Static and Dynamic Pupillometry in 2q37 Microdeletion Syndrome in a Turkish Child

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ABSTRACT

The current study aimed to evaluate a child with dysmorphism and attention-deficit/hyperactivity disorder with cyto- and molecular genetic testing and automated pupillometry. The genetic analysis detected a 4337 kb deletion in 2q37 and a 34 mb duplication in the 4q32 region. The karyotype was 46, XY, der(2;21) (2pter→ 2q37.3::21p13→ 21p10::20p10→ 20pter), der(20) (21qter→ 21q10::20q10→ 20qter). In static pupillometry, scotopic measurement was 5.39 mm in the right eye (RE), 9.24 mm in the left eye (LE), mesopic was 4.89 mm in the RE, 2.22 mm in the LE, and photopic was 4.35 mm in the RE and 0.73 mm in the LE. Dynamic pupil diameter was 4.55 mm in the RE and 2.23 mm in the LE at the 0th second; 2.12 mm in the RE and 6.45 in the LE at the 10th second, and 2.02 mm in the RE and 6.95 mm in the LE at the 18th second. In conclusion, the pupil dilation speed of the case was moderately low on static and dynamic pupillometry. This needs further corroboration in other cases.

Key Words: *2q37, Microdeletion syndrome, Automated pupillometry, Dysmorphism*.

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INTRODUCTION

2q37 microdeletion syndrome (del2q37, OMIM 600430) is a very rare autosomal dominant inherited chromosomal disorder. The characteristic features of this chromosomal disorder are developmental delay/intellectual disability, brachymetaphalangia at grades 3-5 (usually 4 digits alone), short stature, obesity, hypotonia, characteristic facial appearance, autism or autism spectrum disorder, and joint hypermobility.[1] Patients can present with various clinical findings: congenital heart and skeletal malformations, gastrointestinal, renal, genitourinary, and central nerve malformations. Up to 30% of patients have neurodevelopmental disorders and are known as Albright hereditary osteodystrophy-like syndrome (AHO-like). Anomalies such as epilepsy, hypotonia, seizures, and autism are also seen in the syndrome, which was first reported in 1952. Since then, more than 115 cases have been notified worldwide.[2,3]

Herein, we report a child with dysmorphism and attention-deficit/hyperactivity disorder with cyto- and molecular genetic testing and automated pupillometry.

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CASE REPORT

A 6-year boy was the only child of healthy, non-consanguineous, Turkish parents. No genetic or chronic disease was found in the family. The 2.65kg (25th-50th percentile) child was born by cesarean section at 36 weeks. Conventional chromosome analysis revealed 46, XY. Although he had a mild learning disability, he attended a regular school.

Dysmorphic facial features of the patient were droopy ears, curved ear auricle, brow arch protrusion, notched nostril, and short-flat lip philtrum. He had a prominent forehead and dysmorphic features including relative macrocephaly, a flattened nasal bridge, short hands and feet without prominent columella and metacarpal / metatarsal shortening. At the age of 3 years, he was diagnosed with myocarditis with heart failure. At the age of 4 years, he was diagnosed with attention-deficit and hyperactivity disorder after being diagnosed with brachydactyly mental retardation (BDMR) syndrome. Then, a chromosomal microarray study was performed with Affymetric Cytoscan Optima (315 k) chips from DNA obtained from peripheral blood. A 4337 kb deletion was detected in the 2q37.3 region. Deletions of this region are defined as 2q37 microdeletion syndrome (OMIM 600439) and are reported as pathogenic in the literature. In addition, approximately a 34 mb duplication was detected in the 4q32 region containing many genes. It was thought that both changes affected the patient's phenotype together. Reciprocal translocation was detected between the q37 and q31.3 regions of the 2nd and 4th chromosomes in the mother. No numerical or structural chromosomal anomalies were detected in the father (Figure 1).

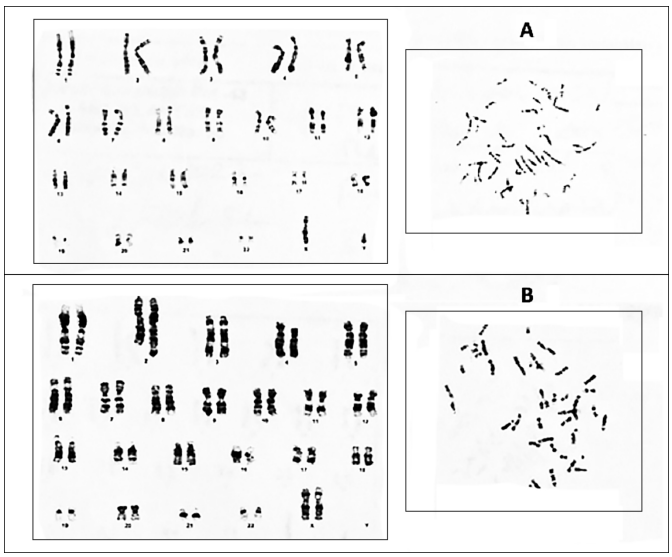

Figure 1: Cyto-genetic testing of the child's parents. (A) Reciprocal translocation in the mother. (B) No chromosomal anomaly in the father.

