SLIPPED UPPER FEMORAL EPIPHYSIS AND PRIMARY JUVENILE HYPOTHYROIDISM


From Alder Hey Children's Hospital, Liverpool

The pathogenesis of slipped upper femoral epiphysis is unknown but the condition has been linked with various endocrine disorders. Nine patients with slipped epiphyses in association with primary juvenile hypothyroidism are presented. In all patients, slipping occurred or symptoms developed in the affected hip before the hypothyroidism was diagnosed. A generalised pathology was suggested by the absence of trauma (8 patients), by bilateral slipping (6 patients), and by obesity and short stature in all patients. All cases had delayed skeletal maturation and characteristic metaphysial changes were seen on their radiographs.

The clinical diagnosis of juvenile hypothyroidism can be difficult but it merits consideration in patients who have a slipped upper femoral epiphysis in association with short stature, obesity, delay in skeletal maturity, or any one of these.

The aetiology of slipped upper femoral epiphysis has remained a matter of considerable speculation despite the voluminous literature on the subject. Waldenström (1940) noticed the signs of a mild form of dystrophia adiposogenitatis in one-third of his patients and described altered function of the pituitary and the sex glands. In 1950 Harris, following his experimental work on the shearing strength of the upper tibial epiphysis in rats, proposed that it was the imbalance between growth hormones and sex hormones which was responsible for the slipping. On the contrary, Razzano, Nelson and Eversman (1972) did not find any such abnormality of growth or sex hormone levels in patients at the time of slipping.

The prevalence of slipped upper femoral epiphysis in obese children has been reported by several authors (Boyd, Ingram and Bourkard 1949; Cleveland et al. 1951; Burrows 1957; Wilson, Jacobs and Schecter 1965). This was not found to be the case in tall children, according to Burrows (1957) and Sørensen (1968). A number of obese children had slower than average skeletal maturation; this combination is considered to heighten the risk of slipping (Sørensen 1968; Kelsey, Acheson and Keggi 1972).

Several factors suggest the presence of a generalised abnormality. These include obesity, delayed skeletal maturation, occurrence during the adolescent growth spurt, a high incidence of bilaterality (Hall 1957; Jacobs 1972) and the frequent absence of trauma. This view is supported by reports (Shea and Mankin 1966; Chioff, Sears and Slaughter 1974) of slipping in various metabolic and endocrine disorders (Tables I and II).

Interest in the association between slipped upper femoral epiphysis and hypothyroidism was first aroused by Lewin (1928) who noticed bilateral slip in a nine-year-old girl who appeared to be clinically hypothyroid. Subsequent papers (Table II) report only 18 patients with both conditions, the largest two series of four patients each being reported by Crawford, MacEwen and Fonte (1977) and Hirano et al. (1978).

PATIENTS AND METHODS

Nine patients with juvenile hypothyroidism and slipped upper femoral epiphysis were studied. The relevant details are listed in Table III. The diagnosis of the hip disorder was established from anteroposterior and frog-lateral (Lowenstein) radiographs. The bone age was assessed from radiographs of the hand, using the TW2 method (Tanner et al. 1975).

RESULTS

Five girls and four boys were affected. Slipped upper femoral epiphysis was diagnosed at the average age of 13 years 2 months and juvenile hypothyroidism at 13 years
Table I. Published reports of slipped upper femoral epiphysis associated with endocrine disorders other than juvenile hypothyroidism

