EDITORIAL

Slowly melting the urate snow in joints: Explaining gout attacks to patients

1 | INTRODUCTION

Generally, gout patients believe that a gout attack or flare occurs when serum urate levels (SU) are abnormally high. However, gout attacks often occur even with a normal SU. Furthermore, a gout attack does not always occur when the SU exceeds 7.0 mg/dL, eg, 10 mg/dL. This phenomenon makes it difficult not only for patients but general practitioners to understand the relationship between gout attacks and SU. It causes confusion about how to regulate SU in various situations of gout treatment. These misunderstandings can cause treatment to be interrupted or terminated before gout control is achieved. As a result, gout attacks will recur, risking complications such as urolithiasis formation, progressive renal damage, and the eventual formation of multiple tophi.

We designed a simple and effective method that we are implementing to improve patient compliance. In order to help patients easily understand the need for continuous long-term treatment, we have devised explanatory illustrations that utilize snowfall, snow cover (Figure 1), avalanches (Figures 2 and 3), and slowly melting snow (Figures 4 and 5) to depict various states of SU conditions and successful treatment.1

FIGURE 1 Hyperuricemia. We compared hyperuricemia to snowfall and the state of accumulating monosodium urate crystals to snow cover. When snowfall continues, snow cover gradually increases on the roof (joint lining). The snow cover eventually reaches a dangerous level on the roof.

FIGURE 2 Crystal shedding. When the monosodium urate burden exceeds the limit of stability, triggered by a variety of stimuli, a block of crystals sheds into the joint cavity. This crystal shedding (avalanche) evokes acute gouty arthritis, otherwise known as a gout attack or a flare.
In body fluid with pH 7.4, 99% of uric acid is dissociated or exists as urate, and most urate exists in the form of monosodium urate (MSU). Urate has a small molecular weight (168 g/mol) and passes freely from serum into the synovium and synovial fluid. Therefore, measuring SU effectively measures the urate level in joint fluid.

The upper limit of MSU solubility in body fluids with pH 7.4 approximates at 7.0 mg/dL (0.42 mmol/L). This value indicates a branch point concerning whether MSU is soluble or insoluble in the joint fluids. When SU and hence synovial fluid urate exceeds 7.0 mg/dL (hyperuricemia), MSU crystals gradually accumulate on the surface of joint synovium as microtophi (Figure 1).

When surface MSU accumulation exceeds the limit of stability, triggered by a variety of stimuli, a block of crystals is shed from the microtophi into the joint cavity. This concept was proposed as “crystal shedding.” Macrophages and neutrophils recognize the needle-like MSU crystals dislodged from microtophi into joint fluid as harmful enemies and start reacting violently against the crystals. Here, an acute gouty arthritis or gout attack is evoked (Figure 2).
4 | SLOWLY MELTING URATE SNOW IN JOINTS

For about a month after a gout attack, the crystals accumulated on the joint lining are very unstable and easily break off. Abrupt reduction of SU due to over-administration of urate-lowering drugs often evokes unexpected, repeated, and prolonged gout attacks (Figure 3). If the treatment procedure is not successful, such instability might persist for 2-3 months or more. At this stage, it is extremely important for accumulated crystals to be dissolved slowly and gently, as shown by the illustration of the sun slowly melting the snow on the roof (Figure 4). This is recommended in the 2020 American College of Rheumatology Guidelines for Management of Gout, which state that a “lower starting dose of urate-lowering therapy reduces the risk of flares associated with initiation.”

5 | FOR COMPLETE REMISSION OF GOUT ATTACKS

As the crystals accumulated on the inner surface of the joint gradually decrease, the occurrence of crystal shedding gradually diminishes, and eventually avalanches occur no longer (Figure 5). When this condition is attained, SU should be controlled using the minimum dose of urate-lowering drugs that achieves a target SU with 6.0 mg/dL. In the illustrations, this stage is depicted as cloudy or pale sun shining down on the roof and the absence of snow accumulation.

Lifestyle disorders such as regular overeating, drinking, and obesity resist normalization of SU. When management and guidance from the doctor or patient compliance is suboptimal, SU cannot be maintained within the target value. No matter how much time passes, the accumulated snow will not melt and gout attacks will continue to occur.

These explanatory illustrations utilizing snowfall, snow cover, and an avalanche to depict various states of SU conditions have proven very useful to understanding the relationship between gout attacks and SU, and has improved patient compliance for gout treatment.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.