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Ultrasound and MRI of the foot in children and adolescents newly diagnosed with juvenile idiopathic arthritis

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Abstract

Aim: To evaluate the spectrum of inflammatory features in foot joints which may be detected on routinely performed ultrasound (US) and magnetic resonance imaging (MRI) in children newly diagnosed with juvenile idiopathic arthritis (JIA). **Material and methods:** Two groups of children hospitalized in a reference center for rheumatology, newly diagnosed with JIA and suspected of foot involvement in the course of JIA were included in this retrospective study. In the first group of 47 patients aged 1–18 years, the imaging was restricted to US. The second group of 22 patients aged 5–18 years underwent only non-contrast MRI of the foot. **Results:** The most frequent pathologies seen on US included effusion and synovial thickening in the first metatarsophalangeal joint (MTP1), followed by the tibiotalar joint. Synovial hyperemia on color Doppler US images was present most frequently in the Chopart and midtarsal joints (64%; 7/11 cases), followed by the tibiotalar joint (45%; 5/11), and MTP2–5 joint synovitis (40%; 4/10). Grade 3 hyperemia was present only in four cases; grades 1 and 2 were detected in the majority of cases. On MRI, bone marrow edema was the most frequent pathology, found mostly in the calcaneus (45%; 10/22 cases), while alterations of the forefoot were rare. No cases of bursitis, enthesitis, cysts, erosions or ankylosis were diagnosed in either of the analyzed groups. **Conclusions**: Routine US of the foot is recommended for early detection of its involvement in JIA in daily clinical practice. Although MRI can identify features of various JIA stages, it is particularly useful for the detection of bone marrow alterations.

Introduction

Juvenile idiopathic arthritis (JIA) is the most common inflammatory arthropathy in childhood and one of the most common chronic diseases in the pediatric population, with a prevalence close to that of type I diabetes mellitus[1,2]. This heterogeneous group of idiopathic inflammatory arthritis occurs in children younger than 16 years of age, with symptoms persisting for longer than six weeks[3,4]. The disease predominantly affects the peripheral skeleton, most often the knee, followed by the wrist and hand joints, the ankle and midfoot with the metatarsophalangeal joints being less frequently involved[4]. Nevertheless, other analyses of patterns of joint involvement in JIA show that the first metatarsophalangeal joint is the most commonly affected joint in the forefoot[5].

The hallmark of the disease is joint synovitis leading to hyaline cartilage and bone damage with a complex background engaging the innate and acquired immune system and proinflammatory cytokines[6]. Lower extremity inflammatory changes in the synovium are frequently underestimated on clinical evaluation, especially in the small joints of the foot, which is why imaging examinations are beneficial in detecting subclinical disease[7,8].

Ultrasound (US) is a well-suited modality for the evaluation of inflammatory synovium in small peripheral joints[9], in periarticular locations including the bursae and tendon sheaths, as well as enthesitis[10].

Another source of joint damage develops in the subchondral bone, where a similar inflammatory process (osteitis) leads to bone destruction and erosions[11]. Magnetic resonance imaging (MRI) provides information on all tissues affected by JIA, including the subchondral bone and soft tissues. It is also superior to US in the detection of late inflammatory lesions, including erosions, inflammatory cysts, and cartilage lesions due to access to all joint surfaces[9]. In addition, it is the only modality that can detect bone marrow edema, which can be an exclusive finding in the pre-erosive stage[4], although some analyses show that the utility of MRI in predicting the occurrence of radiographic bone erosions in the metatarsophalangeal joints is low[12].

The most common pathology in JIA is synovitis, which is difficult to accurately diagnose on non-contrast MRI in the small joints, especially in the midfoot and forefoot. Precise differentiation between effusion and synovitis requires contrast administration. However due to a risk of gadolinium deposition in the brain and kidneys[13,14] contrast injection in children for the evaluation of multiple joints requires very careful consideration, especially bearing in mind the potential need for MRI evaluation of multiple joints that might be affected in the course of JIA. Therefore, in non-contrast MRI studies a common term "effusion/synovial thickening" has been introduced[15]. A similar approach was proposed for the US. According to the Outcome Measures in Rheumatology (OMERACT), an updated definition of synovitis in children encompasses synovial hypertrophy and/or effusion[16].

In our study, we aimed to evaluate the spectrum of inflammatory features in the foot seen on US and non-contrast MRI in children newly diagnosed with JIA.

