

Case Report

Rare case of congenital ocular disease with low intelligence level and extremity abnormalities in two siblings

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Abstract: We report a case of concomitant congenital ocular disease, low intelligence level and extremity abnormalities in two siblings. A 20-year-old Chinese male with distinctive craniofacial features and extremity abnormalities was diagnosed with bilateral keratoconus and congenital cataract. Craniofacial features included ptosis, small palpebral fissure, epicanthus, hypertelorism and a broad nasal bridge. He also suffered congenital deafness of uncertain etiology. His younger brother also had bilateral congenital cataract who similarly presented with hypertelorism, a broad nasal bridge and extremity abnormalities. Both the siblings had a lower intelligence level than their contemporaries. We hypothesize that the two siblings have a distinctive phenotype, which may represent a previously undescribed syndrome.

Keywords: Keratoconus, congenital cataract, extremity abnormalities, new syndrome

Introduction

Keratoconus (KC) is characterized by apical and paracentral thinning of the cornea. Some associations may point towards a common genetically determined cause; others may potentially cause corneal ectasia by recurrent mechanical trauma [1]. Herein, we report a case of two brothers who exhibited contaminant distinctive facial dysmorphism, bilateral KC and congenital cataract, low intelligence level and extremity abnormalities.

Case presentation

A 20-year-old male visited Department of Ophthalmology at First Hospital of Jilin University in January 2008, and complained of decreased vision in both eyes, which started at age 14 and had progressively worse. He had been diagnosed as bilateral KC and congenital cataract at 15 and therefore cataract extraction with no intraocular lens implantation had been successfully performed in the left eye. He was not prescribed glasses postoperatively even in childhood. Six months ago, his right eye was hit

by a basketball. We carried out a complete ocular examination. His best-corrected visual acuity (BCVA) was 0.02 in the right eye and count fingers in the left eye. Anterior segment slit-lamp examination showed that central corneal thinning with ectasia and posterior stromal striae (Vogt's striae) occurred in both eyes. The central corneal thickness (CCT) determined by Visante optical coherence tomography (OCT; Carl Zeiss Meditec, Dublin, CA) was 0.16 mm in the right eye and 0.24 mm in the left (**Figure 1A**). The pupils were normal in size, but the right one was irregular induced by posterior synechia of iris. The anterior chamber depth in both eyes was normal. The right lens was opacified and dislocated to the vitreous. The left lens was absent. Fundus examination could not be achieved because of high astigmatism induced by severe KC.

Craniofacial features of this male included ptosis, small palpebral fissure, epicanthus, hypertelorism and a broad nasal bridge (**Figure 1B**). The interphalangeal joints of his hands exhibited flexion deformity and the 2nd to 5th metacarpophalangeal joints exhibited back stretch

