Linear growth and body mass index in pediatric patients with Cushing’s disease or simple obesity

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ABSTRACT. Background: Increasing prevalence of childhood obesity has resulted in an accelerating rate of referrals of overweight patients to pediatric clinics for exclusion of endocrine or metabolic etiologies. The exclusion of Cushing’s disease (CD) requires complex and potentially invasive investigations. Objective: to evaluate the sensitivity of accurate measurements of height, weight and body mass index (BMI) in discriminating between simple obesity and CD. Methods and patients: Height, weight and BMI were measured at diagnosis in 25 patients with CD; 14 males, 11 females, mean age 12.9 yr (6.4-17.8) and 41 patients with simple obesity (SO), defined as BMI >2.0 SD; 20 males, 21 females, mean age 9.4 yr (3.5-15.6). Results: Mean (±SE) BMI SDS in the CD patients was 2.41±0.5 and in the SO patients 3.71±1.3. Height SDS in the CD patients was −1.88±0.24 and in the SO patients 1.18±0.19 (p<0.05). The mean (±SE) BMI SDS to height SDS ratio was significantly decreased in the CD compared with the SO patients; −1.81±0.54 vs +0.90±1.17 (p<0.0001). Conclusions: Simple, accurate measurement of height and BMI SDS values provides a quick, and sensitive diagnostic discriminator in pediatric patients with CD or SO, thus potentially avoiding complex investigations.

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INTRODUCTION
Prevalence of obesity within Western societies and developing nations is increasing at an alarming rate (1-4). Evidence suggests that long-term morbidities associated with obesity begin in early life, leading to potential disability in adult life (5). As a result, there is now a greater understanding of the need for referral of overweight children for investigation. The predominant cause for obesity remains increased energy intake compared to expenditure. However, patients are increasingly referred for exclusion of primary genetic, neurological and endocrine causes (6).

One of the causes of obesity is Cushing’s syndrome (CS). The incidence of CS in children and in particular ACTH-dependent Cushing’s disease (CD), which is the commonest cause of CS over the age of 7 yr, is very low (7). However, CD can be difficult to diagnose and a series of standardized biochemical and radiological investigations is required (8, 9).

The typical clinical features of CS are increase in body weight (7, 10) with variable restriction in height (11). We have carried out a retrospective comparison of height SDS and body mass index (BMI) SDS recorded in patients with proven diagnoses of CD and simple obesity, in order to assess if accurate auxological measurement prior to biochemical investigation was a sensitive indicator of the diagnosis.

PATIENTS AND METHODS
Patients
Twenty-five patients (14 males, 11 females), diagnosed with CD at mean age 12.9 yr (6.4-17.8 yr) and 41 patients with simple obesity (SO) (20 males, 21 females) with mean age 9.36 yr (3.5-15.6 yr) seen between 1984 and 2005 were studied.

Methods Diagnosis of Cushing’s disease
All patients were investigated in the Department of Endocrinology of the Royal London and St Bartholomew’s Hospitals, London. CD was diagnosed on the basis of loss of serum cortisol circadian rhythm with elevated midnight sleeping cortisol (>50 nmol/l), lack of suppression of serum cortisol (<50 nmol/l) during low-dose dexamethasone sup-

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expression test (LDDST) (0.5 mg 6-hrly x 48 h), suppression of serum cortisol to >50% of baseline level after high-dose dexamethasone suppression test (2 mg 6-hrly x 48 h) and increased cortisol response in a CRH test (1 µg/kg bolus iv) (9). In addition, localization of pituitary-dependent ACTH secretion was confirmed in 21 patients by bilateral inferior petrosal sinus sampling (IPSS) (12,13).

**Diagnosis of simple obesity**

All patients were investigated in the Department of Respiratory Pediatrics at the Royal London Hospital, London. Patients had a BMI >+2.0 SDS or greater than the 99th percentile as defined by Cole et al. (14) with no specific etiology. The patients underwent a dietetic assessment with investigation of thyroid function, liver function, fasting lipids, glucose and insulin.

**Auxology**

Auxological observations were performed at initial review in both groups using standard anthropometric techniques. Height was expressed as SD score (SDS) and BMI was calculated from the formula: weight (kg)/height² (m). SDS scores were calculated from the 1990 British reference data (14,15).

**Statistical analysis**

Comparison of the relationship between height SDS and BMI SDS was performed using the calculation of the Spearman rank correlation coefficient. Analysis of differences between patient groups in relation to height SDS and BMI SDS was performed using a Mann Whitney paired U-test. Analyses were performed using Graphpad 4 Prism software.

**RESULTS**

Results are expressed as mean±SE.

**Auxology**

Details of clinical and auxology variables in the patients studied are given in Table 1. There was a slight predominance of males in the group of patients with CD. This has recently been reported in pediatric CD patients (16). The SO patients were diagnosed at an earlier age than the CD patients. The BMI SDS values in the SO patients were slightly higher than those of the CD patients. Height SDS values were significantly higher in the SO patients than in the CD patients; −1.8±0.24 and 1.1±0.19, respectively (p<0.05). The ratio of BMI SDS to height SDS was significantly greater in the SO group than the CD group (p=0.0001) (Fig. 1). Only one patient in the CD group had a BMI to height SDS ratio >1.0.

**DISCUSSION**

The examination of height and BMI in these two diagnostic groups of obese patients is important because of the known association of impaired growth in CD (11) and potentially advanced growth in SO (6).

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**Table 1 - Clinical and auxological details in patients with Cushing’s disease (CD) and simple obesity (SO).**

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>SO</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>25</td>
<td>41</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>14/11</td>
<td>20/21</td>
</tr>
<tr>
<td>Age at diagnosis (yr)</td>
<td>12.9±0.6</td>
<td>9.3±0.5</td>
</tr>
<tr>
<td>Duration of symptoms (yr)</td>
<td>2.7±1.5</td>
<td>—</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>2.4±0.5</td>
<td>3.7±1.3</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>2.4±0.2</td>
<td>3.7±0.1</td>
</tr>
<tr>
<td>Height SDS</td>
<td>−1.8±0.2</td>
<td>1.1±0.2</td>
</tr>
<tr>
<td>Height SDS/BMI SDS ratio</td>
<td>−1.3±0.54</td>
<td>0.90±1.2</td>
</tr>
</tbody>
</table>

Data expressed as mean±SE.