Journal of Advances in Medicine and Medical Research

Volume 35, Issue 19, Page 230-236, 2023; Article no.JAMMR.102196
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Ultrasonographic findings in Hyperuricemia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2023/v35i195155

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/102196

Review Article

Received: 03/05/2023
Accepted: 11/07/2023
Published: 03/08/2023

ABSTRACT

Musculoskeletal Ultrasound is a quick, inexpensive, non-invasive modality for early diagnosis of hyperuricemia and gout. US waves are more intensely reflected by crystalline material than by the tissues around it, which are found to be in the cartilage, synovial fluid, tendon sheaths, and subcutaneous tissue. Power Doppler Imaging is especially helpful for tiny vessels as well as those having low-velocity flow since it has the sensitivity for flow identification. The existence of double contour sign, aggregates, tophi and hyperechoic spots are more specific ultrasonographic findings for diagnosis of gout. Furthermore, Hyperuricemia was found to be linked with cardiovascular diseases which reflected as increase in the carotid artery intima thickness in addition to carotid artery plaque formation that can be easily detected by ultrasound helping in early cardiovascular diseases screening and management.

Keywords: Gout; hyperuricemia; double contour sign; tophi; carotid intima media thickness.

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1. INTRODUCTION

Both an excess of uric acid produced by purine metabolism and an insufficient elimination of uric acid by the kidneys have been associated with hyperuricemia [1,2]. Humans have greater blood uric acid levels because they are lacking the uricase enzyme, which turns uric acid to a more soluble end product. One of the most prevalent forms of arthritis in adults is gout, which is brought on by the buildup of monosodium urate (MSU) crystals in the joints and is accompanied by high levels of uric acid in the blood. However, asymptomatic hyperuricemia (AHU) is a medical disorder in which the blood urate level is elevated with no symptoms or signs of arthritis [3].

The inflammatory substances IL-6, C- reactive protein (CRP), and tumor necrosis factor (TNF)-a, which are all independently related to either coronary artery disease (CAD) or congestive heart failure (CHF), have all been associated with hyperuricemia in epidemiological research [4]. By inducing matrix metalloproteinases, TNF-a may contribute to abnormal ventricular remodeling in CHF and induce myocyte death [5,6]. Both IL-6 and TNF-a have been connected to the degree of coronary obstructions in CAD [7,8].

Uric acid crystals, known to be proinflammatory, triggers complements, neutrophils that produce protease and macrophages, oxidants, and platelets to initiate the coagulation cascade in the presence of endothelial dysfunction brought on by hyperuricemia with diminished acetylcholine-induced vasodilatation and diminished endothelial nitric oxide (NO) release. UA has a negative impact on oxidative metabolism as well as the adhesiveness and aggregation of platelets. In addition, UA plays a part in elevating blood pressure, which in turn promotes atherosclerosis [9,10]. Moreover, the occurrence of chronic and/or recurrent acute gout is linked to systemic inflammation since gout patients' synovial fluid has consistently exhibited inflammatory activity [11]. As a result, it may be stated that ongoing inflammation everywhere in the body can cause atherosclerosis to develop and accelerate, as well as develop a prothrombotic environment that can result in a stroke or an acute coronary syndrome, especially in the presence of chronic diseases like hypertension, especially in presence of other associated chronic diseases like DM and hypertension dyslipidemia [12,13].

2. ULTRASONOGRAPHIC FINDINGS IN GOUT AND HYPERURICEMIA

Synovial fluid, Hyaline cartilage, bones, ligaments, and soft tissues are common MSU deposition sites. A new stage mechanism was just put forth: Stage A is hyperuricemia without indicators of MSU crystal deposits; stage B is MSU deposition of crystals without gout manifestations; stage C is MSU deposition with past or present symptoms of acute gout flares; and stage D is advanced gout needing specialized treatment [14]. This stage method takes into account the fact that MSU crystals may exist even in patients who show no symptoms or warning indications. To verify this system, further research is still required. A new era in our knowledge of gout begins with this new stage system. The so-called 'asymptomatic' hyperuricemic individuals no longer appear to be asymptomatic, as the cause of gout and the gold-standard method of gout diagnosis, MSU crystal in synovial fluid, may be seen in hyperuricaemic individuals without overt symptoms [15]. The most often afflicted joint in gout sufferers is the first MTP joint, which is crucial to the functioning role of the gait cycle throughout the propulsive phase. Furthermore, those who have chronic pain in the first MTP joint show local anatomical and functional abnormalities in this joint, such as decreased muscle strength, restricted joint mobility, and a higher incidence of musculoskeletal deformities [16].

