Ixekizumab and herpes zoster in an erythrodermic patient

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ABSTRACT

Ixekizumab is an injectable monoclonal antibody against IL-17A approved by the US Food and Drug Administration for the treatment of plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. We present what we believe is the first case of herpes zoster (shingles) in a patient 12 weeks after starting ixekizumab for presumed erythrodermic psoriasis. It is important to be aware of potential side effects of immunomodulatory medications, particularly those that are new to the market.

KEYWORDS Erythroderma; herpes zoster; ixekizumab; psoriasis; shingles

Ixekizumab is an IL-17A antagonist approved by the US Food and Drug Administration for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. It is also indicated for active psoriatic arthritis and was recently approved for active ankylosing spondylitis. Interleukin-17 is a pro-inflammatory cytokine that plays an important role in host defense against bacterial and fungal infections. It works by inducing granulocyte-colony stimulating factor production and producing chemokines that attract neutrophils to sites of infection.¹ Absence of the gene encoding IL-17 has been associated with chronic mucocutaneous candidiasis.² It has also been implicated as a key mediator of the inflammation in psoriasis. Adverse reactions reported in patients taking ixekizumab include injection site reactions, upper respiratory tract infections, nausea, and tinea infections.³ To the authors' knowledge, herpes zoster has not been reported in the literature in a patient treated with an IL-17 antagonist. Here we describe a case of herpes zoster in an erythrodermic patient treated with ixekizumab.

CASE DESCRIPTION

A 70-year-old Hispanic man with type 2 diabetes and extensive prurigo nodularis presented to his dermatologist for a severely itchy red rash of 3 months' duration that was out of proportion to clinical findings. Initial biopsy results showed spongiotic dermatitis with eosinophils and a negative

direct immunofluorescence, suggestive of chronic eczematous dermatitis. He was initially treated with potent topical steroids and emollients; however, minimal improvement was noted after 1 month, and mycophenolate mofetil was initiated. His symptoms continued, and he presented to his dermatologist 2 weeks later with erythroderma and severe pruritus. Mycophenolate was discontinued, additional punch biopsies were obtained, and the patient was admitted for management of his erythroderma. Dermatology was consulted during his admission, with biopsy results demonstrating psoriasiform dermatitis with neutrophilic microabscesses. Due to the severity of his erythroderma and a suspected diagnosis of psoriasis, an extensive discussion was undertaken with the patient regarding treatment options. As there are no known cases or mechanisms describing tuberculosis reactivation in patients being treated with IL-17 antagonists, QuantiFERON gold test was sent to the lab and treatment was initiated with an 80 mg/mL injection of ixekizumab subcutaneously for presumed erythrodermic psoriasis. The patient's erythema and pruritus improved quickly and significantly over the next 2 days and he was discharged with topical steroids and plans to enroll in an ixekizumab program through his insurance.

The patient's symptoms continued to improve at his 1-month hospitalization follow-up. He was noted to have a positive QuantiFERON gold test and was referred to infectious disease. Further workup revealed no evidence of active disease on chest radiograph, and his treatment was initiated

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Figure 1. Crusted vesicular rash in a dermatomal distribution consistent with herpes zoster.

through the state department of public health. His only known risk factor for tuberculosis was prior military service in Vietnam many years ago, and he denied any significant weight loss, fatigue, cough, or night sweats. At hospital follow-up, the patient complained of hard nodules that had been present in his groin for weeks. On exam, he had a nontender, palpable subcutaneous cord in the right inguinal fold as well as a nontender nodule in the left inguinal fold. Digital rectal exam revealed an enlarged, smooth, nontender prostate. A prostate-specific antigen level was within normal limits. Ultrasound revealed a microabscess without evidence of lymphadenopathy or deep vein thrombosis, and subsequent magnetic resonance imaging showed no masses or lymphadenopathy. He resumed care with his primary dermatologist, and acitretin was added to his regimen.

The patient's condition was well controlled for 3 months following hospitalization on ixekizumab, topical steroids, and acitretin until he presented again to the emergency department for severe generalized pruritus and a painful vesicular rash on his chest. He was found to have diffuse xerosis, lichenification, and excoriations to his chest, back, and bilateral arms and legs that involved an estimated 75% of his total body surface area. He also had multiple painful, grouped 2 to 3 mm heme-crusting papules in a T4 dermatomal distribution on his left back and chest consistent with herpes zoster (*Figure 1*). Of note, the previously noted swelling in the left inguinal fold had resolved since his previous exam. Due to his continued extreme pruritus and presentation that was atypical for psoriasis, two additional 4 mm punch biopsies were performed to rule out occult mycosis fungoides. He was given prescriptions for clobetasol ointment and gabapentin and instructed to continue taking the valacyclovir given to him by his local dermatologist. Acitretin was discontinued. Biopsies were consistent with chronic eczematous dermatitis, although psoriasis with secondary allergic contact dermatitis could not be ruled out. The dermatopathologist reviewed all prior biopsy specimens, and the patient was transitioned from ixekizumab to dupilumab.

DISCUSSION

Reporting of adverse events in patients treated with immunomodulatory and immunosuppressive agents is vital. This complex patient with herpes zoster and erythroderma on ixekizumab may represent the first case of zoster associated with an IL-17 antagonist. Mild adverse reactions such as upper respiratory infections, nausea, and tinea infections have been reported, but an increased incidence of viral infections has not. While immunosuppressed patients have a 20 to 100 times greater risk of herpes zoster compared to the immunocompetent population,⁴ herpes zoster itself is common and occurs in 1 in 3 people during their lifetime.⁵ Most cases occur in individuals over 50, so whether this patient's herpes zoster infection was due to immunosuppression from ixekizumab or pure chance isn't known. To date, with over 5 years of data and five clinical trials totaling 5066 participants,^{6–8} the authors are unaware of other reported cases of zoster in patients undergoing treatment with ixekizumab. Results from the IXORA-R trial were not available at the time of our literature search.⁸

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