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Letter to the Editor
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Rheumatoid Nodules Presenting in a Healthy Female Patient: Isolated Finding or Early Sign of a Systemic Disease to Come – Single Case Report

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Abstract

We report a case of a 28-year-old female patient with rheumatoid nodules, confirmed by histopathological examination, with clinical or serological evidence of rheumatoid arthritis or any other systemic disease. Therefore, we present a literature review relevant to the topic.

Letter to the Editor

A 28-year-old female patient came for a dermatological consultation due to hard consistency erythematous nodules, with a smooth skin surface, located at both elbows (Figures 1,2). According to the patient, lesions appeared about 1 year ago, evolving with slow and progressive growth. She denied local pain or itching. When questioned, she denied prior trauma. Her work activity and neither her hobbies involve resting on her elbows. Taking into account the aspect of the lesions, we formulate the following hypotheses: annular granuloma, tendinous xanthomas, erythema elevatum diuntinum and gouty tophus. In agreement with the patient, we performed excision of one of the lesions for histopathological examination, which showed a granulomatous inflammatory process, exhibiting a central area of necrosis surrounded by palisading epithelioid macrophages enclosed by granulation tissue containing lymphocytes and histiocytes (Figures 3,4). The histopathological findings were compatible with the diagnosis of a rheumatoid nodule. With the diagnosis, the patient was actively questioned about joint pain, which she denied. Here joints were examined and there wasn't any joint edema or pain during passive mobilization tests. However, laboratory tests were requested: rheumatoid Factor, ANA, sedimentation rate, active C protein and Anti-cyclic citrullinated peptide (Anti-CCP); all tests came out normal. Hemo gram and basic blood chemistry were also normal, including glucose levels (due to annul are granuloma hypothesis) lipidogram (tendinous xanthomas hypothesis) and uric acid (gouty tophus hypothesis). Hepatitis and HIV serologies were also negative. Rheumatoid Arthritis (RA) is a chronic inflammatory arthritis that affects nearly 1.5 million adults in the United States [1] and 2 million in Europe [2]. The predominant feature of RA is synovial inflammation manifested as swelling and tenderness of small, medium, and large joints in a symmetric pattern, with a predilection for the smaller joints of the hands and feet. It is a systemic disease with an array of extra articular manifestations [3]. This wide variety of extra-articular manifestations can develop at any time during de course of the disease, even in the early stages [4]. Cutaneous involvement is very often observe in RA, mainly in patients with more severe disease, with high titers of rheumatoid factor, usually in early disease course [3,5]. Skin manifestations of RA are academic divided in two groups: non-specific, which is more common; and specific ones [6]. The specific ones are more important since the knowledge and correct identification may allow an important diagnostic contribution to RA. Neutrophilic rheumatoid dermatosis, palisaded Neutrophilic granulomatous dermatitis, interstitial granulomatous dermatitis, rheumatoid vasculitis, pyoderma gangrenosum, is the main examples of specific RA skin manifestations. But the most common one and reason for this communication are the Rheumatoid Nodules (RN) [7]. RN occurs in 35 to 40% of patients with RA and, unlike other extra-articular manifestations, are not associated with disease severity or progression. Although rheumatoid arthritis is up to 3 times more frequent in women, RN predominates in men's. Caucasian population seems to be more commonly affected by RN too [3,5]. As the name suggests, RN present more commonly as nodular lesions, however, in initial cases, they may be recognized as small papular lesions, coalescing with the progression, forming plaques and finally becoming nodules. The skin over the lesions is generally intact. The lesions may be erythematous, xanthomatous or even retain similar color to adjacent

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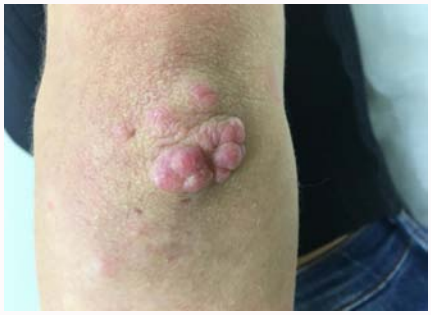

Figure 1: Nodules on the right elbow.

