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Total spleen calcification - a rare clinical manifestation in systemic lupus erythematosus

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ABSTRACT

Splenomegaly, infarction, spontaneous rupture and hyposplenism are among the frequently manifestations of splenic involvement in systemic lupus erythematosus (SLE) patients. Exceptionally, extensive splenic calcifications are found in SLE. This aspect is due to the periarterial thickening in an "onion-skin" model. Discrete, small, circular and diffuse nodules that are distributed at the level of the parenchyma, but that are missing at the capsular and subcapsular level, are the main characteristics of these calcifications. The aim of this report is to present the case of a SLE patient with this rare splenic calcification association.

Keywords: splenic calcifications, systemic lupus erythematosus, hyposplenism, "onion-skin" pattern

INTRODUCTION

Splenic calcifications have been described since the 1930s. The most common splenic calcifications are considered to be sequelae of a previous granulomatous infection; therefore, an extensive differential diagnosis is required for these lesions. Calcified splenic granulomas are often discovered incidentally and are usually due to tuberculosis or histoplasmosis and less frequently secondary to Pneumocystis carinii pneumonia or brucellosis [1-3]. Most splenic masses are benign and of no clinical significance [1,4,5].

For differential diagnosis, Consul et al. propose an algorithmic approach based on computer tomography (CT) which evaluates the morphological features, as well as the pattern of calcification [2]. Their analysis includes manifestations like: splenic hemangiomas, epithelial cysts, epidermoid cysts, pseudocysts, splenic infarction, Gamna-Gandy bodies, hydatid cysts, thorium dioxide exposure, calcified splenic metastases, lymphoma, epithelioid hemangioendothelioma, splenic sarcoma, splenic angiosarcoma, myelofibrosis, autosplenectomy and splenic artery aneurysm [1,2].

Splenic calcifications have been described in many connective tissue diseases (CTD): systemic sclerosis and SLE, rheumatoid arthritis, infections, sickle cell disease, silicosis or celiac disease [6,7]. Through this paper we present a rare case of multiple splenic calcifications in a SLE patient.

CASE REPORT

We report the case of 65-year-old white female diagnosed in 2007 with SLE with articular (inflammatory polyarthralgia), cutaneous (malar rash) and immunological (hypocomplementemia, positive anti-dsDNA antibodies=155U/mL, antiSSA=200U/mL, antiSm>732U/mL) involvement and with secondary antiphospholipid syndrome. She was initially treated with azathioprine 150 mg/day and intermittent corticosteroids (2007-2008). At the time of admission, she is under treatment with hydroxychloroquine 400 mg/day and azathioprine 150mg/day. She complains of mechanical pain in the cervical spine and bilateral knees.

She has a personal history of gastroenterological (gastroesophageal reflux disease and hepatic steatosis), renal (chronic kidney disease stage G3a), cardi-

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ovascular (grade 2 arterial hypertension, chronic venous insufficiency), endocrinological (multinodular goiter with normal function) and degenerative (peripheral and axial modifications) diseases.

Laboratory tests showed positive anti-double stranded DNA antibodies (174 U/mL, reference range: 0-25), the presence of antiphospholipid antibodies (11,2 U/mL, reference range:0-10): anti-beta-2-glycoprotein-I antibodies (90 U/mL, reference range:0-10), anti-beta-2-glycoprotein-I antibodies IgG (20,5 U/mL, reference range: 0-5), anti-beta-2-glycoprotein-I antibodies IgM (9,5 U/mL, reference range: 0-5), a decreased level of complement: C3 (65.8 mg/dL; reference range: 88-252 mg/dL) and C4 (4.1 mg/dL; reference range: 13-75 mg/dL). Renal profile revealed a level of urea of 77.9 mmo/L, creatinine level of 1.31 mg/dl and a glomerular filtration rate of 43.31 ml/min/1.73m^2.

The patient performed a routine chest X-ray which did not show any lung changes, but detected multiple splenic microcalcifications (Figure 1). The same changes were confirmed by abdominal ultrasound. Subsequently, a thoraco-abdominal CT scan was performed, highlighting the same aspect - diffuse splenic calcifications (Figure 2).

Forwards, in order to exclude a possible neoplastic cause, the patient performed a series of complementary investigations. Because a right axillary adenopathy was highlighted, a biopsy and histopathological examination were recommended, which ruled out a tumoral cause. Furthermore, the patient underwent an upper digestive endoscopy and a colonoscopy, the result of which was negative for neoplasms.

