

Double Contour Sign In Early Detection Of Gout Among Asymptomatic Hyperuricemic Filipino Patients: A Single Center Tertiary Hospital Observational Study



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ABSTRACT

Objective Double contour sign (DCS) is considered part of the new gout classification. This study aims to determine the agreement of blinded musculoskeletal sonologists in identifying the double contour sign among asymptomatic hyperuricemic patients.

Methods Participants with asymptomatic hyperuricemia (n=65) underwent a gray-scale ultrasound assessment of both of their 1st metatarsophalangeal joints (MTPJs) done on 3 positions (dorsal, medial, plantar) in longitudinal view. The static images were read by 2 independent blinded sonologists for presence of double contour sign.

Results Among the 130 1st MTPJs, the sonologists were able to positively identify DCS on 48R and 52L, negative in 10R and 10L, with discordant readings in 7R, 3L. The overall kappa agreement was statistically significant at 0.674 (substantial

agreement) and 0.842 (almost perfect agreement) on the right and left respectively, (both $p < 0.001$).

Conclusion and Recommendation There is a high proportion of positive double contour sign seen among persistently asymptomatic hyperuricemic patients. It might be prudent to perform musculoskeletal ultrasound early on to detect monosodium urate crystal deposits in similar patients. A close follow up to monitor clinical gouty arthritis maybe necessary or consider utility of urate lowering drugs in crystal dissolution in prospective studies.

INTRODUCTION

Asymptomatic hyperuricemia is a condition in which the serum urate level is high, but gout—manifested by arthritis or uric acid nephrolithiasis—has not yet occurred. Majority of patients with hyperuricemia remain asymptomatic throughout their lifetimes, up to 20 years before the initial attack of gout. The definitive diagnosis of gout is by demonstration of strongly negative birefringent monosodium urate crystal under polarizing microscopy. Currently, several non-invasive tests such as imaging are used as an alternative to diagnose gout. Nowadays, ultrasound is being used to diagnose gout. The

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characteristic finding is a superficial, hyperechoic, irregular band on the surface of articular cartilage, the so-called "double contour sign" or "urate icing," and nonhomogeneous tophaceous material surrounded by an anechoic rim. [1]

In a cross sectional study done by Bhadu [2], the urate crystal deposition in asymptomatic hyperuricemic individuals were found in the 1st MTPJ (33%) and knees (25%). Furthermore, urate crystals are present in articular tissues even before classic acute monoarthritic presentation of gout is clinically evident and may give further support for the use of urate-lowering therapy in asymptomatic hyperuricemic patients [3].

The American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) collaborated and came up with 2015 Gout Classification Criteria. Ultrasound and Dual-energy Computed Tomography (DECT) are imaging modalities with sufficient published data and investigator experience to support their utility in identifying urate deposition accurately, thus the double-contour sign, is considered a criterion to the new gout classification. [4]

This study aims to determine the ability of musculoskeletal sonologists in a tertiary hospital to detect double contour sign in the presented films taken from asymptomatic hyperuricemic patients.

METHODOLOGY

This is a prospective observational study where patients included were males 20 years old and beyond and postmenopausal women with serum uric acid determination ≥ 7.0 mg/dl not more than a week on day of consult and at least one other occasion within the past 1 year. These patients were recruited from general out-patient clinics and private consults of Rheumatology practice.

Secondary causes of hyperuricemia associated but not limited to malignancy, psoriasis/psoriatic arthritis, chronic hemolytic anemia, myeloproliferative or lymphoproliferative disorders, Paget's disease, sickle cell anemia, and chronic renal failure as well as drug induced hyperuricemia were excluded. Ever use of any urate-lowering agents ie. allopurinol or febuxostat or uricosurics ie. probenecid as well as history of any form of inflammatory mono-, oligo-, or polyarthritis were also excluded.

ULTRASOUND IMAGE INTERPRETATION

All patients underwent ultrasonography of bilateral 1st MTPs using Sonosite HFL50 equipped with a 6-to15-MHz linear transducer. Presence of hyperechoic band over anechoic cartilage (double contour sign) on any or all three different positions (dorsal, medial, plantar) taken in longitudinal view was considered positive for DCS. The static images were interpreted by two musculoskeletal sonologists blinded to all patients' medical information.

The conduct of study was approved by the USTH Research Ethics Committee.

RESULTS

There were 65 patients included in the study, 36 postmenopausal women, 28 men, and 1 undisclosed gender, with 130 1st MTPJs assessed. The mean age was 52.4 years, mean BMI of 24.6 kg/m², and mean serum uric acid level of 8.5 mg/dl. Comorbidities included hypertension in 40%, diabetes in 16.9%, and dyslipidemia at 7.7%. Only 12.3% admitted family history of gout in either father, sibling, or son. (Table 1)

Ultrasound readings of the right and left 1st MTPJs by both sonologists showed overall positive results in 48/65 (73.8%) R and 52/65 (80%) L 1st MTPs. The measure of agreement (kappa) on the various planes of both 1st MTPs ranged bet 0.463 (substantial) and 0.842 (almost perfect) with all p-values <0.05. (Table 2).

Of the 65 patients, only 4 (6.2%) patients were negative for double contour sign (DCS). The remaining 61 patients (93.8%) were positive for DCS in any or all 3 positions in longitudinal view. Plantar views of both MTPs yielded most counts of positive sonographic findings from both readers compared to the dorsal and medial views. The overall percentage of agreement of both sonologists (calculated over 390 paired ratings) as shown in Table 3 is 356/390 views or 91.3%.