Material and methods

Two groups of children hospitalized in a reference center for rheumatology, and newly diagnosed with JIA, were included in this retrospective study. All included patients were suspected of foot involvement in the course of the disease, presenting with pain at the level of the foot, tenderness, swelling and/or difficulties with walking. Retrospective analysis involved the first group of 47 patients, aged 1–18 years, in which the imaging was restricted to the US, and the second group, including 22 patients aged 5–18 years, in whom only non-contrast MRI of the foot was performed. Children with a history of trauma, tumor, previous procedures at the level of the foot and ankle, osteomyelitis, septic arthritis, and congenital foot deformations were excluded from the study.

Informed consent was obtained from the parents or legal guardians of all patients. Local institutional ethics committee approved the study in accordance with the Declaration of Helsinki, as amended (KBT-3/3/2018; KBT-3/5/2018).

US examination of the foot included all joints of the forefoot and midfoot, and the Chopart joint, ankle and subtalar joints, flexors (flexor hallucis longus, tibialis posterior, and flexor digitorum longus), extensors (extensor digitorum longus, extensor hallucis longus, tibialis anterior), and peroneal tendons (peroneus longus and brevis) along with their sheaths distally from the ankle joint, intermetatarsal, retrocalcaneal, subcutaneous calcaneal bursae, and submetatarsal adventitial bursae. The muscles, entheses, and bone contours were scanned for possible features of myositis, enthesitis, cysts, and erosions. The grey-scale mode was used to detect synovial thickening and effusion. Color Doppler US (CDUS) mode was used for hypertrophied synovium based on the three-grade scale of hyperemia proposed by the EULAR-OMERACT consensus (none = grade 0, minimal = grade 1: with up to three single Doppler spots or up to one confluent spot and two single spots or up to two confluent spots, moderate = grade 2: greater than grade 1 but <50% Doppler signals in total area and severe = grade 3: greater than grade 2 >50% of the background grey-scale)[17].

Non-contrast MRI examinations were performed on a 1.5 Tesla scanner (Siemens Avanto) in a dedicated 8 channels coil. The examination was performed according to the standard protocol in three planes: axial, sagittal, and coronal, and detailed MRI acquisitions are listed in Tab. 1. Patients were in supine position and no sedation was used. The field of view ranged from the tibiotalar joint to the distal phalanges. The following joints of the hindfoot, midfoot, and forefoot were evaluated: subtalar, talonavicular, calcaneocuboid, naviculocuneiform, tarsometatarsal, MTP joints, proximal interphalangeal joints, distal interphalangeal joints, and interphalangeal joint of the big toe. Examined tendons included the flexors (flexor hallucis longus, tibialis posterior, and flexor digitorum longus), the extensors

Tab. 1. MRI acquisitions for non-contrast foot MRI examination

Sequence	Plane	TR (ms)	TE (ms)	ST (mm)	Gap (mm)	FOV (mm)	Matrix (mm)
Localizer	All planes	6.9	2.99	3	6	300	205 × 256
T1w	Cor	615	11	3	0.9	150 × 150	240 × 320
T1w FS	Cor	654	11	3	0.9	150 × 150	192 × 256
T2w TIRM	Cor	4690	35	3	0.9	150 × 150	256 × 256
T2w TIRM	Tra	4430	30	3	0.6	290 × 290	154 × 320
PDw FS	Tra	2800	30	3	0.6	280 × 280	224 × 448
PDw	Tra	2800	30	3	0.6	280 × 280	224 × 448
T2w	Tra	3900	83	3	0.6	280 × 280	304 × 512
T1w FS	Tra	590	11	3	0.6	280 × 280	199 × 384
PDw	Sag	2370	30	3	0.6	280 × 280	224 × 448
PDw FS	Sag	3210	30	3	0.6	280 × 280	214 × 384
T1w FS	Sag	654	10	3	0.6	280 × 280	126 × 256

Cor – coronal; FOV – field of view; FS – fat saturation; Sag – sagittal; ST – slice thickness, TE – echo time; TR – repetition time; Tra – transverse; w – weighted

