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Management of acute-stage chikungunya disease: Contribution of ultrasonographic joint examination

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ABSTRACT

Objective: Chikungunya (CHIKV) is an arbovirus that causes acute, debilitating polyarthritis. Its diagnosis can be difficult for clinicians not used to managing joint diseases or detecting synovitis. Joint Doppler ultrasonography (DUS) is a simple, non-invasive examination, able to visualize synovitis. Its diagnostic and prognostic value in rheumatoid arthritis is well-established.
Methods: Patients with serologically proven acute arbovirosis where included. Clinical examination and joint count were performed (DAS score). Ultrasound examination was performed by another clinician — experienced in joint DUS — who also performed ultrasound joint score. Joints were examined by DUS in B-mode looking for: subcutaneous infiltration, effusion, tenosynovitis, erosion and Doppler signal.
Results: In our experience, joint DUS is able to detect effusions in 92.8% of painful joints, with 28.3% of the effusions emitting a high-power Doppler signal. No erosion was observed. Subcutaneous inflammatory infiltration of the ankles (aseptic cellulitis) was found in 28.6% of patients.
Conclusion: Joint DUS is able to detect objective signs responsible for joint pain, which can be useful for practitioners not accustomed to this type of pathology. It also makes possible distinction between articular and periarticular manifestations.

Introduction

Management of chikungunya virus (CHIKV)-related rheumatic disease is complex, as previously reported during the Caribbean outbreak from December 2013 to January 2015 (Marks and Marks, 2016; Blettery et al., 2016). French recommendations (Simon et al., 2015) help clinicians in daily practice, because careful recording of patients' medical histories and serological verification prevent errors inherent to the epidemic context and ensure early therapeutic intervention for these patients. But those recommendations do not include early examination with joint Doppler ultrasonography (DUS).

Although the contribution of joint DUS to early rheumatoid arthritis diagnosis has been shown (Xiao et al., 2014), joint imaging studies on CHIKV-infected subjects are rare, except (Manimunda et al., 2010; Moga et al., 2018; Canella, 2017; Mogami et al., 2017). Joint DUS can confirm the presence of joint effusion, bone edema, synovial thickening, tenosynovitis and erosions in patients with persistent pain >1 month after the acute phase, but no ultrasound data are available for the early stage of the CHIKV disease. During chikungunya there are only ultrasound analyses in secondary and tertiary forms (Manimunda et al., 2010; Moga et al., 2018; Canella, 2017; Mogami et al., 2017).

Joint DUS can be a useful tool for clinicians who are not very familiar with joint diseases or not used to detecting synovitis, can help to make a better clinical evaluation of the articular symptoms, could help to differentiate with other arboviruses, and may predict the late articular evolution of the disease.

By analogy with rheumatoid arthritis, we hypothesized that DUS could be relevant to the evaluation of CHIKV-disease joint and periarticular manifestations. The Echochick Study was part of the work launched by the University Hospital of Martinique (CHUM) at the beginning of the Chikungunya epidemic in 2014. The aim of this preliminary study was to determine whether joint DUS imaging was of clinical interest at the very early phase of CHIKV disease, to confirm the presence or not of arthritis, to help in the positive diagnosis of acute arthritis of Chikungunya and to help in the differential diagnosis with other arboviroses capable of causing joint pain.

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Methods

Patients (>18 years old) consulting at the CHUM in the "crisis unit" organized at the beginning of the epidemic in Martinique for acute arthralgias and/or arthritis of <10 days duration and possibly related to CHIKV infection were included. Acute CHIKV infection was confirmed serologically or by polymerase chain reaction (PCR) (PCR between days 1 and 5, PCR and serology between days 5 and 7, and serology alone after day 7). Exclusion criteria were: history of chronic inflammatory rheumatic disease, oral intake of nonsteroidal anti-inflammatory drugs or corticosteroids, lack of demonstration of acute CHIKV infection.

