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Musculoskeletal Conditions Complicating Stroke Rehabilitation: a Clinical and Ultrasound Study

Paolo Falsetti, Caterina Acciai, Francesco Carpinteri, Barbara Gallai, Rosanna Palilla, Lucia Lenzi.

Neurorehabilitation Unit, Department of Rehabilitation, Local Health Unit 8,

S. Donato Hospital, Arezzo, Tuscany, Italy

Correspondence to:

Dr Paolo Falsetti, e-mail: paolo.falsetti@virgilio.it

Neurorehabilitation Unit, Department of Rehabilitation, Local Health Unit (AUSL) 8,

S. Donato Hospital, via P. Nenni, 52100 Arezzo,

Italy

Fax: +39 (0)575 254520 Tel. +39 (0)575 254521

Running title: Musculoskeletal complications following stroke

ABSTRACT

Objective: the aims of this study were to evaluate incidence and clinical predictors of musculoskeletal complications in patients with stroke in a neurorehabilitation setting, and to describe its clinical and ultrasound (US) features, and its impact on functional recovery.

Methods: in all, 130 consecutive patients admitted in tertiary-level neurorehabilitation unit with diagnosis of ischemic or hemorrhagic stroke, were enrolled. All the patients with symptoms or signs of musculoskeletal pathology, underwent bedside musculoskeletal US.

Results: musculoskeletal pathologies were diagnosed in 66/130 (51%), more frequently in females (p=0.005). In 88% US clarified diagnosis and/or modified therapeutic approach. Shoulder pain was observed in 40/130 (31%). US showed a shoulder subluxation in 82% and a frozen shoulder in 5% of painful shoulders. In all the cases of painful shoulder rotator cuff abnormalities was noted.

Wrist-hand syndrome was observed in 25/130 (19%). US showed mild effusion in wrist joints and tendon sheaths and subcutaneous edema without significant vascularity.

Neurogenic heterotopic ossification were observed in 2/130 (1,5%). US demonstrated the “zone phenomenon” or heterogeneously hypoechoic mass with low resistance vessels within the lesions.

Contractures and spasticity were observed in 27/130 (21%). Relapsing osteoarthritis and acute arthritis were diagnosed in 23/130 (18%) and 10/130 (8%) respectively.

Cortical stroke of nondominant side was associated with musculoskeletal complications (p=0.0249) while posterior circulation stroke showed a reduced incidence of musculoskeletal complications (p=0.0002). Musculoskeletal complications were significantly associated to hemispatial neglect (p=0.018) and depression (p=0.0004).

Significant increase of erythrocyte sedimentation rate (p=0.0008) and lower hemoglobine concentrations (p=0.01) were noted in patients with musculoskeletal complications.

Patients with musculoskeletal complications had lower Katz index scores in discharge (p<0.0026) and more length of hospital stay (p=0.0008).

Conclusion: Musculoskeletal pathologies complicate the course of stroke in about half of patients admitted to rehabilitation, and they delay functional recovery. Patients with cortical stroke of nondominant side and hemispatial neglect are more prone to develop musculoskeletal complications. Bedside US is a cheap and sensitive diagnostic tool and it can aid clinicians to define diagnosis and to choose therapeutic approach.

Keywords: stroke, complications, musculoskeletal pathology, pain, ultrasound.

Introduction

Most of cerebrovascular injuries, can result in secondary musculoskeletal complications that delay functional recovery and affect overall outcome [1-6]. Shoulder pain, shoulder-hand syndrome (SHS), wrist-hand syndrome, neurogenic heterotopic ossifications (NHO), contractures and spasticity are the most common musculoskeletal conditions described in hemiplegia due to stroke [2-7]. These secondary complications can develop at any stage after the onset of a stroke, and the rapidity of clinicians to recognize and treat these complications will improve patient functioning. Diagnostic radiographic and laboratory findings may not be helpful in early diagnosis, and three-phase 99m Technetium bone scanning and magnetic resonance imaging (MRI) have shown variable specificity and they are time consuming and high cost techniques [7,8].

For these reasons previous studies describe incidences of various complications of stroke, but scanty studies provide confirmation of diagnosis by imaging methods [9-11].

