D$_{13}$ ring chromosome syndrome

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McCandless, A., and Walker, S. (1976). Archives of Disease in Childhood, 51, 449. D$_{13}$ ring chromosome syndrome. A case of ring D$_{13}$ chromosome, confirmed by trypsin banding, is described. Reviewing 21 cases from published reports, the most common features of this syndrome are microcephaly and associated mental retardation, poor uterine growth, deformed auricles, hypertelorism, epicanthus, broad nasal bridge, and genital defects in males.

Many reports of D ring chromosomes have been made, of which 21 cases are confirmed as ring D$_{13}$. 16 of these were recognized by radioautography only, the other 5 by chromosome banding techniques which allow accurate identification (see Table). We report a further case identified as D$_{13}$$^b$ by chromosome banding and summarize briefly the clinical findings in these cases.

Case report
A male was born on 26 May 1972. Mother was 23 years and the father 25 years old. Delivery was normal at 34 weeks' gestation, birthweight 1550 g, length 40.6 cm, and head circumference 27.9 cm. The facial appearance was abnormal, the frontal region of the skull was narrow; hypertelorism and almond shaped eyes were present (Fig. 1). A slight epicanthic fold was present on the right. The auricles were large and low set. A broad nasal bridge, micrognathia, and a highly arched palate were apparent. In both hands the thumbs were low lying and there was a contracture of the right thumb. The feet were small and the second and fourth toes overlapped on each foot; bilateral clinodactyly was present in the outer three toes. Examination confirmed the presence of microphthalmos and microcornea, and large choroidal colobomata were present in both eyes. The parents already had 2 normal children.

After diagnosis by chromosome studies, the infant's condition was discussed with the parents and a guarded prognosis was given regarding subsequent mental development. The parents however were anxious to take the child home. At a later date it was discovered that the infant was being kept closed up in a cupboard in the kitchen; feeds were given erratically. He was taken into the care of the Social Services Department. Since then he has gained weight but his height and weight lie below the 3rd centile. A full developmental assessment was done at 2.25 years, developmental quotient 14, equal to a child of less than 6 months. At the age of 3 years the circumference of the head was 44 cm. The upper incisors protrude but there is no overcrowding of the teeth. There is no evidence of

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FIG. 1.—Patient at age of 1 week.
## Table of Cases

<table>
<thead>
<tr>
<th>Case no.</th>
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<th>Birthweight (g)</th>
<th>Gestation (w)</th>
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**Notes:**
- Birth defects include:
  - Microcephaly and mental retardation
  - Microphthalmia
  - Epicanthus
  - Hypertelorism
  - Broad prominent nasal bridge
  - Auricles—large or deformed
  - High-arched palate
  - Protruding upper incisors
  - Micrognathia
  - Heart murmur
  - Small penis
  - Small or bifid scrotum
  - Undescended testes
  - Imperforate anus
  - Hypospadias
  - Renal defects
  - Microcephaly and mental retardation
  - Microphthalmia
  - Epicanthus
  - Hypertelorism
  - Broad prominent nasal bridge
  - Auricles—large or deformed
  - High-arched palate
  - Protruding upper incisors
  - Micrognathia
  - Heart murmur
  - Small penis
  - Small or bifid scrotum
  - Undescended testes
  - Imperforate anus
  - Hypospadias
  - Renal defects

**References:**
- Reisman et al. (1965)
- Gerald et al. (1967)
- Neumann et al. (1967)
- Lejeune et al. (1968)
- Allerdice et al. (1969)
- Stimson & Hecht (1970)
- Cited by Orbeli et al. (1971)
- Mikkelsen & Niebuhr (1969)
- Kistemaker & Pienning (1970)
### D13 ring chromosome syndrome

#### Chromosome 13

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congenital malformation of the heart, and the pyelogram was normal. The testicles are very small but the penis is normal in size. The child is happy and smiles almost continuously during the waking hours.