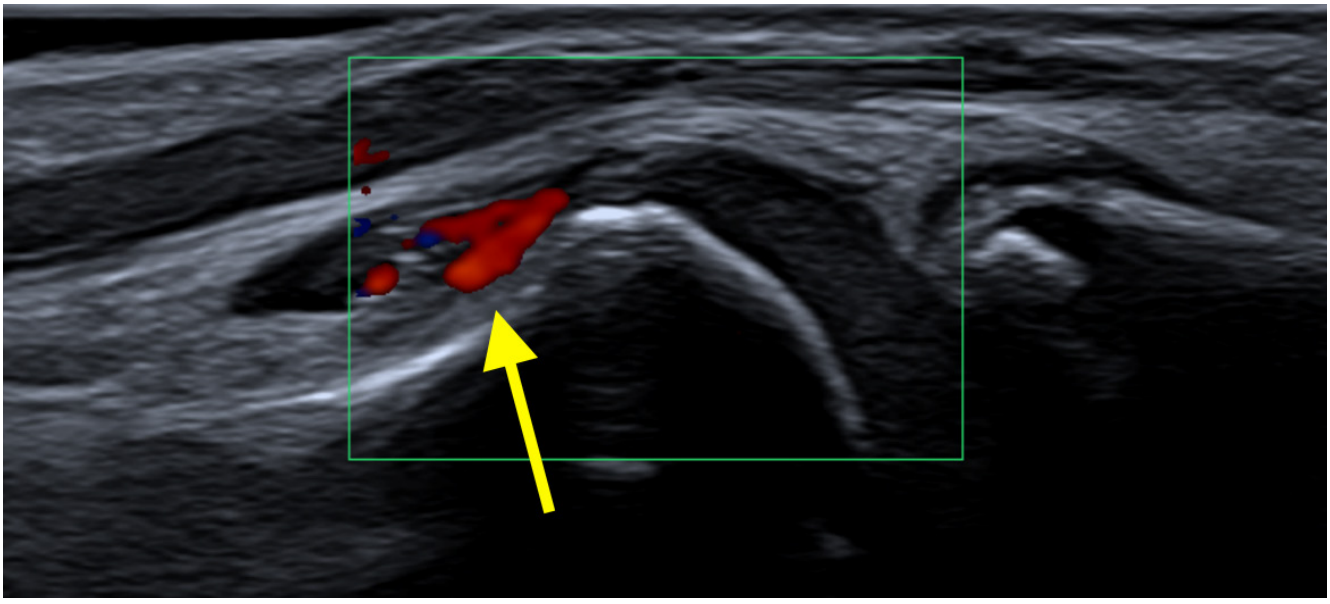

Fig. 1. *US of the MTP1 joint in longitudinal view in a patient diagnosed with JIA, presenting with thickened synovium with hyperemia on color Doppler in grade 2 (arrow)*

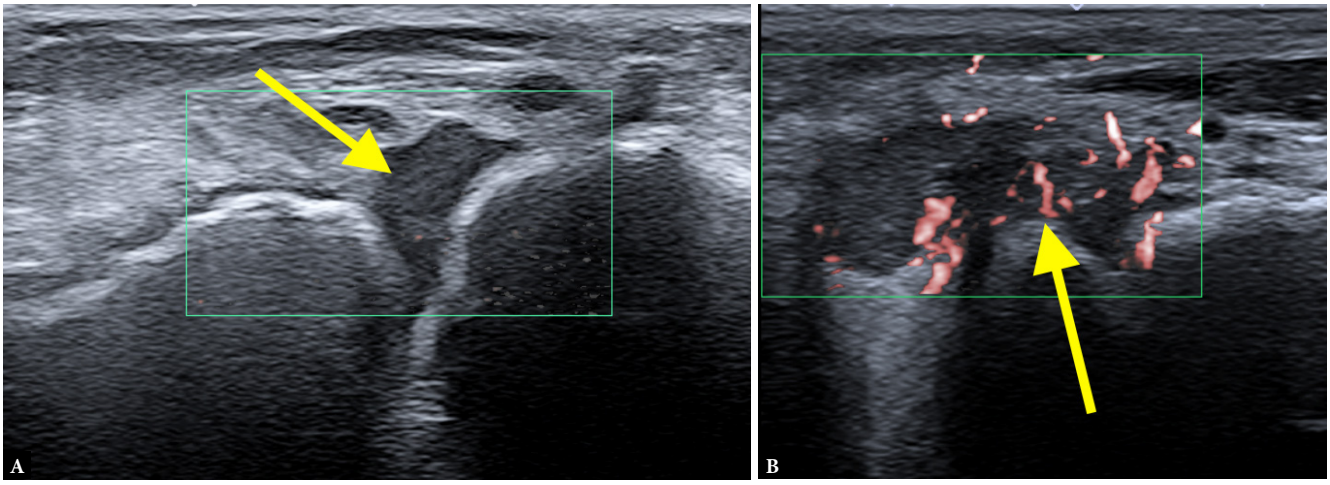

Fig. 2. *US of the Chopart joint in a patient with JIA.* **A.** *Effusion and hypertrophied synovium in gray scale is shown dorsally in the talonavicular part of the Chopart joint. Note that both effusion and hypertrophied synovium may have hypoechoic appearance, and the ultrasound probe pressure maneuver may be helpful in discriminating both entities as fluid will be displaceable and compressible.* **B.** *Grade 2 vascularization is seen in microflow option in the talonavicular part medially*