Gray-scale ultrasoud (US) is proved to be an accurate imaging method in soft tissues lesions [12-14]. US has the advantage of the possibility of bedside application, it is easy to perform, repeatable and inexpensive and requires no radiation. Power Doppler US (PDUS) has proved to be a reliable tool for semiquantitative assessment of the inflammatory vascularity of the soft tissue [13,14]. Only recently gray-scale US has been applied to the study of musculoskeletal complications of stroke with encouraging results [15-18] and the standardization of the use of musculoskeletal US is advocated also in neurorehabilitation and physiatry settings [19,20].

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The aims of this study were to evaluate incidence and clinical predictors of musculoskeletal complications in patients with stroke in a neurorehabilitation setting, and to describe its impact on functional recovery. Moreover we aimed to describe US features of these conditions.

Materials and methods

A 16-bed neurorehabilitation unit in a tertiary-level hospital was the setting for the study. All 130 patients admitted from October 2016 to October 2017 with diagnosis of ischemic or hemorrhagic stroke were included in the study. The demographic and clinical characteristics of study participants are shown in Table 1.

The diagnosis of stroke was always confirmed by computed tomography (CT) and/or magnetic resonance imaging (MRI) and the last scan of each patient was reviewed in order to classify the lesion location (as reported in **Table 1**) and to define the type of stroke (ischemic or hemorrhagic).

Classification of stroke location was made on the basis of the damaged area on CT/MRI following the Oxfordshire Community Stroke Project (OCSP)-derived CT stroke classification with indication of side location [21,22].

The patients were enrolled regardless to their cognitive function, conscious level, grade of collaboration, capability of communication. Presence of hemineglect (defined as a failure to report, orient oneself toward, or respond to stimuli on the controlesional side that cannot be attribuited solely to sensory or motor dysfunction)[23] and post-stroke depression (defined as evidence of depression documented from a psychiatric consult plus a new prescription of antidepressant following admission) [24] were recorded for each patient.

On admission and on discharge each patient underwent neurological and functional assessment, even with compilation of Functional Independence Measurement (FIM) and Katz index.

The presence of specific complications was clinically suspected by clinicians and discussed during the interdisciplinary weekly team conference for each patient. The determination was made by the attending physiatrist or rheumatologist, with input from other members of the interdisciplinary team when it was appropriate (physioterapist, speech therapist, psychiatrist). Clinical suspect of musculoskeletal complications derived from reduction of the range of motion (ROM) of a joint, with or without local swelling, or evidence for local (spontaneous or provoked) pain. All the patients with clinical suspect of musculoskeletal complications underwent bedside US examination. Other imaging techniques were used when they were necessary to confirm diagnosis.

US diagnostic criteria of these lesions were detailed in previous works [12-15, 25].

Bedside US examination were carried out using a SonoSite (Bothell, USA) Titan with a 5-10 MHz linear transducer (frequency variations depending on site and depth of the lesion). Each US examination was carried out with both longitudinal and transverse scans by the same operator

(P.F.), with the same machine setting [12,13]. The technical parameters of PDUS were: lowest pulse repetition frequency (PFR) avoiding flash artifact, highest gain level without background noise and low filter [13,14]. The intensity of vascularity at PDUS analysis was rated on a semi-quantitative 4-point scale as follows: grade 0= no flow signal; grade 1= 1-2 flow signals (only as coloured spot); grade 2= 2-5 flow signals (both coloured spot and/or definite vessels without secondary branching); grade 3= >5 flow signals or vascular tree or diffuse blush with vessel boundaries not distinguishable [13-15]. A spectral Doppler tracing was obtained to confirm that each color signal represented true arterial flow and spectral wave analysis (SWA) was performed in order to define two indices: Pulsatility Index (PI) and Resistance index (RI). In particular the latter, defined as (maximum systolic velocity- end diastolic velocity)/ maximum velocity, was recorded as it correlates with increasing peripheral resistance.

Statistical analysis was performed by GraphPad InStat 3 (La Jolla, CA, USA) software. The chi-square test was used for an overall approach to compare the percentages among groups. Fisher's exact test was used to compare the percentages between two groups. Unpaired nonparametric Mann-Whitney test was applied to compare the means between two groups. Nonparametric Spearman's Rank test were applied to correlate variables without Gaussian assumptions. The level of statistical significance was set at a P level of 0,05.

