Robinow syndrome without mesomelic ‘brachymelia’: a report of five cases

M D BAIN*, R M WINTER†, AND J BURN‡

From *the Section of Perinatal and Child Health, and †Division of Inherited Metabolic Diseases, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ; and ‡Clinical Genetics Unit, Institute of Child Health, London WC1N 1EH.

SUMMARY A family is described in which the father and his two children had Robinow syndrome, but with no consistent brachymelia or dwarfism. Two further sporadic cases are described, one with rhizomelic brachymelia and dwarfism and the other with generalised shortening of the limbs. An attempt is also made to distinguish between the phenotype of autosomal dominant and recessive cases on the basis of the familial cases in this paper and other reported cases.

In 1969 Robinow described a syndrome of characteristic facies, micropenis in the male, and mesomelic limb shortening. There have been several reports of the syndrome documenting both autosomal dominant and recessive inheritance. We describe a family in which three members had the features of Robinow syndrome but without mesomelic brachymelia or dwarfism, unlike other documented cases. Two sporadic cases are also described, one of which had short limbed dwarfism but of the rhizomelic variety, while the other had generalised shortening of the upper limbs. An attempt is made to distinguish between dominant and recessive phenotypes in the light of these further observations.

Case reports

The first three cases are a father (case 1) and two children. The family was ascertained through the daughter (case 2) and subsequently a further affected boy was born (case 3). There was no parental consanguinity and no family history of short stature or unusual facies before the birth of the affected father. It is of interest that the father of case 1 was 52 years of age at the conception of his son, which may have predisposed to a new autosomal dominant mutation.

Case 1 (Fig 1)

This man had all the facial features of Robinow syndrome. He had enjoyed good health and worked as a storeman. His height was 173 cm, which is 1 SD below the mean, and body proportions were normal. The only other feature was a small but functional penis.

Case 2 (Fig 2)

Case 2, a girl, was noted at birth to have unusual facies with a prominent forehead, hypertelorism,
and small nose with anteverted nostrils. Weight, length, and head circumference were on the 50th centile at birth and 2 months of age, but between the 10th and 50th centile by 3 months of age. The genitalia were normal. Just after 3 months of age a urinary tract infection was diagnosed and subsequent investigation showed bilateral renal scarring with grade IV vesicoureteric reflux. Review of the facial features suggested the diagnosis of Robinow syndrome. Prophylactic antibiotics were started and growth returned to the 50th centile. Development was normal.

CASE 3 (FIG 3)
Case 3, a boy, was born 18 months after case 2. Weight, length, and head circumference were well above the 90th centile for gestation. Examination showed the characteristic 'fetal' facies, micropenis, a right undescended testis, and a dislocatable right hip. Clinically there was no limb shortening and radiological measurements were not made until 6 months of age. The dislocated hip was treated with
splintage in a Van Rosen splint. At the age of 10 days, group B streptococcal sepsicaemia with meningitis was diagnosed and successfully treated with penicillin. Subsequent follow up has shown the kidneys to be normal with no vesicoureteric reflux and the hips to be radiologically and clinically normal at 1 year of age. At the age of 1 year both weight and length were on the 50th centile. The right testis was still undescended. Development was normal.

**Radiographs and Detailed Measurements of Limb Lengths**

Review of skeletal surveys on the above three patients did not reveal any vertebral or skeletal abnormalities. Measurements of the length of the long bones according to the methods of Robinow and Chumlea are shown in fig 4. It can be seen that the long bone profiles do not match the two other reported cases for which there are radiological measurements. There is no mesomelic shortening of either the upper or lower limbs in any of the three affected family members.

**Sporadic cases**

**Case 4 (Fig 5)**

This girl was the second child of unrelated European parents. Her brother was normal. She was delivered normally at term and weighed 2.7 kg, with a length of 46 cm and a head circumference of 35 cm. Short limbs, particularly involving the arms, were noted at birth and she had an unusual facial appearance. She was seen at 1 year of age when development was normal. She has been noted to have clicking hips, which required no treatment. Her head circumference was 45.5 cm, length was 68 cm, and span was 61 cm.

The forehead was high and prominent and hypertelorism was present. The nostrils were anteverted and the philtrum smooth with a triangular mouth. The palate was high and the alveolar ridges broad with gum hyperplasia. The ears were small and low set. Mild pectus excavatum and narrow shoulders were noted. Limb shortening was more marked in the arms than the legs and did not appear to be mesomelic. Detailed measurements of radiographs revealed generalised limb shortening (fig 4). No height measurement was taken at the time of the radiographs so that relative bone length cannot be derived. No vertebral anomalies were present.

