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REFERENCES

1. Korman N. Bullous pemphigoid. J Am Acad Dermatol 1987; 16: 907–924.
2. Gammon WR, Briggaman RA, Inman AO, Queen LL, Wheeler CE. Differentiating anti-laminina lucida and anti-sublamina densa anti-BMZ antibodies by indirect immunofluorescence on 1.0 M sodium chloride-separated skin. J Invest Dermatol 1984; 38: 139–144.
3. Kelly SE, Wojnarowska F. The use of chemically split tissue in the detection of circulating antibasement membrane zone antibodies in bullous pemphigoid and cicatricial pemphigoid. Br J Dermatol 1988; 118: 31–40.
4. Scaletta LJ, Occhino JC, MacCallum DK. Isolation and immunologic identification of basement membrane zone antigens from human skin. Lab Invest 1978; 39: 1–9.
5. Woodley D, Sauder D, Talley MJ, Silver M, Grotendorst G, Qwarnstrom E. Localization of basement membrane components after dermal–epidermal junction separation. J Invest Dermatol 1983; 81: 149–153.
6. Logan RA, Bhogal B, Das AK, McKee PM, Black MM. Localization of pemphigoid antibody—an indirect immunofluorescence study of 228 cases using a split-skin technique. Br J Dermatol 1987; 117: 471–478.
7. Bystryn JC, Sabolinski M. Effect of substrate on indirect immunofluorescence tests for intercellular and basement membrane zone antibodies. J Am Acad Dermatol 1986; 15: 973–977.
8. Goldberg DJ, Sabolinski M, Bystryn JC. Bullous pemphigoid antigens. Arch Dermatol 1985; 121: 1136–1140.
9. Gammon WR, Merritt RR, Lewis DM, Sams WM, Wheeler CE, Carlo J. Leucocyte chemotaxis to the dermal–epidermal junction of human skin mediated by pemphigoid antibody and complement: mechanism of cell attachment in the in vitro leucocyte attachment. J Invest Dermatol 1981; 76: 514–522.
10. Sams WM, Jordon RE. Correlation of pemphigoid and pemphigus antibody titres with acitivity of disease. Br J Dermatol 1971; 84: 7–13.

Clonidine-induced Immune Complex Disease

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We report upon a 46-year-old woman, who developed immune complex disease after treatment with clonidine for one year. The diagnosis was verified with histological demonstration of IgG and IgM complexes as well as complement C1q, C3c and C4 between muscle fibres and at the dermo-epidermal junctions. The patient's symptoms abated and the abnormal results of blood tests reverted to normal following cessation of clonidine therapy.

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Local deposition of circulating immune complexes or complex formation "*in situ*" may lead to inflammatory injury to the tissue, i.e. immune complex disease (ICD) (1). Drug-induced ICD is rare, but it has been reported following treatment with hydralazine, procainamide, α-methyldopa or chlorthalidone (2, 3). Clonidine is an α_2-receptor stimulating agent used for treatment of hypertension, prophylaxis of hemicrania, and treatment of menopausal flushes. The most common adverse effects are drowsiness and dryness of the mouth (4). In this report we present a case of clonidine-induced ICD.

CASE REPORT

The patient is a 46-year-old woman, who was formerly completely healthy. Due to menopausal flushes she had been treated with tablets of clonidine 25 μg twice a day for one year. During the last 9 months prior to admission, she had noticed an increasing depigmentation of the skin of her right upper extremity, including diffuse swelling of the forearm and tingling in the first, second and third fingers. Similar, though less distinct symptoms appeared at the same time on the left arm.

The physical examination of the right arm showed a depigmented skin area beginning on the upper arm and ending in the middle of the forearm on the ulnar side. The edema and the solid induration included the hand. The symptoms of the

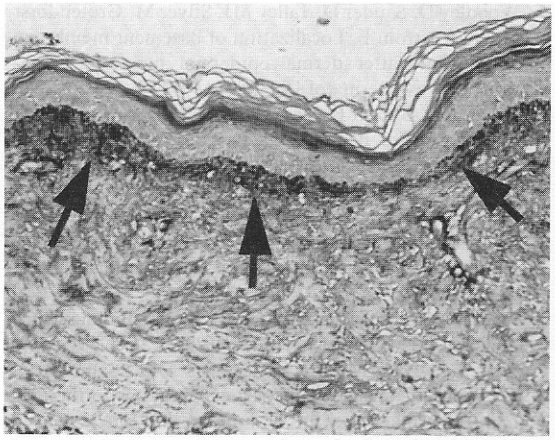

Fig. 1. Subepidermal deposits of IgM demonstrated by means of immune peroxidase technique. The epidermis is atrophic and the subepidermal tissue is edematous.