Results

Musculoskeletal complications were clinically diagnosed in 66/130 (51%) patients and all underwent US. Eleven patients with musculoskeletal pathologies (17%) underwent other imaging modalities to confirm diagnosis (radiographic assessment for 8 patients, computed tomography for 1 patient, MRI for 2 patients).

In 58/66 (88%) US examination clarified diagnosis and/or modified therapeutic approach.

Shoulder pain was observed in 40/130 patients (31%). In 33 patients (82% of painful shoulders) a variable grade of shoulder subluxation could be observed. US showed increased acromio-humeral distance, compared with the not hemiplegic side. Moreover, in 2 cases of shoulders with subluxation a cortical fractures of greater tuberosity (Hill-Sachs lesion) and lesser tuberosity (McLaughlin lesion) (Fig.1) were respectively noted.

In only 2 cases a diagnosis of frozen shoulder could be made (5% of painful shoulders). In these cases US showed gleno-humeral effusion and mild synovitis of the long head of biceps tendon (LHBT) in the intracapsular tract, with no significant abnormalities of rotator cuff. Moreover PDUS showed scanty signals in the rotator cuff outlet. Diagnosis were supported by MRI.

The 5 cases without subluxation or frozen shoulder, were classified as nonspecific painful shoulder.

Independently from clinical syndromes US always revealed rotator cuff abnormalities. LHBT sheath effusion (31/40, 77%) was the most common abnormality observed with US. Subacromial-subdeltoid (SA-SD) bursal effusion (12/40, 30%), tendinosis of the supraspinatus tendon (20/40, 50%) and subscapularis tendon (16/40, 40%), partial-thickness tear of the rotator cuff (17/40, 42%) and full-thickness tear of the rotator cuff (8/40, 20%) were also noted. Gleno-humeral effusion was observed in 11/40 (27%). No NHO could be observed in shoulders.

Wrist-hand syndrome was observed in 25/130 patients (19%). US showed mild to moderate effusion in radio-carpal and mid-carpal joint and in both extensor and flexor tendon sheaths, with mild thickening of tendons and rare vascular signals on PDUS into the radio-carpal and mid-carpal joints. A subcutaneous edema with extensive dilatation of lymphatics was always observed without significant vascularity at this level.

NHO were observed in 2 patients (1.5%): a case with hip NHO and a case with elbow NHO. In the case with NHO of the hip US demonstrated the classical pattern of zone phenomenon [15,16] (Fig.2), and PDUS demonstrated vascular signal within mineralized NHO and in outer hypoechoic area. No vascular signal was observed in the central hypoechoic core. In NHO of elbow only a heterogeneously hypoechoic mass or hyperechoic mineralized mass were respectively evident, with vascular signals within the lesions at PDUS. Spectral wave analysis (SWA) always demonstrates low resistance vessels in NHO.

Contractures and spasticity were observed in 27/130 (21%). These findings were most common in the upper arm (18 patients) than in the lower extremities (13 patients). Twelve patients with spasticity were treated with US-guided injections of Botulinum toxin A (BTX-A). In these cases US allowed easy identification of target muscle and reliable guidance for needle insertion and BTX-A injection.

Relapsing osteoarthritis was diagnosed in 23/130 (18%) patients (19 with knee osteoarthritis, 3 with hip osteoarthritis, 2 with low back pain in spondylosis).

Acute arthritis was diagnosed in 10/130 (8%) patients (3 knee synovitis and 3 wrist synovitis due to a relapsing calcium pyrophosphate deposition disease, CPDD; 3 knee synovitis and one metatarsal-phalangeal synovitis due to relapsing gout). In these cases US showed hypoechoic effusion and synovial proliferation into the joint space. In all the cases hyperechoic deposits (crystals) can be detected in the fibrocartilaginous menisci or insertional tract of tendons (in CPDD), within the hyaline cartilage of femur (in CPDD), over the hyaline cartilage of femur and into the joint effusion (in gout). PDUS and SWA revealed vascular low resistance vessels within synovial proliferation and/or along the capsular layer (Fig. 3).

For laboratory variables significant differences between groups occurred for erythrocyte sedimentation rate (ESR) which was increased in patients with musculoskeletal complications ($p=0.0008$) and hemoglobine, which was reduced in these patients ($p=0.01$).