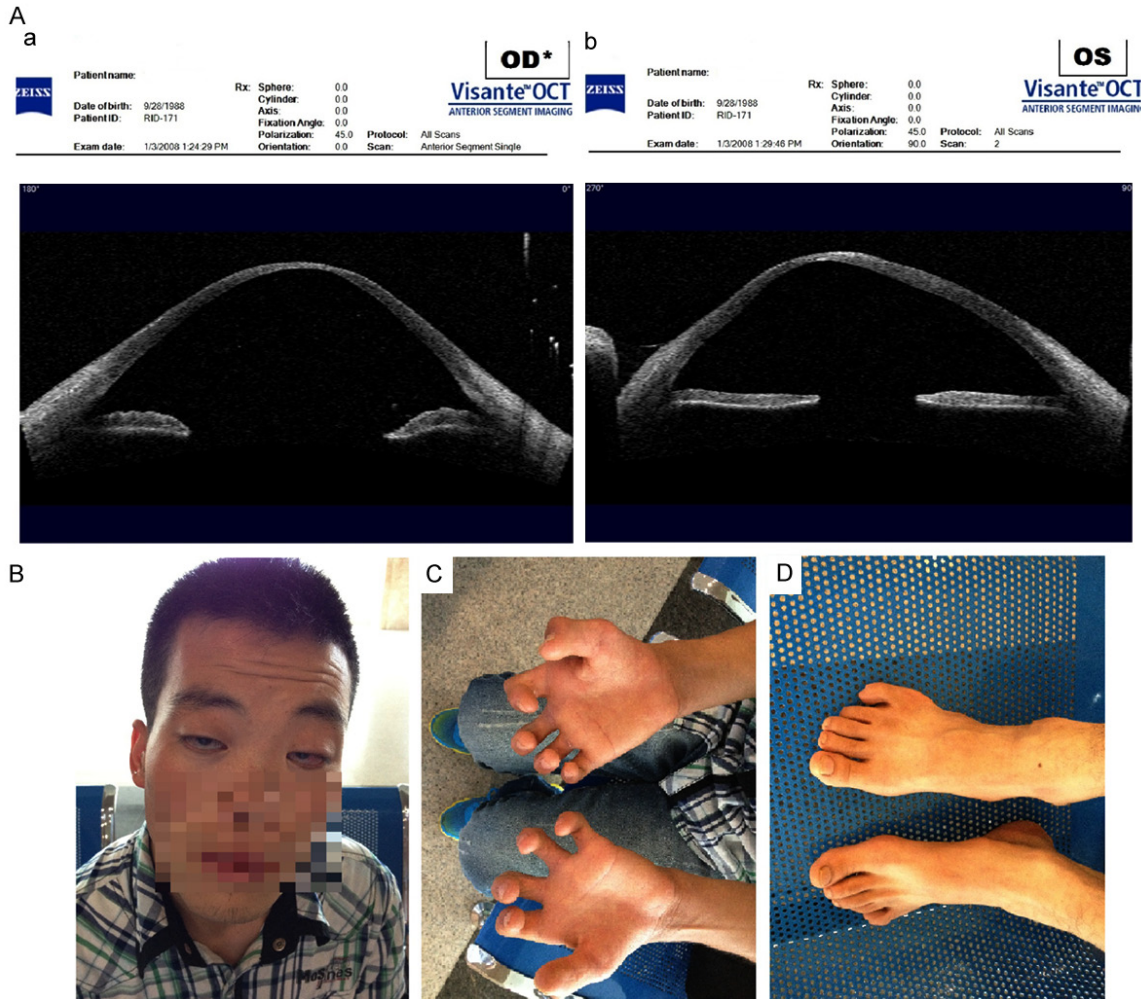


Figure 1. A. Central corneal thickness was determined by Visante OCT. The central corneal thickness was 0.16 mm in the right eye (a) and 0.24 mm in the left eye (b). B. Craniofacial features of the older brother included ptosis, small palpebral fissure, epicanthus, hypertelorism and a broad nasal bridge. C. The interphalangeal joints of both the older brother's hands exhibited flexion deformity and the 2nd-5th metacarpophalangeal joints of both hands exhibited back stretch deformities. D. The 4th-5th interphalangeal joints of both the older brother's feet exhibited flexion deformity. Permission has been obtained from the patient's parents for presentation.

deformity (**Figure 1C**). The 4th and 5th interphalangeal joints of both feet exhibited flexion deformity (**Figure 1D**). The stature was normal. His intelligence quotient score was 75.

We performed penetrating keratoplasty (PKP) in both eyes of this older brother. Because dislocated lens of the right eyes was close to the macular area, we did not perform the cataract extraction for him instead of maintaining the dislocated lens in the vitreous temporarily. The corneal grafts remained transparent (**Figure 2**). The 5-year follow-up showed that his BCVA was 0.12 in the right eye and 0.2 in the left eye and no further specific treatment was needed.

This patient was the first child of healthy, unrelated parents. He had a younger brother with a diagnosis of bilateral congenital cataract (**Figure 3A**), while there was no obvious abnormality in his corneas. Corneal topography showed that keratometric values in the right eye were 46.0 D at 116.6° and 44.4 D at 26.6°, the corneal thinnest point was 408 μm. Keratometric values in the left eye were 45.4 D at 60.1° and 44.4 D at 150.1°. The corneal thinnest point was 411 μm (**Figure 3B**). The younger brother presented with hypertelorism and a broad nasal bridge (**Figure 3C**). Extremity abnormalities included flexion deformities in the interphalangeal joints of both hands and the 2nd, 4th

