Clinical Manifestations and Diagnosis of Gout

Fernando Perez-Ruiz, MD, PhD[a,*], Edwin Castillo, MD[b], Sandra P. Chinchilla, MD[b], Ana M. Herrero-Beites, MD[c]

KEYWORDS

• Gout • Diagnosis • Clinical manifestations • Tophi • Damage

KEY POINTS

- Gout has been academically considered, from the clinical point of view, to be a step-up disease consisting of different stages: acute gout, intercritical gout, and chronic gout.
- In clinical practice, clinicians should consider gout as a single disease with either or both acute (most commonly, episodes of acute inflammation) and persistent clinical manifestations, but not restricted to chronic synovitis.
- Monosodium urate crystal (MSUC) deposition and subclinical inflammation related to MSUCs are also to be considered as (asymptomatic) gout, in contrast to asymptomatic hyperuricemia with no deposition.

Gout is to be considered as the nucleation and aggregation of monosodium urate crystals (MSUCs) in tissues, mostly cartilage, synovial structures, bone, and skin, independently of the presence or absence of clinical manifestations. Further addition of descriptive terms may help to characterize the burden of disease.

INTRODUCTION: CONCEPTUAL ISSUES

Although most textbooks state that gout comprises the clinical manifestations of MSUC deposition, recent investigation using high-resolution and highly specific imaging techniques has shown that deposition and chronic inflammation may be present in

Disclosures: F. Perez-Ruiz: consultancies for Astra-Zeneca, Menarini, Metabolex, Novartis, Pfizer, SOBI. Speaker for Menarini International. Educational programs for Savient and Menarini. Investigation grants: Asociación de Reumatólogos del Hospital de Cruces; Ministerio de Sanidad (Gobierno de España); Fundación Española de Reumatología; E. Castillo, S. Chinchilla: nothing to disclose and A.M. Herrero-Beites: Investigation grants: Asociación de Reumatólogos del Hospital de Cruces.

[a] Division of Rheumatology, BioCruces Health Institute, Hospital Universitario Cruces, Pza Cruces sn, Baracaldo 48903, Spain; [b] Division of Rheumatology, Hospital Universitario Cruces, Pza Cruces sn, Baracaldo 48903, Spain; [c] Division of Physical Medicine, Hospital de Górliz, Astondo Ibiltoki, km. 2, Górliz 48630, Spain

* Corresponding author. Servicio de Reumatología, Hospital Universitario Cruces, Pza Cruces sn, Baracaldo 48903, Spain.

E-mail address: fernando.perezruiz@osakidetza.net

Rheum Dis Clin N Am 40 (2014) 193–206

http://dx.doi.org/10.1016/j.rdc.2014.01.003 **rheumatic.theclinics.com**

0889-857X/14/$ – see front matter

many individuals before the first symptom[1,2] and that they persist after symptoms of acute inflammation have completely subsided.[3] Therefore, MSUC deposition and subclinical inflammation related to MSUCs are also to be considered as (asymptomatic) gout, in contrast to asymptomatic hyperuricemia with no deposition. If this physiopathologic sequence is accepted, gout is to be defined as the presence of MSUCs in tissues as a consequence of long-standing hyperuricemia, despite the absence or the presence of acute or persistent clinical manifestations. To show this issue, consider that hemochromatosis, a well-known deposition disease, is defined as evidence of iron overload in the target organ, independently of the presence or absence of signs, symptoms, or organ dysfunction.

Academically, gout has been reported frequently as acute gout, intercritical gout, and chronic gout, as if these are different and an obligatory sequence of the stages of the natural history of the disease or even different diseases. We would like to take a more comprehensive approach, considering only acute clinical manifestations (mostly episodes of acute inflammation [EAIs]) and persistent clinical manifestations (chronic signs and symptoms). Again, as an example, it is not appropriate to talk about asymptomatic diabetes, acute diabetes, intercritical diabetes, or chronic diabetes but of acute and chronic clinical manifestations of diabetes. We suggest considering gout as the deposition of MSUCs in tissues (a true chronic deposition disease) with either or both acute and persistent, but even with absent clinical, manifestations.[4]

From a clinical point of view, gout has either acute (most commonly, but not restricted to, acute inflammatory episodes) or persistent clinical manifestations (including palpable tophi, joint limitation, persistent inflammation, and joint deformity). Gout should be considered a chronic disease from the beginning.

ACUTE CLINICAL MANIFESTATIONS OF GOUT

EAIs

Crystal-induced acute inflammation is the hallmark of gout and is well recognized by both patients and clinicians. Nomenclature of EAIs is variable, referred to as gout flares, gout attacks, gouty bouts, gouty arthritis, and so on. EAIs could be defined as the appearance of signs and symptoms of acute inflammation induced by MSUCs in any structure of the musculoskeletal system.

The time from the onset of hyperuricemia to tissue nucleation and growth of MSUCs is not known. The time from the onset of hyperuricemia to the development of clinical manifestations of gout seems to be directly related to the level of hyperuricemia and to the time that the individual is exposed to the hyperuricemic state.[5]

EAIs involve mainly synovial structures of joints, tendons, and bursae, thereby inducing acute arthritis, tendonitis, and bursitis. According to topographic distribution, the peripherally located structures are more commonly involved than those structures centrally located, and those of the lower limbs more frequently than that of the upper limbs. Nevertheless, in patients with long-standing gout, involvement of centrally located joints[6] and even the joints of the axial skeleton is possible. However, an absence of association between spinal pain and computed tomography (CT) of the spine showing changes suggesting gout has been reported,[7] despite the infrequent occurrence of spinal location as a presentation of gout.[8]

Therefore, involvement of the most peripheral structures of the lower limbs, such as the first metatarsophalangeal (MTP) joint, classic podagra, is a hallmark of, although not restricted to, gout. EAIs involving the first MTP joint are the presenting location in close to half, and they are involved in up to or more than 80% of untreated patients, including those without target therapeutic serum urate levels.