A detailed ophthalmological examination was performed. At presentation, a refractive error of +0.25/-1.50x175 diopter (D) was measured for the right eye (RE) and +1.00-2.25x175 D for the left eye (LE). The best corrected visual actuality (BCVA) was 0.20 logMAR in his RE and 0.20 logMAR in LE. Anterior segments and fundus examinations were normal. The intraocular pressure (IOP) as measured using Goldman applanation tonometry was 12 mmHg in the RE and 14 mmHg in the LE while central corneal thickness was 511 µm in the RE and 520 µm in the LE.

Direct and consensual pupillary light reflex tests were done and were normal. Pupillary parameters were performed by automatic pupillometry of Sirius 3-D rotating Scheimpflug Topographer (CSO, Firenze, Italy). Pupillometry measurements were made at the same time of day by the same clinician (08:00 am–12:00 noon). Firstly, the static pupillometry which was implemented under three distinct illumination settings was applied after a 5-minute dark adaptation. Scotopic measurement was 5.39 mm in the RE, 9.24 mm in the LE, mesopic was 4.89 mm in the RE, 2.22 mm in the LE, and photopic was 4.35 mm in the RE and 0.73 mm in the LE.

Afterwards, dynamic pupillometry was also performed. Dynamic pupil diameter was 4.55 mm in the RE and 2.23 mm in the LE at 0th second; 2.12 mm in the RE and 6.45 in the LE at 10th second and 2.02 mm in the RE and 6.95 mm in the LE at 18th second.

DISCUSSION

The study reported static and dynamic pupillometry findings in a Turkish child with a 4337 Kb deletion in the 2q37 region and a 34 Mb duplication in the 4q32 region.

Objectively, pupil examination can be done with automatic pupillometry using infrared rays. Pupillometry, which is a non-invasive method, gives an important clue about the balance between the parasympathetic and sympathetic nervous systems.[4-6]

Baseline fluctuation is observed with pupil dilation at a steady state. Neurological abnormalities are taken into account in cases of significant pupillary size differences, and these are called anisocoria, which are estimated to affect at 4% of the general population. Normal pupillary reaction times are about one second for initial constriction and five seconds for dilation.[7,8] In the present case, the patient had anisocoria, and the pupil reactions were abnormal in both eyes. In previous studies, none of the reported patients with 2q37 microdeletion syndrome were evaluated by automated pupillometry. Since it is a very rare condition, static and dynamic pupillometry parameters could not be evaluated with other similar patients.

In conclusion, quantitative evaluations were performed by automated pupillometry in a child with 2q37 microdeletion syndrome. The pupil dilation speed of the case was moderately low, but the finding should also be investigated in other individuals with 2q37 microdeletion syndrome before they can be generalised.

PATIENT' S CONSENT:
An explicit consent has been obtained from the patient's parents to publish this case.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHOR'S CONTRIBUTION:
CT: Substantial contribution to the conception or design of the work, drafting and critically revising the manuscript for important intellectual content.

REFERENCES

1. Falk RE, Casas KA. Chromosome 2q37 Deletion: Clinical and molecular aspects. *Am J Med Genet C Semin Med Genet* 2007; **145**:357-71. doi: 10.1002/ajmg.c.30153.
2. Wilson LC, Leverton K, Luttikhuis MEMO, Oley CA, Flint J, Wolstenholme J, *et al*. Brachydactyly and mental retardation: An Albright hereditary osteodystrophy-like syndrome localized to 2q37. *Am J Hum Genet* 1995; **56**: 400-7.
3. Leroy C, Landais E, Briault S, David A, Tassy O, Gruchy N, *et al*. The 2q37-deletion syndrome: An update of the clinical spectrum including overweight, brachydactyly and behavioural features in 14 new patients. *Eur J Hum Genet* 2013; **21(6)**:602-12. doi: 10.1038/ejhg.2012.230.
4. Zhang F, Jaffa-Dax S, Wilson RC, Emberson LL. Prediction in infants and adults: A pupillometry study. *Dev Sci* 2019; **22(4)**:e12780. doi: 10.1111/desc.12780.
5. Fountoulakis KN, St Kaprinis G, Fotiou F. Is there a role for pupillometry in the diagnosis approach of Alzheimer's disease? A review of the data. *J am Geriatric Soc* 2004; **52**:166-8. doi: 10.1111/j.1532-5415.2004.52030_7.x.
6. Bhatnagar R, Birnbaum AD, Baqai J, Volpe NJ. Automated pupillometry as an adjunct to clinical examination in patients with acute vision loss. *J Neuroophthalmol* 2021; **41(2)**:239-45. doi: 10.1097/WNO.0000000000000919.

7. Ciuffreda KJ, Joshi NR, Truong JQ. Understanding the effects of mild traumatic brain injury on the pupillary light reflex. *Concussion* 2017; **2(3)**:CNC36. doi: 10.2217/cnc-2016-0029.

8. Lynch G. Using Pupillometry to assess the atypical pupillary light reflex and LC-NE system in ASD. *Behav Sci (Basel)* 2018; **8(11)**. 108. doi: 10.3390/bs8110108.