Diabetes mellitus in idiopathic haemochromatosis

Diabetes mellitus in patients with idiopathic haemochromatosis (IH) is widely believed to be due to islet cell destruction by iron. This view has recently been challenged, and it has been suggested that diabetes associated with IH may be of genetic or multifactorial origin. 1, 2 We investigated this question by studying a-cell responses in patients with diabetes and IH. In idiopathic diabetes plasma pancreatic glucagon concentrations rise after arginine stimulation. By contrast, in diabetes secondary to chronic pancreatitis or transfusional haemochromatosis glucagon responses are impaired. 3 If diabetes associated with IH results from islet cell damage, glucagon responses would be expected to be impaired.

Patients, methods, and results

Ten patients aged 55 to 79 years with diabetes and IH were investigated. They had diabetes for 1 to 23 years and IH for 1 to 16 years. Five of the eight patients tested were HLA type A3B7. Six were on insulin, three on oral hypoglycaemic agents, and one on diet alone. All had undergone venesection and at the time of the study the serum iron concentration was raised in three patients. Nine patients with idiopathic diabetes matched for sex, age, duration of diabetes, treatment, and percentage ideal body weight were controls. A standard arginine stimulation test was carried out in the fasting state. Venous samples were withdrawn for measurement of blood sugar and plasma glucagon (SRB).

The mean blood sugar values for the patients with IH did not differ significantly from those of the controls (P > 0.05). The basal glucagon values were similar in both groups, and after arginine infusion plasma glucagon concentrations showed the expected rise in the controls. In the patients with IH the concentrations also rose, being significantly higher than control values at 15 minutes (P < 0.05).

Comment

That diabetes associated with IH results from islet cell damage by iron is supported by reports of a high incidence of diabetes in patients with IH 3 and the reduction in insulin dose in some patients after venesection. That the diabetes is not due simply to iron deposition, however, is suggested by the high incidence of diabetes in relatives of patients with IH with normal iron stores 3; 4 observations that after iron depletion carbohydrate metabolism is sometimes unaltered or even deteriorates; and the poor correlation between the degree of iron overload and the presence of diabetes. 1

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Serum prolactin (PRL) concentrations before and after treatment

<table>
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<th>Patient No</th>
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<th>Serum PRL (mU/l)* After</th>
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<td>16</td>
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Mean (± SEM) 43-4 (±2-6) 281-9 (±19-9) 174-4 (±15-5)

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*Normal = up to 500 mU/l.
Partial mastectomy for breast cancer

Survival from breast cancer depends mainly on whether general and progressing disease is present at diagnosis, and clinicians look for treatment that, while controlling local recurrence, causes the least mutilation and morbidity. Crile et al. reported that results of partial mastectomy without supplementary radiotherapy equalled those of total mastectomy. I carried out a pilot study of partial mastectomy without radiotherapy.

Patients, methods, and results

I studied 44 patients with histologically proved invasive carcinoma. The series was consecutive apart from patients excluded because they had more than one primary growth in the same breast; fixity of the primary growth or affected axillary nodes to the deep fascia; widespread "peau d’orange"; or less than 2 cm between the nipple and the growth’s palpable edge nearest the nipple (because it seemed pointless to preserve the breast without the nipple). Thus some extremely large growths and central growths were excluded.

The growth was excised with 2 cm of apparently normal tissue all round (overlying skin, breast substance, and deep fascia over pectoral muscles). If the axilla contained nodes thought to be diseased it was dissected.

Follow-up was three-monthly for the first three years and lasted for 36-72 months. Several deaths occurred.

Initial lesions

Size and position of lesions—Growth diameter was 0.5-5.0 cm (average 2.0 cm). Five growths were in the medial and 28 in the lateral halves of the breast; seven were in intermediate positions. Axillary nodes were thought to be diseased and were dissected in 13 out of 40 cases, but in only nine was malignant disease confirmed histologically. Six axillary recurrences occurred in the remaining 27 patients.

Recurrences

Tumours recurred in the same breast in 14 out of 38 patients (37 %) who survived for three years or more. Recurrences developed 6-41 (average 25) months after operation. Eight of the 28 patients with lateral tumours, two of the five with medial tumours, and three of the seven with tumours in the intermediate zone developed recurrence in the same breast. Diameter of tumours recurring in the same breast was on average 2.3 cm. General disease became apparent in 14 of the 44 patients (31 %). The manifest disease-free interval was 4-40 (average 23) months.

Further management—All patients with histologically proved recurrences underwent total mastectomy or axillary dissection, or both.

Comment

This high rate of recurrence in the same breast contrasts with the results of Crile et al. The two largest growths (5-0 cm diameter) and one of the smallest (0.5 cm) were recurrences, so inadequate excision may have been a factor. In all but one case the recurrence lay in or immediately deep to the operation scar, suggesting that the wound became colonised by malignant cells migrating through apparently normal tissue.

Greening et al. studied a small series of carefully selected patients with small growths and no axillary disease. Treatment was by quadrant excision and axillary dissection alone. Although only half their patients had been followed up for three years at the time of the report, the rate of recurrence in the same breast was already 15 %. Other workers have found local recurrence rates of 15 % without and 4 % with radiotherapy after simple mastectomy, and of 9 % and 18 % after extended tylactomy and radiotherapy.

This pilot trial was concluded immediately the trend towards a local recurrence rate of 37 % became apparent. Simple mastectomy with or without radiotherapy appears to be the minimum treatment likely to control local recurrence. Fortunately most patients accept this calmly, and in this series patients were not noticeably relieved to hear that they were to lose part rather than all of the breast. The incidence of systemic disease at three years was 31 %, compared with 25 % reported for mastectomy with or without radiotherapy. This difference was probably not significant.


Long-term survival after resection of carcinoma of the oesophagus

In 1913 Torek reported the case of a patient who survived for 13 years after resection of a carcinoma of the oesophagus. Since then no comparable survival has been recorded. I describe here a patient who survived for 31 years, in good health, after resection of carcinoma of the oesophagus.

Case report

In 1947 a 54-year-old woman was referred to Hammersmith Hospital in a condition of extreme emaciation. Several months earlier she had developed dysphagia; this had become progressively worse and on admission was almost complete. Her condition was such that even investigations could not be carried out safely until her nutrition had been improved. According to her feeding jejunostomy was made. Her condition improved rapidly and investigations showed what appeared to be a carcinoma near the lower end of the thoracic oesophagus. Three weeks after the start of jejunostomy feeding she was judged fit for operation.