<table>
<thead>
<tr>
<th>Author</th>
<th>Diagnosis</th>
<th>Age at diagnosis of SUFE (years)</th>
<th>Sex</th>
<th>Skeletal age (years)</th>
<th>Thyroid function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Müller 1888</td>
<td>Pituitary basophilic adenoma</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Farrow 1953</td>
<td>Post-traumatic Simmond’s disease</td>
<td>20</td>
<td>M</td>
<td>—</td>
<td>BMR 10% below normal</td>
</tr>
<tr>
<td>Löfgren 1953</td>
<td>Hyperpituitarism Craniopharyngioma</td>
<td>14</td>
<td>F</td>
<td>16</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Burrows 1957</td>
<td>Pituitary disorder (no precise diagnosis)</td>
<td>14</td>
<td>F</td>
<td>—</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Goldman et al. 1963</td>
<td>Hypopituitarism (fractional) with gigantism</td>
<td>27</td>
<td>M</td>
<td>—</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Sarver et al. 1964</td>
<td>Hypopituitarism (fractional) with gigantism</td>
<td>27</td>
<td>M</td>
<td>—</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Tissink 1964</td>
<td>Craniopharyngioma</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Zimmerman et al. 1967</td>
<td>Hypopituitarism</td>
<td>29</td>
<td>M</td>
<td>14–16</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Primiano and Hughston 1971</td>
<td>Hypogonadal male (Klinefelter’s mosaic)</td>
<td>19</td>
<td>M</td>
<td>14</td>
<td>Normal</td>
</tr>
<tr>
<td>Rennie and Mitchell 1974</td>
<td>Selective GH deficiency (on GH treatment)</td>
<td>17</td>
<td>F</td>
<td>9</td>
<td>Normal</td>
</tr>
<tr>
<td>Fidler and Brook 1974</td>
<td>Craniopharyngioma (on GH treatment)</td>
<td>16</td>
<td>M</td>
<td>14</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Heatley et al. 1976</td>
<td>Craniopharyngioma</td>
<td>27</td>
<td>M</td>
<td>15</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Optic glioma</td>
<td>Craniopharyngioma</td>
<td>13</td>
<td>F</td>
<td>11</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>Craniopharyngioma</td>
<td>19</td>
<td>M</td>
<td>16</td>
<td>Hypothyroid</td>
</tr>
<tr>
<td>Moorefield et al. 1976</td>
<td>Craniopharyngioma</td>
<td>13</td>
<td>F</td>
<td>11</td>
<td>Hypothyroid</td>
</tr>
</tbody>
</table>

SUFÉ, slipped upper femoral epiphysis  
BMR, basal metabolic rate  
GH, growth hormone  
—information not available

4 months. The range for both was from 8 years 8 months to 19 years 2 months.

In eight patients bone age was delayed by an average of three years; the minimum delay was two years and the maximum six years. A radiograph of the hand was not available in one of the patients (Case 8), but he clearly had delayed skeletal maturation because slipping occurred at the age of 19 years 2 months.

Body weight and total height were recorded at the time that the hip condition was diagnosed. This information was not available in Case 8 though, in clinical records, he was described as short and obese. Clinically most of the other eight patients appeared also to be obese in relation to their short stature (Figs 1 and 2). On standard weight charts none of these patients was above the 97th centile, but when weight was plotted against skeletal age seven patients were at or above the 95th centile (Table II). This correlation between obesity and delayed skeletal maturation was considered to be a significant factor predisposing to epiphysial slipping.

All eight patients were of short stature: six were below the 3rd centile and the other two at the 10th and 20th centile respectively.

**Slipped upper femoral epiphysis**

**Symptoms.** Pain was the predominant symptom and was localised to the affected hip in all but one patient (Case 9); his pain was mainly in the ipsilateral knee.  
**Duration.** This ranged from two months to four years. It is noteworthy that all the patients sustained a slipped epiphysis or developed symptoms in the affected hip before hypothyroidism was diagnosed.  
**Trauma.** Only one patient (Case 3) gave a history of possible trauma during a high jump at school. In all other patients symptoms developed spontaneously.  
**Laterality.** Bilateral slips occurred in six patients—an incidence of 66.6%. As the slipping was asymptomatic in all six this was considered to be highly significant.
Table II. Published reports of slipped upper femoral epiphysis associated with juvenile hypothyroidism

