Calcified fibrous nodules in masseter muscle - A case report and possible etiologies

**Abstract:**
Fibro-calcified nodules represent a rare group of lesions that are composed of fibrous connective tissue with calcified areas. The etiology of fibro-calcified nodules may be related to secondary changes that are caused by trauma, infectious and autoimmune diseases, or calcified thrombi. The purpose of this paper is to report the presence of a lesion of a fibro-calcified nature in the masseter muscle and its possible etiologies. The patient, a 35-year-old melanoderm female, presented with a nodule in the left masseter region with 12 months of progression. Considering the accessibility of the lesion, an excisional biopsy was performed. A histopathological examination revealed residual fibro-calcified nodules with central foci of coagulation necrosis surrounded by fatty tissue and striated skeletal muscle fibers. The test for acid-alcohol-resistant bacillus (BAAR) was negative. Two years after the surgical procedure, there were no signs of lesion recurrence. Thus, the results of histochemical staining ratified the fibro-calcified aspect of the lesion, which suggested dystrophic calcification.

**Keywords:** autoimmune diseases; calcification, physiologic; latent tuberculosis, soft tissue infections.
INTRODUCTION

Fibro-calcified nodules represent a group of rare lesions that are composed of fibrous conjunctive tissue with calcified areas. The etiology of fibro-calcified nodules may be related to secondary alterations that result from trauma, infectious and autoimmune diseases or from calcified thrombi.

In the majority of cases, these nodules present as subcutaneous lesions, which may form within striated skeletal muscle tissue. Previous studies have demonstrated evidence of the presence of fibro-calcified lesions after bacterial and helminthic infections, including tuberculosis and cysticercosis, respectively. The most common sequela of primary tuberculosis is the Ghon nodule, which comprises a calcified area that forms over caseous necrosis, which is normally surrounded by epithelioid macrophages, lymphocytes and fibroblasts. When the granulomatous lesion develops in an extra-pulmonary location, the clinical condition is defined as scrofula. In addition, fibro-calcified lesions have also been documented in individuals who are infected by Taenia solium larvae. Cysticercosis muscle infection is unlikely to be identified in a live patient because it exhibits no specific clinical signs and/or symptoms. The presence of extensive calcifications has been reported in the soft tissues of individuals with systemic lupus erythematosus as well as in dermatomyositis and progressive systemic sclerosis. Particularly in these cases, the mechanisms of calcification involving calcium phosphate deposition have not yet been completely elucidated. Other authors pointed out the presence of fibro-calcified nodules related to vascular thrombi. In this case, they resulted from traumatic lesions that had affected the endothelium. The aim of this case report was to describe fibro-calcified nodules in the masseter muscle and discuss the possible etiologies related to this lesion type and its clinical and histopathological characteristics.

CASE REPORT

The patient, a 35-year-old melanoderm female, presented to the Bucmaxillofacial Surgery and Traumatology Service of an University Hospital in Salvador, Bahia, complaining of an increase in volume in the masseter region on her left side, with approximately 12 months of progression. The lesion had a slow growth pattern and was painless.

The patient’s medical history was insignificant. No systemic pathology was mentioned, and no episodes of trauma were found in her report.

In the clinical exam, a discrete volume increase was observed in the inferior third of the left masseter region, which was painless and mobile and measured approximately 2 cm in diameter at the largest point, without any associated phlogistic signs or functional limitations (Figures 1 and 2). There were no associated lymphadenopathy/megalias.

In an ultrasonography of the face, a solid nodule with regular outlines was observed in the left mandibular region. No echographic alterations were observed in the local musculature or skin (Figure 3).

A parasitology exam to test for proglottids was negative. No notable alterations were observed in magnetic resonance imaging of the central nervous system. The Mantoux test and FAN were negative. In addition, laboratory tests, such as a complete hemogram, Prothrombin, Bleeding and Thromboplastin time were performed.

The lesion was biopsied under local anesthesia and completely removed. The lesion was located in the masseter muscle and its clinical and histopathological characteristics. The lesion was radiologically confirmed as a fibro-calcified nodule.
region within the bundle of the superficial masseter muscle. The post-operative period progressed with esthetic cicatrization of the skin and without any neuromuscular sequelae; there were no adverse events.