DISCUSSION

Point-of-care musculoskeletal ultrasound offers several advantages to patients with refractory hyperuricemia. Aside from being readily accessible in most hospital facilities, it also does not use ionizing

Table 1. Demographic profile of the participants with Gout. (N=65)

Gender, n (%)	
Male	28 (43.1)
Female	36 (55.4)
Not disclosed	1 (1.5)
Age (in years)	
mean (SD)	52.4 (15.5)
range	24-83
BMI (kg/m ²), mean (SD)	24.6 (4.2)
Serum uric acid (mg/dl), mean (SD)	8.5 (2.2)
Family History of gout, n (%)	8 (12.3)
Comorbidities, n (%)	
Hypertension	26 (40)
Diabetes mellitus	11 (16.9)
Dyslipidemia	5 (7.7)
CAD	0 (0)

radiation, is relatively less expensive, patient-friendly, and offers reproducible results. It has multiplanar imaging capability and is efficacious as a method of guidance for invasive procedures as well. However, among its shortcomings are its reliance on getting a good acoustic window to visualize a joint and its being generally less sensitive than MRI in detecting joint inflammation and structural changes [3].

The study of Pineda in Mexico [5] showed that the mean serum urate of the 50 patients with AH included was 8.1±0.9 mg/dl, DCS positive in 25 of the 100 1st MTP joints (50 patients). This study also focused on subclinical structural damage in both intra- and extra-articular structures of the knees and ankles where 52% had synovial fluid/hypertrophy and erosion in 12% with enthesopathies as well.

Asymptomatic hyperuricemia patients with positive DCS (36%) in the study of Stewart [6] were mostly of European descent (83%), with lower mean serum urate levels (7.7±0.8mg/dl) compared to our study. Though the same study also mentioned presence of sonographic evidence of mild joint effusion in AH

Table 2. Detection of double contour sign among participants with Gout and measure of agreement between two sonologists

	Reader 1	Reader 2	κ	p	95% CI
R (dorsal)					
Positive, n (%)	16 (24.6)	18 (27.7)	.761	< .001	0.581, 0.941
Negative, n (%)	49 (75.4)	47 (72.3)			
R (medial)					
Positive, n (%)	3 (4.6)	9 (13.9)	.463	< .001	0.118, 0.808
Negative, n (%)	62 (95.4)	56 (86.1)			
R (plantar)					
Positive, n (%)	49 (75.4)	47 (72.3)	.682	< .001	0.478, 0.886
Negative, n (%)	16 (24.6)	18 (27.7)			
R Overall					
Positive, n (%)	53 (81.5)	50 (76.9)	.674	< .001	0.453, 0.895
Negative, n (%)	12 (18.5)	15 (23.1)			
L (dorsal)					
Positive, n (%)	12 (18.5)	16 (24.6)	.728	< .001	0.526, 0.930
Negative, n (%)	53 (81.5)	49 (75.4)			
L (medial)					
Positive, n (%)	4 (6.2)	8 (12.3)	.637	< .001	0.316, 0.958
Negative, n (%)	61 (93.9)	57 (87.7)			

Table 2. Detection of double contour sign among participants with Gout and measure of agreement between two sonologists (continued)

	Reader 1	Reader 2	κ	p	95% CI
L (plantar)					
Positive, n (%)	53 (81.5)	50 (76.9)	.767	< .001	0.574, 0.959
Negative, n (%)	12 (18.5)	15 (23.1)			
L Overall					
Positive, n (%)	54 (83.1)	53 (81.5)	.842	< .001	0.668, 1.016
Negative, n (%)	11 (16.9)	12 (18.5)			

L, left; R, right

Table 3: Agreement on sonographic findings from both sonologists (N=390 views)

Right	Positives	Negatives	Left	Positives	Negatives
Dorsal (R1)	14	45	Dorsal (L1)	10	49
Medial (R2)	3	56	Medial (L2)	4	59
Plantar (R3)	43	13	Plantar (L3)	49	11
Total	60	114	Total	63	119

(22%) more than in gout patients (9%), erosion in 1, synovial hypertrophy in 2, and synovitis in 2.

Our study showed an unexpectedly high proportion of asymptomatic hyperuricemia patients with positive double contour sign at 95.4% (62/65). With such a high yield of positive DCS and statistically significant kappa coefficients, possible other morphostructural changes involving the hyaline cartilage, tendons, and presence of tophi or erosions - could have also been present in some if not most patients. We did not expect this high positivity rate, therefore not able to fully maximize the utility of ultrasound in this cohort of patients with AH. This finding though should be duplicated in a larger sample and stricter control of confounders and effect modifiers.

CONCLUSION

There is a high proportion of asymptomatic hyperuricemia patients seen in the tertiary hospital

with positive double contour sign. This highlights the importance of early detection of monosodium urate deposits in an easily accessible asymptomatic joint of individuals with persistent hyperuricemia.

RECOMMENDATION

It is not clear how soon after the presence of DCS will patients develop the clinical expression of gouty arthritis. Therefore, follow-up study of these patients to determine whether initiation of urate lowering therapy will prevent or retard the development of acute gout or even lead to the disappearance of ultrasound features [7].

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