<table>
<thead>
<tr>
<th>Author</th>
<th>Age at diagnosis (years)</th>
<th>Delay in skeletal maturation (years)</th>
<th>Weight centile related to age</th>
<th>Height centile related to age</th>
<th>Trauma</th>
<th>Laterality</th>
<th>Silent slips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewin 1928</td>
<td>9</td>
<td>— F</td>
<td>15</td>
<td>&lt; 3</td>
<td>Nil</td>
<td>Bilateral</td>
<td>Right</td>
</tr>
<tr>
<td>Benjamin and Miller 1938</td>
<td>11</td>
<td>5 M</td>
<td>15 &lt; 97</td>
<td>&lt; 3 &gt; 97</td>
<td>Fall from bicycle</td>
<td>Left</td>
<td>Nil</td>
</tr>
<tr>
<td>Epps and Martin 1963</td>
<td>22</td>
<td>9 F</td>
<td>&lt; 3 30</td>
<td>&lt; 3 &lt; 3</td>
<td>Nil</td>
<td>Left</td>
<td>Nil</td>
</tr>
<tr>
<td>Moorefield et al. 1976</td>
<td>12</td>
<td>7 M</td>
<td>50 &gt; 97</td>
<td>&lt; 3 &gt; 97</td>
<td>Nil</td>
<td>Left</td>
<td>Nil</td>
</tr>
<tr>
<td>Crawford et al. 1977</td>
<td>9</td>
<td>— M</td>
<td>—</td>
<td>—</td>
<td>Nil</td>
<td>Right</td>
<td>Nil</td>
</tr>
<tr>
<td>Zubrow et al. 1978</td>
<td>9</td>
<td>3 F</td>
<td>25 90</td>
<td>&lt; 3 60</td>
<td>Nil</td>
<td>Bilateral</td>
<td>Nil</td>
</tr>
<tr>
<td>Hirano et al. 1978</td>
<td>9</td>
<td>Nil M</td>
<td>—</td>
<td>—</td>
<td>Right</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Al-Aswad et al. 1978</td>
<td>35</td>
<td>Nil M</td>
<td>—</td>
<td>—</td>
<td>Nil</td>
<td>Right</td>
<td>Nil</td>
</tr>
<tr>
<td>Jayakumar 1980</td>
<td>12</td>
<td>— F</td>
<td>—</td>
<td>—</td>
<td>Nil</td>
<td>Bilateral</td>
<td>Right</td>
</tr>
<tr>
<td>Hennessy and Jones 1982</td>
<td>21</td>
<td>— M</td>
<td>—</td>
<td>—</td>
<td>Nil</td>
<td>Right</td>
<td>Nil</td>
</tr>
</tbody>
</table>

* Treatment stopped at 10 years
SUFE, slipped upper femoral epiphysis
JHT, juvenile hypothyroidism
Chron., chronological
Skel., skeletal
— information not available

Table III. Details of patients in the present series with slipped upper femoral epiphysis associated with juvenile hypothyroidism

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>SUFE</th>
<th>JHT</th>
<th>Delay in skeletal maturation (years)</th>
<th>Weight centile related to age</th>
<th>Height centile related to age</th>
<th>Trauma</th>
<th>Laterality</th>
<th>Silent slips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>y</td>
<td>m</td>
<td>y</td>
<td>m</td>
<td>Sex</td>
<td>Chron.</td>
<td>Skel.</td>
<td>Chron.</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>2</td>
<td>F</td>
<td>85</td>
<td>&gt; 97</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>10</td>
<td>13</td>
<td>10</td>
<td>3</td>
<td>F</td>
<td>80</td>
<td>&gt; 97</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>10</td>
<td>14</td>
<td>10</td>
<td>3</td>
<td>F</td>
<td>55</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>5</td>
<td>14</td>
<td>6</td>
<td>2</td>
<td>F</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>2</td>
<td>F</td>
<td>75</td>
<td>&gt; 97</td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>0</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>M</td>
<td>80</td>
<td>&gt; 97</td>
</tr>
<tr>
<td>7</td>
<td>15</td>
<td>3</td>
<td>15</td>
<td>3</td>
<td>6</td>
<td>M</td>
<td>20</td>
<td>&gt; 97</td>
</tr>
<tr>
<td>8</td>
<td>19</td>
<td>2</td>
<td>19</td>
<td>2</td>
<td>—</td>
<td>M</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>6</td>
<td>14</td>
<td>3</td>
<td>4</td>
<td>M</td>
<td>6</td>
<td>95</td>
</tr>
</tbody>
</table>

SUFE, slipped upper femoral epiphysis
JHT, juvenile hypothyroidism
Chron., chronological
Skel., skeletal
— information not available
Juvenile hypothyroidism

Symptoms and signs. Seven patients, first seen in the orthopaedic department with hip pain, were referred on clinical suspicion for endocrine evaluation. In the remaining two patients hypothyroidism was diagnosed first, and they were referred later for orthopaedic assessment. One of these two (Case 5), a girl diagnosed as being hypothyroid two months before orthopaedic referral, had a history of pain in her left hip over the same period. The other (Case 9), a boy found to be hypothyroid three months before referral, had suffered from intermittent pain in his left knee for 18 months. Thus all patients developed symptoms in the affected leg before hypothyroidism was diagnosed.

