complex disease. In 2 out of 8 cases (1 of PL acuta and 1 of PL chronica) IgM and C deposition were found concomitantly at the DEJ. Hence, it cannot be excluded that, during a certain stage, immune complex formation at this site might play a certain role in the disease. It might, however, be more fruitful to investigate the possibility of other reaction mechanisms in order to cast more light on the pathogenesis of PL.

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Granuloma Annulare: Histopathologic and Direct Immunofluorescent Study

Håkan N. Thyresson, John A. Doyle and Richard K. Winkelmann

Department of Dermatology, Mayo Clinic, Rochester, Minnesota 55901, USA

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Abstract. Eighteen cases of granuloma annulare were classified histopathologically and examined by direct immunofluorescence. The three different histopathologic types of granuloma annulare were compared with the result of immunofluorescence examination. No features of leukocytoclastic vasculitis were seen. Direct immunofluorescence of granuloma annulare does not reveal any consistent diagnostic pattern. Dermal desposition of fibrin in necrobiotic areas were noted in 8 cases of 18. Blood vessel and/or basement membrane deposition of IgM and C3 was inconsistent and does not support an immune complex vasculitis. Direct immunofluorescence is useful in studying the pathogenesis of granuloma annulare. The finding of fibrin, together with the histology, suggests to us a delayed hypersensitivity reaction as the dominant pathogenic event.

Key words: Granuloma annulare; Direct immunofluorescence; Delayed hypersensitivity; Fibrin

We report here 18 cases of granuloma annulare examined by direct immunofluorescent technique and a comparison of these findings with the histologic features. The histopathology of granuloma annulare is characterized by three different patterns: 1) the mononuclear-histiocytic infiltrative type; 2) the palisading granuloma type, and 3) the epithelioid nodule type (7).

Immunofluorescence studies of granuloma annulare have reported findings of fibrin deposition corresponding to the necrobiotic areas as the dominant feature (6) as well as depositions of fibrin, C_3 and IgM in the blood vessels and along the basement membrane (2). The former have been interpreted as evidence of a delayed hypersensitivity reaction and the latter could indicate a chronic immune vasculitis as the main pathogenic event in granuloma annulare.

The present report was conducted to evaluate whether different patterns of direct immunofluorescence are associated with the different histiologic types seen in granuloma annulare.

METHOD

Histopathology. Eighteen cases of granuloma annulare seen at the Mayo Clinic between 1975 and 1979 were studied. 4 mm punch biopsy material was obtained, fixed in formalin and multiple sections stained with hematoxylin and eosin and were examined for (*a*) the type and degree of mononuclear-histiocytic infiltrate surrounding the vessels and between collagen fibers; (*b*) amount and location of necrobiosis; (*c*) formation of typical palisading granulomas; (*d*) presence of epithelioid nodules, and (*f*) features consistent with leukocytoclastic vasculitis.

Direct immunofluorescence procedure. 4 mm punch biopsy samples from corresponding sites and patients

Table I. *Granuloma annulare histiologic types*

	Cases *n*	%	Direct immunofluorescence: Negative	Direct immunofluorescence: Positive
Mononuclear–histiocytic infiltrate type	14	78	3	11
Palisading granuloma type	3	7	–	3
Epithelioid nodule type	1	5	1	–
Total	18		4	14

were obtained for direct immunofluorescent study. The biopsies were immediately snap-frozen in liquid nitrogen, −70°C; serial 4 μm cryostat sections were examined by standard direct immunofluorescence technique. Using a method previously outlined (4), monospecific FITC-conjugated antisera to human IgG, IgM, IgA, C3 and fibrin (Hyland and Behring Laboratories) were used. Specificity of conjugates was ascertained by Ouchterlony immunodiffusion.

RESULTS

Three distinct histologic patterns could be recognized, as previously reported by Umbert & Winkelmann (7). 1) The most frequent pattern, *the Mononuclear-histocytic infiltrative type:* 14 of 18 cases (78%) consisted of perivascular cuffing predominantly of lymphocytes, and patches of scattered histiocytic cells infiltrating between the collagen fibers with minimal necrobiosis. 2) *Palisading granuloma type:* 3 of 18 cases (17%) showed typical granuloma with central necrobiosis surrounded by a rim of histiocytes and lymphocytes, located in the upper and mid-dermis. All three biopsy specimens were from the distal portions of the extremities in our study. 3) *The epithelioid nodule type:* 1 of 18 cases (5%) showed epithelioid nodules. The histiocytes aggregated in nodular morphology, with occasional giant cells and with no marked necrobiosis.

