Rieger syndrome and a de novo (4;17)(q25;q23.3) translocation

Jorge M. Saraiva [1], Elisabete Engenheiro [2], Niels Tommerup [2], Eunice Matoso [3], Isabel Marques [3]

[1] Serviço de Genética Médica, Hospital Pediátrico de Coimbra, Portugal

[2] Department of Medical Genetics, Wilhelm Johannsen Center for Functional Genome Research, University of Copenhagen, Denmark

[3] Laboratório de Citogenética, Instituto de Biologia Médica, Faculdade de Medicina de Coimbra, Portugal

Introduction

Rieger syndrome has been mapped to two loci, one, RIEG1, in 4q25q26 [Murray et al., 1992], and the other, RIEG2, in 13q14 [Phillips et al., 1996]. Mutations in the PITX2 gene, in 4q25q26, have been identified as the cause of several Rieger syndrome cases [Semina et al., 1996]. There are several reports of chromosomal structural abnormalities affecting 4q25 with similar phenotypes. Here we report another example.

Clinical Report

He was the first son of healthy unrelated parents. Growth and development were normal. He had broad nasal bridge, hypertelorism (inner canthal distance 3 cm ->+2SD- and outer canthal distance 7.5 cm -+2DS), short philtrum, maxillary hypoplasia (Fig. 1), coloboma of iris and an abnormal umbilicus with failure of involution of the periumbilical skin (Fig. 2). At 12 months of age he had only two central incisors in the mandible without any other teeth. The ophthalmologic observation described the presence of most features of Rieger anomaly (iris hipoplasia and posterior embryotoxon) and a diagnosis of Rieger syndrome was made.

Figure 1

Figure 2

Cytogenetics

The patient had a de novo reciprocal translocation involving the 4q25 region [46,XY,t(4;17)(q25;q23.3)] (Fig. 3). The following BACs were found to be deleted on chromosome 4q25: RP11-1023k13, RP11-112h6, RP11-610p19, RP11-313b13, RP11-777n19, RP11-316m24, RP11-621b23, RP11-326n15, RP11-716b14, RP11-531e5, RP11-255i10, RP1177n9 and RP11-269f21. The proximal BAC with signals on both chromosomes 4 and der(4) is RP11-433b3 and the distal is RP11-477g18.

Discussion

A deletion of approximately 2 Mb affecting the PITX2 gene has been found at the breakpoint in 4q25. The cytogenetic data that implies that functional haploinsufficiency of the PITX2 gene is the pathogenic mechanism of Rieger syndrome is in accordance with the molecular data. Most of the chromosome abnormalities in Rieger syndrome are de novo. Although there may be bias of ascertainment the number of such cytogenetic abnormalities described is surprisingly great. This may be due to a feature of 4q25 that makes it particularly susceptible to rearrangements