Benign rheumatoid nodules in a woman with chronic lymphocytic leukaemia and borderline lepromatous leprosy

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Abstract

Objectives—To report benign rheumatoid nodules in a woman with chronic lymphocytic leukaemia and borderline lepromatous leprosy and to summarise the features of the patients with adult onset benign rheumatoid nodules.

Methods—A 66 year old woman with chronic lymphocytic leukaemia and borderline lepromatous leprosy who presented with subcutaneous elbow nodules, which were at first suspected to represent either progression of her haematological disease or leprosy, is described. The clinical characteristics of our patient and previous reports of another 24 subjects with adult onset benign rheumatoid nodules are reviewed.

Results—Biopsy of the patient’s subcutaneous lesion disclosed the histopathology of a rheumatoid nodule; serological and clinical evaluations for rheumatoid arthritis and other rheumatoid nodule associated systemic diseases were negative. Adult onset benign rheumatoid nodules are clinically and histologically identical to those found in patients with rheumatoid arthritis. They often appeared in women during their 20s, frequently resolved spontaneously or were adequately treated by excision, and recurred in about one third of patients. The lesions were located in the ocular adnexa in 60% of patients. The most common lesional sites in patients with non-ocular benign rheumatoid nodules were the elbows, feet, and knees. None of these patients subsequently developed rheumatoid arthritis or other rheumatoid nodule associated diseases during follow up periods of as long as 20 years.

Conclusion—The appearance of subcutaneous nodules is often the harbinger of an associated systemic disorder. Although benign rheumatoid nodules occur infrequently in adults, they should be considered in the differential diagnosis of new nodular lesions.


Benign rheumatoid nodules usually appear in childhood and are morphologically and histologically indistinguishable from the subcutaneous nodules found in patients with rheumatoid arthritis. We describe the case of a 66 year old white woman with chronic lymphocytic leukaemia and borderline lepromatous leprosy who developed benign rheumatoid nodules. Her subcutaneous nodules initially appeared at the age of 61 years and have remained asymptomatic. To the best of our knowledge this subject is the oldest reported patient with benign rheumatoid nodules and the only reported case of this disorder in a person with leukaemia and leprosy.

A review of the literature shows that adult onset benign rheumatoid nodules have previously only been reported in 24 subjects. Underlying disorders in several of these patients have included hypertension, local trauma, and pregnancy, though most subjects had no associated disorder. As in our patient, no clinical nor serological evidence of rheumatoid disease developed, even after long term follow up.

Case report

A 56 year old woman was diagnosed with chronic lymphocytic leukaemia in January 1982. She was treated intermittently with chlorambucil and prednisone over the next three years. Beginning in November 1986, monthly treatment with fludarabine was initiated for progressive disease. She achieved a partial remission in April 1987 after receiving five courses of this treatment.

In February 1987 a chronic rash on her right arm was noted to have become erythematous. By April 1987 additional infiltrative lesions were present on her arms, legs, abdomen, and back. A lesional biopsy sample established the diagnosis of borderline lepromatous leprosy; additional information was obtained that armadillos were present around the patient’s house in Sealy, Texas. Treatment with clofazimine and dapsone by mouth was started. She stopped developing new lesions and her ulcerated plaques and nodules progressively healed. In September 1991 her lepromatous disease was found to be inactive, yet she continues her life long treatment with dapsone.

When the cutaneous lesions of leprosy began to develop, the patient also noted the appearance of tender subcutaneous nodules overlying her elbows. The nodules were thought to represent neural disease secondary to leprosy. Initially the nodules became less
painful and softened after antimycobacterial treatment was started. However, despite an improvement in her leprosy related skin lesions, her elbow nodules persisted. When the patient was seen in November 1990 her chronic lymphocytic leukaemia had progressed. Treatment with subcutaneous interferon and prednison by mouth for five days each month was begun, with partial control of her disease.

Clinical examination in August 1991 showed asymptomatic, bilateral, 1·0×1·5 cm subcutaneous nodules at the olecranon (fig 1). They were not fixed to the underlying bone; the overlying skin did not adhere to the nodules and could easily be moved. The histological features of a lesional biopsy sample were characteristic of a rheumatoid nodule. There was a palisading granuloma surrounding a central area of fibrinoid necrosis located in the deep dermis and subcutaneous fat. The inflammatory infiltrate was predominantly composed of monocytes adjacent to the central necrosis and lymphocytes located more peripherally; there was no evidence of malignancy (fig 2). Special stains were negative for fungi and mycobacteria.

No joint pain or morning stiffness was present; repeat examination did not show any bony abnormalities of the hands or other sites. Serological evaluation for rheumatoid factor was negative. Thus clinicopathological correlation of the lesions that had been present for five years was consistent with the diagnosis of benign rheumatoid nodules.

Discussion

Benign rheumatoid nodules are subcutaneous nodules, histologically indistinguishable from those occurring in patients with rheumatoid arthritis, that typically occur in otherwise healthy children who have neither clinical nor serological manifestations of an associated rheumatological or other disease. These nodules have also been designated as non-rheumatoid rheumatoid, palisading granuloma nodosum, pseudorheumatoid, pump bumps, rheumatic-like, rheumatoid-like, and subcutaneous palisading granuloma. Microscopic examination shows a homogeneous central area of fibrinoid necrosis surrounded by palisading fibroblasts, macrophages, and monocytes; vascular connective tissue with lymphocytes and plasma cells comprise the peripheral zone of the nodule. In addition to benign rheumatoid nodules, subcutaneous nodules with similar histopathological features may be observed in patients with agammaglobulinaemia with polyarthritis, subcutaneous granuloma annulare, Jaccoud’s syndrome, necrobiosis lipoidica, rheumatic fever, rheumatoid arthritis, rheumatoid nodulosis, and systemic lupus erythematosus.