Specific findings: Double contour sign, aggregates, and tophi are the three distinct characteristics that are thought to be indicators of gout. OMERACT criteria for gouty lesions were just recently provided [17].

A double contour sign (DCS), which may be recognized from the cartilage interface sign, is described as an aberrant hyperechoic band across the superficial boundary of the articular hyaline cartilage, regular or irregular, intermittent or continuous [18,19]. DCS has a sensitivity of 46.3% and a specificity of 99%, making it one of the pathology's most precise aspects. It is more usually seen in problematic joints, notably the hyaline cartilage of the knees and the metatarsophalangeal (particularly the 1st) and metacarpophalangeal joints (Fig. 1). In joints with a narrow acoustic window for cartilage evaluation, in joints with osteoarthritis, and in the existence of effusion, which causes a posterior echo amplification, the observation of DCS may be challenging. It's interesting to note that DCS

has been identified in people with asymptomatic hyperuricemia and that it may go away with treatment [14].

Tophi, which are extracellular deposits of MSU, are common clinical symptoms of gout. The three types of granulomas—soft, hard, and mixed—can be identified everywhere and are surrounded by foreign body giant cells and mononuclear cells, generating a granuloma-like structure (Fig. 2) [20].

The hallmark of gout is thought to be aggregates, which are caused by the deposition of crystals of MSU in synovial fluids and other tissues including cartilage and soft tissues. Compared to the nearby tissues, those aggregates reflect ultrasonic beams more strongly. There have been reports of "bright stippled foci," "hyper-echoic cloudy areas," "hyper-echoic spots," and a "snowstorm" look. It is assumed that MSU crystals in synovial fluid or tissue are the cause of these descriptions because they produce tiny light echoes [21].

Aggregates less than 1 cm, often homogenous, and devoid of a posterior acoustic shadow are referred to be hyperechoic cloudy regions (sometimes known as "cottony images"), and they are extremely receptive to treatment [18].

Non-specific findings: Individuals with gout may be found to have structural lesions such as bone erosions as well as inflammatory anomalies such as joint effusion and synovial hypertrophy [19].

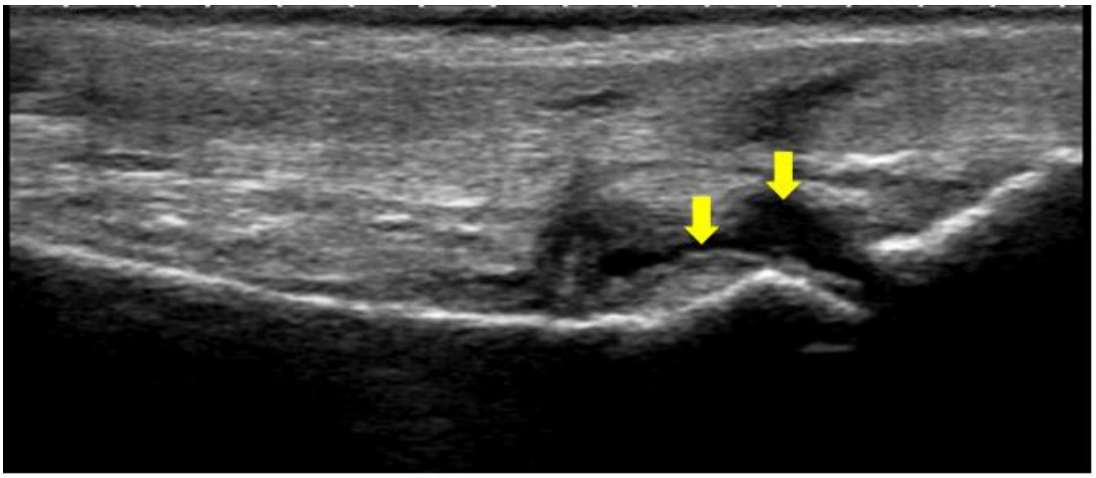

Fig. 1. MSUS longitudinal scan of 1st MTP jointshowing double contour sign and effusion