(extensor digitorum longus, extensor hallucis longus, tibialis anterior), and the peroneal tendons (peroneus longus and brevis). The report also included bone marrow edema in the bones of the foot, and the presence of distended bursae (intermetatarsal, retrocalcaneal, subcutaneous calcaneal, adventitial submetatarsal), myositis, enthesitis, cysts, erosions, joint space narrowing (JSN), ankylosis, osteophytes, and developmental disorders[4].

Results

The first group, in which only US was performed, included 47 children, 29 female and 18 male, aged 1–18 years. A total of 22 patients were diagnosed with oligoarthritis, 11 with polyarthritis, one with systemic, 11 with undifferentiated and two with seronegative subtypes of JIA.

The first metatarsophalangeal joint (MTP1) was the most frequently affected one, with effusion observed in 23/47 cases (49%) and hypertrophied synovium in 23/47 cases (49%) (Fig. 1). In only 17% of cases (4/23 patients of detected thickened synovium in MTP1) synovial vascularization was seen in CDUS images in grade 1 and grade 2. Synovial hyperemia was present most frequently in the Chopart and in midtarsal joints (7/11cases; 64%) in grades 1–3 (Fig. 2). The second most common abnormality was effusion in the tibiotalar joint, found in 16/47 cases (34%), with synovial hypertrophy at this level noted in 11 cases (23%) and detectable vascularization in 5/11 cases (45%) in grades 1–3. In the toes, the most commonly affected joint was the interphalangeal joint of the big toe (IP) (Fig. 3). Tenosynovitis was found in 10/47 cases (21%), mostly affecting the flexor tendons (Fig. 4). Periarticular dorsal edema of the subcutaneous tissue was found in three cases. Destructive lesions including cysts and erosions were not detected by US, and neither

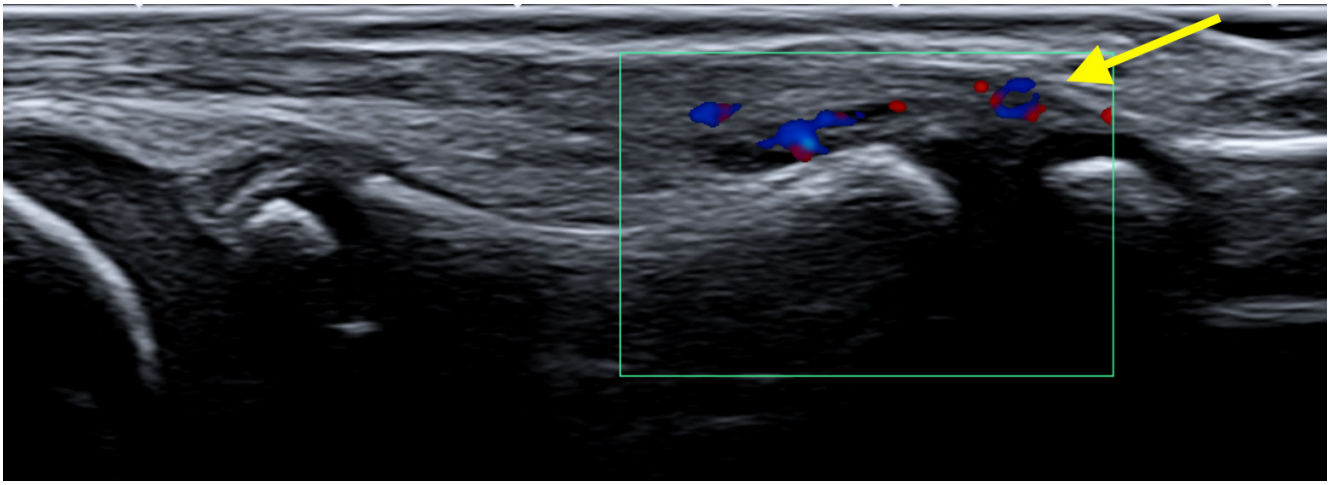

Fig. 3. *US of the interphalangeal joint of the big toe (IP) in longitudinal view in a patient diagnosed with JIA, presenting with thickened synovium with grade 2 hyperemia on color Doppler (arrow)*