Spearman analysis did not show any significant correlation between laboratory variables and single musculoskeletal pathology. Alkaline phosphatase was elevated in the two patients with NHO without statistical significance.

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Patients with musculoskeletal complications had lower Katz index score in discharge ($p<0.0026$), they had more length of hospital stay ($p=0.0008$).

Cortical stroke of nondominant side was directly associated with musculoskeletal complications ($p=0.0249$) while posterior circulation stroke showed a reduced incidence of musculoskeletal pathologies ($p=0.0002$). Musculoskeletal complications were significantly associated to hemispatial neglect ($p=0.018$) and post-stroke depression ($p=0.0004$)(Table 1).

Discussion

Musculoskeletal complications were clinically diagnosed and US confirmed in 51% of patients with stroke admitted to rehabilitation. This data is comparable with those reported in previous clinical studies on stroke survivors [1-6,26-28]. Shoulder pain and wrist-hand syndrome were the most frequently observed musculoskeletal complications with a prevalence of 31% and 19% respectively, followed by contractures and spasticity (21%), relapsing osteoarthritis (18%), acute arthritis (8%) and NHO (1.5%).

Shoulder pain were observed in about a third of patients and in 82% of painful shoulders a variable grade of shoulder subluxation could be observed. These data are comparable with previous observations [27]. US seems to gain a prominent role in the diagnosis of subluxation of hemiplegics' shoulder, as reported in recent works [16-18]. In fact US can easily performed at the bedside, can measure inferior and anterior shoulder subluxation with high reproducibility and correlation with clinical scores and it can be used for serial evaluations without exposure to ionizing radiations [18]. In our series US two cortical fractures could be diagnosed. In both cases routine plans radiographs fail to reveal these abnormalities.

The clinical evidence of restriction of shoulder passive motion in all planes in a patient with stroke should induce clinicians to suspect a frozen shoulder. In our series this condition was diagnosed in 5% of painful shoulders. US gave useful information showing gleno-humeral effusion and mild synovitis of the LHBT in the intracapsular tract, and scanty vascular signals in the rotator cuff outlet at PDUS. The absence of relevant abnormalities of rotator cuff was indicative of a primary capsular inflammatory involvement.

Moreover, in all painful shoulders US revealed rotator cuff pathology, independently from clinical syndromes. Rotator cuff degeneration and tears are age-related changes, and they could not be directly related to hemiplegia. However, in our experience, when US showed prevalent inflammatory abnormalities, a short course of corticosteroids or a local corticosteroid injection were associated to physical therapy and orthesis, with high effectiveness on pain.

Results of our series show that US is a valuable imaging technique in the study of hemiplegics' shoulder and it should be associated to clinical examination to support therapeutic approach. In recent works an imaging investigation is recommended in post-stroke shoulder pain prior to treatment in order to exclude fracture or large rotator cuff tears [27].

In wrist-hand syndrome following stroke US can define a typical pattern with a subcutaneous edema with extensive dilatation of lymphatics with moderate effusion in radio-carpal and mid-carpal joint and in both extensor and flexor tendon sheaths, with mild thickening of tendons, without vascular signals on PDUS, that could represent the clinical entity defined as simple post-stroke hand edema (PSHE), the most frequent edema of hand and wrist observed in hemiplegic patients [11]. The absence of inflammatory hypervascularization is the most prominent aspect of this pattern and this is compatible the relative low grades of referred pain. This data supports the role of loss of muscle tone and pump activity and increased venous and lymphatic congestion as etiology of PSHE [11]. A mild thickening of extensor and flexor tendons is confirmed in a recent work [30]. The PDUS findings should modified therapeutic approach. The patients with the typical US pattern of PSHE should be treated with analgesics, orthesis, cautious mobilization and arm positioning, whether the patients with frankly inflammatory pattern (arthritic) could be promptly treated with corticosteroid, colchicine or local steroids injection.

Relapsing crystals induced arthritis has been frequently described in patients with stroke, in particular in the paretic side [31], and it is confirmed by our data. Moreover US has been demonstrated to be a diagnostic tool in these arthitides [32] as it can depict the presence of crystals in sinovial spaces, cartilages, fibrocartilages (as menisci) and tendons [33] with a sensibility superior to conventional radiography. On this basis US should be used as the first-step diagnostic tool when a synovitis is suspected in the course of stroke rehabilitation.

