



Pediatrics

Isotretinoin induced urethritis: A case report & review of the literature

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ABSTRACT

We report a case of urethritis in a 17-year-old non-sexually active male that developed after starting isotretinoin treatment for his acne. Clinicians must be vigilant about this adverse effect and elicit a thorough medication history prior to administering antibiotics in patients taking isotretinoin treatment for acne.

Introduction

Isotretinoin is a highly regarded drug for severe nodulocystic acne and is commonly used in pediatric and young adults. Isotretinoin has mucocutaneous and systemic effects including xerosis, cheilitis, skin fragility, palmoplantar desquamation, epistaxis, and fetal retinoid syndrome among childbearing women.¹ Although teratogenicity and common side effects of oral retinoids have been widely studied, little is known about isotretinoin as a cause of urological symptoms. We present a case of urethritis/meatitis that developed in a pediatric patient after starting isotretinoin treatment for his acne.

Case presentation

A 17-year-old non-sexually active male with acne on twice-daily isotretinoin 30 mg was referred to a Urology clinic for evaluation of possible urethral web. He initially presented to a dermatology appointment with a two-week history of "urine stream issues". He had been on isotretinoin for approximately five weeks when he noticed a scab at the urethral tip that prevented him from urinating. This occurred twice before while on isotretinoin. He manually opened his urethra to allow for urination which worked until five days prior to presentation. He denied any sexual history, prior hematuria, or issues with his urinary stream. He was noted to have a rash on his hands and lips. No penile discharge was noted, although signs of meatal mucosal irritation were present. He was prescribed topical halobetasol 0.05% twice-daily for one week as needed while on isotretinoin. His symptoms were adequately managed with this regimen. The patient remained on isotretinoin for a total of five months, stopping medication after five months of treatment. In his subsequent follow-up visits to his

dermatologist, he did not report the return of urological symptoms.

Discussion

Isotretinoin is a rare cause of urethritis with multiple mechanisms at play. One proposed mechanism is the interaction of retinoids with their skin-specific receptors, RAR γ and RXR α , resulting in stratum corneum thinning and increased transepithelial water loss. Keratolysis is another, which alters skin structure through desmosomal loss.^{1,2} The increase in skin fragility and dehydration of the urogenital mucosa from these mechanisms predisposes the area to infection and inflammation contributing to the symptoms of urethritis/meatitis observed in our patient.

Review of the literature suggests that these mucocutaneous side effects are dose-dependent. Kellock *et al.* described cases of isotretinoin-induced urethritis improved by dose reduction. The first, a 30-year-old male who presented with dry cracked lips, dry eyes, epistaxis, penile discomfort, and bloody urethral discharge two weeks after initiating isotretinoin 100 mg daily. After a negative workup, he was treated with antibiotics without improvement. Symptom resolution occurred after reducing isotretinoin to 50 mg.³ In another case, a 25-year-old male on 60 mg daily of isotretinoin for three months had a one-week history of dry and painful urethral meatus suspected of penile candidiasis. He was treated with clotrimazole cream and antibiotics with no improvement in symptoms. Workup for infectious causes was unremarkable, and he was given a provisional diagnosis of nonspecific urethritis. Symptoms spontaneously resolved during the fourth month of treatment with no symptom recurrence following completion of isotretinoin treatment.³ Similarly, Alli *et al.* described a 23-year-old male presenting with dysuria and meatitis on isotretinoin 40 mg daily for four months. After a

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negative workup, he was diagnosed with retinoid dermatitis affecting the external urethral meatus. Symptom resolution occurred two weeks after dosage reduction and use of topical corticosteroids and dexpanthenol.^{1,2} Ballout *et al.* described a 28-year-old male with urethritis, clear penile discharge, and meatitis, whose isotretinoin dose was increased to 60 mg from 40 mg daily, five days before presentation. His dose was reduced back to 40 mg after a negative workup, with symptom resolution afterward.⁴

Additionally, urethritis is known to resolve within days to weeks after discontinuation of isotretinoin. Kellock *et al.* described a 20-year-old male with a two-week history of dysuria and urethral discharge on 60 mg isotretinoin for the past six weeks. The patient was subsequently treated with doxycycline for 14 days, requiring cessation of isotretinoin. He re-presented with similar symptoms one month later, noting his symptoms completely resolved while on a drug holiday from isotretinoin. Edwards *et al.* described two cases of urethritis that resolved with isotretinoin cessation. The first, a 23-year-old male who presented with meatal soreness and clear discharge upon initiation of a second course of isotretinoin. In another case, a 35-year-old male, presented with three days of urethral discharge one week after starting isotretinoin, reporting similar symptoms one year ago when previously on isotretinoin. Both patients were treated with a tetracycline, with symptom resolution upon isotretinoin cessation.⁵ While our 17-year-old patient was not treated with antibiotics, his symptoms resolved with isotretinoin cessation. Isotretinoin's pharmacokinetics, which has a half-life of 10–20 hours, best supports the resolution of these side effects.^{3,5}

These studies demonstrate the correlation between isotretinoin usage or discontinuation and the presence or resolution of symptoms of urethritis, respectively. In contrast to other cases, where infectious workup was performed, no extensive workup to exclude infectious causes of urethritis/meatitis was performed for our patient. It was through review of his medication history, where we realized that his presentation may be an adverse effect of his isotretinoin treatment.

The case presented highlights the link between isotretinoin use and urethritis. This is critical in the pediatric and young adult population, as isotretinoin is commonly prescribed for acne treatment. This case underscores the importance of a thorough history and examination, particularly of the patient's medication history. In addition to eliciting a thorough review of medications, clinicians should be aware of this

adverse effect and manage accordingly whether by dosage reduction or cessation of treatment altogether. Antibiotics or antivirals should be avoided in these patients in the absence of an immunocompromised state, positive STD workup, or positive urine culture.

Conclusion

Though uncommon, isotretinoin has been shown to present with urethritis which is often overlooked. This is a diagnosis of exclusion and can be treated by dose reduction or cessation of isotretinoin. Clinicians must be vigilant about this adverse effect and elicit a thorough medication history prior to administering antibiotics or antivirals in patients on isotretinoin treatment for acne.

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Declaration of competing interest

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