The histopathological analysis revealed residual fibro-calcified nodules with central foci of coagulation necrosis (Figure 4) and negative for alcohol-acid resistant bacillus (BAAR) using Fite-Faraco staining. The nodules were surrounded by adipose and striated skeletal muscle tissues. Other types of histochemical staining were performed to determine the nature of the lesion, including Masson Trichrome, Sirius red for collagen and Weigert Orcein for elastic fibers (Figure 5). The sections stained with Sirius red and Masson Trichrome exhibited the connective nature of the lesion, with regular and concentric bundles of collagen. The slides stained with Wigert Orcein revealed no elastic fibers.

After 2 years of follow-up, no new lesions have developed.

**DISCUSSION**

The present clinical case report describes a type of lesion whose development may be related to multiple etiologies. Fibro-calcified nodules have been described in the literature as the direct consequence of inflammatory events subjacent to various pathological processes, such as tuberculosis, cysticercosis, some types of autoimmune diseases and traumatism. Dystrophic calcifications are characterized by the abnormal deposition of calcium and mineral salts in damaged or necrotic tissues and present with greater frequency in muscle trauma, systemic lupus erythematosus, burns, scleroderma and dermatomyositis. None of these clinical conditions were confirmed in the clinical history of the patient in this case study. Other additional diagnostic possibilities were considered, including infectious diseases.

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory, multi-systemic disease of an autoimmune nature with polymorphic clinical manifestations and periods of exacerbation and remission. In SLE, calcifications develop in subcutaneous soft tissues, skeletal muscles and, rarely, in the arteries in the extremities. The calcification occurs by phosphate and calcium deposition in necrotic tissues. According to the American College of Rheumatology (ACR), an SLE diagnosis requires the presence of at least four of the eleven factors that are listed in Chart 1. Although it is rare, it is possible to identify patients who have the disease without the presence of four of the eleven classification criteria. The SLE diagnosis was discarded in this clinical case because the patient did not mention any signs and/or symptoms.
classified as a criterion for the clinical diagnosis of SLE. Among the laboratory exams performed, the FAN exhibited a negative result. FAN test positivity serves as triage because the test exhibits a high degree of sensitivity (over 95%) and a high negative predictive value.

**Chart 1.** Some signs that must be considered to Systemic Lupus Erythematosus diagnosis.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar erythema</td>
<td>Erythematous lesion fixed in the malar region, flat or in relief</td>
</tr>
<tr>
<td>Discoid lesion</td>
<td>Erythematous lesion, infiltrated with adherent keratotic scales and follicular coving that developed as an atrophic and dichromate scar</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Unusual reaction caused by exposure to sunlight</td>
</tr>
<tr>
<td>Oral/nasal ulcers</td>
<td>Oral or nasopharyngeal ulcers, usually painless</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Non erosive arthritis involving two or more peripheral joints</td>
</tr>
<tr>
<td>Serositis</td>
<td>Pleurisy or pericarditis</td>
</tr>
<tr>
<td>Renal compromise</td>
<td>Persistent Proteinuria or abnormal cylindruria</td>
</tr>
<tr>
<td>Neurological alterations</td>
<td>Convulsion or psychosis</td>
</tr>
<tr>
<td>Hematological alterations</td>
<td>Hemolytic anemia or leucopenia, Lymphopenia or plateletopenia</td>
</tr>
<tr>
<td>Immunological alterations</td>
<td>Native anti-DNA or anti-Sm antibody, or presence of antiphospholipid antibody</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
<td>Abnormal antinuclear antibody titer by indirect immunofluorescence or equivalent method</td>
</tr>
</tbody>
</table>

Source: Adapted from Sato et al., 2002.

In dermatomyositis, a disease of the conjunctive tissue that results in myopathy and characteristic cutaneous manifestations, the calcifications occur as thin plates that affect the muscles. Calcium deposits may appear in the intermuscular facial planes, a finding that is rarely observed in other conjunctive tissue diseases. Patients who exhibit calcinosis or dystrophic calcifications have normal serum levels of calcium and phosphorus, unlike those patients with metastatic calcifications (which may be evidence of hyperparathyroidism) who may have elevated levels of these metabolites. In the majority of cases, dermatomyositis is associated with muscle weakness, fatigue or generalized muscle pain. In the present case, although the patient exhibited normal serum levels of calcium and phosphorus, the diagnostic hypothesis of dermatomyositis was excluded because calcinosis occurs more frequently in the pediatric age group, which comprises approximately 70% of the cases. Moreover, other indications of dermatomyositis, including muscle weakness, elevation of the serum levels of muscle enzymes and the presence of gastrointestinal compromise, were not observed in the patient in question.