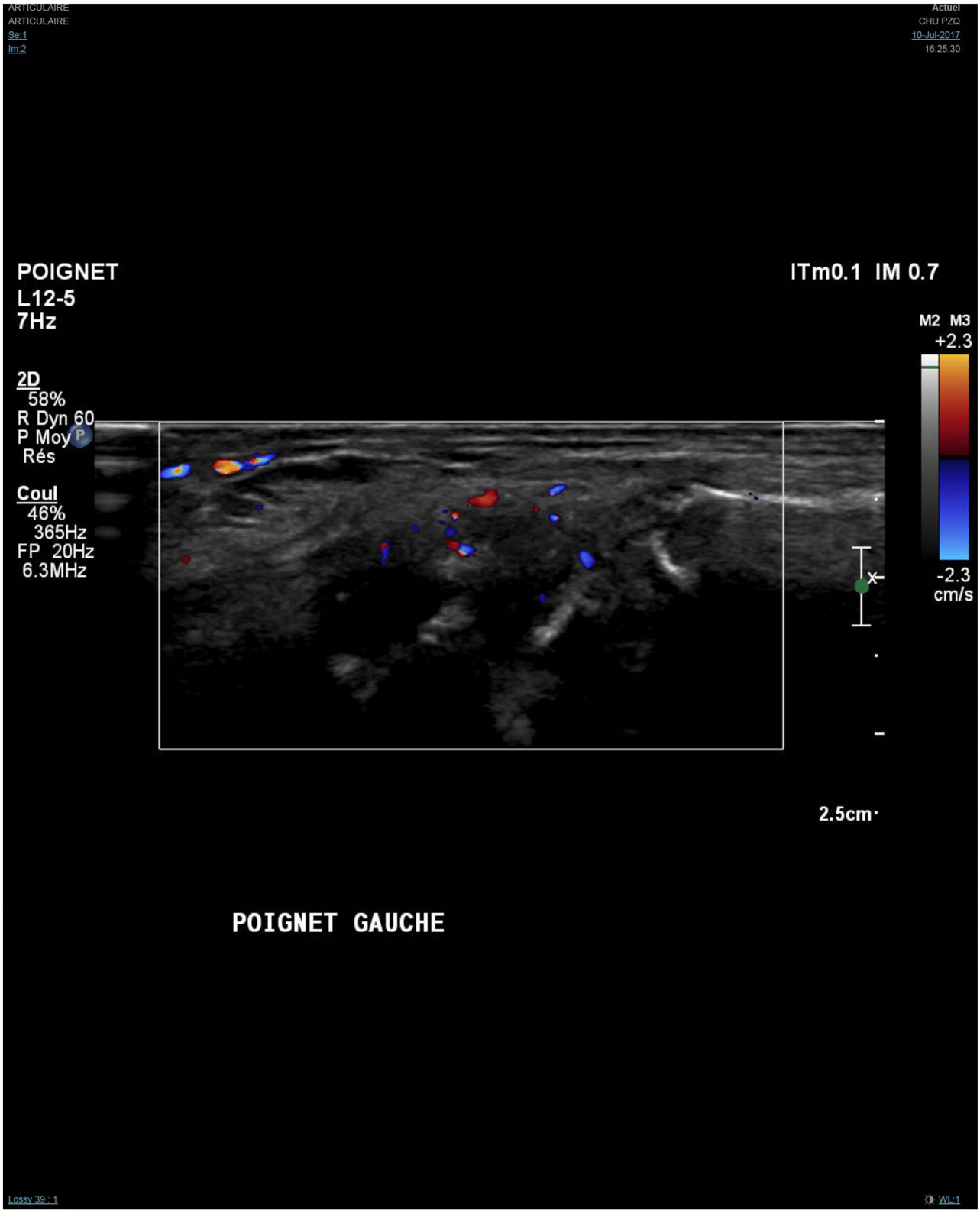

Figure 1. Doppler ultrasound examination of a left wrist. Presence of synovitis, with effusion and positive Doppler effect (grade 2, Szkudlarek' classification).

Demographic data and physical examination findings were recorded. The joint count (according to DAS 28) was performed by the clinician who managed the patient using the same management method as in rheumatoid arthritis.

Ultrasound examination was then performed by another clinician who also performed an ultrasound joint score. Joint imaging was performed by a senior rheumatologist experienced in joint DUS (LB). Hands, wrists, feet and ankles were systematically examined, for the other joints, the 3 most painful and/or swollen joints were examined and if abnormal findings were observed, the contralateral joint was systematically examined. Joints were examined by DUS in B-mode looking for 5 items: subcutaneous infiltration, effusion, tenosynovitis, erosion and Doppler signal.

Ethics statements

The study was approved by a regional French Ethic Committee ("Comité de Protection des Personnes, Sud-Ouest et Outremer III" ; CCP number : 2014/50, ref : 2014-A00875-42). Written informed consent was obtained from all patients. No child was included in the study. All patients were adults.

