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Malignant Diabetes Mellitus—a Case Report

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ABSTRACT

A 30-year-old man presented at the diagnosis of an insulin dependent diabetes mellitus with pronounced and multiple complications, such as retino-, nephro-, dermo- and neuropathy. His diabetes had a malignant course and he died from uremia within one year after diagnosis. There were no signs of atherosclerosis at autopsy but in several organs there were pronounced diabetic small vessel lesions.

Key words: Diabetes mellitus, retinopathy, nephropathy, dermopathy, neuropathy, smoking

INTRODUCTION

Different factors have been considered to influence the development and course of late diabetic vascular complications, e.g. smoking (15), hypertensive (16), coagulative (1, 2) and genetic factors (12, 18) but mostly the vascular lesions have been reported to be due to the metabolic derangement per se (5, 13). One of the underpinnings of this latter opinion is that vascular complications are only rarely found at the beginning of diabetes (13). However, typical late vascular complications are sometimes to be found already at diagnosis of type 2-diabetes (4, 10, 11) and also in patients with normal glucose tolerance test curves (6, 9, 23).

In patients with type 1-diabetes, clinical vascular complications upon diagnosis of diabetes were reported by Solar and coworkers (22). They described 10 patients, 21-39 years old, with retinopathy. All, except one, had only so-called background retinopathy. Two of them also had asymptomatic proteinuria.

In the following we will describe a young man with type 1-diabetes who had multiple complications when his diabetes was diagnosed. Of additional interest is that his diabetes had a malignant course and he died within one year from a progressive uremia although his diabetes was well regulated during this time.

CASE REPORT

This male patient was an electrician, 30 years old, who previously had been healthy. His mother had a mild type 2-diabetes and his brother, 43 years, had type 1-diabetes of 40 years' duration with proliferative retinopathy, neuropathy and asymptomatic proteinuria. Because of his brother's diabetes, our patient throughout the years had often checked his urine for glucosuria. He had smoked 20 cigarettes a day since he was 16 years old but he ceased smoking when his diabetes was diagnosed. In connection with treatment of a fracture of a lower leg, moderate glucosuria and hyperglycemia (17 mmol/l) were discovered.

His body weight was 60 kg and his height 176 cm. His blood pressure was 130/90. He had no increased thirst or polyuria and had not lost weight. He had no peripheral edema and the pulmonary x-ray was normal. He had typical diabetic dermopathy on his legs, such as shin spots (14), purpuric lesions and pigmentation (10). He also had bilateral absence of knee and ankle jerks. At ophtalmoscopy, performed by an ophtalmologist, there were bilateral fundus lesions, in the form of small red dots and white hard exudates in abundance. There was no bacteriuria.

It was impossible to control his diabetes with diet alone, he had increasing blood glucose values, with a peak of 34.9 mmol/l, and ketonuria. Insulin was administered with good effect, generally he had 20 IU daily of an intermediate insulin. He lived about 11 months after his diabetes was diagnosed. During this time his blood sugar levels usually were in the normal range. His renal threshold for glucose was normal.

Two months after the diagnosis of diabetes he was troubled with diarrheas and also with postural hypotension. He was discovered to have steatorrhea; the fecal fat content was 36.8 g/day (N < 6 g/day). He had normal values of vitamin B and folic acid and the D-xylose test was in the normal range. He had normal amounts of complement factor C3 (1.04 d/l) and an increased amount of C4 (1.48 g/l). The HLA genotype was A1, A2, B7, B12.

Further examinations during the following months: Cystometry revealed a neurogenic dysfunction of the urinary bladder without signs of sensitivity and detrusor function. Renal papillary calcifications were observed on an intravenous pyelogram. Micturition-urethrocystography demonstrated a very large urinary bladder with emptying difficulties. Electromyography disclosed pronounced, general and symmetrical peripheral lesions of the polyneuropathy type both in upper and lower extremities but particularly in the lower. Already at the time of diagnosis he had constant proteinuria, however, serum electrolytes were then normal, including serum albumin and creatinine (81 umol/l, N 53-97). The level of creatinine gradually increased and his condition deteriorated. He died from uremia, serum creatinine was 2310 umol/l just before death. Extensive clinical investigations revealed no other cause than diabetes to his various lesions. Dialysis and transplantation of a kidney was judged not feasible to perform, mainly because of his severe and generalized polyneuropathy.