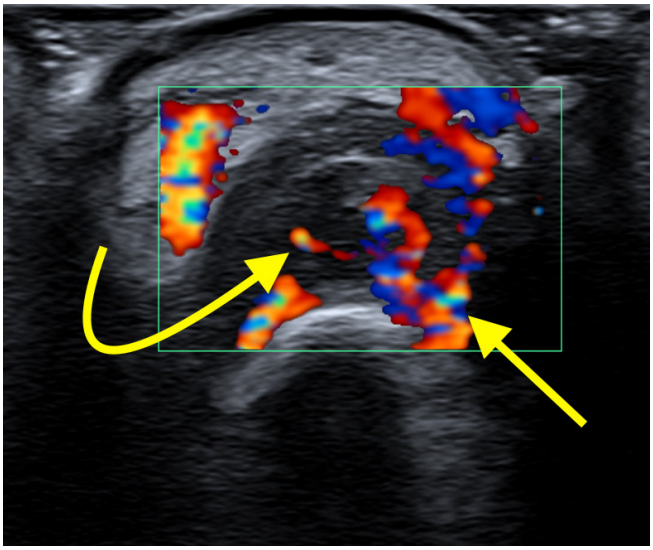

Fig. 4. *Short axis US of the flexor tendon at the level of the third toe in a patient diagnosed with JIA presenting with tendinopathy of the flexor tendon. On color Doppler, there is severe vascularization within the thickened tendon sheath (arrow) and inside the flexor tendon (curved arrow)*

were bursitis, enthesitis, and myositis. All pathologies identified on foot US are listed in Tab. 2.

The second group, in which only non-contrast MRI of the foot was performed, included 22 children diagnosed with JIA, 10 female and 12 male, aged 5–18 years. Seven patients were diagnosed with oligoarthritis, two patients with ERA, and 13 with the undifferentiated form. Bone marrow edema was the most common pathology and was most frequently located in the calcaneus (10/22, 45% cases), followed by the talus, navicular and cuboid (9/22, 41%) (Fig. 5). Among all patients examined by MRI in 4/22 cases (18%) bone marrow edema was the only pathology detected in the foot. Ankle region included in imaging FOV was still the most frequent location for effusion (10/22, 45% cases). Joint effusion was only found in three cases in the Chopart joint (13%). Periarticular soft tissues involvement in MRI of the foot was seen in isolated cases, including enthesitis (one case) and tenosynovitis (one case) detected only in the flexor hallucis longus tendon sheath. Detailed data on pathologies detected on non-contrast foot MRI are listed in Tab. 3.

Tab. 2. Pathologies reported on foot ultrasound examination in children diagnosed with JIA. According to three-grade scale of color Doppler hyperemia proposed by the EULAR-OMERACT consensus (no hyperemia = grade 0, minimal = grade 1: with up to three single Doppler spots or up to one confluent spot and two single spots or up to two confluent spots, moderate = grade 2: greater than grade 1 but <50% Doppler signals in total area and severe = grade 3: greater than grade 2 >50% of the background grey scale)[17]

Location	Effusion	Synovial hypertrophy
Chopart /midtarsal joint	9/47 (19%)	11/47 (23%) (color Doppler hyperemia: grade 1: 1 grade 2: 3 grade 3: 3 no hyperemia: 4)
First metatarsophalangeal joint (MTP1)	23/47 (49%)	23 /47 (49%) (color Doppler hyperemia: grade 1: 1 grade 2: 3 grade 3: 0 no hyperemia: 19)
Metatarsophalangeal joints 2–5 (MTP2–5)	8/47 (17%)	10/47 (21%) (color Doppler hyperemia: grade 1: 3 grade 2: 1 grade 3: 0 no hyperemia: 6)
Interphalangeal joint of the big toe (aIP)	11/47 (23%)	8/47 (17%) (no color Doppler hyperemia)
Proximal interphalangeal joints (aPiP)	4/47 (8.5%)	4/47 (8.5%) (no color Doppler hyperemia)
Tibiotalar joint	16/47 (34%)	11 /47 (23%) (color Doppler hyperemia: grade 1 : 1 grade 2 : 3 grade 3 : 1 no hyperemia: 6)
Other pathologies: tenosynovitis flexors: 10/47 (21%); tenosynovitis peroneal: 3/47 (6%); tenosynovitis extensors: 2/47 (4%); dorsal edema subcutaneous tissue: 3/47 (6%)		