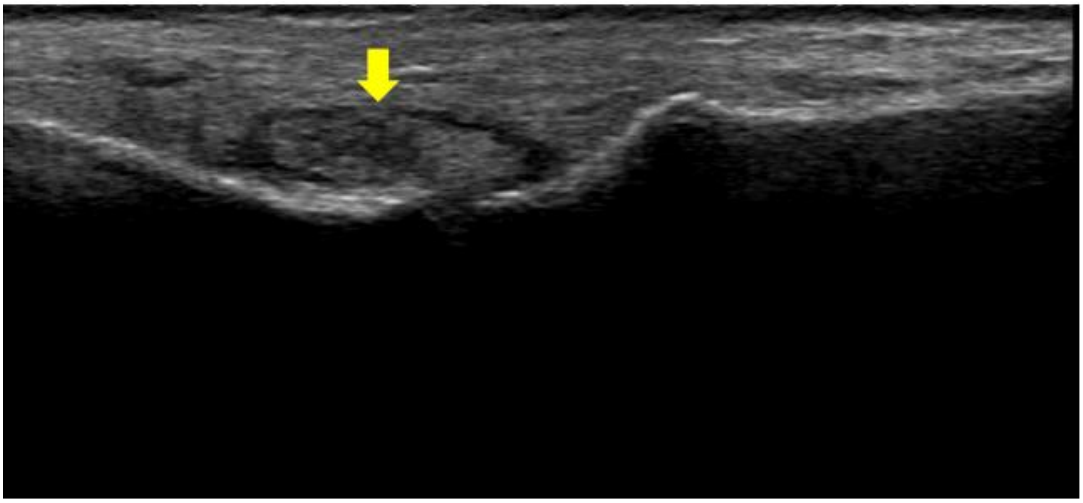

Fig. 2. MSUS longtudinal scan of 1st MTP joint showing large Tophus on 1 MTP joint

Joint effusion is defined by OMERACT as an abnormally hypoechoic or anechoic IA material which can be compressed and displaced but lacks a doppler signal. That may be distinguished from SH, which is characterized by a material that is typically hypoechoic, non-displaceable, and poorly compressible and may display a Doppler signal [22,23]. The US has been able to assess the level of synovial vascularity owing to the usage of PD. This can be evaluated quantitatively by measuring the number of vascular flow pixels in the area of interest with an automated analysis system, or semi-quantitatively by rating the quantity of PD signals inside the joint capsule on a 0–3 scale. It has been demonstrated that Power Doppler is an effective tool for evaluating the vascularity of the synovium and for correlating synovitis in inflamed joints that has been histologically identified. Similar to this, Fig. 1 shows the semiquantitative score for doppler synovitis.

Grade 0: No synovial fluid flow.
Grade 1: signals with a maximum of three single spots, 2 confluent spots, or 1 confluent spot with a maximum of two single spots.
Grade 2: fewer than half of the synovium exhibits vessel signals.
Grade 3: greater than half of the synovium exhibits vessel signals [22-24].

Furthermore, the "snowstorm" of synovial fluid, which is assumed to represent moving crystals inside the fluid that is reported in acute gout, could not be unique to gout. In the first MTP joint, ankle, knee, wrist, and second MCP joint, synovitis is most often seen, according to modern exploratory research in gout. Subclinical synovitis was shown to exist in gout in both of the acute and inter-critical stages according to other recent, minor research on the condition. The frequency of clinically active joints reduced in the inter-critical phase of the one US research evaluating subclinical synovitis longitudinally, but subclinical inflammatory condition did not change throughout the acute and inter-critical phases. This could affect how the gout-related disease burden and disease activity are assessed. It is important to note that in this short trial, the blood uric acid level was not sufficiently controlled, and it is unclear if subclinical inflammation would have long-term consequences for structural joint deterioration or comorbidities [22,23].

An abnormally hypoechoic intraarticular tissue with poor compressibility and displaceability is the hallmark of synovial hypertrophy. Although they are non-specific findings, synovial hypertrophy and hyper-vascularization can also be found, and the potential existence of cloudy areas or hyperechoic spots in the synovial fluid is strongly suggestive of gout [25].

A high frequency doppler signal suggests ongoing inflammation, just like in other types of arthritis. It can occasionally be seen in joints that are not clinically inflamed, highlighting a subclinical situation of inflammation. Additionally, it has been shown that the signal may diminish following treatment [16].

Tenosynovitis: According to the OMERACT group, tenosynovitis is a thickened tissue that is anechoic or hypoechoic on 2 perpendicular planes and may or may not contain tendon sheath fluid and a doppler signal [16].

