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CASE REPORT

A Novel Case of Bilateral High Myopia, Cataract, and Total Retinal Detachment Associated with Interstitial 11q Deletion

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ABSTRACT

Purpose: Jacobsen syndrome, also known as 11q deletion syndrome, is a rare condition characterized by multiple anomalies, including developmental delay, cardiac abnormalities, blood dyscrasias, distal limb abnormalities, craniofacial anomalies, and variable ophthalmic manifestations. The syndrome's phenotype is due to a terminal deletion and is usually severely debilitating, frequently associated with fatality. Interstitial deletions, not involving the terminal end, have been associated with a more variable and less severe phenotype.

Methods: Herein, we describe a case of interstitial 11q deletion in a 16 year-old female with associated systemic and craniofacial abnormalities as well as a novel combination of ocular findings, specifically strabismus, high myopia, bilateral cataracts, and bilateral total retinal detachments.

Results: This case report highlights the necessity for a detailed ophthalmic examination of patients with both interstitial and terminal deletions of the long arm of chromosome 11.

KEYWORDS: Interstitial 11q deletion; Jacobsen Syndrome; Chromosome 11; Retinal detachment; Cataract; High myopia

INTRODUCTION

Jacobsen syndrome, also known as 11q deletion syndrome, is a rare condition characterized by multiple anomalies. These anomalies include developmental delay, cardiac abnormalities, blood dyscrasias, distal limb abnormalities and craniofacial anomalies including trigonocephaly, depressed nasal bridge and micrognathia.[1–8] Jacobsen first described a contiguous gene deletion disorder caused by a translocation between chromosomes 11 and 21.[4] While the original description involved the (11;21) translocation, more recent data has attributed the syndrome's phenotype to deletion of the terminal end of the long arm of chromosome 11.[9–12] Involvement of 11q24.1 is the critical deletion required for the Jacobsen syndrome phenotype.[9–12] The fragile point at which many deletions take place has been identified at 11q23.3.[13,14] When this terminal end is involved, the resultant phenotype is severely debilitating and associated with fatality in the first 2 years of life in 25% of affected individuals, usually secondary to cardiac anomalies.[8,15] Other interstitial deletions of 11q arising between 11q14 and 11q23 have additionally been reported. Interstitial deletions, not involving 11q24.1, have been associated with a more variable and less severe phenotype.[15–17]

Lee reported a series of 10 new cases of Jacobsen syndrome and reviewed 63 previously reported cases to further describe the ophthalmic manifestations of this syndrome. They found that strabismus and refractive error were quite widespread among patients. Facial dysmorphism was additionally commonly observed, specifically ptosis, hypertelorism, epicanthal folds, and up-slanting or down-slanting palpebral fissures.[1–4,7,15,18–20] Specifically, hypertelorism has been observed in deletions involving the 11q24.1 critical region, and ptosis has been associated with involvement of 11q23.[7,8,12] The ptosis can be variable,

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ranging from mild unilateral drooping to bilateral complete absence of levator function.[1,21] Uncommon ophthalmic findings consisted of ectropion, colobomas of various sizes, correctopia, Peters corneal anomaly, nuclear cataract, persistent pupillary membrane, retinal vascular tortuosity, retinal pigmentary abnormalities, glaucoma, and amblyopia.[1,2,7,8,12,19,21–24]

Herein, we present a 16 year-old female with chromosome 11 interstitial deletion involving 11q14–q22. The patient had many typical phenotypic features of this chromosomal abnormality, including growth retardation, developmental and cognitive delay, kidney anomaly, microcephaly, scoliosis, and mild facial dysmorphisms, as well as severe feeding deficits, apneic episodes, and recurrent respiratory infections. However, we believe this case to be the first patient with 11q deletion described in the medical literature with high myopia, bilateral cataracts, and bilateral total retinal detachments.

CASE REPORT

A 16 year-old female with known interstitial 11q deletion presented for pediatric ophthalmic evaluation at Cole Eye Institute in Cleveland, Ohio. Her parents noted a several-week history of decreased vision. Her past ocular history was significant for strabismus and high myopia. The strabismus had resolved in childhood without surgical correction.

The patient was the fourth child of healthy parents, born at 40 weeks gestation following induced vaginal delivery. A three-generation family history revealed no known consanguinity or other birth defects, developmental abnormality, growth problem, or potential genetic disorder. There was additionally no family history of ocular abnormalities, including juvenile-onset cataract, high myopia, or retinal detachment. The pregnancy had been initially uncomplicated with normal fetal activity, use of prenatal vitamins, without teratogenic exposures or illness. However, the 35-week prenatal fetal ultrasonography revealed intrauterine growth retardation, absent left kidney, and dilated cerebral ventricles. The latter two findings were later diagnosed as ectopic, hyoplastic left kidney and grade 3 intraventricular hemorrhage. From birth to throughout childhood, the patient's height and weight were at the 5th percentile for age with her head circumference lying far below the 2nd percentile.

Cytogenetic analysis at 5 months of age revealed a female karyotype with an interstitial deletion on the long arm of one #11 chromosome, involving breakpoints at 11q14.2 and 11q22.3 (46,XX,del(11)(q14.2q22.3)). Approximately 25 percent of chromosome 11q was involved in this deletion.

