Table 2 *Duration and severity of colic: total hours with colic/No of symptomatic days (difficult colic in parentheses). The longest duration of each child is in bold*

Case No	*Milk feed*			
	Breast milk	*Breast milk treated with lactase*	*Formula*	*Formula treated with lactase*
1	0·6 (0·2)	3·4 **(3·2)**	**5·2** (1·6)	1·2 (1·0)
2	0·6 (0)	1·5 (0)	1·5 (0)	**2·8 (1·6)**
3	0·5 (0·5)	0·1 (0)	0·9 (0·7)	**3·8 (3·8)**
4	8·1 (7·3)	4·3 (2·5)	6·9 (3·3)	**17·0 (17·0)**
5	**5·2** (1·6)	4·6 (1·0)	0·8 (0·8)	4·3 (**3·5**)
6	0·2 (0·2)	0·2 (0·2)	0·1 (0·1)	**0·4 (0·3)**
7	1·5 (1·5)	1·1 (1·0)	1·0 (0·6)	**2·2 (2·2)**
8	0·7 (0·6)	2·0 (2·0)	**2·9 (2·9)**	1·8 (0)
9	**2·8 (0·8)**	1·5 (0·4)	1·9 (0·6)	1·2 (0·4)
10	**5·5 (5·5)**	2·7 (2·2)	1·2 (0·9)	3·5 (3·3)

Two way analysis of variance: F for overall colic=1·8, df=3/27, p>0·05; F for difficult colic=1·9, df=3/27, p>0·05.
Student's *t* test: cow's milk formulas *v* breast milks, p>0·05; lactose containing *v* lactase treated milks, p>0·05.

There were no differences between the milks in daily duration of colic (Table 2). Not even regrouping cow's milk formulas versus breast milks or lactose containing versus lactase treated milks showed any differences. Severity of attacks was also unaffected. In five children the total duration of colic and in six children the duration of difficult colic was, however, longest on cow's milk treated with lactase.

Discussion

The aetiology of infantile colic may be multiple, different causes operating in different children and perhaps one child's colic even being a result of several factors. To minimise the effects of confounding factors we conducted this investigation as a crossover study.

Colic was present on 89% of the days on cow's milk feeding and on 71% of the days on breast milk feeding. This difference was significant (p<0·05), but 71% is still high: colic is not cured by breast milk. No differences were found regarding severity of colic on those days when the disease was observed. Healthy infants may have physiologic lactase deficiency during several weeks,[6] but infantile colic is not a symptom of lactose malabsorption. Other factors than milk must be crucial.

We are grateful to Valio Ltd for donation of formulas and treatment of milks with lactase.

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Somatomedin C deficiency in Asian sisters

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SUMMARY Two sisters of Asian origin showed typical clinical and biochemical features of primary somatomedin C (SM-C) deficiency (Laron dwarfism). Abnormalities of SM-C binding proteins were observed, one sister lacking the high molecular weight (150 Kd) protein.

In 1966 Laron *et al* first described a form of familial dwarfism characterised by the clinical features of severe growth hormone (hGH) deficiency and high concentrations of plasma immunoreactive hGH.[1] Low plasma somatomedin activities before and during treatment with hGH indicate that the primary defect is in the production of somatomedin.[2] Most reported cases of this autosomal recessive disorder are in oriental Jews,[3] although a few patients of European origin have been described.[2] We report two Asian sisters with Laron dwarfism

and describe abnormalties of somatomedin C (SM-C) binding proteins in their sera.

Patients

Case 1. This girl was born at term, weighing 2950 g, with a length of 45·0 cm (−2·5 standard deviation score (SDS)), to apparently non-consanguinous parents from Pakistan. The heights of both parents and three older male siblings were between the 25th and 50th centiles. She was 'jittery' shortly after birth, but hypoglycaemia was not confirmed. She grew poorly and at 2 years 3 months was referred to a paediatric endocrine unit. On examination her height was 67·5 cm (−5·6 SDS), weight 7·46 kg (−3·9 SDS), and triceps and subscapular skinfolds >97 centiles and she had typical somatic features of hyposomatotropism (Figure).

A full blood count, karyotype, tests of renal, hepatic, and thyroid function yielded normal results. Her bone age was 10 months. Serum prolactin concentrations rose from 112 mU/l to 1530 mU/l after intravenous thyrotrophin releasing hormone stimulation. Serum hGH concentrations ranged from 65 to 150 mU/l (mean 108 mU/l) during a 12 point 24 hour profile and from 54 to 100 mU/l (mean 80 mU/l) in an arginine provocation test. Serum insulin concentrations were <4 mU/l during arginine provocation.

