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THU0420

ULTRASOUND SHOWS GREAT ACCURACY FOR THE DIAGNOSIS OF CRYSTAL ARTHRITIS IN PATIENTS WITH RECENT-ONSET SYNOVITIS

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Background: The value of ultrasound (US) in the diagnosis of crystal arthropathy, such as gout or calcium pyrophosphate deposition disease (CPPD), in patients with recent onset synovitis has been evaluated only by a few studies.

Objectives: To investigate, in patients with acute arthritis, the accuracy of US for the diagnosis of crystal arthropathy.

Methods: Consecutive patients with recent onset (<6 weeks) acute arthritis were enrolled. The US examinations were performed a rheumatologist blinded to clinical data. Calcium pyrophosphate and monosodium urate crystal deposits were identified in the joint affected by synovitis (target joint), as well as in the classic sites for gout and CPPD (set of joint) (Table 1), according to the OMERACT definitions.

Table 1. Anatomical targets of ultrasound examination

	Gout	CPPD	Both
Wrist	Radiocarpal j Intercarpal j	Triangular FC complex Scapho-lunate ligament	/
Hand	DC in the II MCPj HC	Deposits within the II MCPj HC	II MCPj
Knee	Popliteal groove DC in the femoral condyle's HC	Meniscal FC Deposits within the femoral condyles' HC	Supra-patellar recesses
Hip	DC in the femoral head's HC	Deposits within the femoral head's HC	Hip j
Foot	DC in the I MTPj HC	Acetabular FC Deposits within I MTPj HC	I MTPj

Legend. DC: double contour, FC: fibrocartilage, HC: hyaline cartilage, MCPj: metacarpophalangeal joint, MTPj: metatarsophalangeal joint, j: joint.

The diagnostic accuracy of US and synovial fluid analysis (SFA) was evaluated taking the classification criteria for gout and CPPD as gold standard (1,2). Moreover, the US and SFA results were compared in the joints in which the SFA was performed.

Results: One-hundred and four patients were enrolled: 22 CPPD patients, 23 with gout and 59 disease controls. Table 2 reports the diagnostic accuracy of US and SFA, using the classification criteria as gold standard.

Table 2. Diagnostic accuracy of US and SFA

	Sensitivity	Specificity	Positive LHR	Negative LHR
US (target joint)				
Crystal arthritis	0.84 (0.7-0.93)	0.91 (0.8-0.97)	9.5 (4.1-22)	0.2 (0.1-0.3)
CPPD	0.91 (0.71-0.99)	0.91 (0.80-0.97)	10.2 (4.4-23.8)	0.1 (0-0.4)
Gout	0.83 (0.61-0.97)	0.91 (0.80-0.97)	9.1 (3.9-21.4)	0.2 (0.1-0.5)
US (set of joints)				
Crystal arthritis	0.96 (0.85-0.99)	0.87 (0.76-0.95)	7.6 (3.8-15.3)	0.1 (0-0.2)
CPPD	1 (0.85-1)	0.88 (0.76-0.95)	8 (4-16)	0 (0-0.2)
Gout	0.91 (0.72-0.99)	0.88 (0.76-0.95)	7.3 (3.6-14.8)	0.1 (0-0.4)
SFA				
Crystal arthritis	0.9 (0.77-0.97)	1 (0.94-1)	/	0.1 (0-0.2)
CPPD	0.90 (0.7-0.99)	1.0 (0.94-1)	/	0.1 (0-0.3)
Gout	0.91 (0.71-0.99)	1 (0.94-1)	/	0.1 (0-0.3)

Legend. LHR: likelihood ratio

SFA was performed in 67 knees (64.4%), 10 wrists (9.6%), 10 ankles (9.6%), 5 I MTP joints (4.8%), 5 hips (4.8%), 4 elbows (3.8%), 4 shoulders (3.8%).

The total agreement between US and SFA was excellent (93.8% in CPPD and 90.2% in gout). SFA positive/US negative results occurred in 1 patient with CPPD (1.2%) and in 4 patients with gout (4.9%). On the contrary, US positive/SFA negative results occurred in 4 patients with CPPD (4.9%) and in 4 patients with gout (4.9%).

Figure 1 provides a pictorial evidence of the US appearance of crystal deposits. A: anterior suprapatellar transverse scan of the femoral condylar HC. HC calcifications (arrows) B: anterior longitudinal scan of the hip. FC calcification (asterisk) C: anterior longitudinal scan of the ankle. DC sign (void arrow) D: dorsal longitudinal scan of distal interphalangeal joint. DC sign (void arrow).