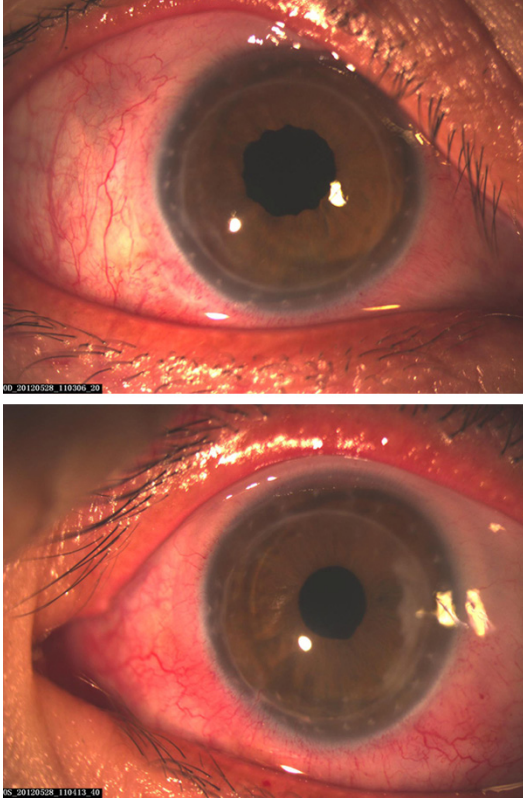


Figure 2. The corneal grafts remained transparent after 5 years postoperatively.

and 5th interphalangeal joints of both feet (**Figure 3D, 3E**). The stature was normal. His intelligence quotient score was 88. The brothers were born at full term following a normal pregnancy and delivery.

Discussion

KC is a non-inflammatory corneal ectasia that is usually bilateral, asymmetrical and progressive and it has a potential association with Down syndrome, Leber's congenital amaurosis and mitral valve prolapse [2]. Approximately 6% of Down syndrome patients have concomitant KC [3]. In this case, the siblings also demonstrated some features of Down syndrome, but the chromosome karyotype by a single nucleotide polymorphisms array did not conform to Down syndrome (**Figure 4**).

It has been known that familial inheritance, discordance between dizygotic twins, and association with other known genetic disorders are all evidence of the genetic etiology of KC [4]. Tuft

et al. [5] found that the severity of KC is more concordant in monozygotic than in dizygotic twins. To remove the environment factor, we carried out a detailed investigation into the living environment of the two siblings. There were no known physical or chemical risk factors which could have had an impact on birth defects. Their mother's nutrition during pregnancy was good and she had no contact history of any known teratogenic substances.

From the published cases, we did not find any previously described syndrome which accorded with the features of the two cases. Sinnerbrink and Adès [6] had described a brother and sister with craniofacial dysmorphism, short stature, relative obesity, sensorineural deafness, and severe mental retardation. The sister had bilateral KC and intermittent left divergent strabismus. The brother had a right iris coloboma (without KC). The two scholars thought it might be an unrecognized autosomal recessive disease. Similar conditions seem to exist in our case. We believe that the two cases have a distinctive phenotype. The features of the patients described here may represent a previously undescribed autosomal recessive condition, or it could be caused by other mechanisms such as a point mutation.

In summary, the features of congenital ocular disease, low intelligence level, and extremity abnormalities in the two cases are both striking and distinct from other known syndromes. A subtelomeric chromosomal alteration or a subtle submicroscopic deletion may be responsible for their condition, and recurrence in two siblings of normal parents would support these hypotheses.

Acknowledgements

The patients gave their written informed consent for this case report to be published.

