Syndrome of the month

Edited by D Donnai and R Winter

Floating–Harbor syndrome

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Many syndromes are named in an eponymous fashion after the original authors, or occasionally after the original patients, but the name of this syndrome is derived from the hospitals where the first two patients were described. In 1973 Pelletier and Feingold¹ described a boy seen at the Boston Floating Hospital with short stature, delayed speech development, and a striking facial appearance. A further report of a similar case was published in 1974 by Leisti *et al.*² Their patient attended the Harbor General Hospital, Torrance, California. They suggested the term Floating–Harbor syndrome, which for its memorable quality is likely to become established.

Since the original reports there has been one further publication on this syndrome. Robinson *et al.*³ reviewed six further patients from different centres in 1988.

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This review includes a further seven patients whose clinical features are included in the table and five of whose facial features are illustrated in figs 1 and 2.

Clinical features

The syndrome is characterised by a triad of (1) short stature with significantly delayed bone age, (2) expressive language delay, usually in the presence of normal motor development, and (3) a triangular face with a prominent nose and deep set eyes.

GROWTH

Prenatal growth may be affected with the birth weight and length between the 3rd and 10th centile for gestational age. However, the growth delay becomes noticeable in the first year of life and during childhood is 4 to 6 SD below the mean. There have been four patients who completed puberty and they remained significantly short (131 to 142 cm).³ The relative proportions of the trunk and limbs are normal. The head circumference remains around the 50th centile, giving the appearance of a relatively large head.

The bone age is significantly delayed (–2 SD) and appears to be a consistent feature in all patients. The closure of the epiphyses, however, takes place at puberty, which is not significantly delayed. Endocrine studies of growth hormone, somatomedin C, and thyroid function are normal. In one male patient, a three year course of fluoxymesterone did not bring the child's height within the normal range.³ There have been no systematic studies of endocrine treatment in this syndrome and at present the therapeutic effect of synthetic growth hormone has not been evaluated.

DEVELOPMENT

Speech delay is a consistent feature. The speech

Figure 1 Facial features of four patients reviewed in the table. The numbers refer to the patients in the table: (a) patient 1, (b) patient 2, (c) patient 6, (d) patient 7.

difficulties may be related to immobility of the palate. Whether this is the result of a lack of coordination or a specific lower motor neurone lesion is unclear. There is no evidence of other abnormality in the cranial nerves and hearing is normal.

Assessment of general psychomotor development may be difficult in view of the considerable problems in expressive speech. Of the six cases reviewed by Robinson *et al*³ and the seven cases in the table, five out of 13 patients have had some general developmental delay but none has been moderately or severely retarded.

CRANIOFACIAL FEATURES

The most striking facial features of this syndrome are around the nose and upper lip (fig 1). The nose is broad and bulbous with a prominent nasal bridge. The columella is wide. The philtrum is smooth and short with thin upper and lower lips. The mouth is relatively wide. As the cranial growth is not restricted compared to the face, the face appears relatively small and triangular. Long eyelashes and dental malocclusion are also frequently found. The facial features are, perhaps, most recognisable in mid-childhood. In infancy (fig 2) the face is rounder with more prominent

Features of seven cases of Floating-Harbor syndrome.

Patient	Sex	Age (y)	Pregnancy	Birth weight (g)	Bone age	Development	Other features
1	F	5	Diazepam	2500	Delayed	Specific speech delay with immobile palate. Development otherwise normal	Malocclusion. Mild pulmonary stenosis
2	M	5	—	2700	Delayed	Speech delay, motor development within normal range	Constipation. Pakistani family
3	F	8	—	2800	Delayed	Speech delay with poor articulation. General development also delayed	Hirsutism. Finger clubbing
4	M	8	Pre-eclampsia	2890	Delayed	Expressive language delay. Motor development normal	Small nails. Finger clubbing
5	F	7	Minor tranquilisers	2300	Delayed	Speech delay with nasal speech. Development otherwise normal	Accessory thumb. Clavicular pseudarthrosis. Constipation
6	F	8	—	2900	Delayed	Expressive language delay. Development otherwise normal	Hypoplastic nails on 5th fingers. Hirsutism
7	F	5	—	3000	Delayed	Speech delay. Slow in walking	Hirsutism. Fits

Figure 2 Case 5. In infancy (8 months) the facies are well rounded but the broad nose and wide columella offer a means of diagnosis. At 6 years the facies become more characteristic.

eyes. The nasal tip, however, is still broad at this stage. In older children the eyes give the appearance of being deep set.