**Cytogenetic studies.** From peripheral blood cultures in 1972 chromosome counts were made on 60 cells. Of these, 57 contained 46 chromosomes and 3 contained 45 only. Those with 46 chromosomes showed the presence of a ring chromosome apparently replacing a member of the D group. The ring chromosome was missing from cells with 2n=45. Culture of blood from both parents indicated they had normal karyotypes. Reinvestigation in 1975 permitted G-banding of the chromosomes from the patient using a modification of the trypsin method of Seabright (1971). This showed a D13 ring chromosome in all cells with a count of 2n=46 (Fig. 2).

![Fig. 2.—Group D chromosomes of patient. Upper row stained in lactic-acetic orcin; lower row after trypsin banding and Leishman's stain.](image)

**Serology.** Blood groups ABO, CDE, MN, S, K, and Fy were investigated in the patient and his parents. Only in the case of the MNS groups did the patient show heterozygosity, indicating that the MNS loci could not be carried on the deleted sections of D13. The level of haptoglobin in the patient was normal. Immunoglobulins IgA, IgM, and IgG were investigated in the child (age 6 months) and his parents. All were considered normal.

**Discussion**

The most frequent anomalies associated with the published ring D13 cases are recorded in the Table, together with those found in the present case. There is no association with maternal or paternal age. With one exception, maternal age, when given, was below 30 years. The only consistent feature in all cases is microcephaly. Associated with this the intellectual assessment, when done, has shown severe mental retardation. There are also a number of other features which occur in more than 60% of the cases and which can be regarded as characteristic of the syndrome. These are poor uterine growth resulting in dysmaturity at birth, large low-set or malformed auricles, hypertelorism, epicanthus, broad prominent nasal bridge, and genital defects in males. The most frequent genital defects were small or bifid scrotum and undescended testes. Less common were a small penis and hypospadias.

The next most common group of features appearing in more than 30% of the cases are micrognathia, high arched palate, protruding upper incisors, foot or hand anomalies, and heart murmur. In the 8 cases in which cardiac murmurs were found there were no consistent abnormalities. Case 9 (Biles, Lüers, and Sperling, 1970) had an atrial septal defect confirmed at necropsy and Case 13 (Hollowell et al., 1971) Fallot’s tetralogy. Foot and hand anomalies were various. Overlapping of the toes seen in the present case was evident also in Case 2 (Gerald et al., 1967), Case 4 (Lejune et al., 1968), Case 5 (Allerdice et al., 1969), and Case 21 (Fried et al., 1975). Other defects were absent thumbs and fifth toes in Case 18 (Nebuhar and Ottosen, 1973), absent or fused metacarpals with extra digits in Case 9 (Biles et al., 1970), planovalgus in Case 2 (Gerald et al., 1967), and arthrogryposis with multiple skeletal defects in Case 16 (Grace et al., 1971). The low lying thumbs and contracture seen in the present case have not been described previously.

Several authors described the eyes of their cases as oriental or ‘almond-shaped’; this is well shown in our case (Fig. 1). Other than microphthalmia, defects of the eyes were rare, including squint or colobomata of the irides. Only 3 infants had renal defects; Case 5 (Allerdice et al., 1969) and Case 9 (Biles et al., 1970) had prostat of the right kidney; Case 9 also had a hypoplastic left kidney; and Case 19 (Hoo, Oberrmann, and Cramer, 1974) had agenesis of the right kidney. Anal atresia was reported in 5 cases.

As may be expected in an effective chromosome deletion syndrome there is wide variation in the phenotypic expression of the recorded ring D13 cases, probably related to the amount of chromatin lost. However, there are sufficient common features as illustrated above to lead to a possible diagnosis.

We thank Dr. J. Bradley, Mr. W. T. A. Donohoe, and Mr. J. Ireland for the serology, and Miss G. A. Rowlands for technical assistance.
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References


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