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Successful febuxostat desensitization in a patient with febuxostat hypersensitivity: A Malaysian experience

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Abstract

Over the years, allopurinol has been widely used as the preferred choice of urate lowering therapy in patients with gout. However, its role in patients with renal impairment is limited; and adverse reactions are well documented. Febuxostat, a newer oral non-purine xanthine oxidase inhibitor has been proven in several trials to be more effective and tolerable compared to allopurinol and may be used in patients with renal impairment. Here, we describe a case of successful febuxostat desensitization in a patient with a history of allopurinol- and febuxostat-induced adverse cutaneous reaction, as well as the protocol utilized.

Keywords

Febuxostat hypersensitivity, febuxostat desensitization, generalized eczematous photodermatitis

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Introduction

Gout is a chronic inflammatory arthritis associated with hyperuricemia, leading to uric acid deposition in tissue joints as well as other tissues.[1] It is a common and treatable condition which affects almost 4% of adults in the United States.[2] Urate lowering therapy (ULT) is the cornerstone of gout management. This reduces the serum uric acid levels, in effect preventing acute gouty attacks. For many years, allopurinol has been the preferred choice of ULT in patients with gout. Despite that, there are drawbacks to its usage; the most serious adverse effect of which is allopurinol hypersensitivity syndrome (AHS).[3] Febuxostat, an oral non-purine selective and potent xanthine oxidase (XO) inhibitor was approved in 2009 by the US Food and Drug Administration (FDA) for the treatment of chronic gout. It is particularly favorable in patients with previous adverse reactions to allopurinol and in those with renal impairment, as described in the literature.[4–7] Febuxostat hypersensitivity, albeit rare, has been documented.[4,8] Scarce literature is available concerning successful febuxostat desensitization protocols thus far, to our knowledge,[9] and our case is likely the first reported in Asia.

Case report

A 63-year-old male was referred to the rheumatology service for chronic tophaceous gout with frequent relapses. He had a typical gout history with initial podagra; which later progressed into arthritis of the ankles, hands, wrists, and elbows. The arthritis responded to therapy with non-steroidal anti-inflammatory drugs and colchicine. His initial test supported the clinical diagnosis of gout, with a serum uric acid of 600 µmol/L and radiographic evidence of typical gout changes. His serum creatinine was noted to be 260 µmol/L, and ultrasound showed evidence of bilateral renal parenchymal disease with non-obstructive right renal calculi. We started him on allopurinol; however, unfortunately, he was then lost to follow-up. He presented again after 2 years with infected ruptured tophi needing surgical intervention. Allopurinol was re-initiated; unfortunately, he developed generalized exfoliative dermatitis 4 weeks after initiation of therapy. The dermatitis spontaneously resolved following withdrawal of

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Table 1. The febuxostat desensitization protocol utilized.

Day	Concentration (mg/mL)	Amount (mL)
1	0.1	0.1
2	0.1	0.2
3	0.1	0.4
4	0.1	0.8
5	0.1	1.6
6	0.1	3.0
7	0.1	6.0
8	0.1	12.0
9	0.1	24.0
10	10	0.5
11	10	1.0
12	10	2.0
13	10	3.0
14	10	4.0

allopurinol. His condition deteriorated to the extent that he needed intermittent intra-articular corticosteroid injections. These were eventually complicated by frequent episodes of infected ruptured tophi requiring intravenous antibiotics with or without surgical intervention. Febuxostat was commenced at a dose of 40 mg once daily (OD); but after 6 weeks, he developed generalized eczematous photodermatitis. Discontinuation of febuxostat led to resolution of the dermatitis. In view of worsening symptomatology and rising serum uric acid levels to 734 μmol/L, a decision was made to desensitize him to febuxostat. He was admitted for a 14-day febuxostat desensitization protocol (Table 1). The oral febuxostat suspension was prepared fresh daily; given at a concentration of 0.1 mg/mL from day 1 to day 9, followed by 10 mg/mL from day 10 to day 14. No cutaneous reaction was evident throughout hospital stay. He was discharged with a febuxostat dose of 40 mg OD. He reports no relapse of gouty arthritis or cutaneous reaction since, with a latest serum uric acid reading of 429 μmol/L.