According to the literature, other pathologies may be included in the differential diagnosis for cases that exhibit fibro-calcified nodules as clinical characteristics. Cysticercosis and tuberculosis are infections that are described in the literature associated with fibro-calcified nodules.

Cysticercosis is caused by the presence of *Taenia solium* larvae (cysticercus) in tissues. Cysticercosis can affect both humans and pigs because both ingest the eggs that are present in the environment. Humans can also be affected when they become hosts to the adult worms, and the eggs occlude the intestines. Studies have attempted to estimate the frequency of the musculocutaneous and visceral forms of cysticercosis using anatomical-pathological exams and necropsies to diagnose musculocutaneous cysticercosis in patients in the same region. These studies report that 42.4% of the patients with the muscular form of cysticercosis exhibited reactions to the serological tests, whereas 1.8% were nonreactive. The diagnosis of this latter group was based on the findings of hyperdense images that resemble grains of rice in the soft tissue radiographs. As there was no longer any disease activity, these images were produced by dead cysticercus that had calcified. Because the muscle infection by cisterns exhibits no clinical signs and/or symptoms and exhibits nonspecific symptomatology, it is unlikely to be identified in a living patient. In the case described here, the diagnosis of cysticercus infection was excluded because the parasitology exam with tests for proglottids was negative and because no notable alterations were observed in the central nervous system magnetic resonance imaging exam.

Tuberculosis is an infectious disease that exhibits distinct clinical forms and is caused by the penetration of *Mycobacterium tuberculosis* (Koch bacillus) into the body, through sputum or air.

McAdams et al. (1995) analyzed the main radiological findings in all of the tuberculosis stages. In the majority of the cases, the areas that were infected by *Mycobacterium tuberculosis* were cured with small pathological residues. Curing large parenchymal lesions may leave fibrous scars or persistent nodules, known as tuberculomas, and both may calcify. In addition, the cure of a secondarily infected site may result in radiologically visible scars and/or calcifications. The majority of tuberculomas are reportedly smaller than 3 cm in size, but lesions larger than 5 cm have been described. Calcified nodules generally occur 6 months or longer after the initial infection and are more common than parenchymal calcification. Nodule calcification is also more common in adults than in children. Nodule calcification may occur in extra-pulmonary sites, which are known as scrofula, and may occur by the lymphatic hematogenic dissemination of latent microorganisms. The calcified nodule presents as a
painless, slow growing nodule that is sometimes accompanied by systemic signs and symptoms. When the bacilli disseminate by blood or lymphatic metastasis involving various internal organs, the condition is termed miliary tuberculosis. In the majority of individuals, the result of primary tuberculosis is a fibro-calcified nodule (Ghon nodule) forming at the initial site of involvement, which may exhibit latent living microorganisms for several years or throughout a lifetime. Histologically, the areas of infection demonstrate collections that are circumscribed by epithelioid histiocytes, lymphocytes and multinucleated giant cells (frequently with central caseous necrosis, denominated granulomas). Calcium deposition commonly occurs in the necrotic areas.

The histological aspects of the present clinical case were consistent with this description. The presence of a circular nodule circumscribed by collagen fibers was observed and revealed by Sirius red staining. Using hematoxylin-eosin staining, the focal areas of calcification were visualized, and the conjunctive nature of the lesion was observed with Masson Trichrome staining. There was a scarcity of monomorphonuclear cells, which could characterize the longtime of progression of the nodule, which was described by the patient. Nevertheless, the laboratory exams did not reveal any apparent alterations that could be related to this pathology.

Although the clinical and laboratory findings did not contribute to the diagnosis, the morphological characteristics of the lesion strongly suggested that it was a type of dystrophic calcification that most likely resulted from an infectious process or a traumatic vascular thrombus because vascular lesions are common in the masseteric region and can regularly produce calcified thrombi with similar microscopic features.

**FINAL CONSIDERATIONS**

During the diagnostic investigation, the exam results exhibited no evidence of a relationship between the pathologies described in the literature and the lesion in question. Despite this result, the results of histochemical staining ratified the fibro-calcified aspect of the lesion, which suggested dystrophic calcification.

**REFERENCES**