• Letter to the Editor •

A case of 9p deletion syndrome with congenital infantile glaucoma, effective method of diagnosis, and treatment

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Received: 2016-07-18 Accepted: 2016-11-29

DOI:10.18240/ijo.2017.02.23

Jia X, Liu XY, Duan XC. A case of 9p deletion syndrome with congenital infantile glaucoma, effective method of diagnosis, and treatment. *Int J Ophthalmol* 2017;10(2):318-320

Dear Editor,

I am Dr. Jia X from the Department of Ophthalmology, Second Xiangya Hospital, Central South University, Changsha, China. I write to present a rare case report of 9p deletion syndrome with congenital infantile glaucoma in an infant, accompanying with an effective method of both diagnosis and treatment.

On March 14th, a 5-month-old female infant was taken to our Ophthalmology Department by her parents because they observed that the anterior surface of her left eye was cloudy for a month. They also discovered the left eye was photophobic and the girl had become accustomed to using her right eye. There were no associated symptoms, such as conjunctival hyperemia, lacrimation, increased secretions, *etc*. Ophthalmological examination under anesthesia revealed the left eye had undergone some pathological changes (Figure 1). These changes included the cornea being edematous and opaque, the corneal horizontal diameter was also big (about 15 mm), the anterior chamber angle was wide, with its axial length at 21.25 mm (18.85 mm on right eye), and intraocular pressure (IOP) (using Goldmann tenonometer) was 37 mm Hg (18 mm Hg on the right eye). As a consequence of the cloudy cornea, the lens and fundus could not be clearly examined. It was observed through detailed clinical examination that the right eye was normal from cornea to fundus (cup-disc ratio 0.3), with the exception of the slightly larger corneal horizontal diameter, which was about 13 mm.

The infant was born with congenital aplasia, including apparent trigonocephaly (craniosynostosis with small frontal lobes through Magnetic Resonance Imaging) (Figure 2), an umbilical hernia, a saddle bridge to the nose, and patent ductus arteriosus. According to a Neonatal Behaviral Neurological Assessment (NBNA), the infant also had mental deficiency. Her NBNA score was 29, far below the normal range value (≥35). The mother's history of pregnancy and delivery was also considerably abnormal. This infant was her first child, she was an elderly parturient women of 40 years old, and the infant was forced to be delivered by cesarean section at the 41st week by III° polluted amniotic fluid.

Affymetrix Cytoscan 750K Array was utilized to detect genome-wide copy number variation and any genetic imbalances within the patient. All identified experimental data were analyzed by software ChAS with references from the database of ISCA (International Standards for Cytogenomic Arrays) and OMIM (Online Mendelian Inheritance in Man), and a comprehensive literature review was conducted to determine whether the identified results were pathogenic. Cytoscan 750K Array revealed a terminal loss of the p arm of chromosome 9: 46XX, Loss (9p22.1pter). The size of lost chromosome 9 was about 18.859 Mb (Figure 3). Microarray data analysis also found a segment gain of the p arm of chromosome 7: 46XX, Gain (7p22.1). But the size (about 442 kb) was too small to bring attention to and no relatable references can be found. Both parental karyotypes were normal.

After being diagnosed, complex trabeculectomy associated with external trabeculotomy were successfully performed on the left eye. The outcome and surgical efficacy were both postoperatively investigated on the first day, the third day, the first week, and the first month. We found that on the first day following the operation, the corneal symptoms of being edematous and opaque had markedly been relieved, although remained slightly hazy. The cornea cleared over the first month and the IOP oscillated between 10-14 mm Hg. The axial length of the left eye shrank to 19.98 mm. The appearance and position of the left eye's lens was normal. Fundus examination revealed that the vertical cup-disc ratio was 0.3 and optic appearance was normal. The baby had normal binocular visual. The right eye had normal pursuit eye movement.

As it is known, the 9p deletion syndrome (MIM 158170) is a rare condition caused by the loss of the partial portion of

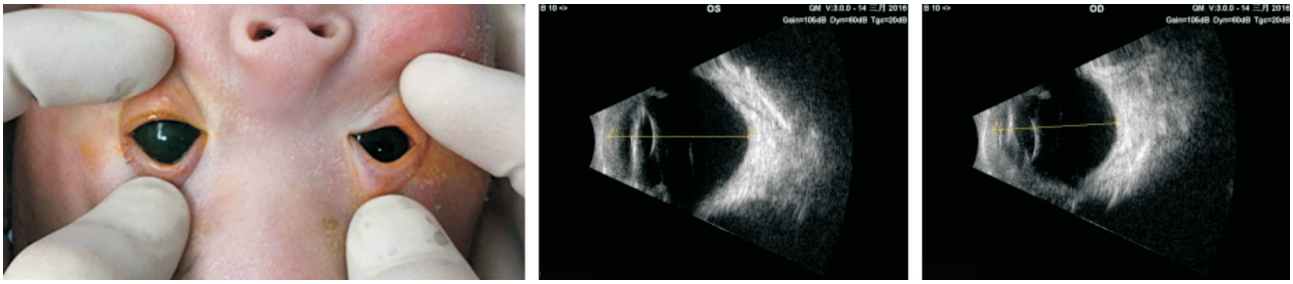

Figure 1 Ophthalmological examination under anesthesia revealed that the left eye had undergone some pathological changes.

