Adalimumab-induced facial erysipelas and its successful resolution with azithromycin in a 19-year-old female

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Abstract

A 19-year-old female with severe hidradenitis suppurativa (HS), treated with adalimumab for 10 months, developed facial erysipelas following an episode of pharyngitis. The infection presented with fever, severe cough, and a rapidly progressing erythematous plaque with edema on the left cheek, forehead, and periocular region. Laboratory tests confirmed a streptococcal infection. Due to allergies and intolerance to first-line antibiotics, azithromycin was administered, leading to complete resolution. This case highlights the increased risk of severe infections in immunosuppressed patients and underscores the importance of careful antibiotic selection and close monitoring for infections in patients receiving TNF-α inhibitors.

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Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disorder often requiring systemic immunomodulatory therapy.[1,2] Adalimumab, a monoclonal antibody targeting TNF-α, is widely used for HS treatment due to its ability to reduce inflammation and disease activity.[1] However, TNF-α inhibitors also impair innate immunity, particularly macrophage activation and neutrophil recruitment, increasing susceptibility to infections.[1,2] Erysipelas is an acute bacterial skin infection primarily caused by *Streptococcus pyogenes*. It is characterized by erythematous plaques with well-demarcated borders, often accompanied by systemic symptoms such as fever and malaise. While erysipelas typically affects the lower extremities, immunosuppressed individuals may experience atypical presentations, including facial involvement.[3] This case highlights how TNF-α inhibition can predispose patients to severe infections and underscores the importance of infection surveillance in immunocompromised individuals.

Case Report

A 19-year-old female with a history of severe HS had been undergoing treatment with adalimumab (40 mg weekly) for 10 months. She presented with acute symptoms of fever and a severe cough, followed by the rapid onset of facial erythema. On clinical examination, a well-demarcated erythematous plaque was observed, encompassing the left cheek and extending to the forehead and periocular region. The plaque was characterized by significant edema, which led to facial swelling and minor desquamation (Figure 1a). Laboratory findings indicated a marked inflammatory response, with elevated C-reactive protein (CRP) at 79.2 mg/L, erythrocyte sedimentation rate (ESR) at 30 mm/h, and high anti-streptolysin O titers (759 U/mL), consistent with a recent *S. pyogenes* infection. The patient reported a recent history of pharyngitis, which likely served as the entry point for the bacteria. The immunosuppressive effect of adalimumab, a TNF-α inhibitor, may have facilitated the spread of the streptococcal infection through the lymphatic system, culminating in facial erysipelas.[4,5] Due to a documented history of immediate hypersensitivity reactions to penicillins and cephalosporins, beta-lactam therapy was contraindicated. Additionally, clindamycin, an alternative for penicillin-allergic patients, was avoided due to the patient's history of severe gastrointestinal intolerance. Azithromycin (500 mg once daily, three days a week for six weeks) was selected as an

alternative treatment. Azithromycin provides excellent oral bioavailability, allowing high tissue penetration, including the skin. Additionally, it exerts immunomodulatory effects, which may benefit patients with inflammatory conditions like HS. Given local epidemiological data indicating low resistance rates of group A *Streptococcus* to macrolides in the patient's geographical area, azithromycin was deemed an appropriate alternative. The patient showed a complete resolution of the erythematous plaque and edema (Figure 1b). Follow-up laboratory tests demonstrated normalization of CRP and ESR, and no recurrence of erysipelas was observed in subsequent visits.

Discussion

Adalimumab is a TNF-α inhibitor widely used for the treatment of HS, effectively reducing inflammatory activity and improving clinical outcomes.[6] However, TNF-α plays a fundamental role in innate immunity, contributing to macrophage activation and neutrophil recruitment to infection sites. Its inhibition can significantly weaken the immune response, increasing susceptibility to opportunistic infections.[6,7] This case demonstrates how TNF-α blockade can predispose patients to severe bacterial infections. The patient's preceding episode of pharyngitis likely served as the bacterial entry point. At the same time, the immunosuppressive effect of adalimumab facilitated the spread of *S. pyogenes* through the lymphatic system, ultimately leading to facial erysipelas.[8] The interplay between biologic therapy and infection susceptibility highlights the importance of close clinical monitoring in immunosuppressed patients, particularly after upper respiratory tract infections. In this context, antibiotic selection requires careful consideration. Beta-lactams remain the first-line treatment for erysipelas, but alternative regimens must be considered for patients with allergies or intolerances. In this case, azithromycin was chosen due to the patient's documented hypersensitivity to penicillins and cephalosporins, as well as intolerance to clindamycin. Azithromycin's high oral bioavailability and excellent tissue penetration made it a suitable alternative, while its immunomodulatory properties may have provided additional benefits in the setting of HS. This case underscores the necessity of heightened vigilance in patients receiving TNF-α inhibitors. The increased risk of bacterial infections, particularly following respiratory illnesses, necessitates proactive monitoring to enable early detection and intervention. Tailored antibiotic therapy is essential to balance antimicrobial efficacy with individual patient factors. Future treatment protocols could benefit from incorporating individualized risk assessments based on infection history, medication response, and comorbidities. A refined clinical approach focusing on infection surveillance and antibiotic stewardship may help optimize therapeutic outcomes while minimizing infection-related risks.

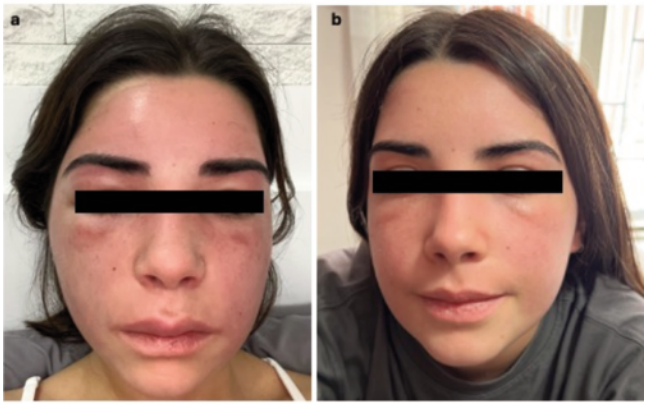

Figure 1. Clinical presentation of facial erysipelas before and after treatment with azithromycin. **a**) The patient exhibits a well-demarcated erythematous plaque with significant edema and minor desquamation involving the left cheek, forehead, and periocular region; **b**) complete resolution of the erythematous plaque and associated edema following a six-week course of azithromycin, with restored normal skin appearance.

Conclusions

This case highlights the dual nature of TNF-α inhibitors in managing HS, offering significant therapeutic benefits while increasing the risk of severe infections like erysipelas. Immunosuppressed patients require close monitoring, particularly after respiratory infections that may serve as bacterial entry points. Early recognition and appropriate antibiotic therapy are crucial to preventing complications. The successful resolution of erysipelas in this patient underscores the importance of individualized antibiotic selection and proactive infection surveillance. Strengthening clinical protocols with routine monitoring and patient education can further reduce infection risks while ensuring the safe and effective use of TNF-α inhibitors.

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