Conclusion: US is useful for the diagnosis of gout and CPPD in patients with acute synovitis. Extending the US evaluation to the joints which are most commonly involved in gout and in CPPD, other than those affected by synovitis, increases the sensitivity of US.

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THU0421

TUMOR-INDUCED OSTEOMALACIA: DATA FROM A MONOCENTRIC EXPERIENCE ON 16 PATIENTS

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Background: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome due to a phosphaturic tumor, which overproduces fibroblast growth factor-23 (FGF-23), causing hyperphosphaturia, hypophosphoremia, low 1,25(OH)₂ VitD₃ and osteomalacia. Locating the tumor is critical, because lesions are typically small, benign mesenchymal tumors, anywhere in the body; the delay between onset of symptoms and diagnosis ranges from 2.5–28 years. Surgical removal is the only effective therapeutic approach.

Objectives: To retrospectively evaluate patients affected by TIO, investigating clinical management and disease outcome.

Methods: We retrospectively collected data of patients affected by TIO referred to a tertiary Rheumatology Center between Sep 2000 and Jan 2020.

Results: We included 16 patients with a definite diagnosis of TIO, mean age±standard deviation 62.4±14.6 yrs, 56.2% females, mean age at symptoms onset 48.0±14.3 yrs (53.8±13.1 at diagnosis). Mean diagnostic delay between symptoms onset and tumor detection was 6.8±6.4 yrs. All patients complained bone pain, muscle weakness, and fractures before diagnosis of TIO. Biochemical findings were: mean serum Phosphorus (PS) 1.4±0.4 mg/dL (reference range (RR) 2.5-4.6), mean serum Calcium 9.4±0.7 mg/dL (RR 8.4-10.2), mean serum 1,25(OH)₂VitD₃ 30.5±23.4 ng/L (RR 25-86). Intact-FGF-23 was dosed in 9 patients, always resulting elevated: mean 396.6±707.3 pg/mL (RR 25-45). PTH was increased in 30% of cases, while serum alkaline phosphatase was increased in 87.5%. 24h-Urine Phosphorus (PU) was increased in only 13% of patients, but, when renal phosphate

wasting by tubular reabsorption of phosphate (TRP) was calculated, PU resulted increased in all.

Tumor was localized in all cases (Fig.1) and were localized in bone and soft tissue, by using functional imaging, followed by anatomical techniques. Before the introduction in routinely practice of ^{68}Ga -DOTATATE-PET-CT in 2013, Octreoscan-SPECT/CT and ^{18}F FDG-PET were used as imaging modalities. Since 2013, diagnostic delay consistently reduced, from 8.6 ± 8.3 yrs (7 patients) to 4.5 ± 2.6 yrs (9 patients), confirming higher diagnostic accuracy of ^{68}Ga -DOTATATE-PET-CT.

Figure 1.

13 patients underwent surgery; in two cases surgery was not possible due to tumor location, so pharmacological support with phosphate supplements and calcitriol was started; a patient underwent to TC-guided radiofrequency ablation. After surgery, 7 patients experienced a complete remission, 3 had a persistence of the disease, and 3 an overtime relapse, even after a long-standing normalization of PS (6 years). After surgical tumor removal, PS significantly increased in few days (from 1.36 ± 0.39 to 2.9 ± 1.1 , $p=0.0001$), while iFGF-23 levels tended to rapidly decreased (from 396.6 ± 707.3 to 62.8 ± 78.4). Before the introduction of ^{68}Ga -DOTATATE-PET-CT, 6 patients underwent to imaging-guided closed biopsy to confirm tumor localization; by using ^{68}Ga -DOTATATE-PET-CT only 2 subjects had closed biopsy. Furthermore, in our population only patients who had biopsy to detect the lesion (7 patients) had relapses compared to patients who did not.

Conclusion: To our knowledge, this is the widest European cohort of patients affected by TIO reported in the last two decades. We confirm an important delay between symptoms onset and diagnosis. To locate tumor, a stepwise approach is recommended, starting with a thorough medical history and physical examination, followed by functional imaging, preferring ^{68}Ga -DOTATATE-PET-CT. Tumor biopsy is not recommended due to the potential cell spilling. Surgery is considered the only definitive treatment, aiming to a wider excision. Active surveillance is always needed, due to the possible relapses, even after a long period of complete clinical and biochemical remission.

