CJO JCO

Original Article

Ocular manifestations in Koolen–de Vries syndrome: an international study

Dafna Shalev,[*,†] David A. Koolen,[‡] Bert B.A. de Vries,[‡] Sharon Blum Meirovitch,[§] Jean-Louis Mandel,[‖,¶] Pauline Burger,[‖] Alik Rosenfeld,[†,**] Guy J. Ben Simon,[*,†,††] Daphna Landau Prat[*,†,††]

Objectives: Koolen–de Vries Syndrome (KdVS) is a rare multisystem neurodevelopmental disorder. Ocular manifestations, including strabismus, ptosis, and hyperopia, have been reported in KdVS patients, but detailed clinical data are limited. This study aims to investigate the already known ocular malformations and their frequency while uncovering novel ocular associations.

Methods: This was an international cross-sectional study. An anonymous questionnaire was sent to 237 KdVS patients registered in the GenIDA database. The questionnaire inquired about demographic data, ocular symptoms, findings reported by ophthalmologists, and ophthalmologic surgical interventions. The main outcome measures included ocular findings and surgical interventions.

Results: Sixty-seven respondents worldwide completed the questionnaire, most (n = 53; 79%) under 18 years of age. Ophthalmologic abnormalities, noted in 79% of patients, included refractive errors (n = 35; 52.2%), strabismus (n = 23; 34.3%), amblyopia (n = 13; 19.5%), and eyelid ptosis (n = 9; 13.4%). Lacrimal disorders were present (n = 6; 9.0%), as were retinal findings (n = 7; 10.4%), including retinal hyperpigmentation or hypopigmentation (n = 4; 7.5%), Sjögren's pigment epithelial reticular dystrophy (n = 1; 1.5%), and macular chorioretinal coloboma (n = 1; 1.5%). Other manifestations included ocular surface disorders (n = 5; 7.5%), cataracts (n = 3; 4.5%), Brown syndrome (n = 1; 1.5%), glaucoma (n = 1; 1.5%), cerebral visual impairment (n = 1; 1.5%), and optic atrophy (n = 1; 1.5%). Fourteen patients (20.8%) had undergone surgical interventions.

Conclusions: KdVS is associated with various ophthalmic findings, such as amblyopia, refractive errors, strabismus, and eyelid ptosis. We describe, for the first time, a high rate of nasolacrimal disorders and retinal abnormalities consisting mainly of pigmentary findings, including a rare case of Sjögren's pigment epithelial reticular dystrophy. A comprehensive ophthalmic evaluation is therefore recommended for all KdVS patients at initial diagnosis or at 4–6 months of age for diagnosed newborns.

Koolen–de Vries Syndrome (KdVS), also known as the 17q21.31 microdeletion syndrome,[1–3] is a rare condition characterized by congenital malformations in multiple organs, hypotonia, developmental and speech delay, intellectual disability, epilepsy, and characteristic facial features.[4] Associated structural malformations include renal and urologic anomalies (25%–50%), cryptorchidism (71% of males), and congenital heart defects (25%–50%).[5] Behaviour in most cases is described as friendly and amiable.[5] Craniofacial features in KdVS include blepharophimosis, eyelid ptosis, epicanthus, upslanted palpebral fissure, bulbous or pear-shaped nose, and protruding or large ears.

While the rarity of KdVS has limited our knowledge regarding its various medical presentations in the past, international databases, such as GenIDA, have expanded our knowledge about the syndrome in recent years. The GenIDA International Project is an online cohort study focused on patients affected by intellectual disabilities and (or) autism spectrum disorders (https://genida.unistra.fr/). KdVS is among the disorders documented in the database, with 237 confirmed cases registered from 31 countries, including the United States (42.0%), France (12.9%), the United Kingdom (7.2%), and Australia (6.6%).

Ocular manifestations are a common feature in patients with KdVS, but data characterizing the various abnormalities and their frequency are limited. There are currently no large-scale studies describing the ocular manifestations in KdVS patients in the literature. In this international cohort study, we aim to characterize the already known ocular manifestations in greater detail and to describe novel ocular associations.

Methods

An anonymous questionnaire regarding ocular manifestations and interventions was sent to all KdVS patients or patients' parents registered in the international GenIDA database (Appendix 1, available online). The questionnaire was available only in English, with a translation offered in French. All patients who were registered in the database had genetically confirmed KdVS, and their caregivers gave informed consent to GenIDA allowing the use of data that were obtained for clinical research. In addition, 3 patients shared data from ophthalmic visits, and 2 of them also shared retinal optical coherence tomography examination results.

https://doi.org/10.1016/j.jcjo.2023.11.021
ISSN 0008-4182