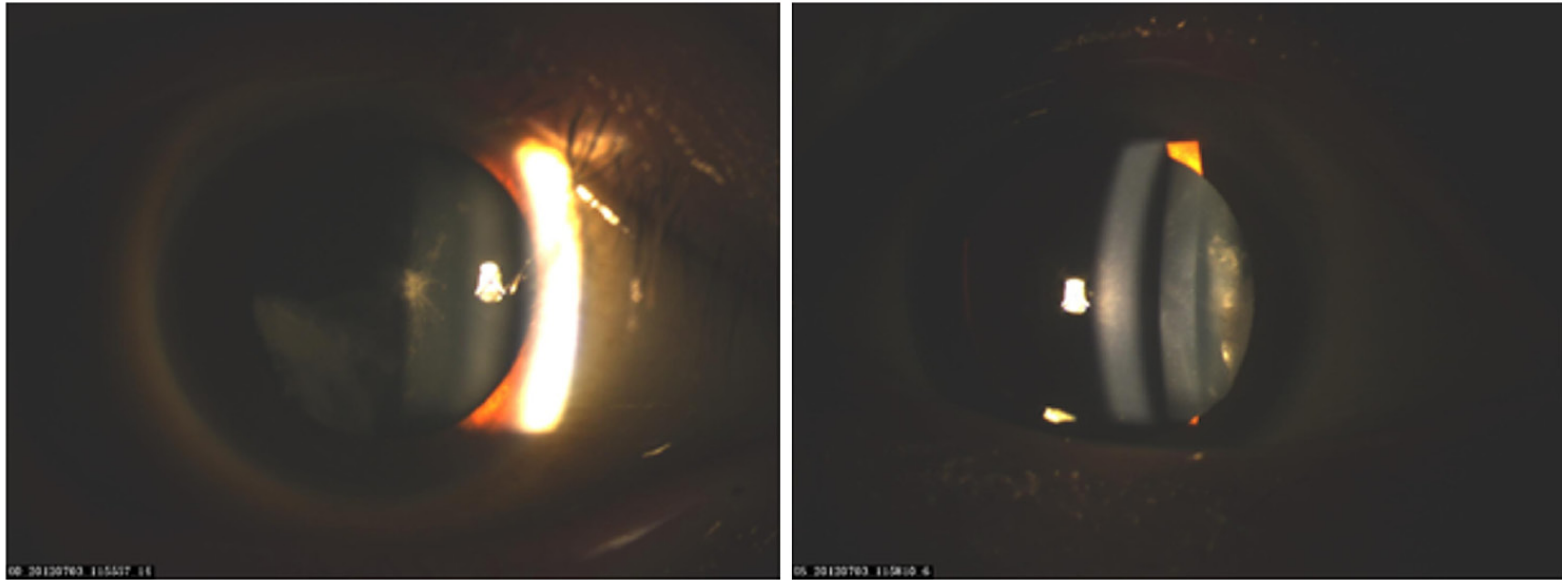
Disclosure of conflict of interest

None.

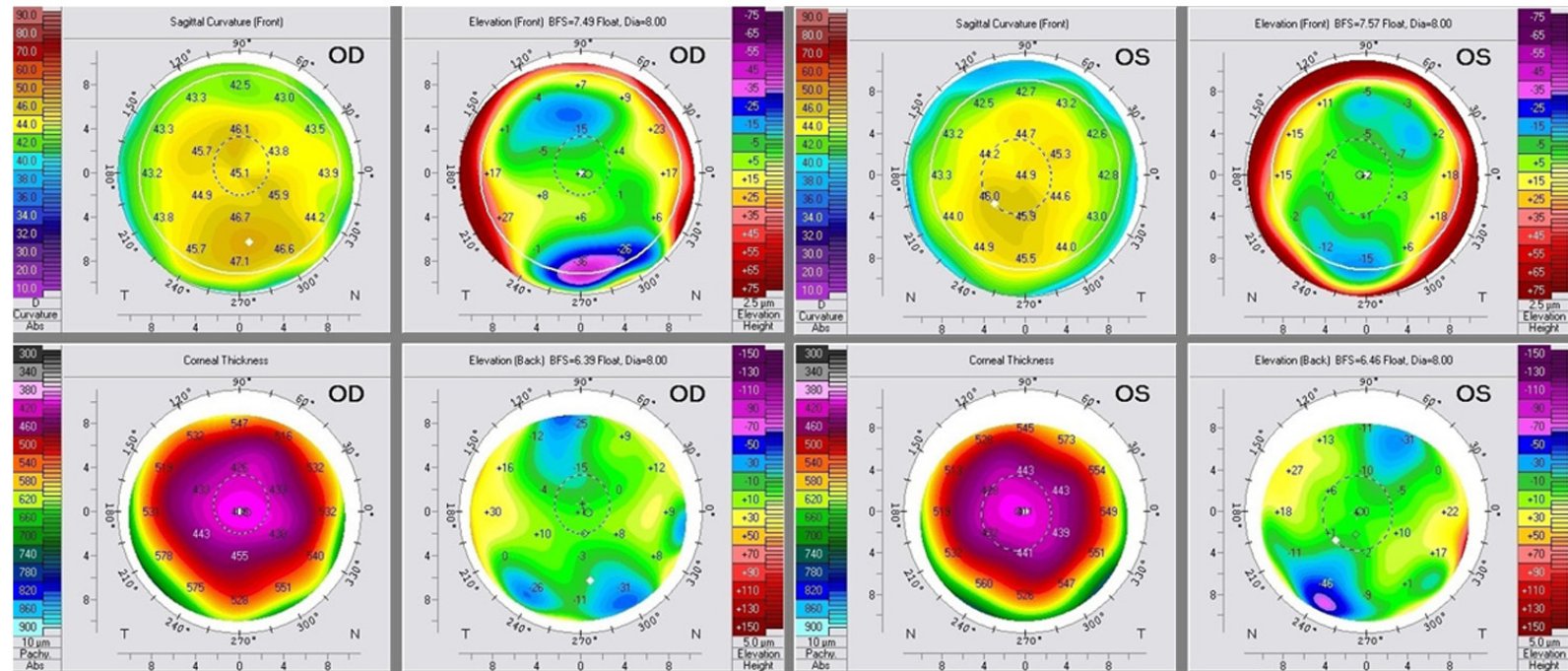
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New specific constellation of features