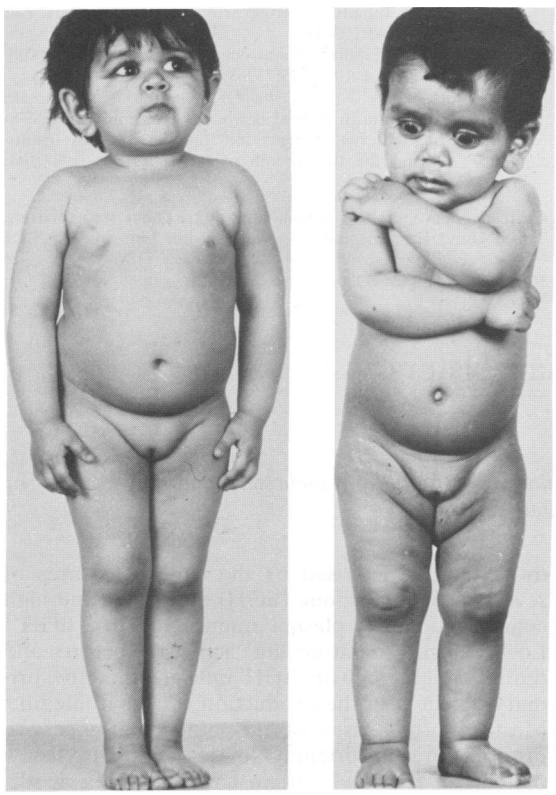

Figure *Case 1 (left) and case 2 (right).*

Before treatment with hGH, serum SM-C was 0·46 U/ml, serum somatomedin activity 0·32 to 0·45 U/ml during a 24 hour profile, and 24 hour urinary hydroxyproline/creatinine ratio 55; normal ranges at this age are 0·47–1·44 U/ml, 0·4–0·7 U/ml, and 45–204, respectively.

Serum binding of [^{125}I]Sm-C showed an absence of the specific 150 Kd binding protein and the presence of binding to proteins ranging from 20 Kd to 100 Kd, the greatest binding being of 40 Kd to 60 Kd.

After two weeks of treatment with hGH (4 IU intramuscularly three times a week) there was no increase in serum SM-C (0·2 U/ml), serum somatomedin activity (0·33 U/ml), and 24 hour urinary hydroxyproline/creatinine ratio (57). Despite a small increase in height velocity of 1 cm/year in the first month, this was not sustained over an eight month period.

Case 2. The sister of case 1 was born at 37 weeks' gestation with a weight of 3200 g, but her length was not documented. She had asymptomatic hypoglycaemia and early feeding difficulties. At 1 year her height was 61·4 cm (−5·1 SDS), weight 6·1 kg (−3·8 SDS), and triceps and subscapular skinfolds >97th centiles and she had typical features of hyposomatotropism.

Her karyotype and thyroid function were normal. Serum prolactin concentrations rose from 346 to 1400 mU/l after intravenous thyrotrophin releasing hormone. Serum hGH concentrations ranged from 45 to 135 mU/l (mean 91 mU/l) during a 12 point 24 hour profile and from 35 to 120 mU/l (mean 64 mU/l) during an arginine provocation test. Serum insulin concentrations were <4 mU/l during arginine provocation. Basal serum SM-C concentrations ranged from 0·12 to 0·23 U/ml (mean 0·18 U/ml) and basal serum somatomedin activity from 0 to 0·37 U/l (mean 0·16 U/l).

Serum binding of [^{125}I]SM-C showed the presence of the specific 150 Kd binding protein and small amounts of binding activity at higher and lower molecular weights, especially in the 40–60 Kd region.

Methods

hGH was measured by double antibody radioimmunoassay and somatomedin biological activity by

the porcine costal cartilage bioassay. SM-C was measured by radioimmunoassay as previously described[4] after the removal of somatomedin binding proteins by extraction with acid-ethanol. The somatomedin binding proteins themselves were detected by their competition with activated charcoal for [^{125}I]SM-C, as previously described,[4] after the fractionation of serum on Sephadex G200 eluted with 0·05M phosphate buffer.

Discussion

The clinical and biochemical features of these two sisters strongly support the diagnosis of primary somatomedin deficiency, which was confirmed by failure of response to treatment with hGH in the older child. hGH injections did not produce somatomedin generation, although the small increase in height velocity, which has also been reported in other cases,[1 2] led us to continue the therapeutic trial for eight months. It was not considered appropriate to offer treatment to the younger sister.

Circulating SM-C (insulin like growth factor 1), with its binding proteins, may predominantly reflect paracrine activity in growing tissues, have a true endocrine role, or represent the sum of paracrine and endocrine activity. SM-C is known to be hGH dependent in normal individuals, however, and is characteristically deficient in Laron dwarfism, despite high concentrations of endogenous hGH or treatment with exogenous hGH. SM-C does not exist in a free form in the plasma but is bound to proteins of various molecular weights, including a specific large molecular weight carrier protein (150 Kd) that is itself hGH dependent and may be a hexamer of subunits of 24 Kd.[5] An additional 40 Kd binding species is present in various body fluids but is not dependent on growth hormone. The 150 Kd protein was absent in the older sister but present in the younger. It has been suggested that Laron dwarfism is due to defective hGh receptors;[6] thus heterogeneity of production of the hGH dependent 150 Kd protein is puzzling and may reflect quantitative differences of receptor number. This warrants further study.

The occurrence of Laron dwarfism in an Asian family should alert clinicians to consider the possibility in other Asian children with extreme short stature, relative adiposity, and high circulating hGH concentrations. Other features may include shortness at birth, neonatal hypoglycaemia, and a characteristic and appealing 'babyish' face with small central facial structures, relatively large calvarium, and occasionally a 'surprised appearance' due to slight proptosis. Hypogenitalism is noticeable in boys with this disorder. The condition is rare and is more likely to occur in a population with a high degree of consanguinity. It is hoped that in the future a trial of SM-C treatment may be of benefit.

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