The occurrence of Z-type diabetes (tropical pancreatic diabetes) in the South African Indian

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Summary

The presentation of diabetes in the young South African Indian is atypical in that insulin-dependent diabetes mellitus is rare, while non-insulin-dependent diabetes mellitus is common. In addition, youthful onset of tropical diabetic syndrome (J-type diabetes) is extremely rare. To date there appear to be no reports on a further tropical malnutrition diabetic syndrome associated with pancreatic fibrosis and calcification (Z-type diabetes). Four Indian patients with features consistent with the diagnosis of Z-type diabetes are described. All were asthenic, came from a poor socio-economic background and developed insulin-requiring diabetes in their youth; 3 of the 4 patients had pancreatic calcification.

The atypical presentation of diabetes in the young South African Indian has been highlighted previously. While insulin-dependent diabetes mellitus with onset in youth is rare, the syndrome of non-insulin-dependent diabetes in the young is common. In addition to the above two subtypes, which have been recorded globally in most populations studied, workers have drawn attention to the existence of a rare youth-onset tropical diabetic syndrome, J-type diabetes, in the South African Indian. The salient characteristics of J-type diabetes, as reported from India and Africa, are: antecedent malnutrition, leanness of the patients, substantial insulin requirements and resistance to ketosis. A further tropical malnutrition-diabetes syndrome associated with pancreatic fibrosis and calcification (Z-type diabetes), has been documented from Indonesia, Africa, Brazil and certain parts of India, especially the state of Kerala. The features of Z-type diabetes are similar to those enumerated for J-type diabetes with the additional characteristic of pancreatic fibrosis and calcification. To date, there appear to be no reported cases of Z-type diabetes in the South African Indian population. In this communication we report, for the first time, the occurrence of Z-type diabetes in South African Indian patients.

Case reports

Case 1
A 19-year-old Indian female presented to the diabetic clinic at R. K. Khan Hospital with symptoms of polyuria and polydypsia. Her mass was 44.5 kg and her height 151 cm (95% of desirable mass). She came from a poor socio-economic background and had no family history of diabetes. There was no history of alcoholic intake or biliary disease. However, she admitted to frequent bouts of intermittent abdominal pain. Clinical examination revealed an asthenic patient without any parotid enlargement. The pulse rate was 80/min and blood pressure 110/70 mmHg. There was no evidence of retinopathy or neuropathy. The diagnosis of diabetes was confirmed by urinalysis which revealed glucosuria without ketonuria, and a plasma glucose level of 15.3 mmol/l. Radiological examination of the abdomen revealed pancreatic calcification (Fig. 1). The patient was then subjected to a 100 g oral glucose load; glucose and insulin responses and the resultant biochemical profile are depicted in Tables I and II. It is evident that she had a delayed and attenuated insulinaemic response compared with that of non-obese Indian volunteers. She did not appear to have any renal impairment; urinalysis failed to reveal albuminuria, and serum concentrations of urea, creatinine and β2-microglobulin were in the reference range. The low serum albumin level is consistent with subnutrition, since both liver and renal function were normal. She was initially treated with diet and glibenclamide with little success. While on this therapy, she defaulted and presented 8 months later with diabetic keto-acidosis (plasma glucose 38.9 mmol/l; ketonuria and severe glucosuria, Na+ 122 mmol/l, HCO3− 8 mmol/l). Having recovered from this episode of diabetic keto-acidosis, she was stabilised on Monotard insulin 85 U/d. She has now defaulted from the diabetic clinic once again.

Fig. 1. Radiograph showing pancreatic calcification in case 1.

Case 2
This patient was diagnosed as a diabetic at the age of 16 years when she presented with acute abdominal pain. She came from a poor socio-economic background. There was no history of mumps, biliary disease, alcohol or drug intake. Clinical examination revealed...
TABLE I. INSULIN AND GLUCOSE RESPONSE OF PATIENT 1

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Plasma glucose (mmol/l)</th>
<th>Serum insulin (mU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>13,9</td>
<td>16</td>
</tr>
<tr>
<td>30</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>60</td>
<td>23,3</td>
<td>28,5</td>
</tr>
<tr>
<td>90</td>
<td>28,5</td>
<td>27,9</td>
</tr>
<tr>
<td>120</td>
<td>29,4</td>
<td>34</td>
</tr>
<tr>
<td>180</td>
<td></td>
<td>34</td>
</tr>
</tbody>
</table>

