Baricitinib rapidly and sustainably relieves a patient from chronic pruritus of unknown origin refractory to dupilumab

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Key words: baricitinib; chronic pruritus of unknown origin; quality of life.

INTRODUCTION

Chronic pruritus of unknown origin (CPUO) is defined by chronic itch lasting for longer than 6 weeks in the absence of skin manifestations or other known causes.[1] CPUO poses a challenge to dermatologists, as the condition is refractory to conventional treatments and patients' quality of life is severely impaired.[2] We present the case of a woman whose CPUO responded rapidly to baricitinib and did not reappear after discontinuation of the drug after 2 weeks of treatment.

Abbreviations used:

CPUO:	chronic pruritus of unknown origin
DLQI:	Dermatology Life Quality Index
JAK:	Janus kinase
NRS:	numerical rating scale

CASE REPORT

A 71-year-old woman presented to our department with severe chronic pruritus of 14 months duration. She reported the onset of symptoms the day after a flu vaccination with intermittent pruritus involving her thighs and breasts. Shortly thereafter, the pruritus spread over her entire body with maximal intensity (numerical rating scale [NRS], 10/10). She complained of constant itching throughout the day with subsequent substantial impact on her quality of life and sleep (Dermatology Life Quality Index (DLQI) = 19; ItchyQoL = 86 points).

The patient had a history of thyroidectomy, hypertension, glaucoma, and orthopedic interventions due to herniated discs of the thoracic vertebrae and spinal stenosis. The clinical examination revealed inconspicuous skin findings without signs of primary skin lesions. All laboratory findings, which were tested repeatedly, were unremarkable, including a normal complete blood cell count (including ranges of hemoglobin from 11.8 to 12.8 mg/dL, leukocytes from 7.2 to 9.4 cells/nL with lymphocytes 2.3-2.9 cells/nL and <2.5% eosinophils); normal renal, liver, and thyroid values (including a normal thyroid-stimulating hormone of 0.5-0.8 mU/L); total immunoglobulin E; hemoglobin A1c; antinuclear antibody; and anti–bullous pemphigoid antibodies. Furthermore, no signs of acute or chronic infections (eg, normal C-reactive protein levels, negative test results for hepatitis B and C and tuberculosis) were observed, and a search for malignancies (including gynecological assessment, chest x-ray, abdominal sonography, lab analyses, and physical examination) was negative.

In the past, numerous therapeutic attempts to suppress pruritus, including moisturizers, topical steroids and topical calcineurin inhibitors, high-dose H_1-antihistamines, ultraviolet therapy, gabapentin, and sertraline, failed. A single dose of intravenous fosaprepitant 150 mg was able to reduce the pruritus for 4 weeks; however, the second dose was ineffective. According to recent reports on the efficacy of dupilumab, a monoclonal antibody against interleukin 4Rα, in CPUO,[3] we introduced dupilumab 300 mg subcutaneously every 2 weeks. However, the patient reported only a slight reduction of pruritus (7/10 NRS) lasting for up to 8 days after each injection; on the remaining days, her pruritus was at NRS 10/10.

From the Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin.
Funding sources: None.
IRB approval status: Not applicable.
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JAAD Case Reports 2021;15:36-8.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.06.028

In view of the insufficient effects of any therapy given, we stopped dupilumab treatment after 4 months and introduced baricitinib 2 mg/d, an inhibitor of the Janus kinases (JAKs) 1 and 2. On the fifth day of intake, the patient documented the following in her calendar: "the itch has almost been reduced to 0 (1/10 NRS)." After 2 weeks, she discontinued baricitinib treatment on her own when she was virtually symptom-free (1/10 NRS). During her visit 2 weeks later, she stated that she was still almost symptom-free (itch over the day 1/10 NRS; DLQI = 4; ItchyQoL = 45). This effect persisted and improved even more over time when she was completely relieved of her pruritus (0/10 NRS; Fig 1) a month later (DLQI = 1; ItchyQoL = 23; Fig 2, *A* and *B*). At a 3-month follow-up, she continued to report complete freedom from itch (0/10 NRS).

