Developmental Glaucoma With Chromosomal Abnormalities of 9p Deletion and 13q Duplication

We recently encountered a case of developmental glaucoma with systemic malformations including polydactyly, retained testis, hydronephrosis, and epilepsy. The patient showed partial monosomy 9p23-pter and partial trisomy 13q31-qter, and this chromosomal translocation has not been reported in the literature to our knowledge.

Report of a Case. The patient, born by cesarean delivery at 38 weeks’ gestation and weighing 3760 g, was the first child (male) of healthy parents. Bilateral polydactyly was observed at birth (Figure, A). At 2 months of age, he was admitted to another hospital and developmental glaucoma was suspected based on findings of enlarged corneal diameter, ocular hypertension, and bilateral optic atrophy. At age 4 months, he was affected by an incomplete type of the mucocutaneous lymph node syndrome (Kawasaki disease), and myoclonic epilepsy appeared in the same period. Hydronephrosis in the right kidney and bilateral retained testis were also found. However, there were no other systemic abnormalities including the face, nose, teeth, umbilicus, fingernails, or hearing. Brain magnetic resonance imaging showed hypoplasia of the corpus callosum and mild cerebral atrophy of the frontal lobes.

At age 6 months, ophthalmological examination based on informed consent from his parents was conducted under general anesthesia and revealed features of developmental glaucoma (Table). The angle showed flat posterior insertion without iris abnormalities like hypoplastic changes. There were Haab striae but no embryotoxon or corneal edema in both corneas. The vertical cup to disc ratio was 0.95. The pupil, lens, retina, and vitreous appeared normal bilaterally. Trabeculotomy was performed in both eyes on the same day. At age 27 months (21 months after surgery), the examination under general anesthesia revealed that the intraocular pressure in both eyes remained within the reference range (Table). The patient’s mental development was arrested, although the height and weight were within the reference ranges of the growth curve.

Together with G-band analysis, fluorescence in situ hybridization demonstrated that reciprocal translocation of the breaking point was 9p23 and 13q31, demonstrating partial monosomy 9p23-pter and partial trisomy 13q31-qter (Figure, B). The karyotypes of the parents could not be examined under the circumstances.

Comment. This patient had monosomy 9p23-pter and trisomy 13q31-qter, which has not been reported in the literature to our knowledge. The tyrosinase-related protein, mapping to 9p23, is associated with pigmentary glaucoma in mice but not in humans.1 This patient also does not show the pigmentary glaucoma phenotype. To our knowledge, there is only 1 reported case showing devel-

Figure. Patient with partial monosomy 9p23-pter and partial trisomy 13q31-qter. A, Photograph of the right hand. Polydactyly (circle) is connected by cord-shaped tissue. B and C, Comprehensive karyotyping of this patient, with chromosome staining by reverse 4’,6-diamidino-2-phenylindole and spectral karyotyping using fluorescence in situ hybridization. Chromosomes 9 (B) and 13 (C) are simultaneously hybridized with a combination of 24 labeled chromosome painting probes. White indicates chromosome 9; red, chromosome 13. A fragment of chromosome 13 is detected on a lacking region of chromosome 9, indicating partial monosomy 9p and partial trisomy 13q.
opmental glaucoma by monosomy 9p23 with trisomy 8q22.2 The investigators attributed the responsible area of glaucoma to 8q22, not 9p23, because GLC1D maps to 8q22. That case also showed retained testis and hydrenephrosis, similar to our patient. Interestingly, 2 previously reported cases1,2 of monosomy 9p24-pter (near the 9p23 locus) manifested developmental glaucoma. Therefore, partial monosomy 9p might be causative for developmental glaucoma.

Chromosome 13 seems essential for development of the eye. Trisomy 13 often results in severe ocular defects, including developmental glaucoma. One case of developmental glaucoma and polydactyly with trisomy 13 was reported,3 which is compatible with our case. In a French family with congenital microcoria, axial myopia, and juvenile open-angle glaucoma, genetic linkage to 13q31-32 was suggested to result in these ocular findings.4 Although our patient had a normal pupill phenotype, trisomy 13q31 might be responsible for the developmental anomaly of angle.

Taken together, it is suggested that the abnormalities of chromosome 9p23 and/or 13q31 are associated with developmental glaucoma with other systemic anomalies.

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Autoantibodies Against Bestrophin in a Patient With Vitelliform Paraneoplastic Retinopathy and a Metastatic Choroidal Malignant Melanoma

Paraneoplastic retinopathies are rare disorders caused by the immune system's response to distal tumors. Autoantibodies generated against distant tumor antigens cross-react with different retinal proteins, resulting in retinal degeneration. Paraneoplastic retinopathies are usually divided into 2 major groups, cancer-associated retinopathy and melanoma-associated retinopathy (MAR).

Cancer-associated retinopathy is usually seen in patients with small-cell carcinoma of the lung and is associated with autoantibodies against recoverin and α-enolase.1-2 The autoantibodies in cancer-associated retinopathy induce apoptotic death of the photoreceptors, resulting in a severe retinal degeneration affecting both cones and rods.3

Melanoma-associated retinopathy is usually seen in patients with cutaneous malignant melanoma. The disorder often appears at the stage of metastases with a sudden onset of night blindness, photopsias, shimmering, and a varying degree of visual loss.4 Melanoma-associated retinopathy has been associated with autoantibodies against the retinal bipolar cells,5 and the typical full-field electroretinogram (ERG) shows a markedly reduced or absent dark-adapted b-wave and a preserved a-wave, confirming a defect in bipolar function.6

Melanoma-associated retinopathy usually has a normal retinal appearance.7 However, more recent studies have described patients with MAR or MAR-like symptoms with posterior uveitis, pigment epithelium changes, paracentral scars, optic disc pallor, and retinal vessel attenuation.4,7,8 A few patients with vitelliform retinal changes or serous retinal detachments resembling Best macular dystrophy (BMD) have also been described.9,12 In 3 of these patients, the primary tumor was a choroidal malignant melanoma.9,11,12

In this article, we describe a patient with a history of choroidal malignant melanoma in the left eye and a vitelliform macular appearance in the right eye, and we show for the first time to our knowledge the presence of circulating autoantibodies against bestrophin-1. The clinical appearance, including that on electro-oculography (EOG), resembled BMD.

Methods. A 45-year-old man had fluctuations in visual acuity and difficulties in dark night vision of a few months' duration in his right and only eye. Ten years prior, his left eye had been enucleated because of a choroidal ma-