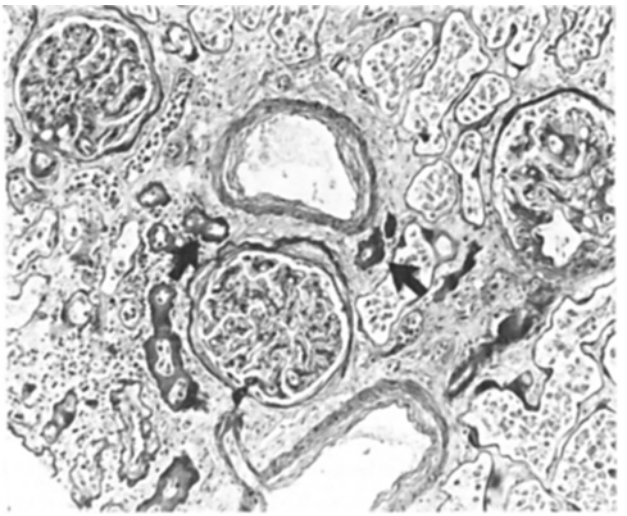

Fig. 1. Kidney. Thickening of the walls of small vessels (arrows). Also the basal membranes of the capillaries of glomeruli are thickened. PAS x 220.

At autopsy, no signs of atherosclerosis were seen, neither macroscopically nor microscopically. There were no signs of heart disease. Microscopically, PAS-positive thickening was seen in the small vessels of the kidneys including the capillary walls of the glomeruli (Fig. 1). PAS-positive thickening of the walls of the small vessels were also seen beneath the epithelium of the skin of the lower legs. In the muscles of the lower legs, signs of atrophy were observed. In the pancreas, the islands of Langerhans were atrophic and few, they had signs of fibrosis and hyalinization. There were no signs of pancreatitis. There were no deposits of amyloid in the different preparations. Electromicroscopic examination was not performed because of the long time between autopsy and death (4 days).

DISCUSSION

This case report demonstrates two remarkable features. Firstly, our patient had well established diabetic complications already at the diagnosis of an insulin dependent diabetes and, secondly, his diabetes ran a fast and malignant course.

The development and the course of diabetic vascular complications is most likely influenced by several different factors. The factor which has been subjected to the greatest number of studies and to the most intense discussion is hyperglycemia (6, 8, 13, 20). In experimental studies with diabetic rats, it was demonstrated that treatment with insulin could inhibit or prevent small vessel lesions (5, 19). There is much evidence that this is true also for human diabetics, although it has been difficult to prove it conclusively (8) which, among other things, could be due to lack of attention to the complicated background mentioned in the introduction.

Our patient may have had open diabetes for some time without symptoms, although his diabetes was of the insulin-dependent type. However, because of his diabetic brother, he was conscious of the risk to be diabetic and he now and then checked himself for signs of glucosuria. The stress of lower leg fracture might have caused his diabetes to be metabolically revealed. Anyhow, inapparent and subclinical defects in carbohydrate metabolism may have been present that paralleled the vascular lesions described here.

Smoking is likely to worsen the course of diabetic vascular lesions, such as retinopathy and nephropathy, which has been reported recently (3, 15, 17). Over a long time (15 yrs) the smoking habits of our patient had been considerable and a harmful effect on his small vessels already at a preclinical diabetic state is possible.

Sohar and coworkers reported three patients with mild, well controlled, diabetes mellitus who early in their diabetes developed vascular complications (21). Histologically, these patients had PAS-positive material not only in their blood vessel walls but also in connective tissue outside the blood vessels. Electron microscopic examination revealed this material to be composed of fibrils resembling the findings in systemic amyloidosis and, in analogy, Sohar and coworkers designated their findings as diabetic fibrillosis. However, despite careful examination, we could not find PAS-positive deposition outside the blood vessels of our patient.

Of special interest is that the vascular complications of our patient worsened in a fast and malignant course although his blood glucose levels were well regulated and he had stopped smoking.

This case teaches us that diabetes emerges as a generalized and complex disease of which aberration of carbohydrate metabolism may sometimes be but one facet.

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