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Dupilumab as a treatment for generalized idiopathic pruritus: a report of 2 cases

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Chronic pruritus markedly impairs quality of life has been compared to living with chronic pain (1). Generalized pruritus can be associated with underlying medical diseases or be deemed idiopathic (1). Regarding idiopathic pruritus, guidelines published by the British Association of Dermatologists state that, “various systemic treatments have been used, however, no randomized controlled trials have found any one therapy to be effective and safe” (2). Novel topical agents such as crisaborole are safer than long-term use of corticosteroids, but many patients require systemic therapy. (3) Dupilumab, a human monoclonal antibody that blocks interleukin-4 (IL-4) and interleukin-13 (IL-13), is a life-changing treatment for patients suffering from atopic dermatitis (4). Here we report two patients with chronic idiopathic pruritus (CIP) who significantly improved with dupilumab.

Case 1 was a 68-year-old woman with six months duration of generalized pruritus. Her Worst Itch Numeric Rating Scale (WINRS) in the past 24 hours prior to presentation was 10/10 (5). Past medical history included migraines but was negative for atopic dermatitis, asthma, or allergic rhinitis. Her medications were pregabalin, fexofenadine, and topical corticosteroids. On physical examination, her skin was clear without primary or secondary skin lesions, and she lacked hepatosplenomegaly or lymphadenopathy.

Dermatographism was negative. A systemic work-up for underlying causes of pruritus was unrevealing (Table 1). CBC revealed 0.9% eosinophils with an absolute count of 52 cells/uL (range 15-500 cells/uL). She failed empiric treatment for scabies with topical permethrin. Hematoxylin and eosin (H&E) demonstrated mild perifollicular inflammation with mast cells and direct immunofluorescence (DIF) was negative for bullous pemphigoid. She was started on dupilumab with an initial dose of 600mg injected subcutaneously followed by 300mg subcutaneously every other week. Her WINRS score decreased to 6/10 after two injections, 3/10 after five injections, and was 0/10 five months after starting dupilumab. No side effects were reported.

Case 2 was an 86-year-old man with two years duration of generalized pruritus. Past medical history included heart failure, hypertension, gout, hyperlipidemia, and atrial

fibrillation, but was negative for atopic dermatitis, asthma, and allergic rhinitis. His medications were spironolactone, allopurinol, aspirin, colchicine, apixaban, sacubitril/valsartan, furosemide, metoprolol, rosuvastatin, topical corticosteroids, and anti-histamines. On physical examination, he had generalized excoriations but no hepatosplenomegaly or lymphadenopathy. CBC and CMP were notable for elevated eosinophils (11.4%) [0-8%], elevated absolute eosinophil count of 650 [15-500 cells/mcL] and creatinine of 1.23. The remainder of the systemic work-up was unremarkable (Table 1). He failed topical permethrin and two skin biopsies were negative for bullous pemphigoid. H&E demonstrated mild spongiotic dermatitis with interstitial eosinophils. After failing to improve with broadband UVB or a combination of mycophenolate mofetil and gabapentin, he was started on dupilumab (the same dosing as Case 1). His WINRS score decreased from 10/10 prior to starting dupilumab, to 5/10 after two injections and 1/10 after three injections. His WINRS score was 3/10 at his most recent follow-up, four months after starting dupilumab. No side effects were reported.

There is growing evidence of shared clinical and biomolecular characteristics between CIP and atopic dermatitis patients. On a molecular level, Oetjen et al. demonstrated that gene expression patterns of skin samples obtained from CIP patients more closely resembled those of atopic dermatitis skin compared to control skin (6). The authors also reported five CIP patients treated with oral Janus kinase (JAK)-1 inhibitors who experienced significant improvement (6). Furthermore, neuronal IL-4 receptor α and JAK-1, both in the pathway targeted by dupilumab, are known to play important roles in chronic itch (6). And yet, peripheral eosinophilia, one of the hallmark signs of atopic dermatitis, is used by Patel et al. to distinguish between various CIP patients and identify patients that are more likely to respond to immunomodulating therapies (7). To further complicate matters, we must consider whether CIP is a result of age-related immunosenescence. Indeed, Xu et al. described four patients with CIP who exhibited elevated serum immunoglobulin E (IgE) levels and peripheral eosinophilia, yet also lymphopenia and hypogammaglobulinemia (8).

Given the biomolecular similarities between CIP and atopic dermatitis, it is not surprising that patients exhibiting peripheral eosinophilia, such as Case 2, would demonstrate

marked improvement with dupilumab. In contrast, as alluded to by Patel et al., Case 1 appears to be of a different CIP subtype, lacking peripheral eosinophilia, yet still demonstrated a marked response to dupilumab. Randomized, placebo-controlled trials are needed to further evaluate the efficacy of dupilumab for CIP. Yet we also need guidance on how to categorize various CIP patients; this distinction is important insofar as it may guide treatment algorithms.

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Table 1: Clinical characteristics of two patients with chronic idiopathic pruritus treated with dupilumab		
	Case 1	Case 2
Age/Sex	68/F	86/M
Failed Treatments	Topical corticosteroids, fexofenadine	Topical corticosteroids, anti-histamines, broad-band UVB, mycophenolate mofetil, gabapentin
Laboratory and Imaging Results	CBC, CMP, thyroid function tests, SPEP, and chest X-ray within normal limits	Elevated eosinophil count: 650 Cr: 1.23 Thyroid function tests, iron panel, ferritin, ESR, CRP, serum immunofix panel, and chest x-ray within normal limits
WINRS score before starting dupilumab	10/10	10/10
WINRS score after treatment with dupilumab	6/10 after two injections; 3/10 after five injections; 0/10 at five-month follow-up	5/10 after two injections; 3/10 at four-month follow-up
CBC: complete blood count; CMP: complete metabolic panel; SPEP: serum protein electrophoresis; UVB: Ultraviolet-B; Cr: creatinine; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; WINRS: Worst Itch Numerical Rating Scale		