Sonoelastography may help in the differential diagnosis between rheumatoid nodules and tophi

Sirs,

In selected cases, the differential diagnosis of rheumatoid arthritis (RA) and gout may be difficult because chronic arthritis, radiographic erosions and subcutaneous nodules may occur in both conditions (1, 2). Identification of monosodium urate (MSU) crystals in synovial fluid and tophi is the mainstay of gout diagnosis and should be used when gout is supected. Sonoelastography is a recently developed, non-invasive ultrasound (US) technique that allows *in vivo* assessment of the mechanical properties of tissues (3). Sonoelastography measures the changes of the radiofrequency (the unfiltered ultrasonographic signal) before and after application of a mechanical stimulation (*i.e.* a surface deformation). A conventional B-mode image is obtained using less than 15% of the information contained in the native signal, whereas sonoelastography also reveals raw data that do not concur to the creation of B-mode images. This technique requires induced tissue deformation in order to assess return elasticity. The most common stimulus adopted to elicit structural deformation is gradual manual compression or radiofrequency pulses. The elastogram is visualised as a color image superimposed on the B-mode image. The scale varies from red (soft tissue) to blue (hard tissue), with yellow and green as intermediate grades (4). Sonoelastography is being used to reveal malignant tumours on the assumption that they are less elastic than benign ones (5). We have previously shown that sonoelastography could be helpful in the evaluation of shoulder bursitis in polymyalgia rheumatica (6). To the best of our knowledge, this remains the only anecdotal report on the use of sonoelastography in the field of rheumatology.

We used sonoelastography to assess eight subcutaneous nodules (5 rheumatoid nodules and 3 tophi) of three patients affected by RA (2 males, 1 female; mean age 69.8±11.1 years) and 3 patients affected by tophaceous gout (2 males, 1 female; mean age 69±5.3 years). Diagnosis was performed according to the relevant ACR criteria (7,8). In addition, MSU crystals were aspirated from all tophi. Patients presented with nodular lesions of the elbow (2 patients), hand and wrist (3 patients), and Achilles tendon (1 patient). A radiologist with 20 years' experience in skeletal US and one year's experience in sonoelastography performed the sonoelastograms using a US system (Logos EUB8500 – Hitachi Ltd., Tokyo, Japan) equipped with a 10-6 MHz electronic high-resolution broadband linear array. He was blinded to the diagnoses. A special adapter was applied to the probe, in order to optimise distribution of pressure. Such mechanic stimulation was applied by the operator directly on the probe, acting perpendicularly to the scanned area, in order to produce a deformation of the tissues. To allow reproducibility of the amount of pressure applied, a feedback of it was provided by a specific numeric scale displayed on the monitor of the US equipment. A high-quality elastogram is obtained with a light contact that does not distort the underlying tissues. The images were recorded and independently evaluated by two readers (a radiologist with four years' experience in skeletal US [LMS] and a rheumatologist [MAC], both with one year experience in sonoelastography) blinded to the patients' disease and symptoms. The main colour of the lesions was recorded and translated to a numeric score with 1=blue, 2=light blue, 3=green, 4=yellow, and 5=red. If more than one colour was present in the image of the nodule, the prevailing one was recorded. Median differences of colour in the 2 groups were compared by the Kruskall Wallis test; inter-observer agreement was assessed by the Cohen's κ-test.

All nodules were clearly detectable both at US and sonoelastography. Rheumatoid nodules resulted significantly less elastic than tophi (Fig. 1). The median value of the main color was 1 (range 1-3) for rheumatoid nodules and 5 (range 3-5) for tophi (p=0.024). Inter-observer agreement was excellent (κ=1).