Results

Twenty-eight patients with documented acute CHIKV infection were enrolled: 19 women and 9 men, mean age 50.7 ± 6 years, and we also examined 3 patients with acute dengue fever (2 women, mean age 47 ± 3). The mean duration of the disease at inclusion was 5 ± 1 days after clinical onset of manifestations. Acute Chikungunya was defined by a positive Blood PCR or presence of IgM antibodies alone and the lack of positivity for dengue and zika reactions. Acute dengue infection was diagnosed with negative test for Chikungunya or Zika and positive RT PCR for Dengue or positive IgM antibodies.

For patients with Chikungunya, the average joint count performed by the clinician was 8 ± 4 painful joints and 4.1 ± 3 swollen joints. The ultrasound joint score was identical for the number of painful joints but higher for the number of swollen joints (7.5 ± 2, p 0.02). For patients with dengue fever, the average number of painful joints was 3, none was swollen either clinically or by DUS examination.

In CHIKV patients, doppler ultrasonography of painful joints revealed: effusions in 92.8% of examined joints (75% of hands and wrists, 50% of ankles, and 35.7% of knees were involved, but shoulders and elbows were rarely affected). The majority (75.5%) of effusions detected were unilateral (Figures 1 and 2). We also noted that not all painful joints are synovitis or effusion sites. A high-power Doppler signal (grade 2 or 3, Szkudlarek classification) was emitted by 28.3% of the effusions. Only 2 patients, one with unilateral and the other bilateral involvement, had detectable tenosynovitis, this is quite opposite to what is observed in the chronic phase of chikungunya (Canella, 2017; Mogami et al., 2017).

No erosion was observed. Subcutaneous inflammatory infiltration (cellulitis) was seen in 13/56 (23.2%) ankles and 8/28 (28.6%) of the patients: unilateral in 3 of them and bilateral in 5 (Table 1).

The typical ultrasonographic pattern observed in acute CHIKV disease was subcutaneous ankle infiltration with asymmetric arthritis and a positive Doppler signal in one-third of the patients.

During the study period 3 patients with acute dengue fever were examined by ultrasound and none showed ultrasound joint effusion.

Discussion

The interest of joint ultrasound in the chronic phases of Chikungunya has been demonstrated in several studies (Moga et al., 2018; Canella, 2017; Mogami et al., 2017), allowing an exhaustive joint, periarticular and tendon assessment. No studies