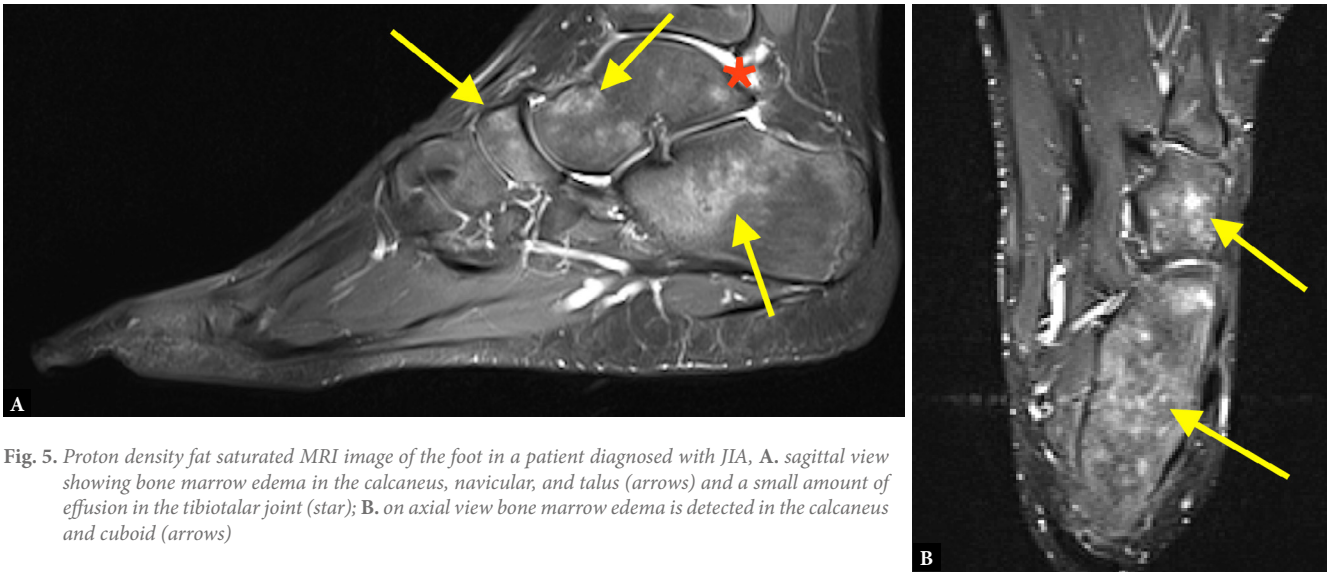

Fig. 5. *Proton density fat saturated MRI image of the foot in a patient diagnosed with JIA,* **A.** *sagittal view showing bone marrow edema in the calcaneus, navicular, and talus (arrows) and a small amount of effusion in the tibiotalar joint (star);* **B.** *on axial view bone marrow edema is detected in the calcaneus and cuboid (arrows)*

Tab. 3. Pathologies detected on non-contrast MRI of the foot in children diagnosed with JIA

Location	Pathology	Number
Subtalar joint	effusion	10/22 (45%)
aIP	effusion	1/22 (4.5%)
Second metatarsophalangeal joint (aMTP2)	effusion	1/22 (4.5%)
Chopart /midtarsal joint	effusion	3/22 (14%)
Talus	BME	9/22 (41%)
Calcaneus	BME	10/22 (45%)
Navicular	BME	9/22 (41%)
Cuboid	BME	9/22 (41%)
Cuneiform intermediate	BME	6/22 (27%)
Cuneiform lateral	BME	7/22 (32%)
Cuneiform medial	BME	6/22 (27%)
1. Metatarsal bone	BME	3/22 (14%)
2. Metatarsal bone	BME	1/22 (4.5%)
3. Metatarsal bone	BME	1/22(4.5%)
4. Metatarsal bone	BME	2/22 (9%)
5. Metatarsal bone	BME	3/22 (14%)
	enthesitis tenosynovitis FHL sclerotization Kager's fat pad	1/22 (4.5%) 1/22 (4.5%) 1/22 (4.5%) 1/22 (4.5%)
	bursitis, myositis, cyst, erosions, chondromalacia, JSN, ankylosis, osteophytes, developmental disorders	0/22
Tibiotalar joint	effusion	14/22 (67%)

Discussion

The most frequent foot pathology detected on US in children diagnosed with JIA was MTP1 joint effusion and synovial hypertrophy (49% cases). The most common soft tissue alteration seen on US was flexor tenosynovitis. Late complications of JIA including destructive bone lesions in our group of newly diagnosed disease were absent, which is consistent with the previous literature data[18].

In foot MRI, bone marrow edema was the most common pathology and was located mostly in the hindfoot, followed by the midfoot. It was recognized as a sole pathology in 18% of patients. Forefoot – bones and joints of the toes tend to be less frequently affected, which was also confirmed in our study[19,20]. This has to be differentiated from the normal foci of high signal in fluid sensitive sequences in the tarsal bones ("starry sky appearance") frequently found in children up to 15 years old, which can mimic true bone marrow edema[21,22].

