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A case of partial 5q trisomy associated with partial 7q monosomy

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SUMMARY A 1-year-old girl with partial 5q trisomy and partial 7q monosomy had ocular abnormalities that included bilateral blepharoptosis and Leber's congenital amaurosis. A single bright-flash electroretinogram (dark-adapted, white stimulation) disclosed subnormal bilateral responses. Her maculas showed a reddish spot surrounded by a broad, greyish retinal zone. Cytogenetic studies disclosed deletion of q22 to the terminal of chromosome 7 and partial trisomy of q31 to the terminal of chromosome 5. Because all reported patients with 5q trisomy have not had Leber's congenital amaurosis, the ocular abnormalities noted in our patient may be explained by the 7q monosomy.

The ability to specify breakpoints and the extent of a deletion have become increasingly reliable with improved techniques that provide elongated chromosomes with detailed banding.[1] Twenty-nine cases of partial deletion of 7q[2-24] and 15 cases of distal trisomy of 5q[25-33] have been reported with corresponding clinical syndromes. Among these, two patients have had intraocular abnormalities, one with unilateral optic nerve coloboma[6] and one with bilateral microphthalmos and a large retinal coloboma.[23] We describe here a patient with partial trisomy of terminal 5q associated a partial monosomy of terminal 7q who had ocular abnormalities, including Leber's congenital amaurosis, and non-specific findings, such as hypertelorism and blepharoptosis.

Case report

A 4-month-old girl was referred to us in August 1982 for bilateral blepharoptosis. The product of a normal, full-term pregnancy, the patient, weighed 2128 g at birth. The Apgar score was 2 at one minute, and supplemental oxygen was administered for one hour. The parents were 35 years old, were not con-

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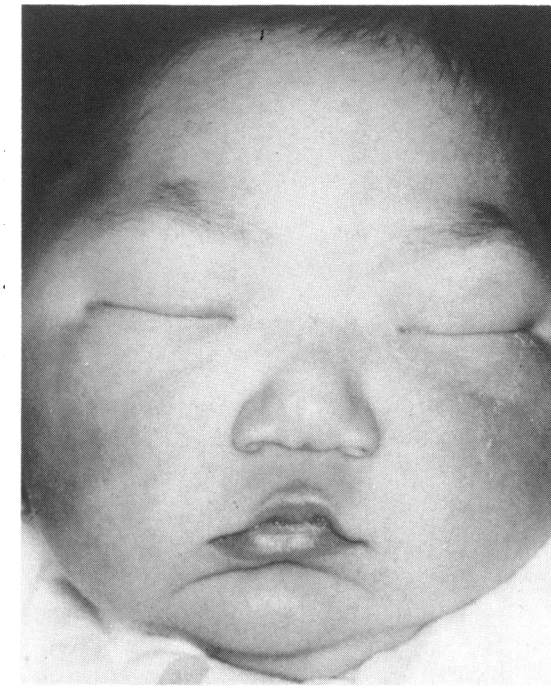

Fig. 1 *Four-month-old girl with telecanthus, broad nose, and microcephaly.*

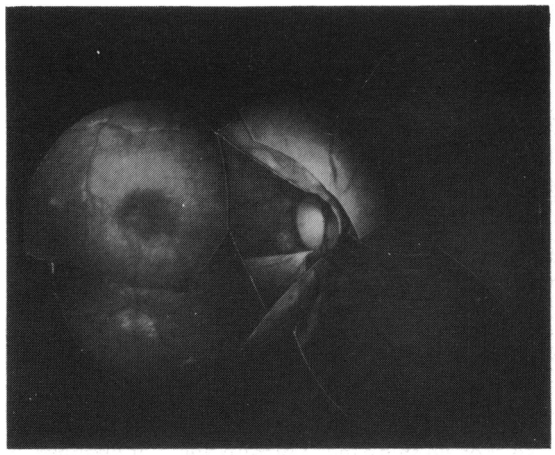

Fig. 2A

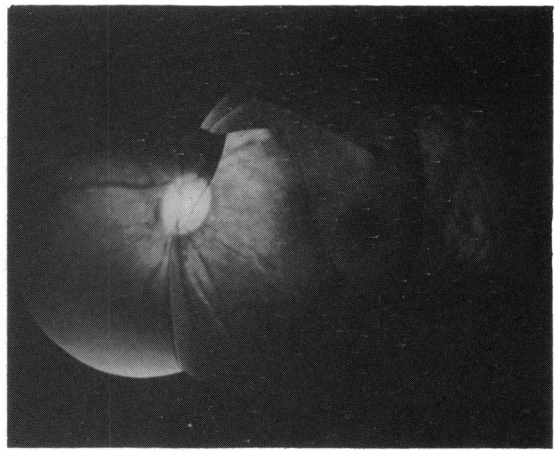

Fig. 2B

Fig. 2 A: *right eye.* B: *left eye. The maculas show a reddish spot surrounded by a broad greyish retinal zone. No macular rings are seen.*

sanguinous, and were in good health. A 3-year-old male sibling was normal.

