

Successful treatment of juvenile generalized pustular psoriasis with infliximab therapy: two case reports

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Abstract

Juvenile generalized pustular psoriasis is a rare, severe type of psoriasis that can be life-threatening. Thus far, treatment for juvenile generalized pustular psoriasis has been challenging, and no standardized guidelines are available. Here, we describe two Chinese boys with juvenile generalized pustular psoriasis who were successfully treated with infusions of infliximab. During 12 months of follow-up, no recurrence or exacerbation was observed in either patient. Herpes zoster was observed as an adverse effect in one patient, following the initial infusion of infliximab; the other patient did not experience any adverse reaction. Although infliximab is effective therapy for patients with juvenile generalized pustular psoriasis, there is a need for close monitoring of adverse effects in these patients.

Keywords

Anti-tumor necrosis factor antibody, generalized pustular psoriasis, treatment, infliximab, child, herpes zoster, papulosquamous skin diseases

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Introduction

Generalized pustular psoriasis (GPP), first described by von Zumbusch in 1910, is a rare and severe form of psoriasis that can be life-threatening. For some patients, conventional systemic agents (e.g., oral retinoids, methotrexate, and cyclosporine)

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may be ineffective; they may also cause toxic effects or severe complications.¹ Infliximab, a chimeric monoclonal antibody against tumor necrosis factor α , is highly effective in treatment of adult patients with GPP that is refractory to other therapies. However, the long-term efficacy and side effect profile of infliximab treatment in patients with juvenile GPP remain unknown.² Herein, we describe two Chinese children with juvenile GPP who exhibited robust responses to infliximab and did not exhibit no recurrence or exacerbation during 12 months of follow-up.

Case reports

Case 1

A 7-year-old Chinese boy presented with a 4-year history of juvenile GPP. He had no family history of psoriasis, and recurrence was typically observed after cold weather or upper respiratory infections. With intravenous dexamethasone treatment (5 mg/day), each recurrence of disease had been stabilized in approximately 10 days. The patient had a history of allergy to cephalosporin. Tonsillectomy had been performed 2 years prior, but the rash had persisted after surgery. The patient's most recent history of treatment included intravenous dexamethasone (5 mg/day) and oral acitretin (20 mg/day). However, the condition remained poorly controlled. The patient's most recent recurrence had developed after an upper respiratory infection, which led to massive exacerbation of juvenile GPP 1 month prior to visiting our hospital. At the time of presentation, the patient exhibited pyrexia (body temperature of 39.0°C). Initial laboratory values revealed leukocytosis ($17.70 \times 10^9/L$ white blood cells; normal range, $3.97\text{--}9.15 \times 10^9/L$) with neutrophilia ($13.56 \times 10^9/L$ neutrophils; normal range, $2\text{--}7 \times 10^9/L$). Coagulation screen, renal profile, liver function tests,

and C-reactive protein level were all within normal limits. Microscopy of a punch biopsy specimen confirmed the presence of pustular psoriasis. Treatment with 100 mg infliximab (3.3 mg/kg for 30-kg patient) was initiated and the patient exhibited rapid improvement. His fever resolved within 24 hours and the pustules disappeared within several days; normalization of leukocyte count was also observed. Subsequently, infliximab (3.3 mg/kg) was administered at 2 weeks, 4 weeks, 6 weeks, and 8 weeks after initial presentation; it was then administered at 8-week intervals as maintenance treatment. Complete remission was achieved within 2 weeks. No relapse of pustules or development of side effects were observed during follow-up (Figure 1). The patient's family provided written informed consent for publication of this case report.

Case 2

A 12-year-old Chinese boy presented with a 7-year history of juvenile GPP. He had no family history of psoriasis and no apparent trigger factors. The typical disease duration was approximately 7 days with topical emollient. Two months prior to presentation at our hospital, the patient had developed juvenile GPP recurrence due to a cold; he did not exhibit improvement with oral amoxicillin, and then developed generalized pustules with high fever. The patient's most recent history of treatment included intravenous prednisolone (30 mg/day), oral acitretin (10 mg/day), and oral cyclosporine (35 mg twice per day). With these treatments, his disease had been stabilized in approximately 8 days; however, recurrence was observed after reduction of prednisone. The patient presented to our department with extensive edematous erythema followed by pustular lesions, as well as pyrexia (body temperature of 38.7°C). Initial laboratory values revealed leukocytosis



Figure 1. (a) Clinical presentation of a 7-year-old boy with juvenile generalized pustular psoriasis, before biweekly treatment with infliximab (3.3 mg/kg). (b) Clinical presentation at 2 months after initiation of infliximab

($11.7 \times 10^9/L$ white blood cells; normal range, $3.97\text{--}9.15 \times 10^9/L$) with neutrophilia ($8.74 \times 10^9/L$ neutrophils; normal range, $2\text{--}7 \times 10^9/L$) and elevated C-reactive protein (61.10 mg/L; normal range, 0–8 mg/L). Treatment with 200 mg infliximab (5 mg/kg for 42-kg patient) was administered on day 4 of admission.