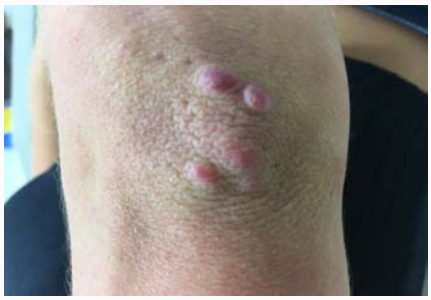

Figure 2: Nodules on the left elbow.

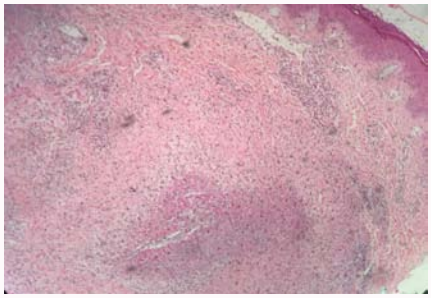

Figure 3: HE, 100x. Palisading necrobiotic granuloma surrounding a fibrinoid necrosis area.

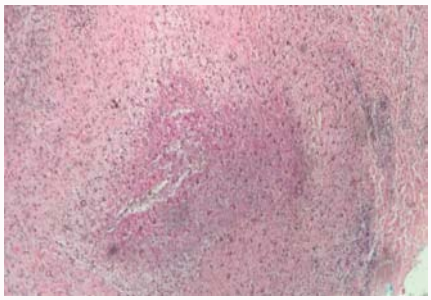

Figure 4: HE, 100x. Closer look at the fibrinoid necrosis area.

skin. Uncommonly, the lesions may present with ulceration. Atypical presentations have already demonstrated linear pathways formed by multiple small RNs [8]. The size of the nodules varies from 2 to 5 cm. They are firm, moveable and painless during palpation. They are usually found on extensor surfaces and areas of pressure or even repetitive trauma. The elbows and backs of the hands correspond to the most common topography. However, they can develop in any tendon-like structures or ligaments such as Achilles tendon and vocal cords [3]. The diagnosis can be made with clinical bases. Imaging exams can complement the evaluation, especially to rule out other pathologies [3]. When needed, histopathological examination can be performed, since the histopathological aspect of the RN is quite specific. We can identify areas of fibrinoid necrosis surrounded by mononuclear cells, characterizing palisading necrobiotic granuloma. The infiltrate consists of lymphocytes and plasma cells. A central red area due to fibrin deposition is usually seen. The lesion stands in the deep reticular dermis [5,9]. Usually specific treatment for the RN, besides the underline disease's treatment, is not necessary, since the lesions are mostly asymptomatic. Specific therapy may be needed when there is pain, nerve entrapment, or interference in function/mobility. In this or similar situations, treatment options include direct injection with corticosteroid preparations or surgical excision [3]. The relevant aspect of this report is the apparently isolated occurrence of RN. Faced with this fact, two lines of thought must be followed. Firstly, if these nodules are not associated not with RA at this moment, since it was investigated and excluded, which other unidentified systemic disease could be associated? There is some rapporteur in the literature of association with chronic hepatitis C, which was ruled out by the negative serology. Other authors mentioned the possibility of other autoimmune diseases associated, either alone or as an overlap of RA [3]. However, being no clinical signs and symptoms, what would be the benefit of insisting on an investigation only through laboratory tests? Another aspect to be considered would be the appearance of the nodules preceding the onset of arthritis, which is rare but already described in the literature, both for rheumatoid nodules in the skin and in the lungs [9,10]. In this case, in agreement with the patient, we decided to surgically excise the present lesions, along with regular follow-up every 6 months, reassuring the possibility of developing rheumatoid arthritis in the future.

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