Discussion

Allopurinol, a purine analog and non-specific competitive inhibitor of XO, is predominantly excreted via the kidneys. Although no confirmation through placebo-controlled randomized clinical trials with regard to its efficacy is available, several head-to-head studies in addition to decades of clinical experience have shown it to be an efficacious, cheap, and well-established ULT for gout; hence, its recommendation as the first line therapeutic agent.[10] However, as with all forms of therapy, it is not without side effects. These side effects range from the mild form, known as allopurinol hypersensitivity with maculopapular eruption to the rare, but life threatening systemic manifestation, universally termed AHS.[3]

The approval of febuxostat by the US FDA in 2009 for the treatment of hyperuricemia of gout in 2009 has provided an alternative avenue in 40 years. Febuxostat, a non-purine inhibitor of XO, is structurally distinct compared to allopurinol and was anticipated to unlikely share the same side effects as allopurinol.[4] Trials by Schumacher et al.[5] and Becker et al.[6] showed febuxostat to be a more effective ULT when compared to allopurinol, even in patients with renal impairment. Chohan,[4] in 2011, demonstrated that febuxostat was a safe and an effective ULT in patients previously documented to have severe allopurinol adverse reactions.

Our patient developed adverse cutaneous reactions toward both ULTs—allopurinol and febuxostat. These were seen to improve upon discontinuation of the therapeutic agents. However, the patient experienced worsening acute gouty attacks as well as ensuing complications, which in some instances required surgical intervention. Taking into account the renal impairment as well as the need to lower his serum uric acid levels, a decision was made to desensitize him to febuxostat, based on the protocol described by Sullivan.[11] The detailed protocol is as given in Table 1. Patient was successfully desensitized after a 14-day hospital stay, with no report of adverse reactions since.

Due to the relatively recent introduction of febuxostat as an alternative ULT in patients with gout, scarce literature is available concerning its adverse reactions. Abeles,[8] in 2012, reported a single case of febuxostat hypersensitivity where patient developed pruritus and fatigue, with renal involvement and peripheral eosinophilia. Our patient experienced generalized exfoliative dermatitis, with no renal involvement or peripheral eosinophilia. Further studies would prove helpful in determining the safety profile of this therapeutic agent; thus enabling its wider usage in the management of gout.

Conclusion

Febuxostat is proving to be a relatively safe and effective alternative ULT in patients with gout, particularly those with previous adverse reactions to allopurinol and renal impairment. Febuxostat hypersensitivity, albeit rare, has been documented. A febuxostat desensitization protocol is a practical and realistic approach in offering treatment to those deemed not suitable to receive allopurinol and with previous documented febuxostat hypersensitivity. More data are needed in determining the most appropriate desensitization protocol; ours appears to be the first successful protocol reported in Asia.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Written informed consent has been obtained prior publication of this manuscript. Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

References

1. Neogi T, Jansen TL, Dalbeth N, et al. 2015 gout classification criteria: an American College of Rheumatology/European League against Rheumatism Collaborative Initiative. *Arthritis Rheumatol* 2015; 67: 2557–2568.
2. Dalbeth N, Merriman TR and Stamp LK. Gout. *Lancet* 2016; 388: 2039–2052.
3. Stamp LK, Day RO and Yun J. Allopurinol hypersensitivity: investigating the cause and minimizing the risk. *Nat Rev Rheumatol* 2015; 12: 235–242.
4. Chohan S. Safety and efficacy of febuxostat treatment in subjects with gout and severe allopurinol adverse reactions. *J Rheumatol* 2011; 38: 1957–1959.
5. Schumacher HR, Becker MA, Wortmann RL, et al. Effects of febuxostat versus allopurinol and placebo in reducing serum urate in subjects with hyperuricemia and gout: a 28-week, phase III, randomized, double-blind, parallel-group trial. *Arthritis Rheum* 2008; 59: 1540–1548.
6. Becker MA, Schumacher HR, Wortmann RL, et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. *N Engl J Med* 2005; 353: 2450–2461.
7. Reinders MK and Jansen TL. Management of hyperuricemia in gout: focus on febuxostat. *Clin Interv Aging* 2010; 5: 7–18.
8. Abeles AM. Febuxostat hypersensitivity. *J Rheumatol* 2012; 39: 659.
9. Di Paolo C, Minetti S, Mineni M, et al. Desensitization to febuxostat: report of two cases. *J Allergy Clin Immunol Pract* 2015; 3: 633–636.
10. Rees F, Hui M and Doherty M. Optimizing current treatment of gout. *Nat Rev Rheumatol* 2014; 10: 271–283.
11. Sullivan TJ. Protocols for rapid and slow drug allergy desensitization, 2009, http://www.scribd.com/doc/22062135/Protocols-for-Drug-Allergy-Desensitization