No features of leukocytoclastic vasculitis were recognized in the 18 cases examined. Table I shows the histopathologic types of granuloma annulare noted, together with the results of the immunofluorescence study. Fourteen cases of the 18 had positive immunofluorescence findings; only 4 were completely negative. The result of the immunofluorescence study in the 14 cases of granuloma annulare within the three histiologic types are shown in Table II. Eleven cases of the mononuclear–histiocytic infiltrative type showed positive immunofluorescence. Of these, 5 cases had positive fibrin depositions in the necrobiotic areas. In 4 cases this was the only finding; the fifth case also had C3 deposit in the necrobiotic area and along the basement membrane. Six cases had a mixture of findings, 4 having IgM cytoid bodies, the other 2 showing fibrin, IgM and C3 in the blood vessels and along the basement membrane. The remaining 3 cases showed no positive immunofluorescence.

The palisading granuloma type. All 3 cases had deposition of fibrin in the necrobiotic areas. One case showed granular IgM and C3 in the blood vessels along the basement membrane and IgM cytoids.

The epithelioid nodular type of granuloma annulare did not show any positive immunofluorescence.

DISCUSSION

Granuloma annulare is a benign reactive process, reversible and generally non-destructive. The clinical picture, evolution and frequent spontaneous resolution are consistent with a type IV hypersensitivity reaction. The anatomical location, age, trauma and the individual immune status will modulate the tissue response. The antigenic stimuli for granuloma annulare are not known, but are prob-

Table II. *Direct immunofluorescence of granuloma annulare*

	Cases *n*	Negative	Blood vessel: IgM	Blood vessel: C3	Blood vessel: Fibrin	Dermo-epidermal junction: IgM	Dermo-epidermal junction: C3	Cytoids IgM	Dermis: Fibrin	Dermis: C3
Mononuclear–histiocytic infiltrative type	14	3	1	2	1	1	2	4	5	1
Palisading granuloma type	3	–	1	1	–	1	–	1	3	–
Epithelioid nodule type	1	1	–	–	–	–	–	–	–	–
Total	18	4	2	3	1	2	2	5	8	1

ably varied. No direct evidence for the presence of circulating immune complexes has been reported. Our previous and present studies have not found a leukocytoclastic vasculitis as a feature in the histology of granuloma annulare, in contrast to other investigations (1, 2). In our experience the main histologic feature present in the three subtypes of granuloma annulare is a macrophage–histiocytic reactivity; the mononuclear perivascular inflammation and focal necrobiosis could be the primary events (8).

Immunofluorescence of granuloma annulare does not reveal an overall consistent diagnostic pattern (5). However, the palisading granuloma type has a consistent finding of only fibrin in the necrobiotic areas. The mononuclear–histiocytic infiltrative type had mixed features, but fibrin deposition was frequent.

Blood vessel and/or basement membrane depositions of IgM and C3 were inconsistent. The histology of granuloma annulare and the inconsistent findings of IgM, C3 do not support an immune complex vasculitis as pathogenic event.

Examination of granuloma annulare by direct immunofluorescence is useful in studying the pathogenesis. The finding of fibrin, together with the histology, suggests to us a delayed hypersensistivity reaction as the dominant pathogenic event (3).

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Antichlamydial Antibodies in Chronic Palmoplantar Pustulosis

Christer T. Jansén, Antero Hollmén, Reino Pajarre and Pertti Terho

Departments of Dermatology and Virology, University Hospital, Turku, and Department of Dermatology, Satalinna Hospital, Satalinna, Finland

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Abstract. Serum antichlamydial antibodies were determined with an immunofluorescence method in 40 patients affected by palmoplantar pustulosis (PPP). Antibody titre ≥16 was found in 53% of the cases, the titre being ≥64 in 38% of the patients. By comparison, a titre of ≥64 was found in 13% out of 55 psoriatics, in 12% out of 41 eczema and urticaria patients, and in 3% out of 37 healthy controls. The difference between the results from the PPP patients and that of the healthy controls was statistically significant ($p<0.01$). In only 8 of the 40 PPP patients was any additional evidence found of a previous venereal infection. The possibility that PPP may represent an abnormal reaction to infectious agents, e.g. Chlamydia, is discussed.

Key words: Palmoplantar pustulosis; Chlamydia; Venereal disease

Palmoplantar pustulosis (PPP) is a chronic dermatosis of the hands and feet, which accounts for some 0.4% of the patient admissions to dermatological clinics (6). The etiology of this disorder is still unknown, but the most long-favoured theory links PPP to the existence of a chronic focus of infection, usually thought to be bacterial in origin (1). Several large patient series, however, have failed to demonstrate any causal relationship between PPP and focal infections (3, 6, 7). Notwithstanding this, textbooks continue to recommend eradication of infectious foci as a therapy for PPP (2, 4, 11), and in many dermatology departments a search for possible infectious foci is included in the routine investigation program of PPP patients. When, in our departments, a test for serum antichlamydial antibodies was included in the search panel, an unexpectingly large number of highly positive titres were encountered. In this paper the chlamydial serology results of 40 consecutive PPP patients is presented, together with data on possible venereal diseases.