The “starry night” (diffuse microcalcific myopathy) – thousands of muscle microcalcifications after 30 years of Trichinella infection detected by ultrasound

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Abstract
Trichinellosis, a parasitosis transmitted through consumption of raw or undercooked meat from pigs and game animals, is responsible for a specific myositis. The calcifications of infected myocytes and larva can be detected during many years postinfection. We present the case of a male patient with a history of severe trichinellosis with disease onset 30 years ago, presenting with generalized muscle microcalcifications detected during musculoskeletal ultrasound evaluation. The ultrasound aspect of the muscles was indeed spectacular; hence, the comparison with a ”starry night”.

Keywords: calcific myositis; trichinellosis; ultrasound

Introduction
Trichinellosis is a parasitic infection caused by nematodes of the genus Trichinella – *Trichinella* spp. being most frequently encountered in humans. Hosts such as pigs and game animals are the major sources of human infection. The transmission of the parasite is related to the consumption of raw or undercooked meat. The disease has an acute stage (weeks) followed by a chronic stage (years) and its severity may vary from asymptomatic to severe forms. The calcification of the host cells (myocytes of the striated muscle tissue) and of the larva can be detected after 6 months postinfection [1-3].

We present the case of a male patient with a history of severe trichinellosis with disease onset 30 years ago, presenting with generalized muscle microcalcifications detected during ultrasound (US) evaluation.

Case report
A 67-year-old male patient was admitted for investigation of small hyperechoic spots detected inside the muscles during a routine musculoskeletal US examination. The patient was diagnosed with tophaceous gout 10 years priorly, with frequent acute episodes of arthritis or tendinitis. No myalgia or impaired muscle function was detected. Laboratory findings revealed muscle enzymes, leukocyte number and C-reactive protein in normal range and increased serum levels of uric acid (8.5 mg/dl, normal range 4-6 mg/dl).

Musculoskeletal US (LOGIQ™ S7 Ultrasound/GE Healthcare, United States, 6-15 and 18 MHz linear transducers) evaluation was first performed on the muscles of the upper arm, afterwards examining the muscles of the thorax, abdomen and lower part of the arms. The same US aspect/pattern was detected in all examined muscles: small hyperechoic spots (0.2-1 mm) diffusely distributed inside the muscles. In some of the larger spots, the comet tail artifact was observed. No posterior acoustic shadow-
ing was detected and dynamic examination (in contraction/relaxation) was normal. No pathological findings related to muscles vascularization or fascia were found. No pathological lymph nodes were identified (fig 1-3, movie 1-3, on the journal site).

Taking into consideration the patient’s history of gout, the preliminary assessment of the hyperechoic spots was of urate deposition myopathy. For this reason, an US guided biopsy (using Bard Magnum system, 16G biopsy needle) of the left pectoralis major muscle was performed. We chose this specific muscle mainly due to the increased number of visible spots in this area.

The anatomopathological exam found in hematoxylin eosin stain a small, isolated, cystic structure lying within the striated muscle fibres, slightly larger in diameter than a normal muscle fibre. Inside the cyst, an intensely basophilic, most likely calcified material, was detected. The thick hyaline capsule excluded an idiopathic or secondary calcification, raising the possibility of a biological structure, calcified and encapsulated. Masson’s trichrome stain highlighted the collagenous nature of the capsule and the outline of a curved, non-viable tubular structure inside the cyst. The anti-desmin immunohistochemistry stained only in the muscle and no inflammatory infiltrate

Fig 1. Transversal (a) and longitudinal (b) grey scale ultrasound of the extensor part of the forearm. Small hyperechoic spots diffusely distributed inside the muscles can be observed.

Fig 2. Transversal (a) and longitudinal (b) grey scale ultrasound of the thenar eminence. Small hyperechoic spots with comet tail artifact diffusely distributed inside the muscles are detected.

Fig 3. Longitudinal grey scale ultrasound of the distal part of soleus muscle (a) and Achilles’ tendon, proximal third. The small hyperechoic spots observed in muscles are different compared to tendon urate deposits (tophi) (arrows).
was detected. The final interpretation was of longstanding, encysted and calcified larvae of *Trichinella spiralis* (fig 4).

