Tocilizumab in a Patient With Tophaceous Gout Resistant to Treatment

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**Abstract**

Gout is a disease characterized by acute episodes of pain, which occur as the result of monosodic urate crystal deposition in the joint and periarticular tissue. In some cases, gout behaves as a severe inflammatory arthropathy that is difficult to manage, generating structural joint damage and functional impairment. We report the case of a 44 years old man with gouty arthritis for 12 years, not responding to NSAIDs, allopurinol, colchicine or corticosteroids. Tocilizumab was started with favorable clinical and laboratory results after treatment.

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**Resumen**

La gota es una enfermedad que se caracteriza por episodios agudos de dolor como consecuencia del depósito de cristales de urato monosódico en las articulaciones y en el tejido periarticular. En algunos casos, la gota se comporta como una artritis inflamatoria severa de difícil manejo, generándose daño estructural articular y alteración funcional secundaria. Presentamos el caso de un hombre de 44 años con artritis gotosa tofácea severa de 12 años de evolución, sin respuesta al manejo con AINE, allopurinol, colchicina y corticosteroideas, a quien se inició tratamiento con tocilizumab, con favorable respuesta clínica y paraclínica.

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**Introduction**

Gout is a disease characterized by acute inflammatory episodes caused by precipitation and deposition of monosodium urate crystals (MUC) in the joints. It is the most common cause of inflammatory arthritis in men under 40 and affects approximately 1% of the adult population.1

Major advances in understanding its pathogenesis and treatment have been made in the last decade and include the identification of genetic and environmental factors, as well as recognition of gout as a major risk factor for cardiovascular disease. Recent studies in animals and humans suggest that MUC elicit an inflammatory response that will trigger nitric oxide, prostaglandins, and tumor necrosis factor alpha (TNF-α), IL-6, proinflammatory cytokines such as IL-1, IL-1β, produced by macrophages, dendritic cells and monocytes as well as the presence of the NLRP3 inflammasome complex (intracellular proteolytic complex).2,3

That is why we evaluated the pharmacological response to IL-1 inhibitors, including rilonacept; the results indicate a reduction in the frequency of gouty attacks during the initial period of treatment with the uricosuric drugs,4 and thus opened the door to evaluate other therapies.

**Clinical Observation**

We present the case of a 44 years old man with severe uncontrollable tophaceous gouty arthritis of 12 years of evolution, with the presence of tophi in knees, elbows, feet, and with polyarticular inflammatory pain that hindered functionality, with a pain visual analogue scale score of 7/10. He had a history of medical treatment and surgical resection of gouty tophi in the feet and
elbows. His previous management included the use of colchicine 0.5 mg/12 h, allopurinol 300 mg/12 h, diclofenac 75 mg/dl, receiving treatment for about eight years, without improvement despite 100% compliance.

On physical examination, the patient had limitation for walking and tophi of 3–5 cm in diameter on the hands, elbows, knees and feet. Radiographs showed multiple punched out erosions that compromised the phalanges of the hands and feet, decreased inter-carpal joint spaces, loss of relationship of the metacarpophalangeal joints, metatarsophalangeal joint subluxation of the left first toe, and remodeling of the left fifth metatarsal.

In the presence of a pattern of severe treatment-resistant tophaceous gout, management was begun with tocolizumab at a dose of 8 mg/kg/month. The evaluation after the start of treatment showed that the patient has had no further gouty attacks and regained his ability to perform basic activities of self-care. There was no evident decrease in the size or number of tophi. Laboratory findings are summarized in Table 1.

### Discussion

Acute treatment of gouty arthritis focuses on the use of NSAIDs, colchicine and glucocorticoids, however adequate chronic treatment is required to decrease the frequency of exacerbations and disease progression. Drugs that have been evaluated for the maintenance of patients can be divided into inhibitors of xanthine oxidase, the uricosuric uricase and those which modulate the inflammatory process. Allopurinol, belongs to the first group and is the cornerstone of chronic treatment, but its adverse effects and the high frequency with which recurrent episodes of gout occur during treatment have led to a search for other drugs.\(^5\)

Among the new drugs highlighted, rasburicase and pegloticase, which catalyze the conversion of urate to allantoin, reduce uric acid levels. The use of pegloticase has shown useful for maintaining uric acid levels below 6 mg/dl in up to 47% of patients,\(^6\) as well as in reducing tophi\(^7\) after 12 weeks. However, it is not available in our country.

The drugs related to the regulation of the inflammatory process in gout are based on the regulation of the high levels of TNF-\(\alpha\), as well as IL-1 and IL-6. These drugs include anti-TNF (infliximab\(^8\) and etanercept\(^9\)), anakinra and rilonacept, which are competitive inhibitors of IL-1,\(^10\) and canakinumab, which neutralizes the bioactivity of IL-1\(\beta\).

Current evidence is limited to cases where anti-TNF (infliximab and etanercept) and competitive inhibitors of IL-1 have been used, with which there is a modulation of pain related to the inflammatory response. Anakinra was used for treatment in a series of 10 cases, in which there was a favorable response in six patients. In the case of canakinumab, Schlesinger et al. conducted two clinical studies, the first in 2011, which demonstrated the superiority of this drug over colchicine for reducing gout symptoms after allopurinol\(^11\) was started. The second shows the effectiveness of canakinumab in improving pain and inflammation, and a decrease in the risk of new acute crises.\(^12\)

The case presented shows an adequate response to treatment with tocolizumab, highlighting disease control from the clinical point of view and the results of laboratory tests, which can be considered as related to IL-6 as a potential therapeutic target,\(^13\) but this is only one report of a successful case and it should be noted that the cost of biologic therapy is more than 100 times the cost of therapy with allopurinol and up to five times the cost of pegloticase.

### Conclusion

We describe an appropriate response to biological treatment with tocolizumab in the context of a patient with severe gouty arthritis. Further studies are required to evaluate the effectiveness of this treatment in the context of this disease.

### Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

**Confidentiality of Data.** The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

### Conflict of Interest

The authors have no disclosures to make.

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