Ocular examination of the patient disclosed bilateral blepharoptosis and telecanthus (Fig. 1). The lid fissure was 3 mm wide in the right eye and 2 mm in the left. The levator function was 0 mm in each eye. A Tensilon test result was negative. Congenital anomalies included microcephaly and a broad nose. Follow-up examination revealed severe mental and physical retardation associated with spastic palsy and hearing impairment. The amino acids in urine and serum were normal. In November 1983 the patient received general anaesthesia to undergo resection of the levator muscle in the right eye through the conjunctiva. Resected material contained no skeletal muscle and only a trace of smooth muscle. The blepharoptosis was not corrected despite a maximal resection.

On the day of the operation additional ocular examinations included electrophysiological studies and fluorescein angiography. The pupillary distance was 50 mm. The anterior segments appeared normal. Ophthalmoscopic examination disclosed no macular rings but showed mottled retina from the posterior to the midperipheral region bilaterally. The maculas showed a reddish spot surrounded by a broad greyish retinal zone (Figs. 2A, B). Fluorescein angiography showed granular hyperfluorescence in the regions that contrasted with the greyish perimacular zones (Fig. 3). A single bright-flash electroretinogram

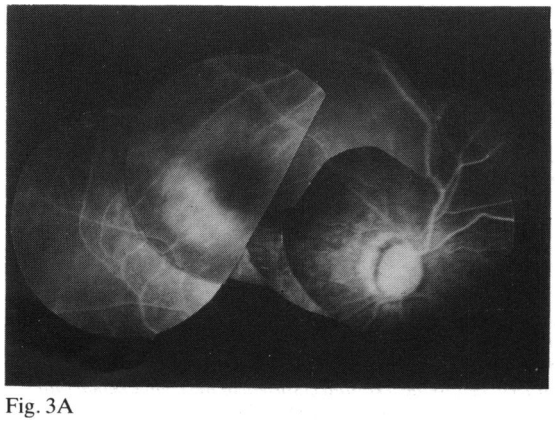

Fig. 3A

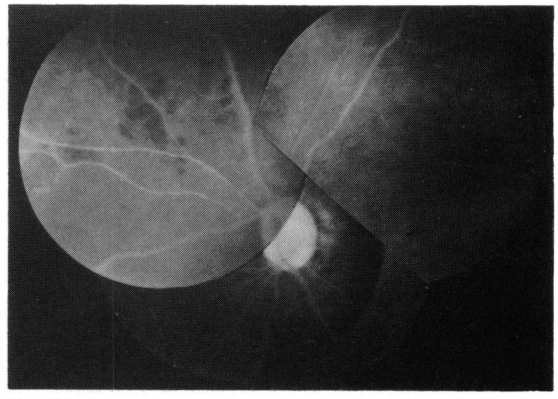

Fig. 3B

Fig. 3 A: *right eye.* B: *left eye. Granular hyperfluorescence is observed in the greyish perimacular regions noted in Fig. 2. No leakage of fluorescein is seen.*

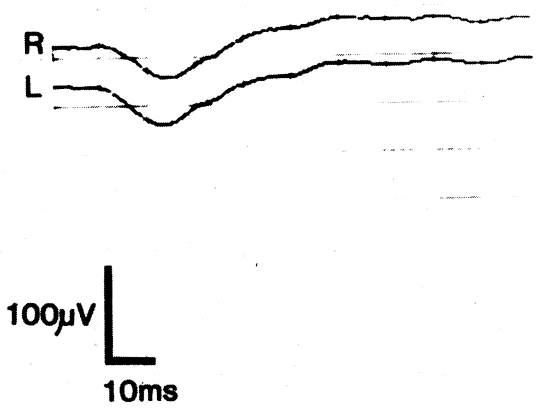

Fig. 4 *Single bright-flash electroretinogram (dark adapted, white stimulation). Both the right* (R) *and left* (L) *eyes show subnormal responses.*

(dark-adapted, white stimulation) disclosed subnormal responses (Fig. 4). Cytogenic studies were performed on peripheral blood lymphocytes. Metaphase chromosomes derived from synchronised cell cultures were treated with trypsin and stained with Giemsa's stain (Fig. 5). The chromosomes showed partial monosomy of the long arm of chromosome 7. The karyotype was 46, XX, −7, +der(7), t(5:7) (q31:q22). A chromosomal study on the mother showed normal findings. The father was unavailable for cytogenic evaluation.