When confronting the patient with the histological result of the biopsy, he admitted to having been hospitalized 30 years anteriorly for a severe form of trichinellosis. We completed the laboratory workups with IgG-specific antibodies which were negative.

The final interpretation was of diffuse (generalized) chronic microcalcific myopathy due to chronic trichinellosis. We concluded that no treatment or follow-up was required.

**Discussion**

Trichinellosis has a 2-stage evolution. After 1-4 weeks of incubation, the acute-stage trichinellosis develops, with fever and gastrointestinal manifestations followed by muscle phase of infection. Myalgia can be severe and associate tenderness, swelling and weakness, sometimes urticaria, symmetrical peri-orbital or facial edema and shivering [2,3]. Myocarditis, thromboembolic disease or encephalitis may complicate the disease course [2,4]. The chronic stage of disease starts 3-4 weeks later and can persist for months or even years [2]. The presence of leucocytosis, eosinophilia and elevated serum muscle enzymes are nonspecific findings, thus requiring the use of the more specific diagnostical procedures for disease confirmation: serologic tests and/or muscle biopsy (rarely needed) [1,2].

Once the *Trichinella* larvae enter the myocytes, they induce a significant inflammatory reaction responsible for the myositis. The host cell transforms into a new phenotype called “nurse cell”; the sarcomere myofibrils disappear and the larva becomes encapsulated. The progressive calcification of larvae may take place after 6 months post infection (first the capsule followed by the nurse cell and the larva). The process may lead to the death of the larvae, but some larvae may survive for years in the same host [2,5]. In a study on 128 patients, 10 years after infection, no calcifications of residual larvae were detected by mammography or muscle biopsy [6]. Muscle calcifications were described in the pectoralis muscle using mammography [6-8] and in extraocular muscles using computed tomography [9]. We found no report regarding the follow-up and the persistence of muscle calcifications after more than 10 years postinfection.

We used the term of “diffuse (generalized) chronic microcalcific myopathy” for the pathological findings in our patient, although PubMed search results did not retrieve any publication pertaining to this topic. Similar terms related to the muscle calcifications included “myositis ossificans” (heterotopic ossification of muscular tissue, divided into two entities: myositis ossificans progressiva – an autosomal dominant disease, and myositis ossificans traumatica) [10,11], “calcinosis” (the abnormal deposition of calcium in skin, subcutaneous tissue, myofascia and muscle related to systemic scleroderma or dermatomyositis) [12] and simple “muscle calcification”. Tawfeeq et al [13] used the term calcific myositis in 2 cases related to COVID-19 infection (streaky calcification of the muscles around the shoulders) as they reported the appearance of muscular calcifications during the acute phase of myositis. Calcifications found in muscles can also be vascular calcifications associated with arteriosclerosis, chronic renal failure or chronic hypercalcemia [14]. Muscle calcifications have been also described in other parasitic infections such as cysticercosis [15].

We found no report about the use of US in neither acute nor chronic trichinellosis. Indeed, there is no role for imaging techniques in the diagnostic work-up of this
parasitosis, but musculoskeletal US has proven a great capacity in identifying the small calcification and may have an important role in patient follow-up, especially in long-term symptomatic patients.

Our first suspected diagnosis was urate myopathy but the generalised microcalcifications coupled with the lack of clinical symptoms and, more importantly, the unawareness about this specific disease entity, determined us to perform muscle biopsy. The histopathological result was indeed unexpected. The US aspect of the muscles was really spectacular; hence, the comparison with the "starry night". To our knowledge this US aspect of the pathological muscles has not been previously described in the literature.

In conclusion, US detection of muscular calcifications can be a challenge in situations in which the clinical aspect is not suggestive for diagnosis. Although rare, trichinellosis should be taken into consideration when assessing the differential diagnosis pertaining to these cases.

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Captions for the movies uploaded to the journal site

Movie 1. Ultrasound examination of the left pectoralis muscles
Movie 2. Ultrasound examination of the right thenar eminence
Movie 3. Ultrasound examination of the extensor part of the right forearm