

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 hypersensitivity reaction as the dominant pathogenic event (3).

REFERENCES

1. Ackerman, A. B.: Histologic diagnosis of inflammatory skin diseases. A method of pattern analysis. Lea & Febiger, Philadelphia, 1978.
2. Dahl, M. V., Ullman, S. & Goltz, R. W.: Vasculitis in granuloma annulare, histopathology and direct immunofluorescence. *Arch Dermatol* 113: 463-467, 1977.
3. Dvorak, H. E., Mihm, M. C. & Dvorak, A. M.: Morphology of delayed-type hypersensitivity reaction in man. *J Invest Dermatol* 67: 391-401, 1976.
4. Jordon, R. E., Triftshauser, C. T. & Schroeter, A. L.: Direct immunofluorescent studies of pemphigus and bullous pemphigoid. *Arch Dermatol* 87: 540, 1971.
5. Niebor, C. & Kalsbeck, G. L.: Direct immunofluorescence studies in Granuloma annulare, Necrobiosis Lipoidica and Granulomatosis Disciformis Miescher. *Dermatologica* 158: 427-432, 1979.
6. Umbert, P. & Winkelmann, R. K.: Granuloma annulare, direct immunofluorescence study. *Br J Dermatol* 95: 487, 1976.
7. — Histologic, ultrastructural and histochemical studies of granuloma annulare. *Arch Dermatol* 113: 1618-1686, 1977.
8. Wolff, H. H. & Maciejewski, W.: The ultrastructure of granuloma annulare. *Arch Dermatol Res* 259: 225-234, 1977.

Antichlamydial Antibodies in Chronic Palmoplantar Pustulosis

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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 unexpectedly 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.

Table I. *Antichlamydial antibody titres in the palmoplantar pustulosis patients and in the three control groups*

Population	Total	Antichlamydial titre			Statistical significance ^a
		≤8	16-32	≥64	
Palmoplantar pustulosis	40	19	6	15	$p < 0.01$
Psoriasis vulgaris	55	37	11	7	NS
Eczema & urticaria	41	27	9	5	NS
Healthy blood donors	37	30	6	1	-

^a Statistical significance of any difference as compared with the healthy blood donor group. NS = not significant.

MATERIAL AND METHODS

Patients and controls

Forty consecutive patients with palmoplantar pustulosis, attending the departments of dermatology of the Turku University Hospital and Satalinna Hospital were included in the study. The diagnosis was based on a typical clinical picture and the exclusion of contact sensitivity and bacterial or fungal infections. The mean age of the patients was 44 years, and the mean duration of the disease was 3.9 years. Twenty-seven of the patients were female.

A group of healthy control persons was represented by 37 consecutive blood donors at the Turku University Hospital blood service; 27 of them were female, and the mean age was 33 years. In addition, a group of 55 psoriasis patients and a group of 41 patients suffering from either chronic urticaria (16 patients) or nummular eczema were studied. The mean age in the psoriasis group was 43 years; 23 were females. The corresponding figures for the urticaria-eczema group were 47 years and 27 females.

Antichlamydial test

Indirect immunofluorescence test (IF) was performed with the single antigen (L2) method reported by Saikku & Paavonen (12) and by Terho (16). Briefly, appropriate serum dilutions were placed on slide-grown L2-infected McCoy cells and incubated for 1 h at 37°C. After washing, antihuman-FITC conjugated antiserum (rabbit) was added and incubated as above.

The fluorescence present in chlamydial inclusions was detected by UV-microscope using an FITC filter, and the titre was determined.

The Chlamydia culture was done as reported by Terho (15).

RESULTS

General findings

Five PPP patients gave a history of a previous genito-urinary tract infection, 3 had had conjunctivitis, and 2 had suffered from minor joint symptoms. One female patient had a history of salpingo-oophoritis and one male reported prostatitis. At the time of the study, the prostatic status of all

men was normal, and no signs of ocular or joint disease were detected in any of the patients. No patient was aware of familial cases of rheumatoid diseases, and the antinuclear antibody test (ANF) proved negative in all cases by the immunofluorescence technique.

Three patients were suspected of having a dental infection, one patient was suffering from sinusitis, and one from tonsillitis. In 13 patients, cultures of throat bacteria had been made, but none grew pathogenic organisms. The anti-streptolysin titre was elevated in 3 out of the 38 patients tested, and the antistaphylolysin titre in one out of 20 patients.

Antichlamydial antibodies

The results of serum antichlamydia IF determinations are given in Table I. A titre of ≥ 16 was found in 53% of the PPP patients, in 33% of the psoriatics, in 34% of the eczema-urticaria patients, and in 19% of the healthy controls. In particular, the proportion of cases with significantly high titres (≥ 64) was prominent in the PPP group (38%) as contrasted with 13%, 12%, and 3% in the other groups. The differences between the results of the PPP patients and those of both the normal controls and the eczema-urticaria group were, in both cases, statistically significant ($p < 0.01$). The difference between the PPP patients and the psoriatics, however, did not reach statistical significance ($p = 0.1$), possibly due to the small number of patients.