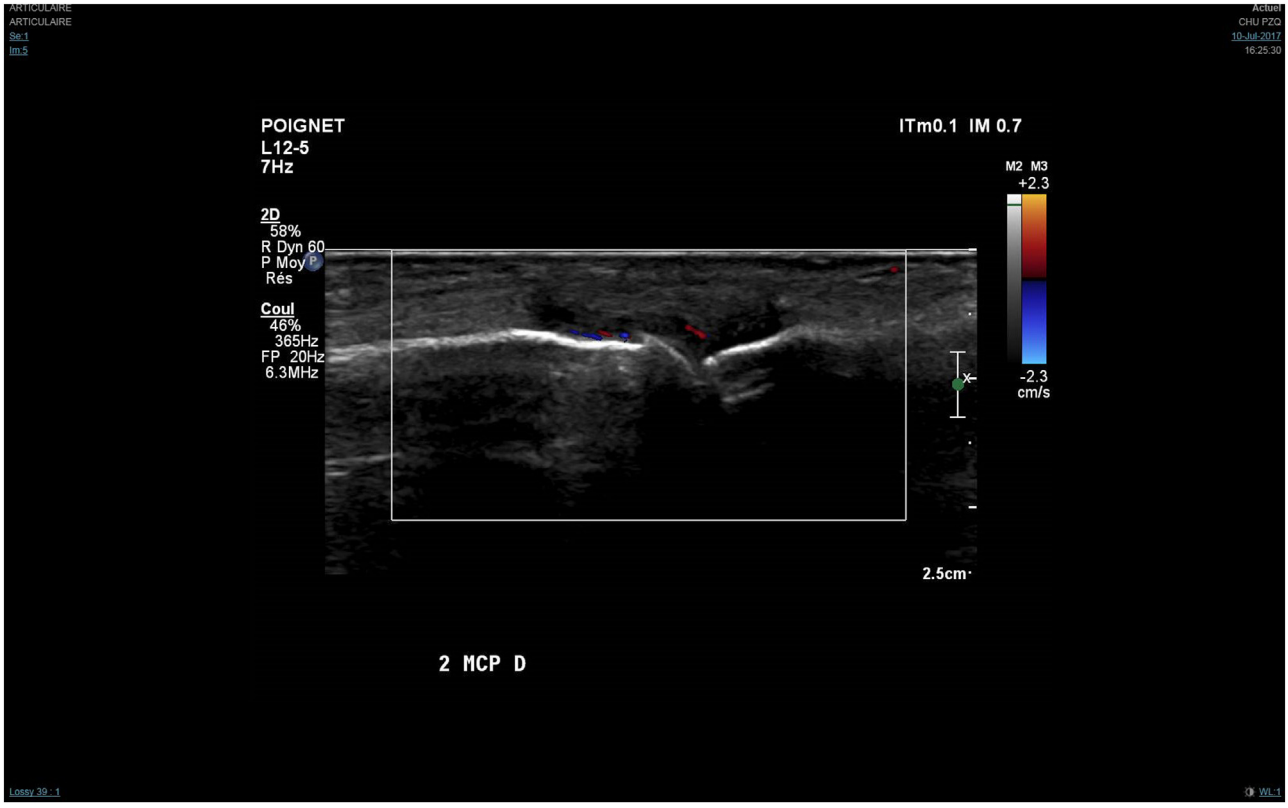

Figure 2. Doppler ultrasound examination of a second MCP. Presence of synovitis, with effusion and positive Doppler effect (grade 1, Szkudlarek' classification).

Table 1
Joint and periarticular Doppler ultrasonography (DUS) findings in 28 patients during the acute phase of Chikungunya disease.

Joint	Subcutaneous infiltration		Effusion				Tenosynovitis			
	Unilateral	Bilateral	Unilateral		Bilateral		Unilateral		Bilateral	
			No DUS	DUS	No DUS	DUS	No DUS	DUS	No DUS	DUS
Shoulder	0	0	0	0	0	0	0	0	0	0
Elbow	0	0	0	1	0	0	0	0	0	0
Wrist	0	0	4	3	3	1	0	1	0	0
Hands (MCP, PIP, DIP)	0	0	6	2	0	2	0	0	0	0
Hip	0	0	2	0	0	0	0	0	0	0
Knee	0	0	7	0	3	0	0	0	0	0
Ankle	3	5	6	4	4	0	0	0	2	0
Foot (MTP)	1	0	3	2	0	0	0	0	0	0

Abbreviations: No DUS, no Doppler effect, hence less aggressive involvement; MCP, metacarpophalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal; MTP, metatarsophalangeal.
Values are the numbers of joints affected.

had looked at this exploratory technique in the acute phase of infection.

However this kind of work is difficult to perform outside an epidemic phase, as it has also been difficult to analyze patients with another arboviroses over the same period. All patients were referred in the acute phase of their condition for suspected arboviroses, which was confirmed in all cases.

Clearly the ultrasound examination makes the diagnosis more often than the clinician and detects more manifestations than the clinician (who was a rheumatologist trained in clinical joint analysis).

In our experience, joint DUS enables detection of objective signs explaining joint pain, which can be useful for practitioners not accustomed to dealing with this type of pathology in an epidemic context or otherwise. It also makes possible distinction between joint and periarticular pathologies.

Despite the very small number of dengue patients in this study it seems that joint ultrasound could also differentiate early between Dengue and Chikungunya, but this must be confirmed on a large scale.

Acute “aseptic ankle cellulitis” is an uncommon clinical sign, usually observed in sarcoidosis (Fernandez-Faith and McDonnell, 2007). The presence of (ultrasonographic or clinical) ankle cellulitis, identical to that seen in acute forms of sarcoidosis, has not been described previously in chikungunya disease and could be a useful sign to diagnose it.

In this study too many patients were lost to follow-up and it was not possible to establish a correlation between the initial joint manifestations and the possible evolution to a chronic form. Long-term follow-up of these patients in future prospective studies will reveal whether the early presence of numerous marked synovitises (with Doppler effect) corresponds to a chronic course and, therefore, justifies early therapeutic intervention.

This preliminary study of ultrasound in the acute phase of an arbovirosis brings elements in favour of the generalization of this approach.

Ethics statements

The study was approved by a regional French Ethic Committee (“Comité de Protection des Personnes, Sud-Ouest et Outremer III” ; CCP number : 2014/50, ref : 2014-A00875-42). Written informed consent was obtained from all patients. No child was included in the study. All patients were adult.

Conflict of interest statement

None of the authors has any financial and/or personal relationships with other people or organisations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

Nothing to disclose for any author.

No conflict of interest.

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