A



B



New specific constellation of features

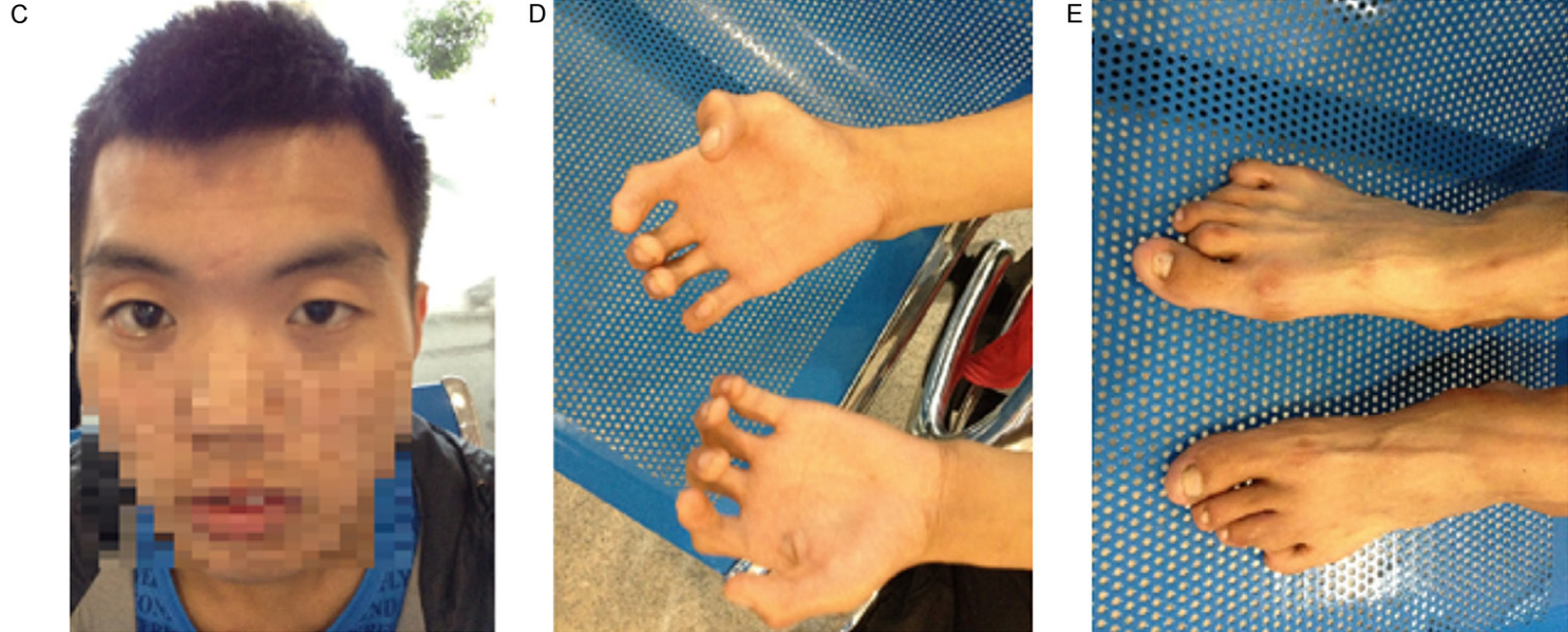


Figure 3. A. The younger brother was diagnosed with bilateral congenital cataract. B. Corneal topography showed that keratometric values in the right eye were 46.0 D at 116.6° and 44.4 D at 26.6°, the corneal thinnest point was 408 μ m. Keratometric values in the left eye were 45.4 D at 60.1° and 44.4 D at 150.1°. The corneal thinnest point was 411 μ m. C. The younger brother presented with hypertelorism and a broad nasal bridge. D, E. Extremity abnormalities of the younger brother included flexion deformities in the interphalangeal joints of both hands and the 2nd, 4th and 5th interphalangeal joints of both feet. Permission has been obtained from the patient's parents for presentation.

