

Bacterial Infection within a Rheumatoid Nodule: A Rarely Reported Finding

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Citation

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Abstract

We describe a palisaded granulomatous skin nodule containing bacterial rods, in a patient with rheumatoid arthritis (RA). The case emphasizes that fact that a known history of RA should not preclude submission of tissue for culture studies or careful histologic review for micro-organisms of any lesion that is interpreted as clinically and/or histologically consistent with a rheumatoid nodule. Cutaneous infection may be an etiological agent in the formation of rheumatoid nodules in a patient with known RA.

CASE REPORT

A 68 year-old male with a known history of rheumatoid arthritis (RA) developed an erythematous nodule on his left pectoral chest, which ulcerated approximately one month later. The patient denied any history of trauma to the site. When the patient was seen by a dermatologist (RG), there was a 0.5cm ulcer, 0.5cm deep, with erythematous undermined borders at the site. A provisional clinical diagnosis of pyoderma gangrenosum was made. A routine bacterial culture of the lesion showed enterococcus spp. (rare) and staphylococcus epidermidis. The patient was started on cephalexin 500mg TID and mupirocin cream. Two weeks later, the ulcer was wider measuring 1.2cm, and was surrounded by a 3.0cm zone of erythema and induration. There was no axillary or cervical lymphadenopathy. A repeat tissue culture showed enterococcus spp. (rare). Blood cultures were not performed as the patient showed no signs of a systemic infection. A complete excision of the lesion was performed. The lesion did not recur following excision.

The patient had a known history of RA (Rheumatoid Factor +) since 1986, with multiple joint involvement, and multiple rheumatoid nodules overlying the elbows, metacarpal-phalangeal joints of both hands, and metatarsal-phalangeal joints of the feet. The patient had a positive family history for RA.

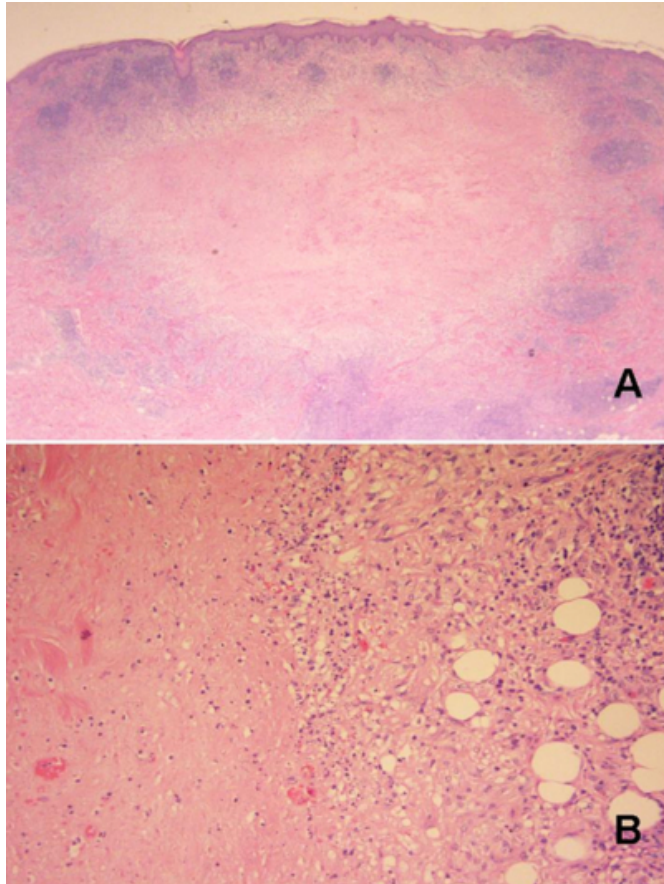
For the past 10 years, the patient had been on methotrexate and was taking 17.5mg per week at the time of presentation, in addition to folic acid, ranitidine, and oxaprolin. Past

medications for RA had included NSAIDs, hydroxychloroquine, azulfidine, aspirin, sulfasalazine, gold and prednisone.

The excisional biopsy demonstrated a large well-circumscribed area of tissue necrosis, nuclear fragments, basophilic debris and fibrin deposition, extending from the superficial dermis to superficial subcutaneous adipose tissue (Fig. 1).

Figure 1

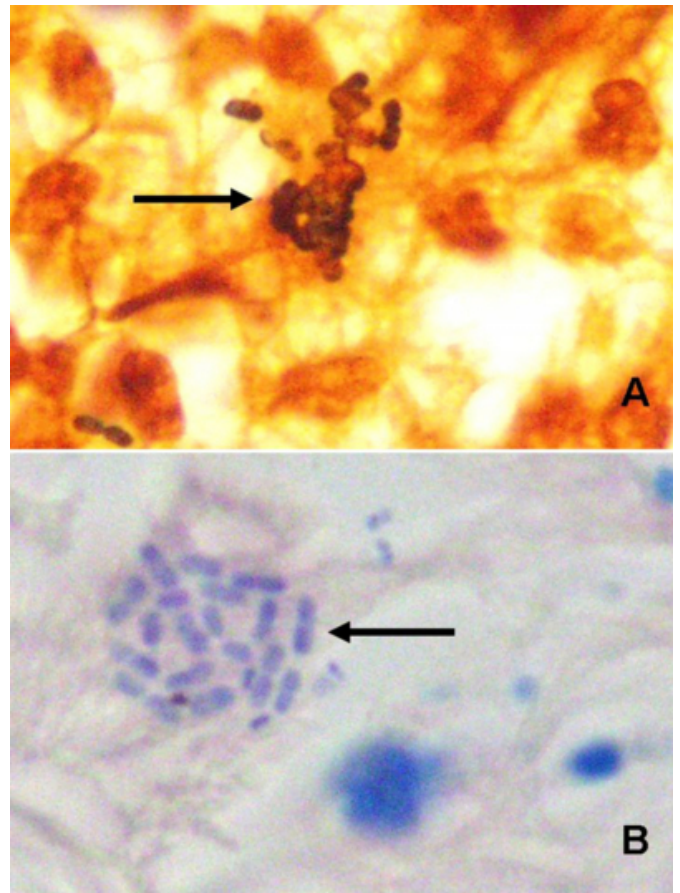
Figure 1: (a) Palisaded granulomatous dermatitis with central necrosis and fibrin deposition (hematoxylin and eosin, 4x). (b) Interface between area of central necrosis and fibrin deposition (left) and peripheral granulomatous inflammation (right) (hematoxylin and eosin, 20x).