Within 72 hours, the pustules cleared, erythema subsided, and body temperature returned to normal. An adverse effect (herpes zoster) was observed 6 days after the initial infusion of infliximab; infliximab infusion therapy was temporarily discontinued and the patient was treated with acyclovir 250 mg every 8 hours for 7 days.



Figure 2. (a) Clinical presentation of a 12-year-old boy with juvenile generalized pustular psoriasis, before biweekly treatment with infliximab (5 mg/kg). (b) Back of patient before treatment (left photo); herpes zoster on the right shoulder blade and upper limb, observed 6 days after initial infusion of infliximab (middle photo); back of patient after treatment (right photo). (c) Clinical presentation at 2 months after initiation of infliximab

The herpes zoster lesions completely subsided within 1 week. Subsequently, infliximab (5 mg/kg) was administered at 2 weeks, 4 weeks, 6 weeks, and 8 weeks after initial presentation; it was then administered at 8-week intervals as maintenance treatment. The patient did not exhibit any relapse of pustules during follow-up (Figure 2). The patient's family provided written informed consent for publication of this case report.

Discussion

GPP is an infrequent clinical variant of psoriasis characterized by widespread sterile pustules on an erythematous background; it occurs only in 1% to 5.4% of children with psoriasis.³ However, the

pathophysiology is not fully understood. Thus far, homozygous or heterozygous mutations in the *IL36RN* gene, which encodes the interleukin-36 receptor antagonist, have been detected in some patients with GPP.⁴⁻⁶

Treatment of patients with juvenile GPP is challenging because of the paucity of randomized controlled trials and standardized guidelines.⁷ The use of traditional therapies (e.g., retinoids, methotrexate, and cyclosporine) may result in adverse effects. The emergence of biological agents provides a new treatment option. To the best of our knowledge, three children with juvenile GPP have been successfully treated with infliximab thus far.⁸⁻¹⁰ Infliximab is a human murine chimeric monoclonal

antibody that specifically binds and neutralizes the soluble tumor necrosis factor- α homotrimer and its membrane bound precursor; it is reportedly effective for GPP and is recommended as a first-line biologic in the National Psoriasis Foundation guidelines for treatment of GPP in adults.¹¹ Infliximab exhibits rapid onset of action, with a median time for pustule clearance of 2 days (range, 1–8 days) in adults with GPP.¹² Thus far, infliximab is regarded as a second-line therapy for juvenile GPP. Our patients exhibited resolution of fever in 24 or 72 hours; pustules disappeared within several days after only 1 dose of infliximab at 3.3 mg/kg or 5 mg/kg. Treatment remained effective during 12 months of follow-up. In a previous report, a child with juvenile GPP received combined infliximab treatment with methotrexate at the initiation of therapy; this may have reduced the immunogenicity of infliximab. That patient exhibited long-term remission with no adverse reactions.⁹ However, another child with juvenile GPP reportedly exhibited relapse after 10 months of infliximab monotherapy; second-line addition of methotrexate conferred no benefit and resulted in side effects. For that patient, switching to etanercept therapy resulted in slow improvement.¹³ The prior reports suggest that the short-term effects of infliximab are satisfactory, while the long-term effects are controversial. In the future, large-scale prospective studies are needed to confirm long-term efficacy.

Despite the effectiveness of infliximab thus far, infections remain an important concern. One of our patients was diagnosed with herpes zoster after the initial infusion of infliximab. Typically, children are not at risk for herpes zoster. The findings in multiple cohort studies, randomized controlled trials, and case reports suggest that the use of infliximab is associated with a high risk of herpes zoster in patients with psoriasis and other inflammatory conditions, relative

to other tumor necrosis factor inhibitor drugs.¹⁴ Pharmacokinetic effects may explain the side-effect profile, because infliximab achieves higher concentrations in tissue microenvironments, compared with other tumor necrosis factor inhibitors; thus, it may be more likely to bind to transmembrane tumor necrosis factor on the cell surface and induce reverse signaling or IgG-Fc receptor-mediated effects.¹⁵

In conclusion, infliximab treatment should be recommended as a choice for juvenile GPP; it has a rapid onset of action and can facilitate achievement of long-term remission. However, close monitoring is needed because of the high risk of herpes zoster in patients with juvenile GPP who receive infliximab. The suitability of herpes zoster vaccine administration should be determined for each patient after discussion with the patient's family and assessment of the risks and benefits.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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