fingers could be reproduced by percussion over the volar surface of the wrist (Tinel's sign), and there was paresis and moderate atrophy of the opponens pollicis muscle. The findings in the left arm were the same, although the pigmentation was considered almost normal. There was no sign of carpal tunnel syndrome. The rest of the skin and subcutis was normal. The patient's minor complaint was dysphagia. Blood tests revealed increased lactic acid dehydrogenase (523 U/l, normal <450 U/l) and aspartate amino transferase (85 U/l, normal <40 U/l) concentrations. Other blood tests proved normal, including a negative test for antinuclear antibodies and normal creatine phosphokinase. EMG showed reduced conductance of the right medianus nerve compatible with carpal tunnel syndrome, and decompression was carried out.

A biopsy was taken from the affected skin and muscle on the right arm. As seen in Fig. 1, the skin showed epidermal atrophy and subepidermal edema. There was stromal basophil degeneration with a slight infiltration of lymphocytes and macrophages around atrophic sweatglands. The muscle fibres showed degenerative changes, with fibrosis, patchy necrosis and atrophy, and an infiltrate of lymphocytes, plasma cells and a few granulocytes. There was no fibrinoid necrosis. IgG and IgM was identified between muscle fibres and at the dermo-epidermal junction by indirect immune peroxidase technique in granular deposits. Direct immunofluorescence with anti-C1q, anti-C3c and anti-C4 showed a strong positive reaction in the dermal connective tissue, with all three antibodies proving the presence of complement C1q, C3c and C4.

The diagnosis was compatible with ICD. The treatment with clonidine was stopped, the patient's skin changes slowly abated, and lactic acid dehydrogenase and aspartate amino transferase values returned to normal. The patient regained normal functions of both hands after rehabilitation under physiotherapy. Six months later the patient developed an area of vitiligo on her right shoulder without any induration of the skin. This was interpreted as being part of the immune complex disease.

DISCUSSION

We report a case of clonidine-induced ICD. Cessation of clonidine therapy reversed the symptoms and abnormal results of blood tests, strongly supporting the hypothesis of clonidine as the etiology of the disease. The diagnosis is supported by the deposition of IgG and IgM in association with the basement membrane of the epidermis and between muscle fibres as well as complement C1q, C3c and C4. The tissue was dominated by fibrosis second to degeneration, without increased deposition of collagen fibres, which would accord with the process being active for almost a year. The immune complex deposits produced inflammation in the tissue below the transverse carpal ligament, resulting in the pressure on the right medianus nerve. The vitiligo which the patient developed months later may be part of the immune complex reaction, as some regard vitiligo as an immune complex disease (5, 6).

Clonidine-induced anogenital cicatricial pemphigoid has been reported by Van Joost et al. (7). The authors identified immune deposits (IgG) and complement along the basement membrane of the perianal epidermis. It is suggested that the underlying factor is local metabolic disturbances causing deposition of immunogens at the site of the basement membrane and subsequently formation of immune complexes.

REFERENCES

1. Salvidio G, Andres G. Immune deposits and immune complex disease. Clin Exp Rheumatol 1986; 4: 281–288.
2. Alarcon-Segovia D. Drug induced lupus erythematosus. Mayo Clin Proc 1969; 44: 664.
3. Feltkamp TEW, Dorhout Mees EJ, Nieuwenhuis MG. Autoantibodies related to treatment with chlorthalidone and α-metyldopa. Acta Med Scand 1970; 187: 219.
4. Steiner JA. In: Dukes MNG, ed. Meyler's "Side effects of drugs" 10th ed. Amsterdam: Elsevier, 1984: 361–363.
5. Naughton GK, Reggiardio D, Bystryn J-C. Correlation between vitiligo antibodies and extent of depigmentation. J Am Acad Dermatol 1986; 15: 978–981.
6. Betterle C, Carretto A, De Zio A, et al. Incidence and significance of organ-specific autoimmune disorders (clinical, latent or only autoantibodies) in patients with vitiligo. Dermatologica 1985; 171: 419–423.
7. Van Joost TH, Faber WR, Manuel HR. Drug-induced anogenital cicatricial pemphigoid. Br J Dermatol 1980; 102: 715–718.