Contractures and spasticity were observed in 21% of patients. In these conditions US can be useful to guide needle placement of BTX-A injections [34]. Moreover, US provides information about muscle size and fibrosis (fibro-adipose degeneration), factors that can be important in decision making.

NHO is a rare but potentially highly disabling cause of reduction of ROM following stroke. In our series this condition has been observed only in 1,5%. Our data confirm that hypervascularization of mineralizing areas is a relevant diagnostic aspect of NHO lesions, as previously observed with angiographic studies [7]. As early detection of NHO and prompt starting of therapy are essential to contain related disability, bedside PDUS seems a useful first-step diagnostic tool when clinical and/or laboratory findings induce suspicion of NHO [15,34,35].

Only a higher ESR and a lower concentration of hemoglobine resulted in our case patients. These data support the limited usefulness of laboratory investigation in early diagnosis of musculoskeletal pathologies following cerebrovascular injuries [7]. Moreover, the low specificity of these laboratory findings should be considered, in particular in critical ill patients (concomitant infection, dysphagia, malnutrition, pressure sores).

The evidence of reduced Katz scores at discharge and more length of hospital stay supports that musculoskeletal pathologies contribute to delay functional recovery and they affect overall outcome of patients with stroke [1,2, 37].

Anterior circulation nondominant side strokes, and hemispatial neglect were significantly associated to musculoskeletal complications. This association is reported in previous work [28,29]. The lack of attention to the left side of body, eventually associated to reduced pain perception, could contribute to expose peripheral (in particular wrist and knee) and axial (shoulder) joints to over-range mobilizations and to inadequate positioning, and to develop focal musculoskeletal pathologies.

This supposition could be supported by the evidence of a significant negative association between posterior circulation strokes to these complications. In these cases a preserved attention and consciousness of body function and relative deficits could be protective to excessive mobilization and inadequate positioning.

Depression resulted significantly associated to musculoskeletal complications in our study. This association has been reported in previous works [27,28,37]. Even if our data are insufficient to define if musculoskeletal complications can contribute to develop depression these data suggest that a prompt treatment of musculoskeletal pain could contribute to limit the development or the severity of reactive depression following stroke.

In conclusion, musculoskeletal conditions complicate the course of stroke in about half of patients admitted to rehabilitation, and they contribute to delay functional recovery. US has proved to be an excellent diagnostic technique also in this field of application and we recommend the use of bedside US in the evaluation of suspected musculoskeletal pathologies in patients with stroke, to define diagnosis (presence of structural damage and grade of inflammation) and to choose the better therapeutic approach.

Conflict of interests

The authors declare that they have no conflict of interest.

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Table legend

Table 1.

Demographic and clinical characteristics of patients.

CRP, C-reactive protein. ESR, erythrocyte sedimentation rate. FIM, Functional Independence Measurement. ns, not significant. SD, Standard Deviation.

	Patients without musculoskeletal complications	Patients with musculoskeletal complications	p value (statistic test)
Number of subjects (%)	64 (49.2%)	66 (50.8%)	
Male / Female (n)	41 / 23	26 / 40	p=0.005 (Fisher)
Mean age in years (range; SD)	75.3 (55-88;9.4)	72.6 (45-93;11.2)	ns (Mann-Whitney)
Days from stroke at admission	23.8	25.9	ns (Mann-Whitney)
Length of stay (range; SD)	26.3(15-120;19)	29.8 (18-90;17)	p=0.0008 (Mann-Whitney)
Serum urate mg/dL [nv 2.6-7] (SD)	4.6 (1.9)	4.5 (1.9)	ns (Mann-Whitney)
Alkaline phosphatase (nv values 40-129 mg/dL for female, 35-104 mg/dL for male)	96.6 (49)	98.7 (82.7)	ns (Mann-Whitney)
Hemoglobine g/dL (nv 11.7-16 g/dL for females, 13.2-17.3 g/dL for males)	12.8 (1.3)	12.1 (1.4)	p=0.01 (Mann-Whitney)
ESR mm/hour [nv 2-25] (SD)	33.5 (25)	51 (26.6)	p=0.0008 (Mann-Whitney)
CRP mg/dL[nv<0.5] (SD)	3 (5.3)	3.7 (5.9)	ns (Mann-Whitney)
Type of recent stroke			ns (Fisher)
• ischemic	53 (82.8%)	50 (83.3%)	
• hemorrhagic	11 (17.1%)	16 (24.2%)	
Classification of stroke location:			p=0.0014 overall (Chi square)
			ns (Fisher)
1.0 TACI/PACI dominant side	22	19	
2.0 TACI/PACI nondominant side			p=0.0249 (Fisher)
3.0 LACI dominant side	10	22	
4.0 LACI nondominant side			ns (Fisher)
5.0 POCI	6	7	
			ns (Fisher)
	7	14	
			p=0.0002 (Fisher)