**Case 5 (Fig 6)**

This boy was the first child of unrelated European parents and was the result of the mother’s first pregnancy. It was the father’s second marriage; the first had resulted in a male infant who had died in the postnatal period. A diagnosis was made by Professor C O Carter of thanatophoric dwarfism, but the records have since been lost. Both parents were of normal appearance and proportions and there was no other family history. Tetralogy of Fallot and abnormal facies were noted in infancy but a firm diagnosis of Robinow syndrome was not made until the age of 5½ years.

The mid-face was concave, the nostrils anteverted, the eyes prominent, and the gums thickened with crowded teeth. Supination of the forearm was limited bilaterally. Height was 5 SD and weight 2 SD below the mean. The penis was small and both upper and lower limbs showed rhizomelic brachymelia, more pronounced in the former. Radiology showed no vertebral or rib abnormalities but there was dislocation of the radial heads. Detailed radiological measurement is shown in fig 4. These show that the limb shortening is distinctly rhizomelic, especially in the upper limbs.

**Discussion**

The five cases reported above have the characteristic facial features of Robinow syndrome, together with other features such as micropenis and gum hypertrophy. The mode of inheritance appears to be autosomal dominant in the three familial cases, in common with other families in published reports.
However, some reported cases appear to be autosomal recessive.

Mesomelic brachymelia and dwarfism, considered almost essential to the diagnosis by other authors, were both absent in the family described here, while the first sporadic case (case 4) had general shortening of the arms and the second (case 5) had rhizomelic brachymelia. Thus, the pattern of limb shortening can be extremely variable. The range of associated features in the cases presented is consistent with other reported cases. A susceptibility to infection has been reported before and may bear some relevance to the group B streptococcal infection in case 3 at the age of 10 days. Urinary tract infection, renal duplication, and moderate hydronephrosis have been reported before, as have dislocated hips and congenital heart disease.

We have combined cases 1, 2, and 3 with the previously reported familial cases (table), in order to compare the phenotypes of dominant and recessive forms. It would appear that the main discriminating factor is the occurrence in recessively inherited cases of multiple rib and vertebral abnormalities. In addition, there is the suggestion that mesomelic brachymelia is more severe in the recessively inherited cases. Thus, Wadia et al described 'distinct shortening' of the forearms and Wadlington and Tucker 'marked shortening' of the arms, and there was a suggestion that the forearm bones were morphologically abnormal in the cases of Wadia et al. Robinow and Chumlea have provided actual measurements of the mesomelic brachymelia in their initial cases and similar data on other cases may clarify the situation.
### TABLE Clinical features of the autosomal dominant and recessive cases of Robinow syndrome.

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<th>Autosomal dominant</th>
<th>Autosomal recessive</th>
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<tbody>
<tr>
<td></td>
<td>Present cases</td>
<td>Vallée et al. ¹</td>
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<tr>
<td>Patient</td>
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<td>V₁ V₁ V₁ V₁</td>
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<tr>
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<td>M F M F M F M F</td>
<td>M F M F</td>
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<tr>
<td>Facial features</td>
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<td>+ + + +</td>
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<td>Oral abnormalities</td>
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<tr>
<td>Dental/gum abnormalities</td>
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<tr>
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<td>-3 -1 8 -2</td>
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<tr>
<td>Mesomelic brachymelia</td>
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<td>- - - -</td>
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<tr>
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<tr>
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<tr>
<td>Hypoplastic genitalia</td>
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<tr>
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<tr>
<td>Dislocation/deforty of</td>
<td>limb bones</td>
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+ present; - absent; / not noted.

The features common to both modes of inheritance are the characteristic facial features, orodental abnormalities, and hypoplastic genitalia. The difficulty in determining genetic hypoplasia in the female infant may explain its variable sex incidence. The two sporadic cases reported here fit more into the autosomal dominant type by virtue of the absence of vertebral and rib abnormalities.

From a description of the published cases, it is apparent that some characteristics run in particular families, for example, the upper limb deformities in the cases described by Wadia et al.,⁴ the small midline cleft lower lip of the patients of Wadlington and Tucker,⁶ and the clefting of the palate in the patients of Shprintzen et al.² This, together with both the autosomal dominant and recessive modes of inheritance and variability of brachymelia and dwarfism, suggests considerable genetic heterogeneity.

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### References


Correspondence and requests for reprints to Dr M D Bain, Section of Perinatal and Child Health, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.
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