CASE REPORT

Febuxostat for Gout: A new treatment for an old disease
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ABSTRACT
Gout is one of the oldest diseases in the medical literature in which patients present with hyperuricemia-induced recurrent attacks of severe monoarthritis. Diagnosis can be confirmed by the demonstration of sodium urate crystals in synovial fluids. For years, allopurinol was the main urate-lowering agent despite many adverse effects including serious drug reactions. In February 2009, febuxostat was approved by Food and Drug Administration as a new urate-lowering agent, thus giving the first alternative to allopurinol-allergic patients. Here, we report a patient who developed fixed drug eruption secondary to allopurinol and tolerated febuxostat without any adverse effects.

KEYWORDS: Febuxostat, Gout

INTRODUCTION
Hyperuricemia is defined as a serum uric acid (sUA) of >6.8 mg/dL, which approaches the limit of solubility of monosodium urate in extracellular fluids.1 Gout is characterized by recurrent acute monoarthritis caused by crystallization of monosodium urate which can be confirmed by the presence of these crystals in synovial fluid.2,3 Allopurinol, a xanthine oxidase inhibitor, remained the main urate-lowering medication, despite its many adverse events leading to discontinuation of therapy in 5% of patients.2,4 In February 2009, the Food and Drug Administration (FDA) approved febuxostat for the management of hyperuricemia in adults with gout.2 Here, we report a patient who developed fixed drug eruption due to allopurinol and tolerated febuxostat without any adverse effects.

CASE REPORT
A 35-year old Saudi male was referred to dermatology clinic with multiple burning skin eruption on the dorsum of both hands for few days after initiation of allopurinol as a treatment for gout. On examination, there were multiple well defined dusky red plaques with central blisters over knuckles bilaterally (Fig. 1). The diagnosis of fixed drug eruption due to allopurinol was rendered and allopurinol was discontinued. Mometasone furoate 0.1% ointment was prescribed to treat the skin eruption which resolved with postinflammatory hyperpigmentation. After discussion with the patient, switching to febuxostat was offered. As febuxostat is not available in Saudi Arabia, the patient obtained it from abroad. We followed the patient for few months on febuxostat without any skin reactions.

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Uric acid is the terminal product of a cascade of metabolic steps catalyzed by xanthine oxidase, whereby purines are degraded and eliminated in urine. Various factors, such as age, body weight, diet, temperature, and pH, are known to influence both the concentration and solubility of monosodium urate.

As the total pool of sUA in the body rises, either because of overproduction or underexcretion, the risk of an acute gout attack increases in a continuous manner. Described for centuries, gout is characterized by recurrent attacks of acute monoarthritis caused by crystallization of monosodium urate from supersaturated body fluids into tissues, particularly joints. If the hyperuricemia is not treated, gout can progress into a chronic stage leading to chronic pain, significant disability and impairment in quality of life. A definitive diagnosis of gout is confirmed by the observation of intracellular needle-shaped, negatively birefringent monosodium urate crystals in synovial fluid aspirated from an affected joint or tophi.

For years, allopurinol has been the mainstay for urate-lowering treatment and until recently was the only pharmacologic agent. Allopurinol is a xanthine oxidase inhibitor with a purine-like structure, and is effective in both underexcretor and overproducer states. However, adverse events lead to discontinuation of therapy in 5% of patients. These include leukopenia, gastrointestinal problems, headache, and skin eruptions. Cutaneous adverse events include toxic epidermal necrolysis, erythema multiforme, allopurinol hypersensitivity syndrome, comprising exfoliative dermatitis, hepatitis, interstitial nephritis, and eosinophilia. In the absence of suitable alternatives, allopurinol has remained the mainstay for the treatment of hyperuricemia until February 2009, when the FDA approved febuxostat to be the first agent approved in the United States for the treatment of gout since allopurinol was first marketed. Febuxostat is a thiazolecarboxylic acid derivative, a selective inhibitor of both the oxidized and reduced forms of xanthine oxidase, and does not resemble a purines or pyrimidines. Febuxostat is readily absorbed after administration and is highly bound to circulating plasma proteins, primarily albumin. It undergoes hepatic metabolism by the cytochrome P450 (CYP) enzyme system and is then eliminated renally.

Because febuxostat lacks purine ring, it is structurally unrelated to allopurinol and thus the probability of developing cross-related intolerance is theoretically low. Indeed, one study that has reported specifically on allopurinol-intolerant patients, like ours, did describe good tolerance to febuxostat. A retrospective study has assessed the safety and efficacy of febuxostat in 13 successively encountered gout patients with prior documented severe allopurinol reactions. In 12 out of 13 gout patients, febuxostat treatment was safe and well tolerated. One patient previously hospitalized...
with documented exfoliative erythroderma due to allopurinol treatment, developed cutaneous leukocytoclastic vasculitis that was probably related to febuxostat.\textsuperscript{11} Being a new medication, caution, careful dose escalation, and close monitoring is warranted when febuxostat urate-lowering therapy of allopurinol-intolerant patients is considered.\textsuperscript{11}

In conclusion, we report a patient who developed a fixed drug eruption due to allopurinol and tolerated febuxostat without any adverse effects.

REFERENCES