The initial appearance of benign rheumatoid nodules in a person aged 18 years or older is rare. Including our patient, only 25 subjects with adult onset benign rheumatoid nodules have been described. Previously reported patients with ‘adult onset benign rheumatoid nodules’ who subsequently developed rheumatoid arthritis or had a positive rheumatoid factor, or both, were excluded from this review. Reports without histological confirmation of the subcutaneous nodules were also not included. Of the subjects, including this patient, with adult onset benign rheumatoid nodules, 14 were women, and eight were men; the sex was not reported for three patients.

When the subcutaneous nodules were initially noted the patients ranged in age from 18 years to 61 years (this paper) (median age 23 years). The nodules were often found around the eyes (15 patients), the elbows (three patients, including this patient), feet (three patients), knee (two patients), ankle, chin, hands, or shoulders (one patient each) (table). One of the patients had ocular and non-ocular benign rheumatoid nodules: a 26 year old white woman with a previous history of recurrent nodules at the lateral and medial canthus of both eyes for five years subsequently developed a similar lesion on her chin.

The benign rheumatoid nodules occurred in eight (36%) of 22 subjects. Follow up of the 25 patients with adult onset benign rheumatoid nodules ranged from less than one year to as long as 20 years; the median follow-up was 4 years.
up time for all patients was five years. None of
these subjects developed serological or clinical
symptoms of rheumatoid arthritis or another
disease associated with rheumatoid nodules
during that period.

Adult onset benign rheumatoid nodules of
the ocular adnexa typically occurred in young
women (10 of 15 patients), often resolved
either after excision or without treatment, and
only recurred in approximately one third of
subjects.² ⁹ ¹⁰ Specifically, the patient’s age at
the onset of their nodules ranged from 18 to
30 years (median 21 years). Thirteen of the
patients were reported by Rao and Font;² they
observed that “the lesions had a tendency to
regress spontaneously.”² Neither treatment nor
follow up was described for a 29 year old
woman with multiple episcleral, eyebrow,
eyelid, and orbital benign rheumatoid
nodules.⁸ The remaining patient with ocular
benign rheumatoid nodules was a 23 year old
woman with multiple recurrent lesions.¹⁰
Although new nodules would appear after
excision, intralesional injection of cortico-
steroids resulted in regression of the lesions.¹⁰

Compared with the adults with ocular
benign rheumatoid nodules, non-ocular adult
onset benign rheumatoid nodules were usually
observed in slightly older women (five of eight
patients) who ranged in age from 20 to 61 years
(median 26 years) (table). The lesions recurred
in half (4/8) of these subjects. Similar to the
patients with ocular benign rheumatoid
nodules, the lesions spontaneously resolved in
several of the subjects with non-ocular benign
rheumatoid nodules: in five (63%) of eight
subjects the nodules regressed without treatment
within four months to 13 years (median seven years).
Although the nodules were adequately excised without subsequent recurrence in two patients, the lesions again appeared after excision in four patients. A 20

year old woman with multiple recurrent
plantar nodules did not respond to several
attempted therapeutic interventions: excisional
biopsy, intralesional methylprednisolone acetate
injections, aufranoin by mouth, rest, or
shoe cushioning.¹ Interestingly, all of her
lesions began to soften within three days of the
delivery of her first child and had completely
disappeared within two weeks of the delivery;
seven months later, two small plantar nodules
reappeared.¹ In contrast, a 26 year old white
woman with multiple benign rheumatoid
nodules noted that the onset of recurrent
lesions was temporarily associated with
pregnancy.³

In association with pregnancy,¹ ³ several of
the subjects with non-ocular adult onset benign
rheumatoid nodules had previous or concurrent,
local or systemic disorders. Injections and trauma
to the deltoid areas of a 26 year old man
preceded the appearance of benign
rheumatoid nodules located on the cor-
responding shoulders.³ Hypertension, requiring
systemic treatment, was present in two
patients.⁴ ⁵ Two patients had also had a splen-
ectomy to treat a traumatic rupture from an
automobile accident⁴ or thrombocytopenic
purpura⁵; the elbow nodules of the latter
patient (which had been present for seven
years) resolved spontaneously during the same
year that the operation was performed.⁴ ⁵

The number of patients with non-ocular adult onset
benign rheumatoid nodules is too small to
establish definitively whether any of these
disorders are indeed causally related to the
development, persistence, or resolution of benign
rheumatoid nodules in these subjects.

¹ Sibley J T. Pregnancy and benign rheumatoid nodules
² Rao N A, Font R L. Pseudorheumatoid nodules of the
³ Williams H J, Bidulph E C, Coleman S S, Ward J R.

Abbreviations: NS = not stated.
† Location of original or recurrent lesions, or both.
‡ Successful or (+) unsuccessful treatment (either no resolution or recurrence of lesion).
§ Recurrence of a nodule at site of previous lesion after successful treatment or spontaneous resolution of previous lesion.
¶ Number of years that the patient has been observed since the benign rheumatoid nodules were diagnosed during which neither rheumatoid arthritis nor any other disease associated with rheumatoid nodules has occurred.
14 Fowler J K. Subcutaneous nodules occurring in an adult not the subject of rheumatism. BMJ 1884; i: 107.
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