Tarsal involvement is characteristic for the initial stages of JIA and may be recognized in up to 1/3 of cases[23,24]. Our results are in conformance with these findings. Talus, navicular and cuboid were affected in in 40% (nine cases), lateral cuneiform in 32% (seven cases), medial and intermediate cuneiform in 27% (six cases). Although post-inflammatory ankylosis in JIA is mostly located at the tarsal level, our group did not show this pathology. Our study included newly diagnosed group of children, while tarsal ankylosis may occur after three to five years from the onset of the disease[18].

Only isolated cases of soft tissue alterations were found on MRI, including enthesitis and flexor hallucis longus tenosynovitis.

Features of inflammation at the level of the forefoot were mostly found on US and rarely on non-contrast MRI. Small peripheral joints of the foot are easily accessible for US, and several previous studies have shown its predominance over clinical assessment[8,25]. The rare involvement of the forefoot on MRI may be the result of the limited spatial resolution of the MRI images for this region. The use of high-resolution probes, both grey-scale and Doppler modes including CDUS and power Doppler US (PDUS), enables good visualization of detailed anatomy and detection of even subclinical synovitis[26]. Consequently, it is widely employed in ambulatory care for real-time imaging of multiple joints[27] and for guidance in corticosteroid injections[8,28]. Recent innovations – including ultra-high frequency ultrasonography (UHFUS) and microflow US assessment – are promising tools for visualization improvement in small struc-