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THU0422

CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION WITHIN TOPHUS LOBULE: A FREQUENT ASSOCIATION OBSERVED IN LONG-TIME COURSE TOPHI

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Background: Calcium pyrophosphate (CPP) crystals and monosodium urate (MSU) crystals are frequently found in the same synovial fluids of gouty patients suggesting an interaction in crystal formation and deposition. This association has never been reported in tophus.

Objectives: we aimed to describe the prevalence of CPP crystal deposition in tophus and to determine the associated risk factors.

Methods: 22 tophi consecutively harvested were fixed in 4% paraformaldehyde and embedded in paraffin. 5- μm thick sections were analyzed by compensated polarized microscopy (CPM) after hematoxylin and eosin staining. Characterization of CPP crystals were performed by scan electronic microscopy (SEM) and Fourier transform infrared (FTIR) spectroscopy. Clinical characteristics were compared between patients having tophus with CPP deposition and patients having tophus without CPP crystals.

Results: All tophi appeared multi-lobulated depositions of MSU crystals separated by fibrous tissue and surrounded by a foreign giant cell reaction. CPP crystals were identified in few lobules of 5 tophi (22.7%) harvested from 3 great toes, 1 elbow bursa and 1 finger of 5 patients. CPP crystals formed aggregate deposition within the lobule of MSU crystals. Both monoclinic and triclinic CPP crystal phases were identified by CPM, SEM and FTIR. Tophi were harvested from 22 male gouty patients with a mean age of 50.8 (28-66) years and a mean BMI of 24.2kg/m² (18.9-29.4). Mean serum urate level (SUL) was $499 \pm 107 \mu\text{mol/L}$. 59% of patients had chronic renal disease stage 2 or 3, 40.9% dyslipidemia, 22.7% type 2 diabetes mellitus, 13.6% hypertension and 50% obesity. Patients with tophi containing CPP deposition were older ($61.2 [56-66]$ vs $47.8 [28-64]$ years, $p=0.009$) and had a longer gout duration ($19 [10-31]$ vs $9 [3-20]$ years, $p=0.007$) and tophus duration ($11.4 [8-16]$ vs $4.5 [1-9]$ years, $p<0.0001$) than patients with tophi alone. Tophi did not display calcification on radiographies performed before surgery. However, the density of tophi containing CPP crystal deposition was higher than the density of tophi without CPP crystals ($51 [25-100]$ vs $21.5\% [0-40]$, $p=0.009$). The proportion of bone erosion and gout arthropathy was similar between the two groups. Similarly, no difference was observed for SUL (467 ± 43 vs $509 \pm 109 \mu\text{mol/L}$), estimated glomerular filtration rate (76.6 ± 11.9 vs $74.9 \pm 15.7 \text{ ml/min/1.73m}^2$) and prevalence of comorbidities. Interestingly, no calcification was detected on knee and wrist radiographies of patients with tophi containing CPP deposition.

Conclusion: These results reported for the first time, in a small sample size, that CPP crystal deposition occurred within tophus lobules. They suggested that long-time course tophi might act as a facilitating agent of CPP nucleation. This hypothesis needs specific confirmation studies

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THU0423

ADHERENCE TO URATE-LOWERING THERAPY IN PATIENTS WITH SEVERE GOUT WHO RECEIVED CANAKINUMAB FOLLOWING A 5-YEAR RETROSPECTIVE ANALYSIS

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Background: The adherence to lowering therapy for gout is low, including in chronic severe gout. Whether interleukin 1 inhibitors may contribute to better adherence is unknown.

Objectives: To compare adherence to urate-lowering therapy in patients with severe gout who received canakinumab versus patients who received standard anti-inflammatory therapy (NSAIDs, glucocorticoids, colchicine).

Methods: Of the 513 patients with gout observed at the V.A. Nasonova Research Institute of Rheumatology, Moscow from 2013 to 2014 y 247 patients with the most severe gout, requiring regular symptomatic treatment, were selected. Of these, 25 patients (3 (12%) women and 22 (88%) men), the average age of 54.5 ± 12.7 g, received (at least 1) canakinumab injection of 150mg subcutaneously as a symptomatic therapy, the remaining 222 patients (men) mean age