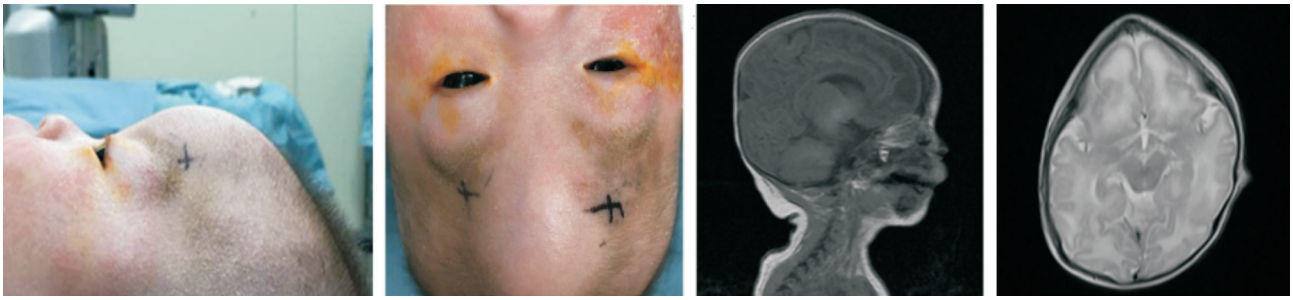

Figure 2 The infant was born with congenital aplasia, including apparent trigonocephaly.

