Use of Dupilumab in Severe, Multifactorial, Chronic Itch for Geriatric Patients

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PRACTICE **POINTS**

- A series of age-related mechanisms within the epidermis, underlying neuropathy, medication side effects, infection, malignancy, thyroid dysregulation, liver disease, and chronic kidney disease may contribute to pruritus in elderly patients.
- Patients with mild kidney disease may still experience a recalcitrant and notable itch burden.
- Dupilumab is efficacious and safe in the management of chronic pruritus, even in complex cases such as elderly patients with multiple comorbidities.

To the Editor:

Today's geriatric population is the fastest growing in history. The National Institutes of Health predicts there will be over 1.5 billion individuals aged 65 years and older by the year 2050: 17% of the world's population.[1] Pruritus—either acute or chronic (>6 weeks)—is defined as a sensory perception that leads to an intense desire to scratch.[2] Chronic pruritus is an increasing health concern that impacts quality of life within the geriatric population. Elderly patients have various risk factors for developing chronic itch, including aging skin, polypharmacy, and increased systemic comorbidities.[3-7]

Although the therapeutic armamentarium for chronic itch continues to grow, health care providers often are hesitant to prescribe medications for geriatric patients because of comorbidities and potential drug-drug interactions. Novel biologic therapies now provide alternatives for this complex population. Dupilumab is a fully humanized, monoclonal antibody approved for treatment-resistant atopic dermatitis. This biologic prevents helper T-cell (T_H2) signaling, IL-4 and IL-13 release, and subsequent effector cell (eg, mast cell, eosinophil) activity.[8-10] The combined efficacy and safety of this medication has changed the treatment landscape of resistant atopic dermatitis. We present the use of dupilumab in a geriatric patient with severe and recalcitrant itch resistant to numerous topical and oral medications.

An 81-year-old man presented to the clinic with a long history of generalized pruritic rash. His medical history was significant for insulin-dependent type 2 diabetes mellitus (T2DM), hypertension, and renal cancer following a right nephrectomy. Laboratory results approximately 14 months prior to the visit revealed a blood urea nitrogen level of 31 mg/dL (reference range, 7–20 mg/dL), creatinine level of 2.20 mg/dL (reference range, 0.7–1.3 mg/dL), and glomerular filtration rate of 29 mL/min (reference range, 90–120 mL/min). Physical examination revealed numerous pink excoriated papules on the face, neck, trunk, and extremities. Lichenified plaques were present on both arms and legs. The patient received the diagnosis of severe atopic dermatitis with greater than 10% body surface area involvement. The investigator global assessment score was 4/4, indicating severe disease burden, and biopsy results reported spongiotic dermatitis. He proceeded to trial various topical corticosteroids, including hydrocortisone ointment 2.5%, betamethasone valerate ointment 0.01%, fluocinonide ointment 0.05%, and mupirocin ointment without benefit. Three subsequent courses of oral steroids failed to provide durable relief. At this point, the peak

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pruritus numerical rating scale (NRS) score was 7/10, indicating severe pruritus, with a negative impact on the patient's quality of life and sleep.

Therapy was switched to tacrolimus acetonide ointment 0.1%, betamethasone dipropionate ointment 0.05%, and triamcinolone acetonide ointment 0.1%. Eleven days later, the patient denied experiencing any response to the topical regimen and sought alternative therapy for the itch and associated poor sleep; the NRS score was 10/10, indicating very severe pruritus. Prednisone 20 mg and doxepin 10 mg were initiated for symptom management until the intended transition to dupilumab. The patient began dupilumab with a loading dose of 600 mg, then 300 mg every other week thereafter. At 2- and 4-month follow-up, the patient reported notable relief in symptoms. The rash had improved, and the NRS score decreased from 10/10 to 3/10. He endorsed improved sleep and quality of life.

Pruritus may arise from a series of age-related mechanisms such as structural and chemical changes within the epidermis, underlying neuropathy, medication side effects, infection, malignancy, thyroid dysregulation, liver disease, and chronic kidney disease (CKD).[5,6,11] Identifying the underlying etiology often is difficult and involves a complete history and physical examination as well as an appropriate contextualized laboratory workup.

Our patient's comorbid T2DM and renal disease may have contributed to the pruritus. Type 2 diabetes mellitus can cause diabetic neuropathy, a sequela known to lead to various complications, including pruritus. One study identified a 4-fold increase in pruritus in those with diabetic polyneuropathy compared with age-matched nondiabetics.[12,13] An additional study found that pruritus was present in 70% of patients with small fiber neuropathy.[14] We needed to consider the role of our patient's insulin-dependent T2DM and potential underlying neuropathy when addressing the pruritic symptoms.

Furthermore, our patient's stage IV CKD and elevated urea level also may factor into the pruritus. The pathophysiology of CKD-associated pruritus (also referred to as uremic pruritus) remains poorly understood. Suggested mechanisms include immune-mediated neural inflammation and erroneous nociceptive-receptor activity.[15,16] Although uremic pruritus is appreciated primarily in late dialysis-dependent disease, research shows that a notable portion of those with lesser disease, similar to our patient, also experience a significant itch burden.[17] Diminishing pruritus is difficult and often aided by management of the underlying renal disease.[18]

In addition to disease management, symptomatic treatment incorporates the use of emollients, corticosteroids, and antihistamines. Unfortunately, the clinical response in the elderly population to such regimens often is poor.[19] Dupilumab is an optimistic therapeutic option for chronic pruritus. By inhibiting the IL-4α receptor found on helper T cells, this biologic inhibits T_H2 differentiation and subsequent inflammatory activity. One report identified an optimistic response to dupilumab in the management of uremic pruritus.[20] The remarkable improvement and absence of adverse effects in our patient confirmed the utility and safety of dupilumab in complex cases such as elderly patients with multiple comorbidities. Such relief may result from inhibition of proinflammatory cytokine activity as well as decreased afferent spinal cord itch stimuli.[10] The positive results from this case cast a favorable outlook on the treatment of chronic itch in the complex geriatric population.

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