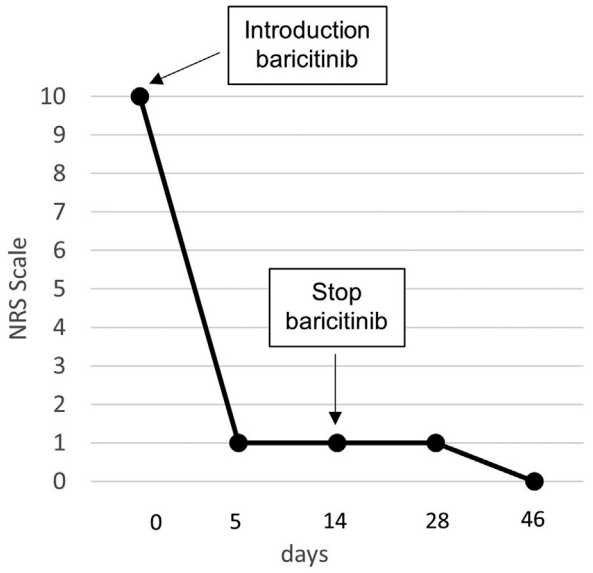

Fig 1. Course of pruritus after the introduction of baricitinib. Average itch intensity was assessed by the patient on a daily NRS. *NRS,* Numerical rating scale.

DISCUSSION

The treatment of CPUO is challenging, as all potential treatments are off-label and often show limited to no effects. Recent findings on the pathophysiology of chronic pruritus have broadened our understanding of itch, suggesting that the type 2 interleukins, interleukin 4 and interleukin 13, and downstream JAK signaling modulate sensory nerves and can be responsible for chronic pruritus, at least in some patients.[4-6] Based on a recent analysis of 40 patients with CPUO, Roh et al[7] concluded that patients with CPUO without increased circulating blood eosinophils are more likely to respond to treatment with gabapentin and less likely to respond to immunomodulators, including dupilumab. Our patient had no elevated eosinophil levels in the blood but failed to show a sustained improvement from treatment with either gabapentin or sertraline. In contrast to the results of Jeon et al,[3] dupilumab treatment also failed to suppress CPUO in our patient. It has recently been reported that the JAK1/3 inhibitor tofacitinib can be effective in CPUO.[4,8] Given the recent European Medicines Agency warning and age and history of cardiovascular disease of our patient, we decided against the use of tofacitinib and initiated treatment with baricitinib. Our observation of a highly effective treatment by the JAK1/2 inhibitor baricitinib, leading to a rapid and sustained relief of itch, indicates a potential role for JAK1 in CPUO. Baricitinib was recently approved in atopic dermatitis[9] and showed rapid effects on the highly bothersome symptoms of itch and sleep disturbance.[10] Its rapid antipruritic properties, as demonstrated in our case study, suggest additional use for refractory chronic pruritus.

Conflicts of interest

None disclosed.

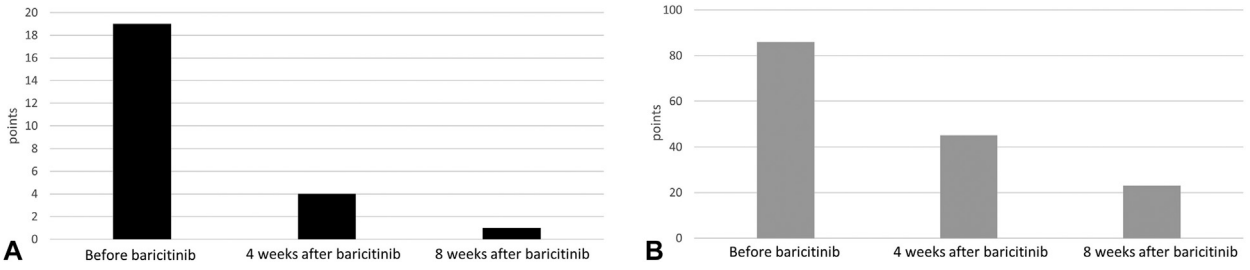

Fig 2. Dramatic improvement of the quality of life after initiation of baricitinib treatment. Quality of life was assessed using (**A**) the Dermatology Life Quality Index and (**B**) the pruritus-specific instrument ItchyQoL.

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