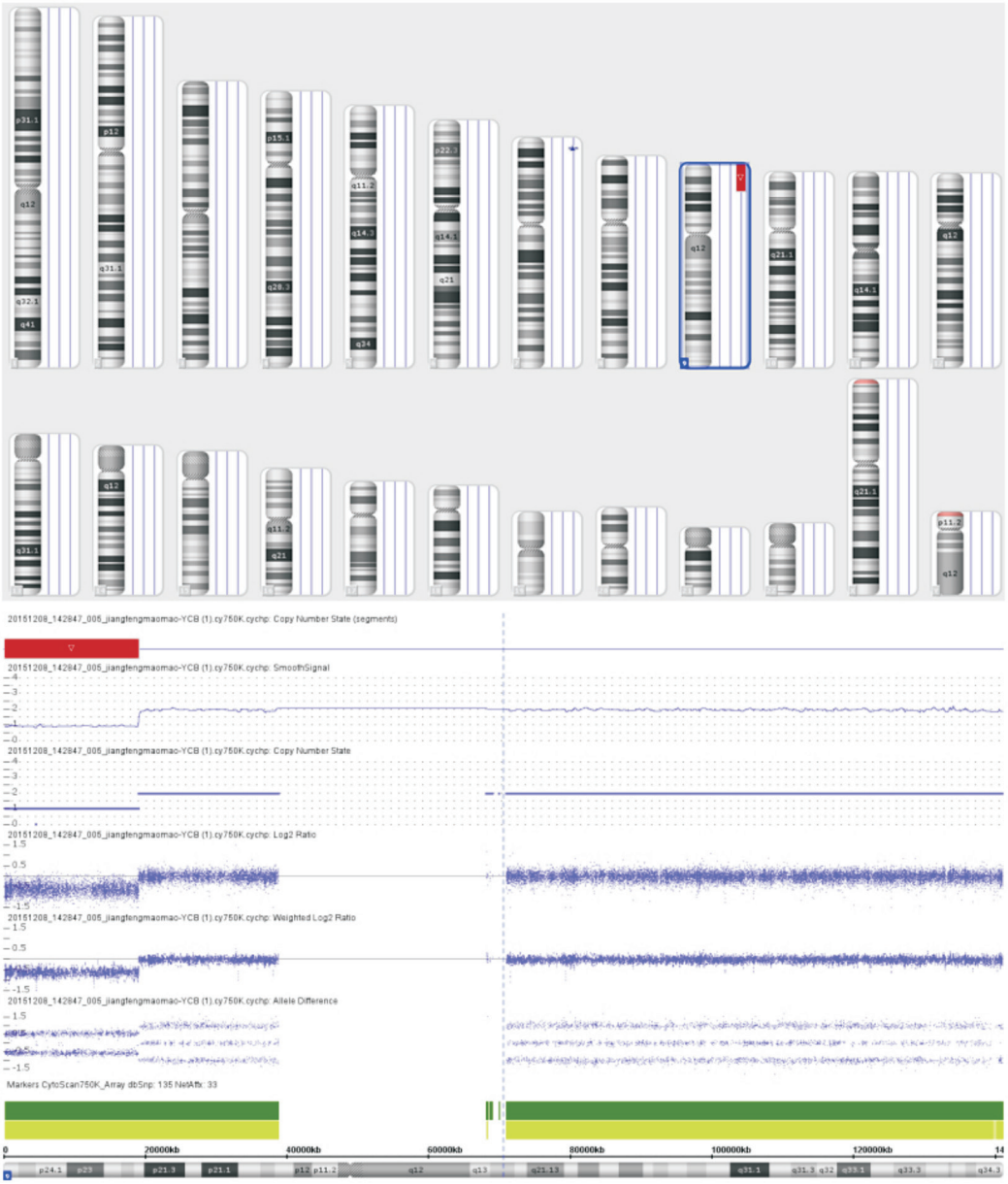

Figure 3 The size of lost chromosome 9 was about 18.859 Mb.

chromosome 9p, always at a distance[1]. The infant who carries the faulty chromosome 9p always displays multiple distinctive phenotypic features, such as trigonocephaly (craniosynostosis), mental deficiency, midfacial hypoplasia, inguinal and/or umbilical hernia, atrioventricular septal defect, *etc*[2-3]. In the majority of cases, the deletion positions are at 9p21, 9p22, 9p22, and 9p24[4]. However, reports of 9p deletion syndrome associated with congenital glaucoma are very rare. According to bibliography retrieval, this infant may be the first case of 9p deletion with congenital glaucoma in an Asian country.

The first case of 9p syndrome associated with congenital glaucoma was reported by Chaves-Carballo *et al*[5] in 1985. A 3-week-old female infant was admitted for evaluation of failure to thrive, which had characteristic features such as unusual facial features, trigonocephaly, and a prominent metopic suture. The karyotype was 46.XX, -9, +der(9).t(9;13)(p22;q14) pat, indicating a translocation between chromosomes 9 and 13, derived from the father. At three months of age, the infant developed bilateral glaucoma, which manifests as goniotomy and trabeculectomy, but the detail situation of glaucoma was not mentioned within the paper. Verbraak *et al*[6] reported a case of partial deletion of chromosome 9 (9p24-pter) with infantile congenital glaucoma. Ophthalmological examination showed the corneas were hazy and IOP was high (palpation) without large corneal diameters. However, the optic nerve and retina were normal. Sakata *et al*[7] reported a case where a 2-month-old male infant was diagnosed with developmental glaucoma associated with 9p deletion. G-band analysis revealed partial monosomy 9p23-pter and partial trisomy 13q31-qter. The karyotypes of the parents were not examined[7]. Trabeculotomy was performed in both eyes at the age of 27 months, the follow-up examination after surgery revealed that the IOP in both eyes remained within the normal range. Saha *et al*[8] presented a case of congenital glaucoma associated with 9p22.3-pter deletion as the sole identified genetic abnormality. Both parental karyotypes were normal. The infant had a typical feature of 9p deletion and congenital glaucoma. IOP were normal after bilateral goniotomy and trabeculotomy, and the optic disc appearance was normal. By one year old, discoid notches related to zonular dehiscence were apparent in both crystalline lenses.

In conclusion, although congenital glaucoma is not an invariant feature of 9p deletion syndrome, it may indicate that the broken regions of 9p21, 9p22, 9p23, or 9p24 can potentially contain the genetic locus associated with glaucoma. Considering the karyotypes of patients' parents are usually normal, the deletion of 9p associated with congenital glaucoma may suggest a single genetic mutation on chromosome 9, rather than it being inherited from the parents. This case presents that late maternal age is one of the significant factors to chromosomal abnormalities. Fortunately, if the congenital glaucoma with 9p deletion can be discovered and diagnosed early, it may not permanently impact the optic nerve or eyeball structure, producing notable results after the goniotomy and trabeculotomy surgeries. Additional works should be carried out to identify whether these breaks involve genetic consensus sequences, as well as to address whether the breaks can be further subdivided. If more genomic resources can become available, it may also allow for more comprehensive phenotype-genotype correlations for infants with congenital glaucoma.

ACKNOWLEDGEMENTS

Foundation: Supported by the Natural Science Foundation of China (No.81370913).

Conflicts of Interest: Jia X, None; **Liu XY**, None; **Duan XC**, None.

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