Abstract A ring chromosome 9 containing an inverted 9p22.3-p24.3 duplication was found in a girl presenting with some of the phenotypic characteristics of ring 9 syndrome such as trigonocephaly, microcephaly, hypotelorism, micrognathia, single palmar crease, and bilateral clinodactyly. The typical facial dysmorphic features of 9p duplication, ascribed to trisomy of the band p22, were not present in this patient. Cytogenetic and molecular studies indicated that the duplicated region of band p22 in the ring is confined to the sub-band 22.3.

Conclusion The chromosome region responsible for the 9p duplication syndrome appears to be restricted to sub-bands p22.1-22.2.

Key words Ring chromosome 9 · 9p duplication · Mild phenotypic abnormalities

Abbreviation FISH Fluorescence in situ hybridisation

Introduction

Ring chromosome 9 is a rare chromosome aberration resulting in mild phenotypic abnormalities, particularly in the newborn period [4]. Duplication 9p leads to a clinically recognisable syndrome in which involvement of band p22 seems to have a predominant role [1, 2].

In this study, we report on a child who has a ring chromosome 9 with very distal breakpoints and a duplication of the segment p22.3-p24.3. The duplication was confirmed by fluorescence in situ hybridisation (FISH) with a chromosome-9 library and YAC DNA probes. The terminal breakpoints of the ring were investigated with specific telomeric 9p and 9q probes.

Case report

The patient, a female, was born at term to a 26-year-old primagravida and a 27-year-old father. Pregnancy was complicated by bleeding in the first trimester and delivery resulted by Caesarean section because of a small maternal pelvis. She weighed 2500 g (3rd percentile) and measured 45.7 cm (3rd percentile) in length. The perinatal period was normal. At 6 months, she was referred to the Paediatric Department of the University of Pavia for evaluation of dysmorphic features. Her length was 63 cm (10th percentile), weight 6420 g (<10th percentile) and head circumference 39 cm (~2 SD). Bone age was 4 months. She presented with trigonocephaly and a relative microcephaly, hypotelorism, micrognathia, single palmar crease, bilateral clinodactyly, hypodensities of the white matter on ultrasound scanning. Developmental milestones were normal. The patient showed a delayed closure of the ductus arteriosus. Haematological investigations revealed haemoglobin 12.4 g/dl, red blood cell count 4,590,000/mm³, white blood cell count 13,000/mm³ and platelets 348,000/mm³. Serum values of total bilirubin, protein, creatinine, alkaline phosphatase and amino transferase activities, cholesterol and electrolytes were within the respective reference ranges. Immunoglobulin levels were within the age-related reference range. The pituitary-thyroid axis was investigated by evaluation of serum T4, free T4 and TSH. Adrenal secretion was estimated on the basis of basal serum cortisol concentrations at 8.00 and 20.00 h. Both thyroid and adrenal functions were normal. No abnormalities were detected on EEG. Ophthalmological examination showed normal findings for the age.
and X-ray evaluation indicated no congenital skeletal anomalies. Cerebral and renal abnormalities were excluded by ultrasonography.

**Cytogenetic investigation**

Routine and high resolution chromosome studies were performed on phytohaemagglutinin-stimulated blood cultures by standard techniques. FISH analysis was carried out using a biotinylated painting library of chromosome 9 (Thecnoc – Genetics) according to the manufacturer’s instructions. FISH was also performed [3] utilising YACs 953A7, 804B2 and 929G12 localised respectively in 9p24.2-24.1, 9p23-p22.3 and 9p22.1 (YAC screening center Osp. S. Raffaele, Milano) and specific telomeric 9p PAC 34H2 and 9q Cosmid 2241c1 probes, localised approximately 100–300 Kb from the telomere [5].

The patient’s karyotype showed a ring chromosome 9. The ring was rather stable at mitosis: on 50 metaphases analysed, 45 showed 46 chromosomes with one ring, 2 had two rings, 1 had a double ring, and in 2 cells the ring was missing. The ring had very distal breakpoints (p24.3 q34.3) and contained additional material. The entire ring chromosome was homogeneously painted by the chromosome 9 library. High resolution banding suggested the presence of an inverted duplication of bands p24.3-p22.3 (Fig. 1). The duplicated region was confirmed by FISH, showing a double fluorescent signal with 953A7 and 804B2 YACs, mapped respectively in 9p24.2-24.1 and in 9p23-p22.3 (Fig. 2, a–b). After FISH with YAC 929G12, localised in 9p22.1, a single signal was detected in the ring (Fig. 2, c). FISH with PAC 34H2 and Cosmid

---

**Fig. 1** Normal and ring chromosome 9: the arrows point to the region duplicated in the ring

**Fig. 2** Fluorescence in situ hybridisation (FISH) with YACs 953A7 (a), and 804B2 (b) reveals a double fluorescent signal on the ring 9, where YAC 929G12 (c) shows a single signal. FISH with PAC 34H2 (d) and Cosmid 2241c1 (e) exhibit, respectively, duplication and absence of hybridisation signal. DAPI staining on the right of each chromosome