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	20	4	
Hemispatial neglect (%)	8 (12.5%)	20 (30.3%)	p=0.018 (Fisher)
Depression	22 (34.3%)	44 (66.6%)	p=0.0004 (Fisher)
FIM (range; SD)			
• at admission	46.2(18-85;20.9)	41.6(18-89;19.2)	ns (Mann-Whitney)
• at discharge	60.9(18-101;25.6)	53.5(18-95;22)	ns (Mann-Whitney)
Katz index (range; SD)			
• at admission	23.4(10-65;15.9)	18.6(10-55;13.5)	ns (Mann-Whitney)
• at discharge	38.7(10-75;20.3)	28.3(10-70;16.7)	p<0.0026 (Mann-Whitney)

Figure legends

Figure 1.

Anterior scans over left shoulder in patient with left hemiplegia, severe hemispatial neglect and shoulder subluxation. On the left side (transverse scan) a large cortical defect (asterisk), compatible with McLaughlin lesion (reverse Hill-Sachs) is visible on humeral head (HH) and its lesser tuberosity (LT). Tendinosis of subscapularis tendon (SSc). On the right side is shown the longitudinal axis of the large cortical defect.

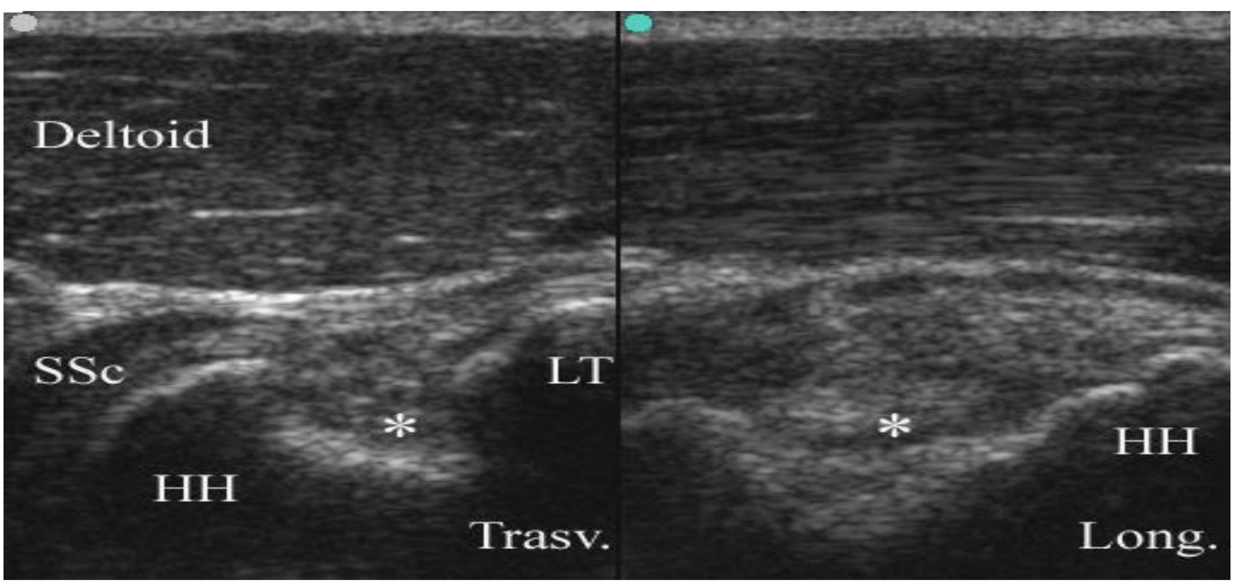

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Figure 2.