Under these conditions and considering the fact that the patient is totally asymptomatic, and the splenic lesions did not show any subsequent evolution (stationary appearance at subsequent evaluations), it was decided to continue the same treatment scheme for SLE. Periodic radiological surveillance was recommended.

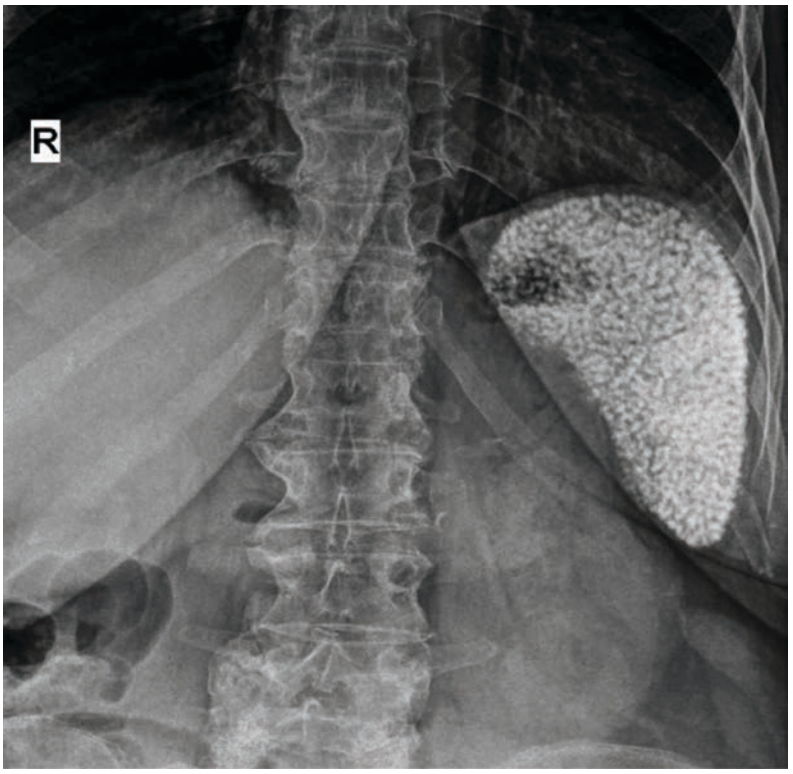

FIGURE 1. Chest X-ray - multiple spleen microcalcifications

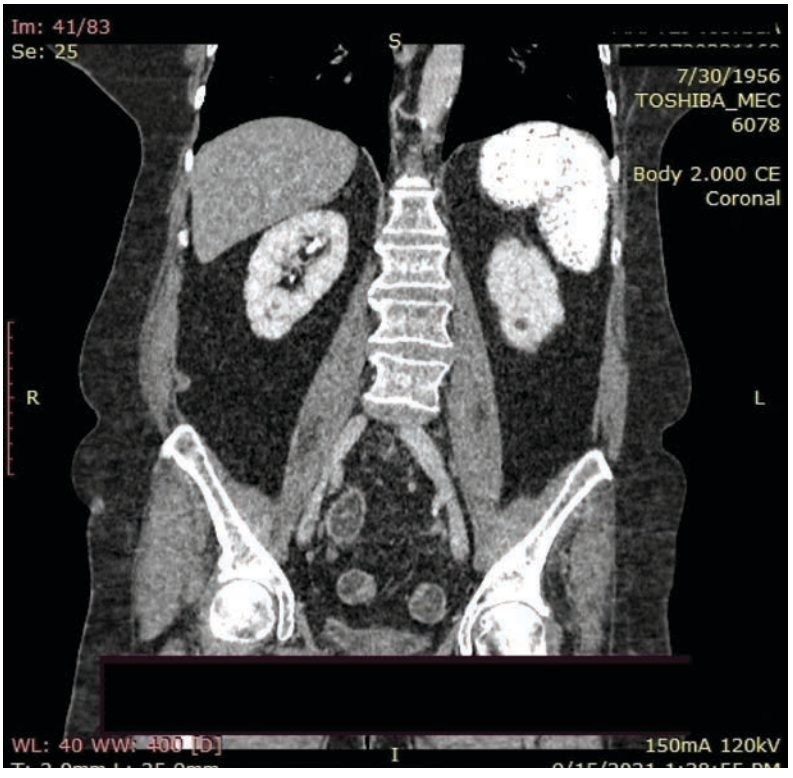

FIGURE 2. CT image - normal spleen size with completely calcified parenchyma

DISCUSSIONS

SLE is a systemic autoimmune disease which can be associated with multiple visceral manifestations, including splenic changes. Splenomegaly, infarction, atrophy, infections, and hyposplenism are some of the most commonly described forms of splenic damage in SLE patients [3,8]. Rarely, a calcification of the spleen can be highlighted in SLE [3,7].