OTHER CLINICAL FEATURES

A range of other clinical features have been observed. There may be clinodactyly of the fifth finger occasionally with a hypoplastic nail on that digit. Finger clubbing has been present in four out of 13 cases. It does not appear to reflect underlying organic disease although it might lead clinically to an extensive search for underlying causes of failure to thrive, such as malabsorption. In one patient³ there was evidence of anaemia and malabsorption with a jejunal biopsy showing features of coeliac disease. Treatment of this child with a gluten free diet improved the anaemia but has not been followed by any improvement in growth. No other case associated with malabsorption has been reported. Three of the patients in the table have had problems with constipation.

Hirsutism has been noted in children from different racial backgrounds. Pulmonary stenosis, an accessory thumb, and abnormal EEG have been isolated features.

Radiology

Radiological examination has shown a number of abnormalities although none of these is specific to the Floating-Harbor syndrome. There is a significant delay in bone age with the capital femoral epiphyses most delayed in maturation. Cone epiphyses may be noted on x ray of the hand. Perthes disease and a clavicular pseudarthrosis have also been observed. Skull and spinal x rays have shown no abnormalities.

Figure 3 The pedigrees of the patients reviewed in the table.

Genetics

There has been no recurrence of this syndrome within families, and with the present limited knowledge it would be appropriate to give parents a low recurrence risk after the diagnosis of an affected child. Only one of the 13 cases has arisen from a consanguineous marriage and that child was the product of a third cousin Iranian marriage.³ The pedigrees from cases in the table are illustrated in fig 3. Chromosome studies have been normal. In two of the children in the table, the mothers took minor tranquillisers in early pregnancy, but no other specific complications of pregnancy have been observed. Intrauterine growth retardation may be noted during pregnancy.

Pathogenesis and incidence

The cause of this syndrome is unknown. There is no evidence as yet to suggest it has a hormonal or metabolic basis. It is probable that many cases of this syndrome are unrecognised in growth or genetic clinics and the incidence of this syndrome is likely to be greater than the few case reports suggest.

Differential diagnosis

This syndrome is likely to be recognised in the genetic assessment of children attending the clinic for short stature. In infancy the round face, broad nasal tip, and palatal abnormalities may resemble Dubowitz syndrome, but the developing facial features and absence of eczema should distinguish it.⁴

Other conditions to consider in the differential diagnosis are intrauterine growth retardation owing to placental insufficiency, Russell-Silver syndrome, and the 3M syndrome. In placental insufficiency there may be a similar pattern of prenatal growth retardation but often there is a 'catch up' of growth after birth. Placental insufficiency is not associated with a characteristic facial appearance or with radiological abnormalities. In the Russell-Silver syndrome there is a similar pattern of growth retardation with a triangular facies and clinodactyly.⁵ In the 3M syndrome the prominent heels and radiological evidence of thin, slender long bones may distinguish the disorder from Floating-Harbor syndrome. These conditions are not associated with the specific expressive speech defect and this may prove to be a mainstay of the diagnosis.

We would like to thank members of the Dysmorphology Group for their helpful discussion when these patients were presented last year.

- 1 Pelletier G, Feingold M. Case report 1. In: Bergsma D, ed. *Syndrome identification*. Vol 1. No 1. White Plains, NY: National Foundation-March of Dimes, 1973:8-9.
- 2 Leisti J, Hollister DW, Rimoin DL. Case report 2. In: Bergsma D, ed. *Syndrome identification*. Vol 2. No 1. White Plains, NY: National Foundation-March of Dimes, 1974:305.
- 3 Robinson PL, Shokat M, Winter RM, et al. A unique association of short stature, dysmorphic features, and speech impairment (Floating-Harbor syndrome). *J Pediatr* 1988;113:703-6.
- 4 Winter RM. Dubowitz syndrome. *J Med Genet* 1986;23:11-13.
- 5 Patton MA. Russell-Silver syndrome. *J Med Genet* 1988;25:557-60.