US has been used to differentiate rheumatoid nodules and tophi by Tiliakos *et al.* (9) and Benson *et al.* (10), although with contrasting results. The US pattern of subcutaneous nodules in patients with rheumatic conditions was reported by Nalbant *et al.* (11), who found that rheumatoid nodules had a more homogeneous structure than tophi. They suggest that this technique could help to distinguish the cause of the lesions, but lacked diagnostic value. In a report by Delle Sedie *et al.* (12), a detailed categorisation of soft, hard, and mixed tophi is described. In our experience (Fig. 1), US B-mode evaluation demonstrated no posterior acoustic shadowing. This would theoretically mean that tophi included in our series are represented only by soft tophi and that probably this could be the reason why thopi are more elastic than rheumatoid nodules. We can suppose obtaining opposite results when considering hard tophi, although soft tophi seem to be more frequent, according to our experience. No other reports have been published on the use of US imaging in the differential diagnosis of nodules in rheumatic patients. We feel that sonoelastography could represent a non-invasive, valuable tool to investigate the nature of nodules by evaluating tissue elasticity, although we recognise that this technique cannot be recommended for the diagnosis of gout on the basis of our results. In addition, there are several limitations to consider: first, the number of observations was very small and inter-observer agreement value may be strongly overestimated, a limitation that could potentially affect the results of the study. Secondly, tophi could be less or more elastic in different patients or in the same patient according to the compactness of the crystal aggregation; this was not the case in our patients with gout, where tophi showed a similar degree of elasticity. Furthermore,

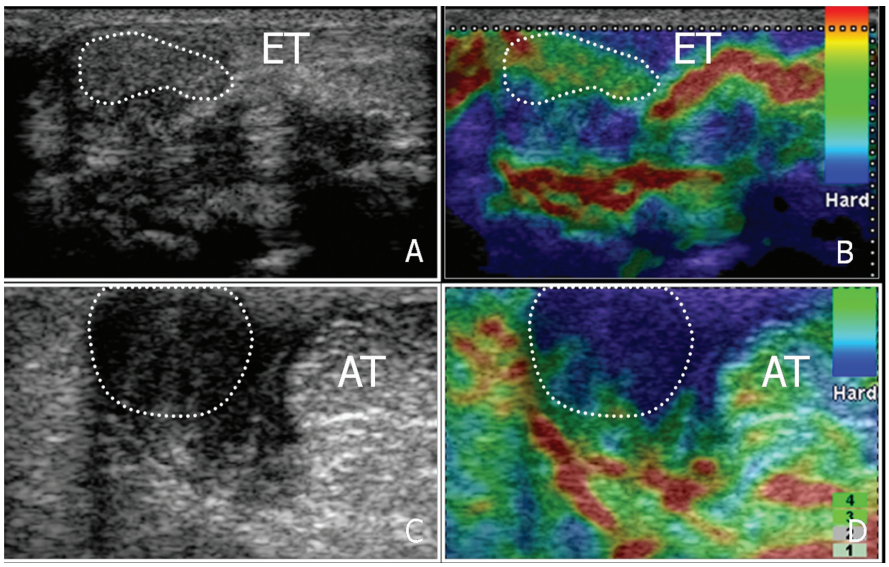

Fig. 1. Long-axis scan performed on the palmar side of a finger: B-mode US in a patient affected by tophaceous gout (**A**) shows an isoechoic nodule (dotted line) embedded within an extensor tendon of the hand (ET); the sonoelastogram (**B**) shows a prevalence of green within the tophus, which is indicative of intermediate elastic property. Axial scan performed on the posterior region of the ankle: (**C**) B-mode US shows a hypoechoich nodule (dotted line) next to the Achilles tendon (AT) of a patient with rheumatoid arthritis. The sonoelastogram (**D**) shows a prevalence of blue within the rheumatoid nodule, which points to poor elasticity.

considering the reported ranges of the main colour values for the rheumatoid nodules (range 3–5) and tophi (range 1–3), there is at least a rheumatoid nodule with value of 3 and at least a tophus with value of 3. Thus, in at least 2 out of the 8 nodules included in our series (25%) sonoelastography could not be of help in the differential diagnosis. However, further investigations on larger cohorts of patients are required to confirm these preliminary data.

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