Venereal disease

During the history taking, every PPP patient was questioned regarding any past venereal disease. In only one case was a positive response obtained, concerning a male patient who had contracted gonorrhoea 20 years earlier; this had been treated with penicillin in adequate doses. The gonococcal

complement fixation test (GCFT) was performed in 25 of the PPP patients. In 7 cases a low-titre positive result (≤ 4) was obtained; 3 of those patients demonstrated a strong antichlamydial reaction, (≥ 64), and in a further 3 patients the antichlamydial titre was weakly or moderately elevated (8 to 32). The *Treponema pallidum* hemagglutination assay (TPHA) was performed in 36 of the PPP patients, always with negative results.

In 8 PPP patients, all below 50 years of age, and where the antichlamydial antibody titre was high (≥ 64), a cervical and/or urethral chlamydial culture was performed. The only positive result was obtained from the cervix of a 32-year-old female, whose dermatosis had lasted for 5 months. During a 12-day course with 1 g tetracycline daily the pustulosis of this patient abated considerably, but it reappeared upon stopping the medication. A post-treatment culture for chlamydia was negative.

DISCUSSION

Our general data conform with the opinion of several authors, that pyogenic infectious foci cannot be held as a common denominator for patients with palmoplantar pustulosis (3, 6, 7). The occurrence of a higher than expected frequency of moderate and high antichlamydial antibody titres in PPP patients, however, is a novel finding, and calls for an explanation.

Besides trachoma and lymphogranuloma venereum, Chlamydia are presently recognized as causative organisms of non-gonococcal urethritis and venereal inclusion conjunctivitis; in addition a pathogenic role for Chlamydia has been demonstrated in salpingo-oophoritis and in cases of neonatal pneumonia (13). As few population studies have yet been made, the actual incidence of positive chlamydial antibody titres in the general population has not yet been reliably worked out. However, the incidence of positive (≥ 16) titres found in our healthy control group (19%) and in the eczema-urticaria patient group (34%) conforms with earlier reports in the literature. Thus, ≥ 16 titres were found in 8 out of 58 females (14%) attending a family planning association clinic (10), and in 9 out of 32 (28%) healthy army recruits (16). In another study, titres ≥ 8 were found in 9 out of 25 healthy male medical doctors and students (9).

Significantly elevated titres (≥ 64) are rare in control populations; in the cited studies frequencies of

respectively 5%, 3% and 12% were reported. Our findings of ≥ 16 titres in 53% and ≥ 64 titres in 38% of the PPP patients contrasts with the observations in our control group and those of others. In our study, this difference reached statistical significance ($p < 0.01$).

Interesting analogies exist between palmoplantar pustulosis and Reiter's disease (RD). In both conditions, the palms and soles are the predilection sites for a deep-seated, sterile cutaneous pustulation. Reiter's disease is accompanied by a psoriasiform, scaling dermatosis in some 10–20% of the cases (5, 8), and PPP has been reported to coexist with psoriasis in 5–30% of the cases (6, 14). Furthermore, positive antichlamydial titres have been found in a substantial proportion of RD patients. Kousa et al. (9) in a study on 104 male RD patients found a ≥ 8 antichlamydial antibody titre in 87% of the cases, using an IF technique similar to ours; in 64% of the cases the titre was 64 or greater. In the same study, 87 out of the 104 RD cases were found to be related to past or recent venereal infection, and 86% of the patients had symptoms or signs of a lower urogenital tract inflammation associated with the first attack of the disease. In contrast, in our PPP series the onset of the disease was temporally related to a recent genital Chlamydia infection in only one case, and only one patient reported a history of a previous venereal disease. In addition, the gonococcal complement fixation test gave a low titre positive result in 7 PPP patients. In a total of 8 out of 40 PPP patients (20%) a past venereal disease could thus possibly be implicated.

Although, therefore, palmoplantar pustulosis cannot be regarded as an indicator of past venereal disease, the association with elevated antichlamydial antibody titres may point towards a proneness to exaggerated immunological reactions to certain infectious agents such as Chlamydia. Interestingly, systemic treatment with tetracycline, an agent possessing antichlamydial activity, has been shown to have a therapeutic effect in some PPP patients (14, 17). Any firmer confirmation of the possible pathogenic role of Chlamydia in palmoplantar pustulosis will require further studies.

REFERENCES

1. Andrews, G. C. & Machalek, G. F.: Pustular bacterid of the hands and feet. *Arch Dermatol Syphilol* 32: 837, 1935.
2. Domonkos, A. N.: *Andrew's Diseases of the Skin*. W. B. Saunders, Philadelphia, 1971.