The patient's subsequent course revealed anomalous kidney, growth retardation, and microcephaly as described, as well as developmental delay, 30-degree S-shaped scoliosis, hypoplastic first rib, and bilateral clubfeet. Additional craniofacial features included trigonocephaly, slightly upslanted palpebral fissures, broad-appearing nasal bridge with short and upturned nose, high palate, bifid uvula, smooth philtrum, thin down-turned upper lip, and small chin (Figures 1 and 2). Hypertelorism, ptosis, and epicantal folds were not observed. As an infant, she had been diagnosed with myotonic jerks and mild cerebral palsy. She had several cyanotic episodes in infancy with subsequent cardiologic evaluation revealing normal anatomy and function. In adolescence, she had several episodes of grand mal seizures, with a diagnosis of likely epilepsy. The patient's family reported no history of repeated head banging or trauma associated with these seizures or other activity. Furthermore, throughout childhood and adolescence she had recurrent ear and respiratory infections, specifically several episodes of aspiration pneumonia. She additionally had been diagnosed with dysphagia secondary to laryngomalacia and gastroesophageal reflux disease associated with severe feeding difficulties requiring gastrostomy placement and revisions. Of note, complete blood counts, kidney function, and liver function tests were normal, specifically with the absence of thrombocytopenia.

Upon presentation for ophthalmic evaluation, she was noted to have severe cognitive delay and mental retardation. She was nonverbal, with Teller card visual acuity assessment revealing 20/250 Snellen-equivalent vision in the right eye (OD), and 20/130 Snellen-equivalent in the left eye (OS) with a correction of -12.00 OD and -12.50 OS. She was very combative and uncooperative during attempted examination, but appeared to have grossly normal ocular alignment. A dense nuclear cataract was observed OD and a relatively less severe inferiorly located nuclear cataract was observed OS. Posterior pole examination was limited both by cataract and patient cooperation.

Subsequent examination under anesthesia confirmed previously observed cataracts. Dilated fundus examination revealed bilateral rhegmatogenous retinal detachments. Both detachments revealed a funnel configuration with proliferative vitreoretinopathy (PVR) grade C2, 4 OD (Figure 3), PVR C2,3,5 OS. B-scan ultrasonography confirmed a total macula-off retinal detachment with no subretinal masses in both eyes. A-scan measurements of axial length revealed 25.6 millimeters OD and 25.04 millimeters OS, with keratometry readings of 47.87 × 52.75 OD and 48.25 × 51.12 OS. Immediately following examination under anesthesia, the patient underwent cataract extraction in the right eye with a 0.00 D lens placed in the capsular bag.

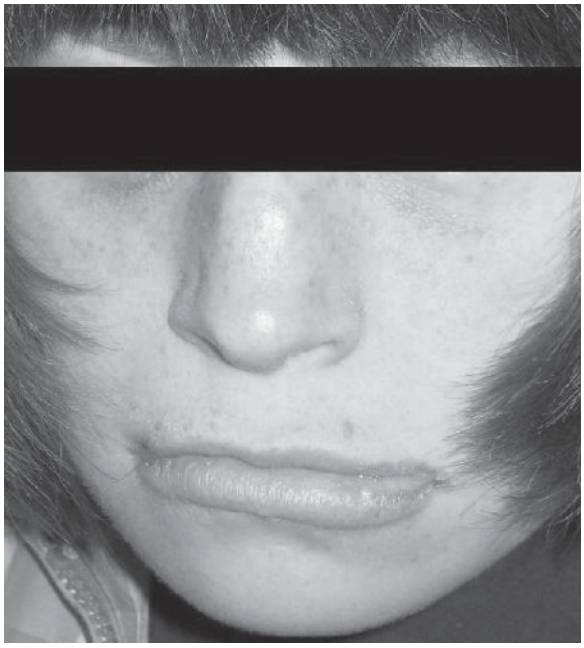

FIGURE 1 Photograph of patient demonstrates various craniofacial features, including broad-appearing nasal bridge, smooth philtrum, thin down-turned upper lip, and small chin.

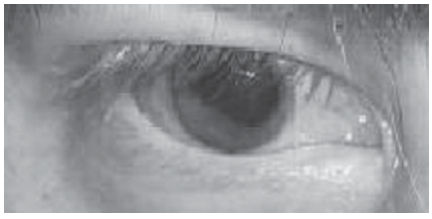

FIGURE 2 Photograph of patient focused on right eye demonstrates slightly upslanted palpebral fissure

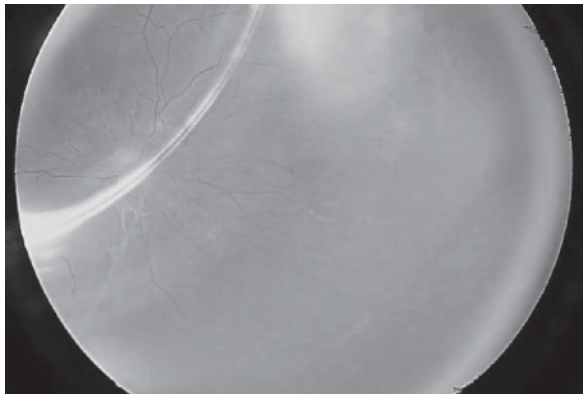

FIGURE 3 Intraoperative photograph of right eye demonstrates total retinal detachment with PVR Grade C2,4. The retina does not show exudation or vascular anomaly consistent with FEVR.

