Type 2 diabetes in obese white children

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We report four white adolescents aged 13 to 15 years (three females, one male) from the south and west region of England who presented with type 2 diabetes mellitus associated with significant obesity (body mass index more than +3SDS) in the past two years. Although these are the first reported obese, white cases from the UK to present with diabetes, we believe this clinical scenario will become more prevalent given the epidemic of childhood obesity in this country.

Type 2 diabetes is still rare in childhood, but recent reports indicate an increasing prevalence in minority populations around the world. This is particularly the case in the USA, but has also been reported in Japan, Libya, Bangladesh, Australia, and Canada. Although a number of cases of type 2 diabetes have been described in UK children, all have been in individuals from ethnic groups known to be at higher risk. There are no published reports documenting the development in obese white children in the UK. Type 2 diabetes is a major cause of morbidity and mortality in adults. Young people developing type 2 diabetes will be at risk of diabetic microvascular and macrovascular disease from a far younger age. In adults, diagnosis may be delayed because of the absence of symptoms early in the disease, so complications can be present at diagnosis. In the USA, a significant proportion of children with type 2 diabetes are found to have hypertension, hypertriglyceridaemia, and microalbuminuria at the time of diagnosis and at follow up; the increasing incidence of childhood obesity in the UK and the inevitable rise in type 2 diabetes from an early age is likely to have a major long term impact on health care systems in the UK.

CASE REPORTS

In our two tertiary referral centres we have identified four obese adolescents (three females, one male; body mass index >35 kg/m²) with either overt clinical diabetes or unrecognised diabetes, diagnosed during oral glucose tolerance testing, over the past 24 months (see table 1).

- Case 1: A pubertal female, aged 15 years, presented with polyuria and polydypsia associated with obesity and acanthosis nigricans. She also had secondary amenorrhoea, acne, and hirsuitism, implying possible polycystic ovary syndrome. There was no family history of diabetes.
- Case 2: A pubertal female, aged 13 years, presented with obesity, enuresis, and glycosuria. Her mother had type 2 diabetes with diabetic retinopathy, requiring insulin.
- Case 3: A pubertal female, aged 14 years, presented with polyuria and polydypsia associated with obesity and acanthosis nigricans. She had a mother with type 2 diabetes.
- Case 4: A pubertal male, aged 15 years, presented in diabetic ketoacidosis. After initial stabilisation, he had rapidly reducing insulin requirements with normal blood glucose and HbA1C measurements. His treatment was changed to diet and metformin after four months. His mother had a normal fasting blood glucose but a raised fasting C peptide concentration, implying a degree of insulin resistance.

All three girls have responded to a treatment regimen using the biguanide metformin, and diet. Islet cell antibodies were negative in all patients at diagnosis. None of these adolescents had severe learning difficulties that can be associated with hyperphagia and severe obesity.

DISCUSSION

The increasing prevalence of type 2 diabetes in the USA has closely paralleled the increase in childhood obesity noted there and across the Western world. Obesity in adulthood is recognised as an independent risk factor for the development of type 2 diabetes, and obesity in adolescence increases the risk of insulin resistance and glucose intolerance. Type 2 diabetes is associated with both insulin resistance and β cell failure, although the primary defect remains unclear. β Cell dysfunction is characterised by raised concentrations of the insulin precursors, intact proinsulin and 32/33 split proinsulin, and studies have shown that raised fasting proinsulin concentrations are highly predictive of the development of type 2 diabetes. We have recently shown that in a selected population of obese, mainly white children, metabolic abnormalities, including hyperinsulinaemia and raised insulin precursors are present, which are associated with a high risk of type 2 diabetes. The increase in childhood obesity in the UK is therefore likely to precede an increase in the incidence of type 2 diabetes in both white and ethnic minority groups.

The mean age at diagnosis reported for type 2 diabetes in childhood is 12–14 years, coinciding with the relative insulin resistance.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>BMI (kg/m²)</th>
<th>BMI SDS</th>
<th>Fasting glucose (mmol/l) (NR ≤ 7.0 mmol/l)</th>
<th>Fasting insulin (pmol/l) (NR ≤ 60 pmol/l)</th>
<th>Fasting C peptide (pmol/l) (NR ≤ 600 pmol/l)</th>
<th>2 h glucose (mmol/l) (NR ≤ 11.1 mmol/l)</th>
<th>HbA1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>15</td>
<td>40.6</td>
<td>+3.7</td>
<td>9.6</td>
<td>354</td>
<td>2715</td>
<td>14.5</td>
<td>7.9</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>13</td>
<td>32.66</td>
<td>+3.07</td>
<td>5.7</td>
<td>68</td>
<td>–</td>
<td>15.6</td>
<td>6.9</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>14</td>
<td>36.9</td>
<td>+3.41</td>
<td>13.1</td>
<td>275</td>
<td>–</td>
<td>–</td>
<td>14.4</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>13</td>
<td>39</td>
<td>+3.64</td>
<td>6.8</td>
<td>21.8</td>
<td>1508</td>
<td>19.8</td>
<td>14.7</td>
</tr>
</tbody>
</table>

BMI, body mass index; SDS, standard deviation score; NR, normal range.
resistance occurring during puberty, which may precipitate glucose intolerance.\textsuperscript{1,4} Although adolescents presenting with diabetes are normally assumed to have type 1 diabetes, this may no longer be the case, even if the patient presents in ketoacidosis requiring insulin treatment.\textsuperscript{4} In recent studies 5–25\% of children with type 2 diabetes presented with ketoacidosis, and ketonuria was present in a further 33\%.\textsuperscript{2,4} The majority of these children will be obese, but the severity of the obesity may be mitigated by weight loss prior to presentation.\textsuperscript{2} These factors may lead to the misclassification of adolescents with type 2 diabetes as type 1, and possibly an underestimation of the current prevalence of this clinical problem.\textsuperscript{2} Other pertinent features in the differential diagnosis include a positive family history (the frequency of a first degree relative with type 2 diabetes has been reported as ranging from 74–100\%).\textsuperscript{2,4} The presence of acanthosis nigricans (fig 1). Acanthosis nigricans has always been regarded as rare in childhood but is strongly associated with obesity and insulin resistance. Maturity onset diabetes of the young (MODY) should also be considered in the differential diagnosis. None of the cases described above fit the criteria for MODY as they show clear evidence of insulin resistance.

As far as we are aware, these are the first cases of type 2 diabetes described in white children in the UK; however, this phenomenon is likely to become increasingly common. It is therefore essential that clinicians appreciate the risk of clinical and unrecognised type 2 diabetes associated with obesity in white children as well as those from high risk populations, as early investigation and appropriate treatment may delay the onset of complications. New research is needed into current national prevalence rates and subsequently, effective methods of prevention and management. Health care providers must particularly recognise the need for targeted screening of at-risk patients, identifying subjects at high risk because of obesity and a family history of diabetes mellitus.

\begin{figure}
\centering
\includegraphics[width=0.8\textwidth]{figure1.png}
\caption{Acanthosis nigricans around the neck in a patient with insulin resistance and obesity.}
\end{figure}

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