Dermatitis herpetiformis and diabetes mellitus

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Summary

Three out of 4 patients with coexistent diabetes mellitus and dermatitis herpetiformis (DH) developed severe renal failure which resulted in death in 2 of them. Diabetes mellitus and DH may coexist more frequently than would occur by chance, and such patients may run an increased risk from severe renal complications of diabetes.

Introduction

Gluten enteropathy indistinguishable from coeliac disease occurs in the majority of patients with dermatitis herpetiformis (DH) (Marks *et al.*, 1968) and both coeliac disease and DH are known to be associated with a number of autoimmune diseases (Davies, Marks and Nuki, 1978). It has recently been suggested that diabetes mellitus occurs more frequently in patients with coeliac disease than in the general population (Walsh *et al.*, 1978), and there have been occasional reports of coexistent diabetes and DH (Davies *et al.*, 1978; Reunala *et al.*, 1976; Walsh *et al.*, 1978).

From a series of 102 patients with DH attending the Royal Infirmary, Edinburgh, the authors have encountered 4 patients with diabetes mellitus. Three of the 4 patients developed severe diabetic complications of which renal failure was most notable.

Case report 1

A 50-year-old female patient with a 19-year history of insulin-dependent diabetes mellitus presented with a blistering skin rash around her neck, shoulders, elbows and on her forearms. The associated intense pruritus was relieved by rupturing the blisters. Histological examination of a biopsy from an affected area of skin showed sub-epidermal blisters containing fibrin and polymorphonuclear leucocytes, which had infiltrated surrounding skin. This rash disappeared rapidly after the commencement of treatment with sulphapyridine which was subsequently required for long-term control of the rash. She developed diabetic retinopathy and persistent

proteinuria which progressed to the nephrotic syndrome and advanced renal failure. A jejunal biopsy was not performed in this patient and she died, 2 years after presenting with DH, in advanced renal failure.

Case report 2

A 32-year-old male patient with an 11-year history of insulin-dependent diabetes presented in 1975 with an itchy blistering skin rash principally affecting the elbows and knees. Intense pruritus was relieved by scratching the blisters. Treatment was initiated with dapsone with relief of symptoms and resolution of the skin rash. Multiple jejunal biopsies demonstrated the presence of subtotal villous atrophy. For 3 years before his presentation with the rash he had been troubled with severe diabetic retinopathy and cataract formation. Severe proteinuria had also been present for at least 6 months and this progressed to the nephrotic syndrome. Renal biopsy showed histological evidence of diabetic glomerulosclerosis. Immunofluorescent staining showed no evidence of an immune nephritis. At present (June 1979) this patient has advanced renal failure with unstable control of diabetes.

Case report 3

A 63-year-old male, insulin-dependent diabetic of 10 years' duration was admitted to hospital with a 12-month history of diarrhoea, bone pain and an itchy, blistering skin rash affecting the elbows, knees, shoulders and buttocks. A skin biopsy from an area affected by the rash showed sub-epidermal microbullae with surrounding acute and chronic inflammatory cell infiltrate. Biochemical tests and skeletal X-rays indicated the presence of osteomalacia, and a jejunal biopsy showed the presence of subtotal villous atrophy. Improvement of the skin rash, diarrhoea and osteomalacia was apparent within one month of treatment with a gluten-free diet vitamin D and calcium supplements. One year after initial presentation to the skin clinic this patient had developed advanced diabetic retinopathy and

TABLE 1. Clinical details and HLA type of 4 patients with diabetes mellitus and dermatitis herpetiformis

Case No.	Age (years)	Response of skin lesions to dapsone, sulphapyridine or gluten free diet	HLA type	Outcome
1	50	*	—	death, renal failure†
2	32	*	A1.A3.B8.B15.CW3	established renal failure‡
3	63	*	A3.AW24.B8.B18.B4	death, renal failure†
4	69	*	A3.A24.B7.B44.CW5	well

* Indicates improvement or resolution of skin rash.

† Diabetic glomerulosclerosis ‡ confirmed at renal biopsy.

persistent, severe proteinuria. The proteinuria progressed to the nephrotic syndrome and the patient died as a result of renal failure.

Case report 4

A 69-year-old female patient presented in 1976 with an itchy excoriated rash affecting her elbows, shins, shoulders and buttocks. Hypothyroidism had been diagnosed in 1962 and diabetes mellitus discovered in 1975. Her diabetes had been adequately controlled by carbohydrate restriction. Immunofluorescence studies of a biopsy from skin unaffected by the rash showed immunoglobulin A deposits at the basement membrane, consistent with a diagnosis of DH. Jejunal biopsy was histologically normal. Dapsone treatment resulted in resolution of her skin rash with symptomatic relief. She remains well with adequate control of her diabetes by carbohydrate restriction but a long-term treatment with sulphapyridine has been required to prevent recurrence of the skin rash.

Discussion

The association between DH and diabetes mellitus in these patients may be a chance event, because diabetes occurs commonly in the general population. Nevertheless, coeliac disease, DH and juvenile diabetes mellitus share the high incidence of the histocompatibility antigen HLA-B8 (Davies *et al.* 1978; Walsh *et al.*, 1978; Bottazzo *et al.*, 1978), suggesting a similar genetic background. Furthermore, it has been suggested from family studies that the gene that determines coeliac disease and DH may be linked with haplotypes A1, B8, A28, B8 and A3 B8 (Reunala *et al.*, 1976). It is of interest that in 2 patients with insulin-dependent diabetes histocompatibility antigens A3 and B8 were encountered (Table 1).

Particular HLA phenotypes are not generally related to diabetic complications (Chuck and

Cudworth, 1977) with the possible exception of severe diabetic proliferative retinopathy which may be associated with HLA-B8 in the absence of HLA-A1 (Larkins, Martin and Tail, 1978). Three of the 4 patients had severe renal failure with clinical features typical of diabetic nephropathy. The incidence of proteinuria in large diabetic out-patient clinics is between 4.9 and 10% (Keen and Jarrett, 1975) and Walsh *et al.* (1978) noted intermittent proteinuria in 5 of 14 patients with coexistent coeliac disease and diabetes mellitus. However, blood urea in the latter group of patients was normal and advanced renal disease was not observed. The significance of renal failure in the present patients is unclear, for although proliferative glomerulonephritis has been recorded in one patient with DH (Toft, Heading and Simpson, 1973) there was no evidence of immune nephritis in patient 3 in the present group.

The apparent increased incidence of diabetes mellitus in patients with DH will require confirmation, but clinicians should be aware that patients with coexistent DH and diabetes mellitus may have an increased risk of severe renal complications.

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