The important clinical features of the juvenile hypothyroidism in order of frequency were short stature, obesity (in relation to height) and lethargy. There was no evidence of intellectual deterioration. Several patients had dry skin and a hoarse voice, and their tendon reflexes had a delayed relaxation phase. Seven patients at about the age of puberty showed delay in development of secondary sexual characteristics.

Biochemical and radiographic investigations. Low thyroxine and high thyroid-stimulating hormone levels were found in all patients, denoting primary hypothyroidism. Thyroid antibodies were identified in varying concentrations in the sera of seven patients, confirming auto-immune (Hashimoto's) thyroiditis. The cause of the thyroid deficiency in the other two patients was not known. Thyroid scanning with $^{99m}$Tc was undertaken in six of the patients with Hashimoto's thyroiditis; all demonstrated a patchy uptake with some gland asymmetry. Radiographs of the skull carried out in six patients did not reveal any abnormality of the pituitary fossa.

Radiographic features. Decreased thyroid function retards growth and delays skeletal maturation; it also delays closure of the growth plate and the appearance of secondary centres of ossification. The retarded bone age

Treatment. Out of a total of 15 slipped epiphyses, 11 were pinned, one (Case 9) had an open reduction and three were treated conservatively without progression. Bilateral slipping in the youngest patient (Case 1) was at first treated conservatively, with traction for eight weeks, because of the fear that pinning might cause premature fusion of the growth plates. She was euthyroid in six weeks (having started on thyroxine when traction began) but both slips progressed from Grade I to Grade II (Figs 3 and 4).

Case 6. The characteristic obesity and short stature of a patient with juvenile hypothyroidism.

Case 1. Figure 3—Bilateral slipped epiphysis in a girl aged 8 years 8 months. Figure 4—Despite traction in abduction and medial rotation for eight weeks and treatment with thyroxine both slips progressed, the left from 20° to 30° and the right from 10° to 22°.
indicates the approximate age of onset of the hypothyroidism. Stippling of various epiphyses (epiphysial dysgenesis), observed characteristically in congenital hypothyroidism, is due to poor and patchy ossification of the epiphysial cartilage (Wilkins 1941); such epiphysial dysgenesis does not occur in juvenile hypothyroidism, perhaps because of its late and gradual onset. The histological and radiological evidence of a weak epophysidiaphysial union in thyroxine deficiency has been reviewed in detail by Benjamin and Miller (1938).

The skeletal changes seen at the upper femoral growth plates in the present series were similar in all the patients though of variable degree. Widening and irregularity of the growth plate in the apparently normal hip as well as in the affected hip was seen on anteroposterior and frog-lateral radiographs. These changes were related in severity to the duration of thyroxine deficiency. In other words, widening and irregularity of growth plates was more marked in those patients who had appreciable delay in bone maturation (Figs 5 to 11). Irregularity of the growth plate was observed largely on the diaphysial side and was indicative of patchy ossification of the cartilage columns.

**DISCUSSION**

Maturation of the skeletal system depends largely on thyroid hormone (Wilkins 1955; Fell and Mellanby 1956); this stimulates hypertrophy and subsequent ossification of the cartilage cells (Silberberg and Silberberg 1943). Ray et al. (1950) have clearly demonstrated in rats that it is thyroxine which is mainly responsible for the process of enchondral ossification; it appears that growth hormones and sex hormones are not essential. It would seem reasonable to infer that thyroxine is responsible for imparting strength to the growth plate by virtue of its specific effect on enchondral ossification.