Anterior longitudinal scan of left hip in patient with left hemiplegia and spasticity consequent to intracerebral hemorrage. The classical aspect of the "zone phenomenon" of heterotopic ossification is evident in iliopsoas muscle, with a inner hypoechoic core (curved arrow) surrounded by a ring of hyperechoic mineralized islands (between arrowhead), and an outer hypoechoic zone adjacent to normal muscle. Hypoechoic effusion (asterisk) is visible within coxo-femural joint capsule. FH, femoral head.

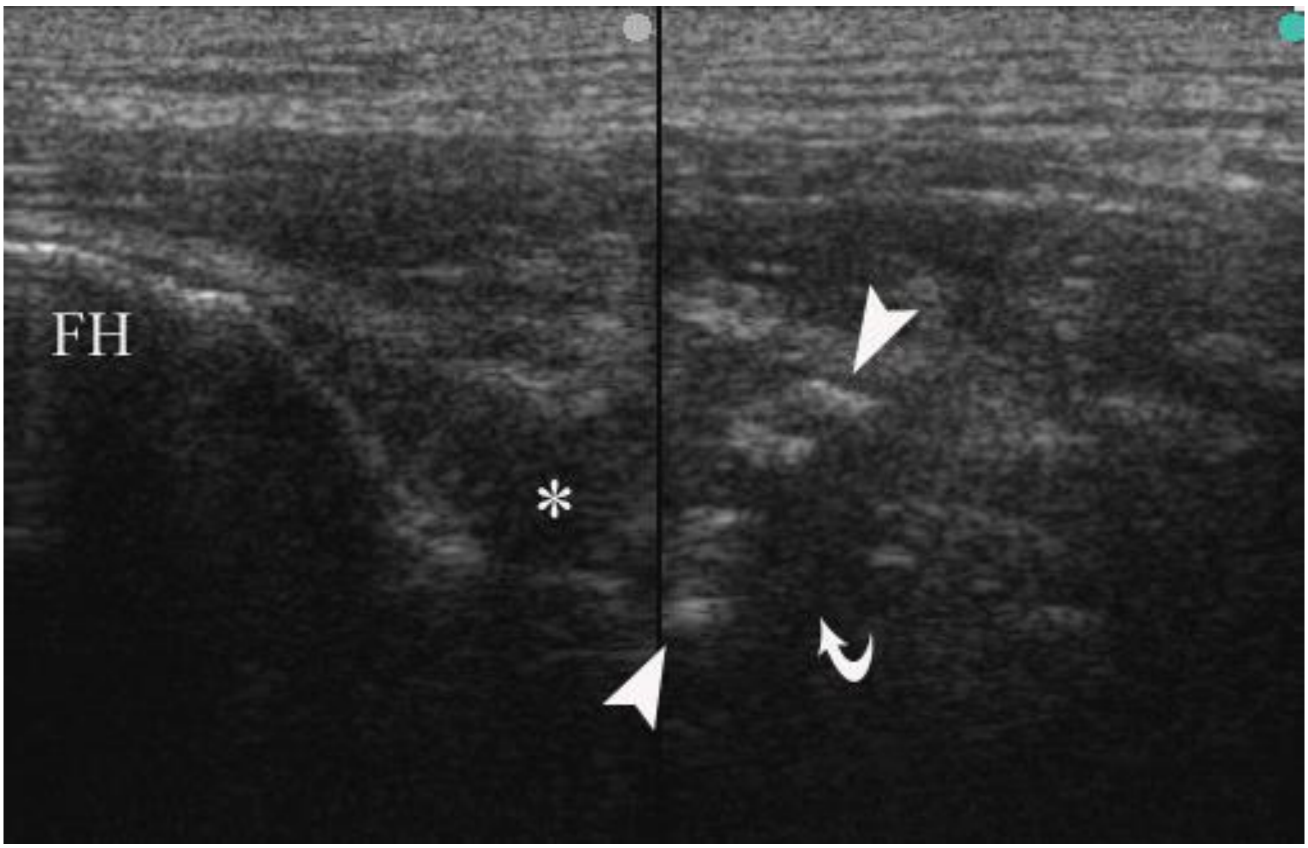
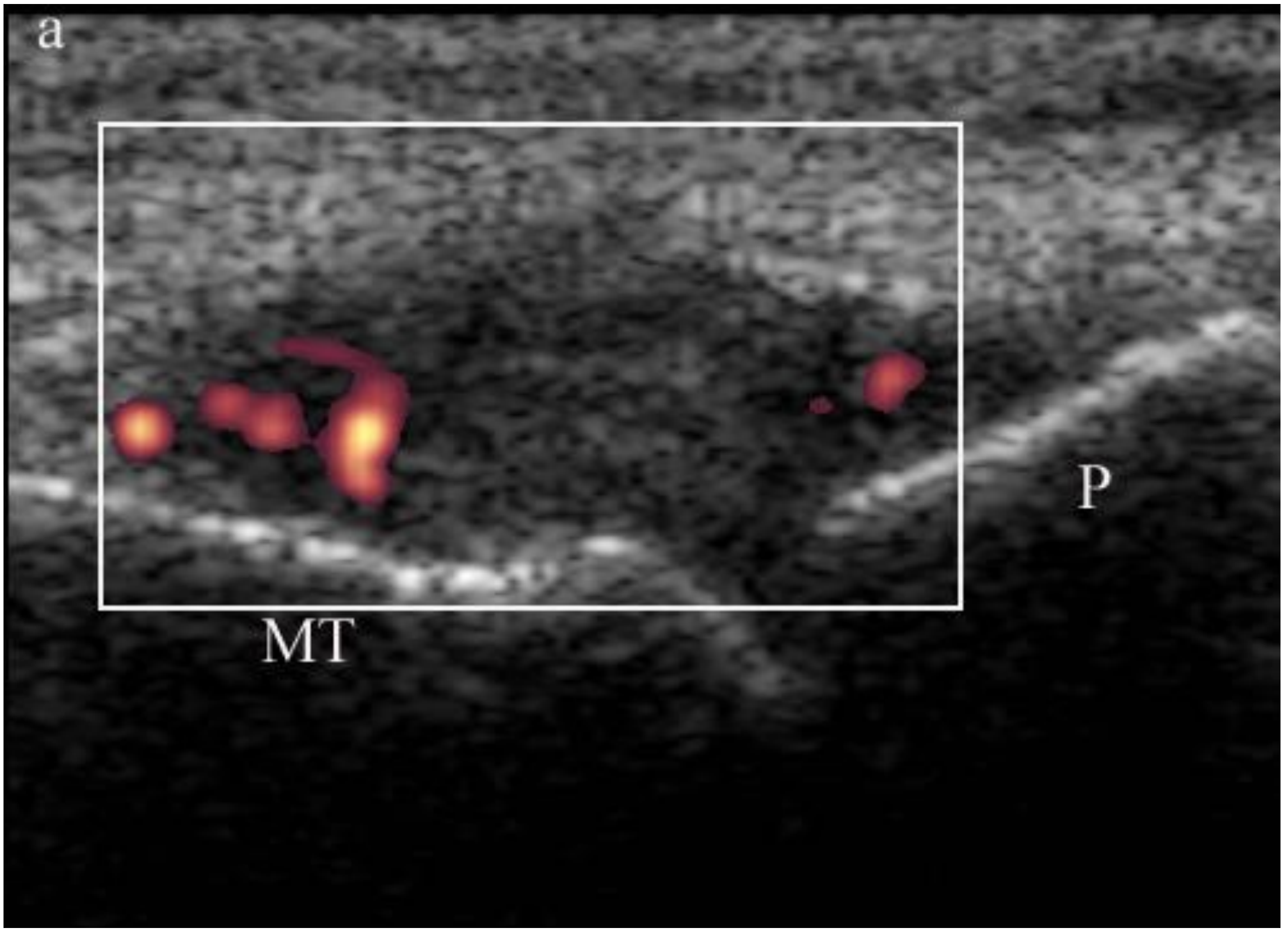


Figure 3.

Acute arthritis of first metatarsal-phalangeal (MT-P) of right foot in hyperuricemic patient with post-stroke right hemiplegia. Sagittal longitudinal scan over first MT-P. Hypoechoic distension of joint, with intracapsular vascular signals at PDUS (grade 2), indicating active synovitis.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