



General Urology

Testicular Pain Associated With Minocycline Use



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ABSTRACT

Two males ages 16 and 23 years presented with new testicular pain while taking minocycline. Both patients experienced resolution of their symptoms only after minocycline discontinuation. Testicular pain with minocycline use has been previously described, however only in the setting of systemic autoimmune reactions (which were absent here). These cases represent probable rare adverse reactions to minocycline. For patients taking minocycline who experience otherwise unexplained testicular pain, a trial discontinuation of this medication should be considered.

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Introduction

Minocycline is a tetracycline antibiotic commonly used to treat inflammatory skin conditions such as acne vulgaris.¹ It has a well-documented side effect profile that includes several rare but serious immunologic reactions such as drug-induced lupus-like syndromes, autoimmune hepatitis, and vasculitis syndromes.^{2–6} Instances of testicular or scrotal pain associated with minocycline use have been described, however only in the setting of systemic minocycline-associated vasculitides.^{7–10} Anecdotally, associations have been made between minocycline use and testicular pain as a lone symptom, however this has not been formally reported. Here we investigate this claim and present cases of minocycline-associated testicular pain in the absence of systemic symptoms.

Materials and methods

Patients were identified from the personal experience of attending urologists at our institution. The patients' medical records were reviewed and the information compiled for this study.

Results

Case reports

Case 1

A 16 year-old Caucasian boy presented to the emergency department with right-sided testicular pain that began while sitting in class. His pain had a waxing and waning quality and further questioning revealed that it had actually begun more subtly 3 – 6 months prior. He could not identify any reason for the acute worsening. He was taking minocycline 50 mg twice daily for acne during this period. Review of systems was also positive for nausea. Additional history was non-contributory. His initial exam in the emergency department was notable for right-sided testicular tenderness and right hemi-scrotal swelling. His urinalysis was normal. A scrotal ultrasound showed no frank testicular torsion or epididymitis. On repeat genitourinary exam later that day his pain had markedly improved (however, this was after pain medication was administered). Because of the nature of his symptoms, intermittent testicular torsion was suspected and the patient underwent a bilateral transscrotal orchiopexy. Intra-operatively both testicles appeared normal with no signs of torsion or previous pathology. One year after this presentation the patient returned to his urologist with right-sided testicular pain of the same quality to his original complaint. His history at the time was notable only for having started taking minocycline again 2 – 3 weeks prior, which he had stopped in the interim following his original surgery. His repeat examination was normal. Because of the suggestive timeline, it was recommended for him to stop taking this medication. The patient's testicular pain resolved within 1 week.

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Case 2

A 23 year-old Caucasian man presented to an outpatient urology clinic with bilateral testicular pain. He had started taking minocycline 100 mg daily 3 weeks prior to this presentation. Additional medical, surgical, and sexual histories were non-contributory and minocycline was his sole medication. His overall exam was normal as was his urinalysis. A scrotal ultrasound showed no evidence of testicular torsion or epididymitis. Due to the suggestive timeline, a trial discontinuation of minocycline was attempted. Additionally, because of the severity of his pain, the patient began taking ibuprofen for symptomatic relief. At 1-month follow-up after stopping minocycline, the patient's pain had almost completely subsided and he no longer required pain medication.

Discussion

Both patients experienced the onset of symptoms after at least several weeks of minocycline use and amelioration of their symptoms only with discontinuation of minocycline. For helping to identify possible adverse drug effects, Naranjo *et al.* suggested a qualifying scoring system.¹¹ Based on this scoring system, the patient in Case 1 had a score of 7 out of 13, or a “probable” adverse drug reaction to minocycline. Similarly, the patient in Case 2 (while he did not experience a “re-challenge” of minocycline) had a “probable” adverse drug reaction as well with a score of 5 out of 13.

Previous reports of testicular pain with minocycline have been in the setting of minocycline-associated vasculitides. Kermani *et al.* reported four male patients with minocycline-associated vasculitis, three of whom reported testicular or epididymal pain as part of their symptoms.⁷ Testicular pain with testicular infarction has been reported to occur in cases of minocycline-associated vasculitides as well. Lenert *et al.* reported a patient with a minocycline-associated “polyarteritis nodosa-like” syndrome who presented with testicular pain and was found to have a testicular infarction prompting orchiectomy.⁸ Lyon *et al.* also reported a case of minocycline-associated vasculitis in which the patient developed testicular pain and was found to have a wedge infarction of the right testicle.⁹ All cases were treated successfully with minocycline discontinuation, in addition to immunosuppression in a select few.

All of the patients found on literature review were documented to have met clinical or pathologic criteria for polyarteritis nodosa, a medium-vessel necrotizing vasculitis. All of the patients in the literature review also had abnormally elevated perinuclear antineutrophil cytoplasmic antibody (pANCA) titers. While pANCA positivity is not classically associated with polyarteritis nodosa, it has been documented in drug-induced vasculitides before.¹⁰ Additionally, it has been suggested that exposure to minocycline alone can induce pANCA positivity, even without the onset of vasculitis symptoms. Marzo-Ortega *et al.* studied patients taking minocycline for acne and found such individuals with abnormally

elevated pANCA titers and no history of vasculitis. While most of these patients with pANCA positivity reported some type of mild-to-moderate symptoms (usually arthritis), there were several who were completely asymptomatic.¹²

Conclusion

Two cases are presented where testicular pain was associated with minocycline use. The circumstances of each case suggest that these were probably adverse drug reactions to minocycline. The cornerstone of management for these patients, in addition to those found literature review, was minocycline discontinuation. For patients taking minocycline who present with otherwise unexplained or poorly-explained testicular pain, stopping minocycline should be considered. It is not known what laboratory tests would be helpful or confirmatory in these cases. An elevated pANCA titer has been suggested as maker for increased risk to developing side effects from minocycline, however this has only been demonstrated in those with previous minocycline exposure on the order of months to years. More study is necessary to fully describe this potential adverse drug reaction and its pathophysiology.

Conflicts of interest

There are no conflicts of interest for this study.

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