Discussion

Cytogenic analyses have shown a number of cases of chromosomal changes in patients with congenital abnormalities. To our knowledge 15 cases of partial trisomy of the long arm of chromosome 5 have been reported. All such cases proved to be inherited from parental insertion or parental translocation, with breakage of the second chromosome at the terminal band. Under these circumstances various cases of partial monosomy associated with partial 5q trisomy may have gone undetected. Our patient may represent the first case of partial 5q trisomy with partial 7q monosomy, although parental translocation could not be proved because the cytogenic data for the father were incomplete. All previously reported patients with partial 5q trisomy had a low birth weight under 3000 g and physical and mental retardation. Cases of partial trisomy of the distal part of 5q (distal to band 5q31 and to 5q33) commonly had inborn dystrophy and severe to moderate retardation of growth and psychomotor development. Our patient also showed this clinical picture and a breakpoint of 5q31.

The ophthalmoscopic appearance of Leber's congenital amaurosis varies. The most common findings are normal fundus, salt and pepper pigmentary changes, a blond fundus with choroidal atrophy or choroideraemia, classic aspect of retinitis pigmentosa, macular changes, or optic atrophy and narrow vessels.

The electroretinogram diagnostic for Leber's congenital amaurosis is extinguished or shows only minimal response.[34] The parents of our case had subnormal responses to the single white flash in dark-adapted conditions. Also noted ophthalmoscopically were lesions in the posterior pole that included a reddish spot in the macula surrounded by a greyish retinal zone that showed granular hyperfluorescence on fluorescein angiography, indicating Leber's congenital amaurosis.

No intraocular abnormalities have been reported

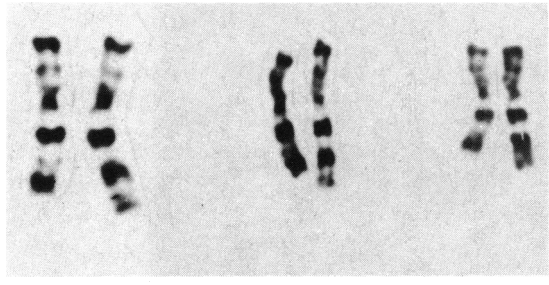

Fig. 5A

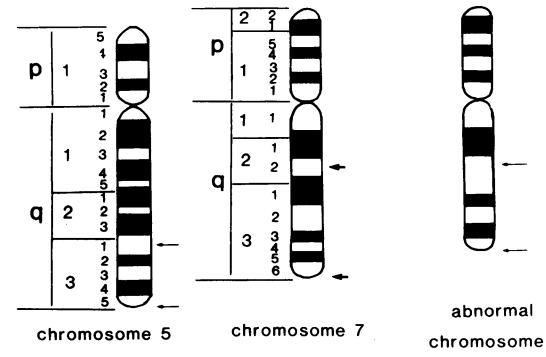

Fig. 5B

Fig. 5 *Partial karyotype of chromosome 7.* A: *three pairs of metaphase chromosome from patient are demonstrated after trypsin-Geimsa banding. Abnormal chromosome with deletion of 7q at q22 to the terminal is shown to the right of each pair.* B: *schematic partial karyotype of our patient. One pair of chromosome 5 is normal, and one pair chromosome 7 is abnormal, having a segment of q31 to the terminal of chromosome 5 instead of a segment of q22 to the terminal of chromosome 7. The karyotype is 46, XX, −7, +der(7), t(5:7) (q31:q22).*

previously in cases of 5q trisomy. The ocular abnormalities noted in our patient, compared with other patients with 5q trisomy who had an almost identical duplicated segment, might be explained by the additional monosomy. Chromosome 7q deletion syndrome has included relatively consistent dysmorphic findings, including growth deficiency, developmental delay, bulbous nasal tip, abnormal ears, cleft lip, and genital abnormalities. Acute non-lymphatic leukaemia, secondary to occupational or therapeutic mutagenic exposure, has also been frequently associated with a 7q abnormality.[35] Only two reported cases of 7q deletion syndrome had, however, associated ocular abnormalities. These were microphthalmos and retinal coloboma[23] and a unilateral optic nerve coloboma,[6] though 14 cases of terminal deletion of the long arm of chromosome 7, terminal to q32 and terminal to q35, have been reported. Because there are no reports of the deletion of chromosome 7q22 to the terminal, we cannot conclude that Leber's congenital amaurosis is pathognomonic for 7q deletion syndrome.

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