After cataract surgery, the patient underwent retinal detachment repair by vitrectomy/scleral buckle/silicon oil injection OD, followed by phacoemulsification/posterior capsulotomy/vitrectomy/scleral buckle/silicon oil OS at a later date. Silicon oil was removed from both eyes without complication after 3 months of tamponade. Both retinas remained attached, and the patient's family reported markedly increased vision and skills in mobility and other daily activities.

DISCUSSION

Our patient is a 16-year-old female with an interstitial 11q14–q22 deletion and associated systemic and craniofacial abnormalities with strabismus, high myopia, bilateral cataracts, and bilateral total retinal detachments. The combination of these latter phenotypic features is unique from the existing literature.

Wakazono reported an infant with an interstitial 11q14–q22 deletion, who suffered from transient hypocalcemia and hypotonia, as well as occasional apneic attacks, feeding difficulties, growth and developmental retardation, dolichocephaly, multiple dysmorphic features, and recurrent respiratory infections. Ocular findings in this infant included telecanthus and bilateral ptosis. Notably, cardiac abnormalities were absent on echocardiography.[17] The nonocular findings of the patient described in this case report, specifically her history of occasional apneic attacks with recurrent respiratory infections and feeding difficulties in the absence of cardiac anomalies, are very similar to Wakazono's report.

Strabismus and refractive error have commonly been observed associated with 11q deletion.[19] Additionally, nuclear cataract has been infrequently reported.[7,23]

Furthermore, retinopathies have also been observed; specifically, the Frizzled-4 (FZD4) and low-density lipoprotein receptor-related protein 5 (LRP5) genes have been mapped to the long arm of chromosome 11 and are responsible for familial exudative vitreoretinopathy (FEVR).[24–26] LRP5, mapping to chromosome 11q13.4, is centromeric to our patient's deletion and likely does not contribute to her ocular pathology.[25,26] Uto reported a patient with an 11q23.3 deletion with peripheral avascular temporal retina and temporal dragging of retinal vessels associated with peripheral vasculopathy.[27] Although this child's findings resembled retinopathy of prematurity, the child was born full-term. The authors attributed these findings to a FEVR phenotype. Li later described a patient with de novo complex chromosomal rearrangements including a translocation-deletion-inversion of chromosomes 11q and 16q causing an interstitial 11q14.1–q23.2 deletion.[28] This patient presented with the FEVR phenotype, as

well as growth retardation, facial anomalies, cleft palate, and minor digital anomalies. The authors postulated that the majority of this patient's retinal findings were secondary to the 11q deletion, specifically resulting from a haploinsufficiency related to the loss of the paternal FZD4 allele at 11q14.3. Upon review of 23 cases with 11q14–23 deletions, the authors constructed a regional deletion map revealing that deletions of the FZD4 gene at the centromeric segment (11q14.1–11q14.3) lead to retinal dysgenesis, while deletions at the gene's telomeric segment (11q21–11q23) account for other features, specifically dysmorphic craniofacial anomalies, growth and mental retardation, and mild digital abnormalities.[28]

Our patient's presentation may well conform to the FEVR phenotype, but significant differences in her clinical exam and intraoperative findings suggest that this was not a FEVR related retinal detachment. Her age of 15 years suggests that if this was FEVR, her presentation with bilateral retinal detachments was late. She harbored no retinal exudates, persistent fetal vasculature, peripheral neovasvcularization, or fibrovascular mass. There were no retinal folds or macular heterotropia. Her preoperative and intraoperative findings revealed a rhegmatogenous origin to her bilateral retinal detachments. We did not obtain a fluorescein angiogram to determine peripheral avascularity. It is also possible that this patient, like patients with acquired abnormal vascular development such as ROP, developed myopia as a secondary consequence to primary vascular disease, which in our case if present is so mild as to not cause any grossly recognizable FEVR phenotype.

The phenotype described in this case report is unique. The aforementioned dysmorphic facial features of abnormal nasal bridge, palebral fissures, and palate, as well as systemic findings of developmental delays, prenatal and postnatal growth retardation, microcephaly, significant feeding problems, single anomalous kidney, and respiratory infections without cardiac anomalies have been reported associated with similar 11q deletions.[5,17,28] However, the associated combination of strabismus, high myopia, cataract, and bilateral total retinal detachment has not been previously described. This case report highlights the necessity for a detailed examination of patients with both interstitial and terminal deletions of the long arm of chromosome 11. While systemic abnormalities as well as facial dysmorphic features are widely known and routinely evaluated, special attention should be given to the possibilities of amblyogenic refractive error and cataract as well as associated retinal detachments, findings that may require examination under anesthesia for accurate diagnosis and treatment.

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