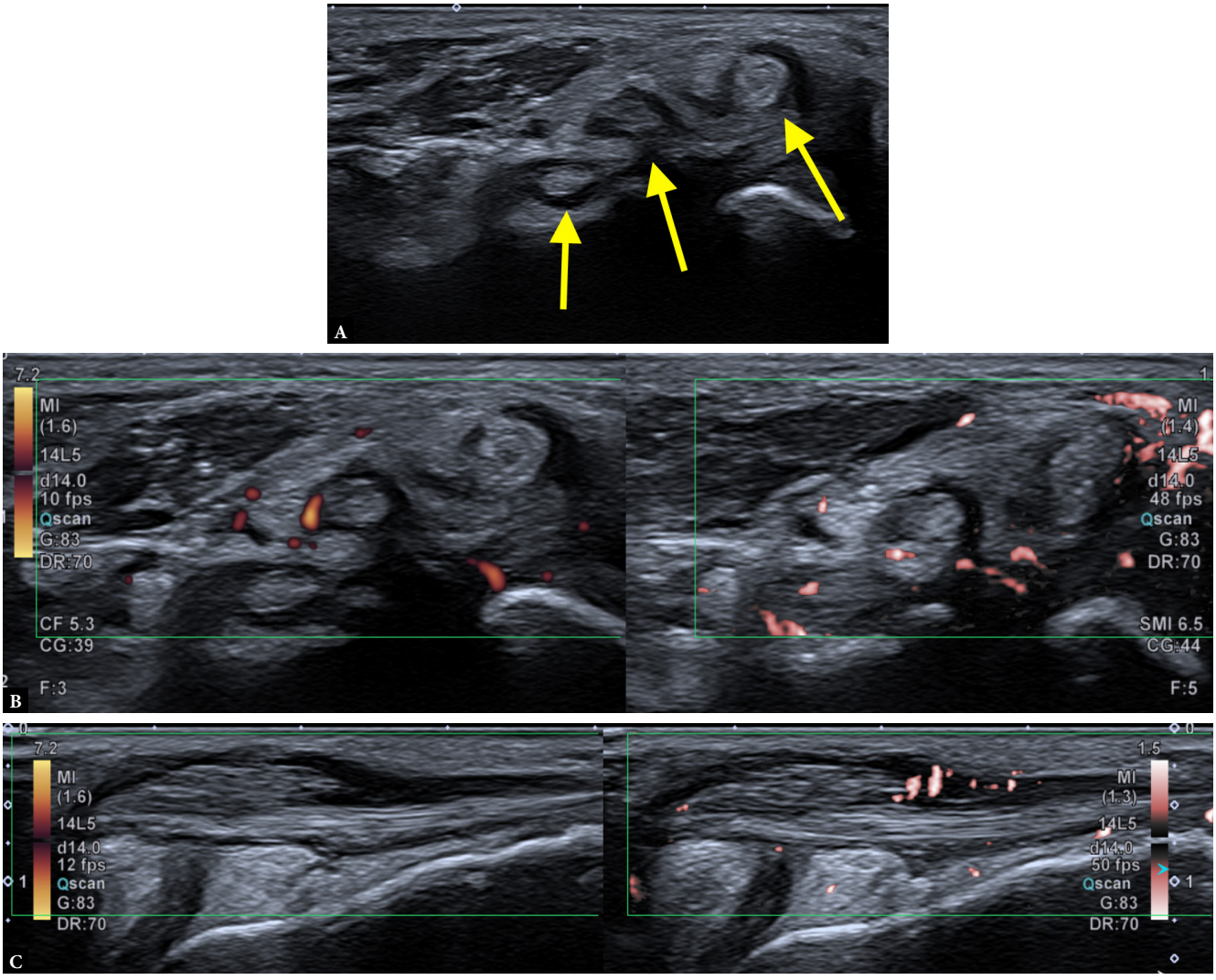

Fig. 6. *Tenosynovitis of the tibias posterior, flexor hallucis longus, and flexor digitorum longus in patient with JIA.* **A.** *Gray-scale US in axial view at the level of the tibiotalar joint presenting with thickened tendon sheaths (arrows);* **B.** *vascularization is detected in the microflow SMI mode (right image) with only subtle hyperemia seen on power Doppler (left image);* **C.** *US of the peroneus longus tendon of the same patient in longitudinal view showing markedly thickened synovium within the tendon sheath with no hyperemia on power Doppler (left image) and detected vascularization in the microflow mode on the same level (right image)*

tures and low-flow velocity vessels. Microvascular imaging is more sensitive than the widely available CDUS and PDUS[29] (Fig. 6).

On US grey scale mode synovitis presents as synovial thickening (hypertrophy), which is a nondisplaceable hypoechoic tissue located within the joint, which may show vascularity depending on its activity. In our study, synovitis was indeed the most frequent pathology, however a thickened synovium mostly did not present detectable vascularization except the Chopart joint, where seven of 11 cases presented different grades of hyperemia (grade 3 in three cases, grade 2 in three cases, and grade 1 in 1 case). Low prevalence of active synovitis could be due to the short duration of the disease.
Joint effusion was found at various levels on US and MRI. Previous studies showed that diverse amount of fluid could be found on the ankle and midfoot MRI in healthy volunteers[30]. Therefore, interpretation of imaging findings should always be done in the context of the patient's clinical picture.

Although MRI is the preferred modality for the diagnosis of foot involvement, it has some limitations which are particularly important in children, including the need for sedation of very young patients and contrast administration to visualize synovitis with high specificity[25]. In our study, children under the age of four had only US, and no MRI with sedation was performed. A limitation of the study is the lack of intravenous contrast administration in MRI. This reflects our practice that contrast MRI should be carefully considered in children frequently presenting with oligo- or polyarthritis, and it is recommended especially in patients with atypical clinical presentation, for the differential diagnosis, in inconclusive US, chronic disease and evaluation of the success of therapy[31]. MRI of the forefoot remains challenging due to volume-averaging artifacts. The principal advantage of MRI is bone marrow edema detection, which may be the only alteration in children with JIA (18% cases in our study group). It is also useful for the evaluation of insufficiency fractures, as JIA children are at a higher risk due to low bone mass and di-

minished bone strength[32] Furthermore, MRI may be beneficial in nonspecific foot and ankle complaints (including avascular necrosis, impingement syndromes, bone coalitions, anatomical variants, and trauma). Although the number of patients examined by MRI in our study was relatively small, more and more clinicians choose this modality nowadays for comprehensive foot evaluation. A broad list of entities from differential diagnosis and coexisting abnormalities may be evaluated by MRI, with particular usefulness in children presenting with unspecific, not precisely located foot complaints.

Conclusions

Routine ultrasound of the peripheral joints and periarticular soft tissues of the foot is widely recommended for early detection of foot involvement in patients with JIA in daily clinical practice. In clinically suspected cases, patients should undergo MRI examination to identify features of early disease, in particular bone marrow edema, which can be the only pathology detected and may determine further patient outcome.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: MP, MO, EM, PG, MM, ISS. Writing of manuscript: MP, MLanc, MLesz, ISS. Analysis and interpretation of data: MP, MO, ISS. Final approval of manuscript: MP, MO, EM, PG, MM, MLanc, MLesz, ISS. Collection, recording and/or compilation of data: MP, MO, EM, ISS. Critical review of manuscript: MP, MO, EM, PG, MM, MLanc, MLesz, ISS.

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