OMERACT defines bone erosions as a disruption of the bone surface that can be seen in 2 perpendicular planes. The US identifies additional joint damage than conventional radiography, particularly in the setting of early illnesses; its limits emerge in locations where there is a weak acoustic window, like in the mid-carpus. Characteristic locations for gout erosions are highlighted by the medial portion of the 1st MTP and MCP joints. Prior asymptomatic MTP joints may have erosions; they are often observed next to tophi and may show a Doppler signal. Compared to other forms of inflammatory arthritis, 1st MTP damages are more typical with gout. The 'inside-out' method of erosion of bones in gout results from the deposit of crystals directly within the osseous tissue, or the 'outside-in' mechanism results from the bone's surface [16-19].

There hasn't been a clear definition by the OMERACT US group, nor has the measurement of cartilage degradation or narrowing of the joint spaces in the US been thoroughly researched. Early research has shown a correlation between conventional radiology findings of narrowing of the joint spaces and directly evaluating thicknesses of the cartilages on the US in the PIP and MCP joints. However, it might not constantly be able to evaluate cartilage directly, for instance when synovitis occurs and there isn't an interface artifact on the surface of the cartilage, which is the upper limitation of cartilage assessment from the subchondral bone's surface. Most recently, research utilizing a semiquantitative cartilage degradation scoring technique (scale of 0–4) was utilized. In general, US cartilage evaluation shows potential, but for now more thorough testing is needed [16,19].

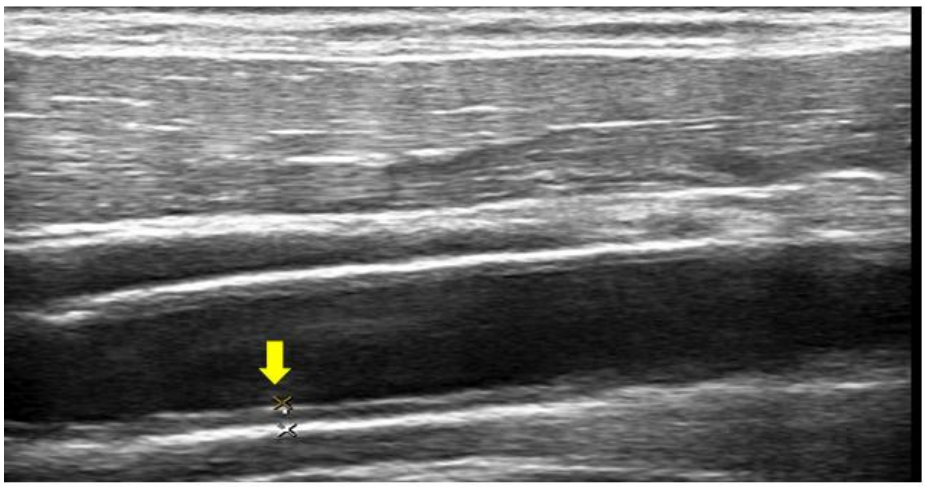

Fig. 3. MSUS longitudinal scan of carotid artery showing increased thickness of intima media in gout patient

Tendon injury is a typical finding in rheumatological illnesses that have been present for a long time because tendon inflammation that is repetitive or chronic may cause structural damage and tendon rupture. The US is more accurate in identifying partial finger extensor tendon tears than MRI [25].

3. CAROTID ARTERY ASSESSMENT BY ULTRASOUND

The measurement of CIMT and evaluation of carotid artery plaque are two independent methodologies that have been utilized to determine CVD risk using carotid ultrasonography. CIMT values <0.8 mm is correlated with normal healthy people (Fig. 3). While any intravascular abnormality measuring 1.5 mm or more or taking up more than 50% of the artery wall was considered to be carotid plaque. Individuals with plaque scores of 0, 1, 2, and 3 were categorized as having neither, mild, moderate, or severe carotid atherosclerosis, correspondingly [26-30].

Carotid intima media thickness represents morphologic process that while subintimal process, carotid plaque, might be more indicative of atherosclerosis than cardiovascular risk markers like hypertension [26,27,31].

4. CONCLUSION

Musculoskeletal ultrasonography is a fundamental tool to detect joint and soft tissue affection in gout and even in AHU help in early management with focusing on individuals who have risk factors and are more liable for developing subclinical atherosclerosis in form of increased CIMT and/or carotid plaque, especially in individuals with old age, hypertension, high BMI, and with longer duration of hyperuricemia.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/102196