Few cases of spleen calcifications in SLE have been reported in the literature [1,3,6,7,9-20]. The first description belongs to a German patient in 1956 and later, in 1963, another case from Chile was published [13,21]. Moreover, association between spleen calcifications and Overlap syndrome [22] or pediatric patients [23] have been mentioned.

Spleen calcifications have a diffuse pattern and are predominantly discrete, small, and circular nodules. Larger, punctate calcifications can be seen in granulomatous infections. In addition, splenic calcifications associated with other CTD may be isolated, smaller, less dense and closer to the capsular region than those highlighted in SLE [6].

Winter et al. focus their attention on the small, dense calcifications that almost cover the spleen and present the specific "pattern recognition" associated with long-standing SLE [1]. This unique and specific calcification pattern guides us on the diagnosis when other secondary causes have been excluded [3,24].

The pathognomonic histological sign of splenic involvement in SLE consists of "onion-skin" pattern [8,25]. Microscopically, the small arteries of splenic pulp typically develop concentric deposition of collagen with at least 3 separated layers of periarterial fibrosis [3,15,26,27].

This described model of calcification: discrete, small, circular, diffuse, but sparring the capsular and subscapular area, may be considered specific to SLE [11,28]. Tieng et al. support the idea that this splenic calcification does not occur by chance, but it develops in direct association with the underlying disease [3]. Based on the systemic perturbance of mineral and bone metabolism, Kelati et al. draw attention to the relationship between spleen calcifications and renal involvement [23]. This is an interesting assumption considering the fact that the presented patient also has kidney damage. Although we have all these evidences, the precise pathological mechanisms of spleen calcification have not been determined [7].

It has been mentioned that these small calcifications into spleen may be due to long-term effects of immune-mediated vascular inflammation during repeated exacerbations of the disease [9].

Moreover, splenic microcalcifications could be related to thrombotic microangiopathy, in which a key role is played by antiphospholipid antibodies [9,10]. Further, segmental splenic infarction is often associated with the presence of anticardiolipin antibodies [6], situation in which our patient finds herself. It is worth mentioning that our patient had no history of any previous infectious or environmental triggers responsible for the appearance of these calcifications. That's why in our case many causes of splenic calcifications were excluded by history, clinical examination, laboratory and imaging findings.

The link between the development of hyposplenism induced by calcified lesions remains to be investigated [6]. As hyposplenism may increase the risk of infections, it should be highlighted the importance of pneumococcal vaccination in these patients [9,10]. In SLE patients, a splenic function test examining the red blood cell morphology on a peripheral blood smear should be performed [3]. Detecting Howell-Jolly bodies on a peripheral blood smear is clear evidence for hyposplenism diagnosis [29].

Splenic calcifications are non-progressive visceral manifestations and treatment is not indicated except if the patient develops symptoms of hyposplenism [3].

According to malignancy history and imaging findings, the American College of Rheumatology (ACR) indicates the need of a follow-up through imaging methods such as nuclear magnetic resonance (MRI) or positron emission tomography (PET) or even biopsy where necessary [1,30].

CONCLUSIONS

Although rare, splenic calcifications in SLE typically have a distinctive pattern. They are tiny, circular calcifications distributed in splenic parenchyma. Calcifications may be considered an atypical immunological response of the spleen to SLE flares. They can be detected incidentally on a routine X-ray. Literature data suggest that these lesions are not progressive and treatment is only required upon the onset of hyposplenism symptoms. On the other hand, this particular splenic calcification pattern should be recognized by rheumatologists and radiologists as it may indicate the presence of SLE. Moreover, splenic lesions must be searched for in patients with diagnosed SLE. Perhaps the awareness of this association will increase case identification and will provide a better knowledge of this rare phenomenon still encountered in SLE patients.

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