Diabetic retinopathy in Cushing's disease

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Summary

A patient with proliferative diabetic retinopathy in long-standing Cushing's disease is described.

Introduction

Most cases of Cushing's syndrome are known to have abnormalities of carbohydrate metabolism (Plotz, Knowlton and Ragan, 1952; Thorn, Renold and Cahill, 1959) and between 10-25% of patients have clinical diabetes mellitus (Thorn *et al.*, 1959). However, the vascular complications of diabetes are reported to be uncommon (Thorn *et al.*, 1959). In the past, adrenalectomy was tried for relieving diabetic retinopathy, but although a few cases had some regression (Malins, 1962; Graef and Maier, 1962) poor results led to abandonment of the procedure. The authors now report what they believe is the first case of proliferative diabetic retinopathy in Cushing's disease.

Case report

The patient, now aged 54 years, had gangrene of the scrotum in 1970; glycosuria was found but not followed-up. In 1975, after his complaining of weakness, his general practitioner detected glycosuria. Diabetes mellitus was diagnosed at the local hospital and he was put on tolbutamide 500 mg thrice/day on which he continued for most of the time. He then noticed muscle weakness and was noted to have hypertension. Cushing's syndrome was suspected and he was referred to a hospital in London where the typical features of Cushing's syndrome were noted. His BP was 180/100 mmHg, he had proliferative retinopathy in the right eye, marked proximal muscle weakness and peripheral neuropathy.

Investigations gave the following results, normal values in parentheses: urine free cortisol, 626 nmol/24 hr (<270); plasma cortisol, 9 a.m. 662 nmol/l (<500), 12 midnight 634 nmol/l (<240); dexamethasone suppression test 8 mg/day, suppressed plasma

cortisol at 12 midnight to 248 nmol/l. Glucose tolerance test basal, 5 mmol/l; 60 min, 12 mmol/l; 120 min, 11 mmol/l. X-rays: small pituitary tumour. A diagnosis of Cushing's disease with radiological evidence of pituitary tumour was made. He was then started on metyrapone 750 mg thrice/day and dexamethasone 0.5 mg twice/day and, in December 1975, was treated with external radiotherapy 4000 rad to the pituitary fossa. During 1976 and 1977 there was no regression of his symptoms despite continuing with these drugs, and in April 1977, when re-assessed off therapy, the results were: plasma cortisol, 9 a.m. 580 nmol/l, 12 midnight 331 nmol/l; plasma ACTH 9 a.m. 165 ng/l (<80), 12 midnight 88 ng/l (<10). Metyrapone was increased to 750 mg 4 times/day and he was continued on the same dose of dexamethasone. However, he continued to deteriorate and developed many leg ulcers which were very slow in healing.

In January 1978 he was assessed with a view to pituitary surgery. During carotid angiography he developed apnoea and required ventilating and it was therefore decided impracticable to consider further surgical intervention of his pituitary gland. He was discharged on his previous dose of metyrapone and dexamethasone. There was still further deterioration in his condition. In September 1978 his left 5th toe was amputated because of gangrene.

He was referred to Hammersmith Hospital in December 1978 from his local hospital. He was chair-bound, obviously Cushingoid, and had many painful ulcers in all limbs. His skin was very dry and paper-thin. There were no pulses palpable below his femorals; BP 150/90 mmHg. Pin-prick sensation was diminished in his feet, vibration sense was absent in his ankles and both ankle jerks were absent. There were expiratory rhonchi (he smoked 20 cigarettes/day). The right fundus showed numerous small flat new vessels, markedly tortuous veins, multiple dot and blot haemorrhages and some hard exudates at the macula (Fig. 1). Investigations

confirmed the initial diagnosis of Cushing's disease with radiological evidence of a pituitary tumour. He was treated with a pituitary implant of ^{90}Y 150 000 rad on 23 January 1979.

FIG. 1. Fluorescein angiogram of right macula in the late phase showing extensive leakage of dye from new vessels arising from the disc and the retinal periphery.

Postoperatively he developed a chest infection which responded to antibiotics and he had to have bilateral above-knee amputations because of sepsis in his ulcers. Over the next few weeks, the Cushingoid features started to regress. The stumps healed.

His diabetic retinopathy did not show any significant change at 13 weeks postoperatively. After he was weaned off steroids he showed adrenocortical deficiency. Insulin hypoglycaemia test on 30 March showed a serum cortisol response <90 nmol/l throughout and he was started on prednisone. He still on prednisone 2 mg/day. At that time plasma ACTH levels were 9 a.m. <11.0 ng/l, 12 midnight <11 ng/l, and a repeat glucose tolerance test gave the following results: fasting 3.4 mmol/l, 120 min 8.4 mmol/l (peak level). The rest of his anterior pituitary function was normal.

Discussion

The possibility arises that patients usually die of Cushing's syndrome before they have time to develop diabetic retinopathy, while this patient's Cushing's disease was slightly controlled by his treatment sufficient to keep him alive, and he developed diabetic retinopathy. One cannot of course exclude that he had co-incident severe diabetes mellitus, but the marked improvement in his glucose tolerance following his remission is against this.

References

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