10:1-4, Mark 3:13-16, and Luke 6:12-16), he is also mentioned as being in the company of Philip. Several other stories of St Bartholomew’s death exist, including one in which he was kidnapped, beaten, and cast into the sea to drown. Subsequently, his body miraculously washed up at Lipari, a small island off the coast of Sicily. There, a large piece of his skin and bones were kept as relics at the Cathedral of St Bartholomew the Apostle. Over time, this church opened a medical center, and St Bartholomew’s name and relics became associated with medicine and skin disease.2

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