Reports of slipped upper femoral epiphysis in association with various endocrine disorders (other than primary hypothyroidism) have referred largely to patients with pituitary dysfunction (Table I). Most slipped epiphyses occurred in patients with hypopituitarism caused by intracranial tumours; significantly, most of these patients had associated hypothyroidism. Harris' hypothesis (1950) implies relatively high growth hormone levels together with low levels of sex hormones as the basis for slipped upper femoral epiphysis. However, most of the patients with hypopituitarism had low levels of growth hormone and low levels of sex hormones. Patients with gigantism and associated fractional hypopituitarism appear to have the most adverse combination of elevated growth hormone and low thyroxine levels leading to delayed skeletal maturation. In these syndromes the stresses of normal or abnormal body weight on the immature upper femoral growth plate probably predispose to epiphysial slipping (Heatley, Greenwood and Boase 1976).
A total of 18 cases of slipped upper femoral epiphysis in juvenile hypothyroidism have been described in the literature (Table II). After Lewin’s first account (1928) of bilateral slips in a nine-year-old girl with hypothyroidism, Benjamin and Miller (1938) added a second case: a cretinous boy who had been on thyroid medication from the age of 17 months. His medication was stopped at the age of 10 years and a year later his left upper femoral epiphysis slipped in a manner similar to that in other hypothyroid patients. Epps and Martin (1963) recorded a slipped upper femoral epiphysis in a 22-year-old mother with myxoedema who was thought to have developed hypothyroidism in her late adolescence. Al-Aswad, Weinger and Schneider (1978) and Hennessy and Jones (1982) also reported older patients, aged 35 and 21 years respectively, who presumably became hypothyroid in their late adolescence. Slipped upper femoral epiphysis in a patient with juvenile hypothyroidism who was receiving thyroxine treatment was reported by Zubrow, Lane and Parks (1978), Moorefield et al. (1976) and Crawford et al. (1971), while reporting their cases of slipped upper femoral epiphysis in juvenile hypothyroidism, advocated thyroid function evaluation in every short and obese child who had a delayed skeletal age and a slipped upper femoral epiphysis.

All patients in the present series had biochemically proven juvenile hypothyroidism. The most significant single observation was that these patients developed slipped epiphyses or had hip symptoms before the hypothyroidism was diagnosed. This fact emphasises the dominant role played by deficient thyroid hormone in the pathogenesis of slipped upper femoral epiphysis, and also that obesity in the presence of delayed skeletal maturity predisposes to slipping in the region of the weak epiphysesdiaphysial zone (Benjamin and Miller 1938). Seven of the nine patients studied in the present series had biochemically confirmed Hashimoto’s thyroiditis—an auto-immune disorder. The idea that there may be a local auto-immune basis responsible for slipping in these patients, put forward by Morrissey, Steele and Gerdes (1983), cannot be ruled out and it remains to be investigated further.

Several authors (Morscher 1968; Sørensen 1968; Reichelt and Rütt 1969) have reported delayed skeletal maturation in a number of obese children with slipped upper femoral epiphysis in the absence of overt endocrine disease. The clinical picture of these patients and those with juvenile hypothyroidism appears to be similar. Is it possible that such children have a degree of sub-clinical hypothyroidism perhaps related to increased metabolic needs, especially during the adolescent growth spurt? It is interesting to speculate whether small doses of thyroxine in these children would promote growth plate maturation in the opposite “normal” hip and thus obviate the need for prophylactic pinning.

With regard to orthopaedic management, some authorities believe that no surgical procedure should be undertaken until an euthyroid state is reached. This can take several weeks during which time the patient may be immobilised on traction or in a plaster cast. Even then progressive slipping may occur. In the present series there were two patients (Cases 3 and 4) who had surgical treatment before the hypothyroidism was diagnosed; neither had complications during or after operation.

We do not recommend conservative management of slipped upper femoral epiphysis in juvenile hypothyroidism. The mechanical deterioration from continued slipping, and the time required to achieve an euthyroid state pre-operatively, may preclude a good result, while early fixation avoids prolonged immobilisation and probably leads to more satisfactory hip function. Prophylactic pinning of the opposite apparently normal hip should also be considered if this is thought to be at risk. It is clear that close liaison between paediatrician and surgeon is mandatory in the management of these patients.

Routine radiography of the pelvis to exclude silent slipping in every juvenile hypothyroid patient, and evaluation of thyroid function in every short and obese child with a slipped upper femoral epiphysis, will help in diagnosing either or both of the conditions at the earliest opportunity.

We would like to thank the following consultant orthopaedic surgeons for access to their patients: Mr C. J. E. Monk, Mr J. F. Taylor, Mr M. J. S. Hubbard, Mr J. Lewis, Mr T. A. Evans and Mr A. G. Pollen.

REFERENCES