Table II: Fasting profile of patients 1 and 2

<table>
<thead>
<tr>
<th>Na⁺</th>
<th>K⁺</th>
<th>Cl⁻</th>
<th>HCO₃⁻</th>
<th>Urea</th>
<th>Creatinine</th>
<th>β₂-microglobulin</th>
<th>Cholesterol</th>
<th>Triglycerides</th>
<th>HDL-cholesterol</th>
<th>HbA₁c</th>
<th>Cortisol</th>
<th>Growth hormone</th>
<th>Total protein</th>
<th>Albumin</th>
<th>Globulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>138</td>
<td>4,6</td>
<td>99</td>
<td>23,9</td>
<td>4,6</td>
<td>60</td>
<td>1,41</td>
<td>3,8</td>
<td>0,89</td>
<td>0,89</td>
<td>13,8</td>
<td>14,5</td>
<td>5,4</td>
<td>66</td>
<td>29</td>
<td>37</td>
</tr>
<tr>
<td>135-145 mmol/l</td>
<td>3,5-5,3 mmol/l</td>
<td>96 - 106 mmol/l</td>
<td>24-32 mmol/l</td>
<td>2,5-6,6 mmol/l</td>
<td>71-133 μmol/l</td>
<td>&lt;2,3 mg/l</td>
<td>3,9-6,5 mmol/l</td>
<td>0,8-2,0 mmol/l</td>
<td>0,96-1,9 mmol/l</td>
<td>5-9,1%</td>
<td>5-25 μg/ml</td>
<td>0-10 ng/ml</td>
<td>60-82 g/l</td>
<td>35-50 g/l</td>
<td>25-32 g/l</td>
</tr>
</tbody>
</table>

Case 3

The sister of the second patient presented with abdominal pain at the age of 25 years and investigations revealed that she was diabetic. She was stabilised on lente insulin 64 U/d. On examination at the diabetic clinic she was found to be asthenic (weight 46 kg, 92,2% of desirable mass), with no evidence of malnutrition, neuropathy or retinopathy; her blood pressure was 110/70 mmHg. A recent biochemical profile revealed normal renal function, a normal serum albumin and a glycosylated haemoglobin level of 10,2%. Radiographic examination of the abdomen failed to show pancreatic calcification.

Case 4

Recently a fourth patient with Z-type diabetes was diagnosed. Clinical examination revealed a 19-year-old lean Indian man (weight 64,5 kg, 92,2% of desirable mass) with insulin-dependent diabetes. He has pancreatic calcification and is a non-drinker but the examination and special investigations failed to reveal any complications of diabetes. He is well controlled on Rapitard 42 U/d (HbA₁c, 8,8%).