3. Everall, L.: Intractable pustular eruptions of the hands and feet. *Br J Dermatol* 69: 269, 1957.
4. Fitzpatrick, T. B., Eisen, A. Z., Wolff, K., Freedberg, I. M. & Austen, K. F.: *Dermatology in General Medicine*. McGraw-Hill, New York, 1979.
5. Hancock, J. A. H.: Surface manifestation of Reiter's disease in the male. *Br J Vener Dis* 36: 36, 1960.
6. Hellgren, L. & Mobacken, H.: Pustulosis palmaris et plantaris. *Acta Dermatovener (Stockholm)* 51: 284, 1971.
7. Ingram, J. T.: Pustular psoriasis. *Arch Dermatol* 77: 314, 1958.
8. Kousa, M.: Clinical observation on Reiter's disease with special reference to the venereal and non-venereal etiology. *Acta Dermatovener (Stockholm)* 58: Suppl. 81, 1978.
9. Kousa, M., Saikku, P., Richmond, S. & Lassus, A.: Frequent association of chlamydial infection with Reiter's syndrome. *Sexually Transm Dis* 5: 57, 1978.
10. Richmond, S. J. & Caul, E. O.: Fluorescent antibody studies in chlamydial infections. *J Clin Microbiol* 1: 345, 1975.
11. Rook, A., Wilson, D. S. & Ebling, F. S. G.: *Textbook of Dermatology*. Blackwell Scientific Publications, Oxford, 1979.
12. Saikku, P. & Paavonen, J.: Single-antigen immunofluorescence test for chlamydial antibodies. *J Clin Microbiol* 8: 119, 1978.
13. Schachter, J. & Dawson, C. R.: *Human Chlamydial Infections*. PSG Publishing Co., Littleton, 1978.
14. Thomsen, K. & Østerbye, P.: Pustulosis palmaris et plantaris. *Br J Dermatol* 89: 293, 1973.
15. Terho, P.: Isolation techniques of *Chlamydia trachomatis* from patients with nonspecific urethritis. *Dermatol Monatsschr* 164: 515, 1978.
16. — *Chlamydia Trachomatis in Male Urethritis. A Clinical, Microbiological and Serological Study*. Academic Dissertation, University of Turku, Turku, 1979.
17. Ward, J. M., Corbett, M. F. & Hanna, M. J.: A double-blind trial of clomocycline in the treatment of persistent palmoplantar pustulosis. *Br J Dermatol* 95: 317, 1976.

Cutaneous Crystal Cholesterol Emboli

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Abstract. One case of cutaneous cholesterol emboli is described. In patients affected with severe arteriosclerosis of the abdominal aorta, cholesterol crystals may become detached from an atheromatous plaque and result in micro

emboli with ensuing skin lesions (livedo reticularis, nodules, purple toes, ulcerations, distal gangrene) on the lower extremities. Histopathologic study is required for diagnosis: the lumens of the arterioles were extensively occluded by macrophagic granuloma which surrounded cholesterol crystals.

Key words: Cholesterol emboli; Livedo reticularis; Nodules; Periarteritis nodosa; Distal gangrene

Cholesterol crystals may become detached from ulcerating atheromatous plaques, and then migrate and settle into the arterioles of various organs. They clog the smaller arteries and are responsible for various clinical pictures such as transient attacks of cerebral ischaemia, amaurosis fugax, hypertension, renal failure, acute or chronic pancreatitis and other abdominal symptoms. When atherosclerosis develops mainly on the abdominal aorta, embolism will be found in the lower extremities; the clogging of the cutaneous arterioles leads to various lesions: livedo reticularis, nodules, ulcerations, distal gangrene and purple toes.

CASE REPORT

A 50-year-old female patient was in excellent health until 6 months before her first admission when she noted a painful violaceous discoloration of her right fifth toe.

In January 1978, examination on admission revealed pregangrenous lesions of the whole of her right big toe with existing dorsalis pedis and femoral pulsation. Her right posterior tibial pulsation was absent. Her other toes and the rest of her foot seemed to have normal colour and temperature. There was no claudication. Arteriography confirmed the atherosclerosis. Right lumbar sympathectomy and the amputation of her toe were performed. An anticoagulant therapy was undertaken.

In April 1978, she came back for examination of the following cutaneous lesions: on her right leg painful erythematous nodules could be seen. There was no fever. On the plantar surface of her right foot there was a livedo reticularis with small ecchymoses (Fig. 1). These cutaneous lesions could not be accounted for by a fresh outbreak of arteritis, since all distal pulses were present except for the tibial posterior one. In the following weeks, a livedo reticularis developed on her right leg (Fig. 2), along with other nodules, these always announced by pain radiating in the lower extremities. Between those outbreaks, the lesions disappeared completely. The cutaneous lesions were not limited to her right-hand side, as a purpuric spot with a whitish centre was observed on her left leg after another painful spell.

A diagnosis of cholesterol crystal embolism was made possible by a cutaneous biopsy performed on one of the nodules. Two arterioles could be seen: the smaller one,