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IS IT TIME TO CONSIDER NEW THERAPEUTIC OPTIONS FOR REFRACTORY GOUT FLARES?

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BACKGROUND

Gout is an inflammatory, painful and potentially destructive disease. Pathophysiology of gout flares involves a pro-inflammatory cascade, which begins with the activation of toll-like receptors 2 and 4 of macrophages and monocytes. The result is the production of IL-1, IL-6, IL-8, tumor necrosis factor (TNF) and oxygen radicals. Management of gout flares is based on immediate control of inflammation with colchicine, NSAIDs or glucocorticoids, often hampered by the presence of frequent comorbidities. The use of IL-1 inhibitors is costly and not approved for gout in Brazil.

CASE REPORT

We present three patients with difficult-to-treat gout flares, in which insufficient response to or side effects from glucocorticoid motivated the use of a TNF inhibitor. Table 1 shows the patients' clinical features and the course and management of refractory gout flares.

Table 1. Case series of 3 male patients with crystal-proven, tophaceous gout presenting refractory polyarticular flares.

	Case 1	Case 2	Case 3
Age (years)	47	37	41
Baseline SU (mg/dL)	9.0	13.0	11.0
Comorbidities	Hypertension Type 2 diabetes mellitus Coronary artery disease (myocardial revascularization three years earlier) CKD stage 3 Pleural tuberculosis (5th month of treatment)	Dyslipidemia Obesity CKD stage 2 (CrCl 65.6 mL/min) Nephrolithiasis	Hypertension Type 2 diabetes mellitus Alcohol abuse Nephrolithiasis
Refractory gout flares	Moderate doses of glucocorticoid resulted in limited improvement and severe side effects. NSAIDs contraindicated. Previous attempts to reintroduce allopurinol failed due to worsening gout flares.	Reentrant severe gout flares, with fever. Attempts to increase allopurinol dose to reach SU target failed due to gout flares. Glucocorticoids resulted in insulin-dependent type 2 diabetes mellitus.	Attempts to increase allopurinol dose to reach SU target failed due to gout flares.
Adalimumab 40 mg 14/14 days	4 doses	4 doses	4 doses
Complications from anti-TNF	Sporotrichosis, successfully treated with itraconazole	None	None
Allopurinol (mg/day)	300	800	800
Outcome	SU < 5 mg/dL Complete tophi resolution	SU 5.1 mg/dL Complete tophi resolution	Partial and slow control of disease

CONCLUSION

Although anti-TNF is not a conventional drug for gout flare management, there is a pathophysiological rationale for this use. In this case series, a short-term of adalimumab created a therapeutic window for the introduction and up-titration of allopurinol, without triggering a new inflammatory process by uric acid mobilization, placing anti-TNF as an important alternative considering the high cost and limited availability of anti-IL1 for gout in Brazil.