This area was surrounded by numerous histiocytes and occasional foreign body-type cells in a palisaded arrangement. The adjacent stroma showed evidence of acute vasculitis and a perivascular and interstitial lymphocyte and plasma cell infiltrate, with occasional eosinophils. The lesion abutted on the overlying epidermis, which was ulcerated. In view of the clinical history and histologic features, a diagnosis of rheumatoid nodule was made. Polarization was negative for a foreign body/material. PAS, Gram, AFB, and AFB-Fite stained sections were negative for definitive fungi, bacteria, or acid-fast bacteria, respectively. However, additional Warthin-Starry (silver) and Giemsa stained sections demonstrated rod-shaped micro-organisms singly and in clusters in the area of necrosis in the deeper portions of the lesion (Fig. 2).

Figure 2

Figure 2: (a) Warthin-Starry and (b) Giemsa stained sections demonstrate large bacterial rods (arrows) within areas of necrosis (100x magnification with oil immersion).



No definitive micro-organisms were seen in the area of ulceration. The case was reviewed within the Department of Laboratory Medicine (Microbiology) at the University of Connecticut Health Center. The organisms were interpreted as morphologically consistent with large bacterial rods, unclassifiable. Tissue from the excision specimen was formalin-fixed and paraffin-embedded, and therefore unavailable for culture studies. Polymerase chain reaction (PCR) on paraffin-embedded tissue was negative for bacteria or acid fast bacilli using 16sRNA, hsp65 and rpoB gene primers.

DISCUSSION

Skin lesions are relatively common in patients with RA, occurring in approximately 20% of patients [1]. The “classic” skin lesion is the rheumatoid nodule, but a spectrum of cutaneous lesions has been defined [1]. Skin lesions usually develop around joints and at acral sites, but other sites of involvement including the trunk, as in this case, have been described [1]. In addition, a superficial

rheumatoid nodule may ulcerate or “perforate” the overlying epidermis [2]. Superimposed infection of rheumatoid nodules has rarely been reported at both extra-cutaneous and cutaneous sites [3,4,5,6,7]. A review of the literature revealed only five reports of rheumatoid nodules complicated by secondary infection [3,4,5,6,7]. In this regard, fungal (aspergillus) colonization of pulmonary rheumatoid nodules [3,4], and *Staphylococcus aureus* [5], *Acinetobacter calcoaceticus* (a rare enterococcus) [6], and leishmaniasis [7] infections of cutaneous rheumatoid nodules have been reported. A recent extensive review of 43 patients with rheumatoid arthritis did not document evidence of infection in associated cutaneous lesions, the most common of which was palisading granulomatous inflammation with necrobiosis (i.e.; rheumatoid nodule) [1].

Herein, we report a case of a rheumatoid nodule containing micro-organisms, morphologically consistent with large bacterial rods. However, the lack of culture or molecular (PCR) confirmation precluded a definitive conclusion about their exact classification. Tissue was not submitted for culture studies. We postulate that the numbers of micro-organisms present was below the level of detection by the PCR technique. In addition, formalin fixation can reduce the sensitivity of PCR assays due to reduced DNA template yield and quality.

Factors that have been implicated in the formation of rheumatoid nodules include an immune-complex mediated vasculitis [1] and/or trauma [8] which result in ischemic damage to subcutaneous tissues and a palisaded granulomatous inflammatory reaction. While this case may represent secondary infection within a previously present rheumatoid nodule in a patient with rheumatoid arthritis, we cannot exclude that the histologic features represent a “rheumatoid nodule-like” response to a primary infectious focus in this patient (i.e.; cutaneous infection producing rheumatoid nodule-like changes in a predisposed individual). Indeed, it raises the question whether cutaneous infection may be another etiological factor in the formation of rheumatoid nodules in patients with known RA. Of note, skin lesions in patients with sarcoidosis (another systemic granulomatous disease) have been described to occur secondary to infection, in addition to trauma and foreign bodies [9]. Furthermore, methotrexate (an immunosuppressive agent), which this patient was taking, has been shown to be associated with appearance and progression of rheumatoid nodules [10].

This case represents a necrotizing skin lesion, with the clinical and histological features of a rheumatoid nodule, but with “superimposed” bacterial infection. The case highlights that a high index of suspicion for the diagnosis of cutaneous infection should be maintained, both by both clinicians facing ulcerating/perforating skin nodules and dermatopathologists reviewing skin biopsies demonstrating rheumatoid nodule-like changes (i.e.; palisading granulomatous dermatitis), in patients with a known history of RA. The histologic features of a rheumatoid nodule do not rule out the possibility of an associated infection. Cutaneous infection may be an etiological agent in the formation of rheumatoid nodules in patients with known RA.

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