New specific constellation of features

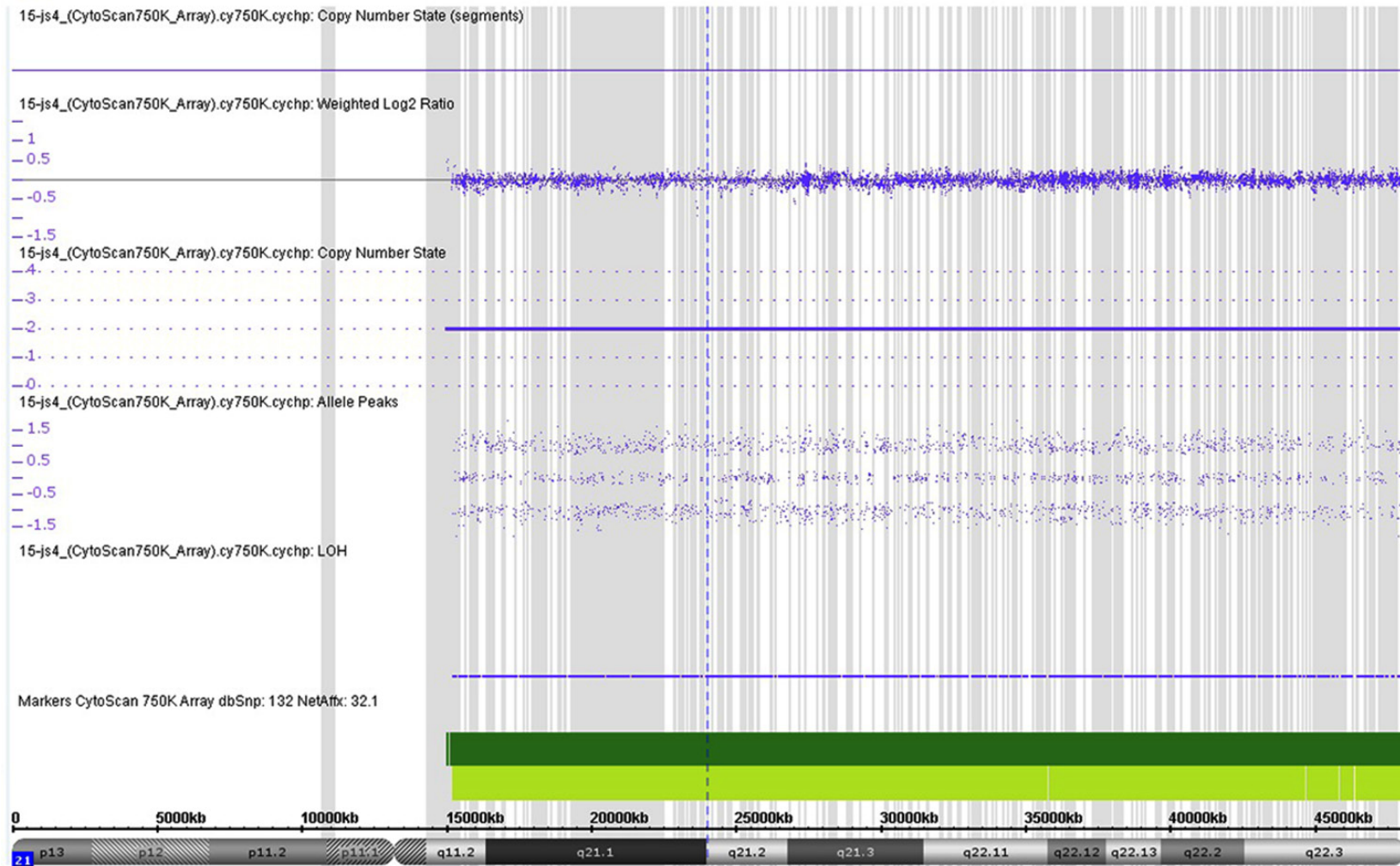


Figure 4. The results of the SNP array showed that the chromosome karyotype did not conform to Down syndrome.

New specific constellation of features

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