Discussion

The syndrome of Z-type diabetes was first reported from Indonesia in 1955 by Zuidema.12 In his original report he described 7 emaciated patients with pancreatic calcification, of whom 6 had insulin-requiring diabetes and none a history of biliary disease or alcoholic abuse. Since this report, numerous studies from various parts of the world have confirmed the existence of this syndrome.13-14 However, this disorder appeared to be non-existent in the Indian population of South Africa and very rare in the black population, since only 2 black patients with Z-type diabetes have so far been reported.5 In this communication, 3 Indian patients who fulfil the criteria for Z-type diabetes are described; all 3 patients were asthenic and came from poor socio-economic backgrounds and the insulin-requiring diabetic syndrome had its onset in youth and was associated with both pancreatic calcification and intermittent abdominal pain. The fourth patient (case 3) has some of the features of Z-type diabetes (insulin-requiring diabetes, asthenia, intermittent abdominal pain and a poor socio-economic background), but radiology of the abdomen failed to reveal calcification. It could be argued that this patient has Z-type diabetes in the pre-calcification phase in which there is only fibrosis of the pancreas.13 This supposition is supported by the fact that while the majority (> 70%) have pancreatic calcification, this is by no means universal.13 Be that as it may, Z-type diabetes is rare in the South African Indian. It is presently not clear why, while this type of diabetes is common in India, it is so rare in the South African Indian. A possible explanation could be that the comparatively higher socio-economic status of the Indian population in South Africa protects them against the development of Z-type diabetes. Furthermore, McMillan and Geevarghese15 have speculated that the pancreatic damage may be related to both chronic malnutrition and the consumption of the cyanogen-containing tropical starch, cassava (tapioca). Cassava is not consumed by an asthenic female (weight 44 kg, 88,2% of desiriable mass), with no signs of malnutrition, retinopathy or neuropathy. Her blood pressure was 105/70 mmHg. An initial diagnosis of acute pancreatitis was entertained. Investigations failed to confirm this diagnosis; the serum amylase level was 330 U/l (reference range 70-300 U/l). However, a radiograph of the abdomen showed pancreatic calcification (Fig. 2), and an elevated plasma glucose level of 13,6 mmol/l revealed that she was a diabetic. A diagnosis of Z-type diabetes was made and she was started on lente insulin 24 U/d. She continued having numerous bouts of abdominal pain with little relief, despite taking antispasmodics. Subsequent investigations which included endoscopy, barium studies, oral cholecystogram and ultrasonography of the liver, were normal. An endoscopic retrograde pancreatocholangiogram showed dilatation of the pancreatic duct. Since her diabetic control was poor on insulin, she was stabilised on Rapitard 52 U/d. At no stage during her illness was she ketogenic and the only complication she has developed to date is cataracts.

The most recent biochemical profile done on her is shown in Table II; it is apparent that she has a normal serum albumin level and normal renal function. Her diabetic control is satisfactory as evidenced by the glycosylated haemoglobin level (11,3%). On direct questioning, the patient stated that both her mother and sister are diabetic. The mother could not be traced for further investigations.

Fig. 2. Radiograph showing pancreatic calcification in case 2.
the South African Indian. However, it should be pointed out that while the geographical distribution of Z-type diabetes coincides with that of cassava ingestion, in other areas where Z-type diabetes is not uncommon, such as in the state of Tamil Nadu in South India, cassava is rarely consumed.14

Finally, it is interesting to note that while in most series there is a male preponderance, in the present study 3 of the patients were females.

Part of the investigations of these patients was undertaken in the MRC Prenatal Diagnostic Chemistry Research Unit, University of Natal.

REFERENCES


Phase II of a successful university-based in vitro fertilisation programme

Changes incorporated

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Summary

The ultimate goal of any clinical programme treating infertility by means of in vitro fertilisation and embryo replacement is to maximise the number of patients who become pregnant in a treatment cycle. A 12% pregnancy rate was previously reported from this unit. Following the instigation of changes and further modifications, an overall success rate of 27% per patient was obtained in phase II. The reasons for this improved success are hard to pinpoint, but experience and changes in methodology probably play a role. These changes are described and the results discussed.


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World-wide during the last 5 years in vitro fertilisation (IVF) clinics have sprung up. This new modality has brought hope to countless infertile couples. IVF has moved rapidly from an esoteric technique to an available method of infertility treatment for many couples; one million may benefit from it in the USA alone.1

A programme of IVF is simple in concept but difficult to accomplish. However, as knowledge and insight and also confidence in this new procedure developed, changes in technique occurred that had a significant beneficial influence on the success rate. Some of these advances were: altered ovulation induction regimens proved beneficial;2 it was learned that 'ugly' looking embryos produced normal pregnancies and babies;3 and immature eggs were found to mature successfully with prolonged incubation.4 Furthermore, numerous recent reports have demonstrated an increasing pregnancy rate with an increasing number of embryos replaced in the uterus.5

The primary goals of our programme have been threefold: (i) to develop a clinical programme for the treatment of infertile couples not treatable by conventional methods; (ii) to apply scientific enquiry to selected aspects of current IVF protocols with the aim of improving overall success rates and increasing our knowledge of basic human reproductive biology; and (iii) to serve as a background against which possible future development, i.e. embryo manipulations including sex determination and early embryonic diagnosis, could be implemented.

The ultimate goal of any clinical programme of IVF and embryo replacement is to maximise the number of patients who become pregnant in a treatment cycle. A 12% pregnancy rate was previously reported from this unit.6 After the instigation of changes and further modifications, the pregnancy rate