Successful Treatment of Intractable Palmoplantar Pruritus With Ondansetron

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REPORT OF A CASE

A 61-year-old woman presented with a 2-year history of intense itching of her palms and soles. The irritation was relieved only by plunging her hands and feet into cold water. She would awaken at least 4 times per night to rub her hands and feet for 15 minutes before falling asleep again. Her symptoms were more marked in the summer compared with the winter. Her medical history included chronic obstructive pulmonary disease, hiatal hernia, nasal polyps, and 3 previous deep vein thrombi. She took sulfalene tablets and ipratropium bromide, albuterol, and beclomethasone dipropionate aerosol inhalers during the winter for her bronchitis.

On examination, her hands and feet appeared healthy. There were no color changes, dryness, or abnormal neurologic symptoms. Investigation showed that the results of a complete blood cell count, electrolyte levels, liver function tests, immunoglobulin profile, total IgE level, and autoantibody profile all were within normal limits. A biopsy of the palm showed a mild chronic inflammatory infiltrate of the upper dermis, mild acanthosis, and no spongiosis. These changes were nonspecific and consistent with rubbing of the skin. A psychological assessment by a clinical psychologist showed no evidence for a psychosomatic cause of her pruritus.

The following treatments were tried for several months per treatment, one after another: 0.5% to 2% menthol in aqueous cream (BP cream, Hillcross Pharmaceuticals, Briercliff, England), 30% emulsifying ointment in purified water, various emollients, oral antihistamines, 10% crotamiton cream twice per day (Emla cream, Astral, Westboro, Mass), 2.5% lignocaine hydrochloride and 2.5% prilocaine hydrochloride cream twice per day, 0.05% clobetasol propionate cream under occlusion twice per day, oral doxepin hydrochloride, 75 mg/d, carbamazepine, 200 mg twice per day, and topical 0.07% capsaicin cream twice per day, all without beneficial effect. She also underwent a twice-weekly course of local UV-B phototherapy for 6 weeks and a twice-weekly course of UV-A phototherapy with topical psoralen paint for 10 weeks, but both of these treatments were ineffective.

THERAPEUTIC CHALLENGE

The degree of discomfort experienced by the patient and the failure of a wide range of therapeutic approaches often considered useful for intractable pruritus made us search for other treatments.

SOLUTION

Ondansetron hydrochloride is a competitive and selective antagonist of serotonin receptors. These receptors are widely distributed throughout the body, including in the peripheral and central nervous systems. Intravenous ondansetron has been used successfully to treat postoperative pruritus following administration of perioperative intravenous morphine and perioperative intrathecal morphine sulfate. Oral ondansetron has been used effectively to treat refractory pruritus in cholestatic jaundice and in chronic renal insufficiency. These reports suggest that ondansetron is an effective agent for pruritus arising from different causes. In our patient, ondansetron hydrochloride was started at 8 mg/d and within a few hours of starting the treatment, her pruritus stopped. She has remained free of pruritus for 1 year with a regimen of 8 mg taken on alternate days during the summer and 8 mg/wk during the winter, without adverse effects and with no change in her liver function test results.

COMMENT

Itch is a skin sensation that leads to a desire to scratch. Soluble mediators found in itchy inflamed skin can cause itching when injected intradermally. These mediators include histamines, opioids, serotonin, interleukin 2, and substance P. Specific antagonists or interventions designed to deplete these mediators will ease or abolish pruritus. Itching of healthy-looking skin in the absence of systemic disease is common. No specific mediators have been identified to explain this phenomenon. One hypothesis suggests that a local intermittent stimulation of a few afferent sensory nerve fibers will produce itch, while a prolonged stimulation of more afferent fibers will gen-
erate inhibition by activation of inhibitory circuits within the spinal cord. Disorders or unusual settings of this central inhibitory mechanism may produce itching without the need for a sensory input from the periphery.

The efficacy of ondansetron in treating different types of pruritus suggests an effect on a common nociceptive pathway, such as the inhibition of serotonin receptors on peripheral nerves or in the spinal cord. Oral ondansetron is rapidly absorbed and has a terminal elimination half-life of between 2.5 and 5.4 hours. Ondansetron is a well-tolerated drug, with adverse effects limited to headaches, dizziness, drowsiness, and occasional abnormal results of liver function tests. Oral ondansetron is rapidly absorbed with a large volume of distribution, including the central nervous system.

Ondansetron is an established treatment for vomiting induced by cancer chemotherapy and radiotherapy and in the prevention of postoperative nausea and vomiting. Blockade of serotonin receptors and dopamine release within the central nervous system are possible mechanisms to explain its effectiveness. Preliminary data have shown ondansetron to have clinical benefit in patients with some pain and neurologic disorders, such as alcohol dependency, opiate withdrawal, intractable vertigo, cerebellar tremor, and Parkinson disease treatment–related psychosis. As in pruritus, many of these claims have been documented as case reports only. The mechanisms by which ondansetron produces its clinical effects in these novel applications are not understood. Serotonin causes pruritus and a serotonin antagonist, such as ondansetron, would appear to block the generation of pruritus. There has been just 1 placebo-controlled trial assessing the efficacy of ondansetron in cholestatic pruritus resistant to other antipruritic agents. This trial showed at least a 50% reduction of itching in all 10 patients.

Itching can only be assessed subjectively. This creates difficulty in interpreting the effectiveness of a given treatment. We believe that our patient had tried multiple treatments without success but has responded to oral ondansetron, and that the success of ondansetron was not placebo related because the response has been maintained for more than 1 year. Although the drug is expensive ($564 for thirty 8-mg tablets), in conditions in which the degree of pruritus is debilitating and cheaper alternatives have been unsuccessful, it should be considered.

REFERENCES


Submissions

Clinicians, local and regional societies, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern. Submit 4 double-spaced copies of the manuscript with right margins nonjustified and 4 sets of the illustrations. Photomicrographs and illustrations must be clear and submitted as positive color transparencies (35-mm slides) or black-and-white prints. Do not submit color prints unless accompanied by original transparencies. Material should be accompanied by the required copyright transfer statement, as noted in “Instructions for Authors.” Material for this section should be submitted to George J. Hruza, MD, Cutaneous Surgery Center, Suite 16+11, 1 Barnes Hospital Plaza, St Louis, MO 63110. Reprints are not available.