**Abstract**

**Introduction:** Mowat-Wilson syndrome is a rare genetic condition resulting in multiple congenital anomalies including facial dysmorphism, structural anomalies of the internal organs, functional disorders and, although less commonly, ocular abnormalities.

**Aim:** To present a child with Mowat-Wilson Syndrome and eye abnormalities.

**Patient and method:** 3-year-old boy born at 37 weeks of pregnancy with dysmorphic features, neurodevelopmental disorders, genetically confirmed Mowat-Wilson syndrome, nystagmus, strabismus and suspicion of congenital glaucoma. Ophthalmic examination was carried out under general anesthesia; eyeball ultrasound and electrophysiological examination (flash - VEP) were also performed.

**Results:** The examinations revealed nystagmus, normal response of pupils to light in both eyes and normal intraocular pressure, i.e., 17mmHg and 18mmHg in the right and left eye, respectively. Corneal thickness was 606 µm in the right and 588 µm in the left eye. Gonioscopy revealed displacement of Schwalbe's line anterior to the limbus of the cornea (posterior embryotoxon). Fundus examination revealed a pink optic disk with a cup-to-disc ratio of 0.5, macular pigment regrouping and normal blood vessels. Flash VEP - P2 latency was normal. P2 amplitude from the left hemisphere was reduced to 50%, P2 amplitude over the right hemisphere was normal.

**Conclusions:** Children with genetically determined congenital anomalies need regular ophthalmic check-ups to accurately assess the eye and determine the prospects of vision function development.

**Keywords:** Mowat-Wilson; ZEB2 gene; Children; Ocular abnormalities.
Introduction

Mowat-Wilson Syndrome (MWS) is a genetically determined rare syndrome of congenital malformations, including craniofacial dysmorphism, developmental anomalies of the central nervous system, kidneys, heart, genitourinary system, Hirschprung disease, small head, neurodevelopmental disorders and, although less commonly, ocular abnormalities [1]. The cause of the syndrome is a mutation of the ZEB2 gene located at 2q22 [1-3]. The gene encodes the transcription factor Zeb-2, also called SIP1, involved in the TGF-β signaling pathway thus being responsible for the normal course of embryogenesis [4]. MWS is more common in males; the male/female ratio is approximately 1.42:1 [5,8].

Aim

The aim of this paper is to present a case of a 3-year-old boy with Mowat-Wilson syndrome and eye abnormalities.

Case report

A 3-year-old boy with Mowat-Wilson Syndrome, confirmed by molecular genetic testing, was referred to the Division of Pediatric Ophthalmology, the K. Gibinski University Hospital Center, Medical University of Silesia, Katowice, Poland for an ophthalmic examination.

The boy is the second child of his parents, born at 37 weeks of pregnancy with a birth weight of 2130 g and Apgar score of 10. In the neonatal period he had been diagnosed with polysplenia syndrome; he also had a history of grade II right and grade I left intraventricular hemorrhage.

At the age of 2 months the child was hospitalized in the Department of Immunology due to hyperleukocytosis and agammaglobulinemia. The results of immunoglobulin tests were within the normal age-specific reference range and the current response to vaccine antigens was found to be normal for the age. Immune responses to vaccinations had been generated. In the first year of life the child was hospitalized in the Department of Pediatrics and Developmental Age Neurology due to facial dysmorphism and neurodevelopmental disorders. Magnetic resonance imaging of the head showed ventricular asymmetry. Electroencephalography revealed generalized abnormalities; no paroxysmal EEG patterns were found. Neurological examination revealed decreased muscle tension in the head-torso axis, contractures in the knee and elbow joints and variable muscle tension with a tendency to increase. The child was also diagnosed with hypospadias, absence of testes in the scrotum and congenital kidney anomalies including hypertrophied column. Due to facial dysmorphism, neurodevelopmental disorders and internal organ abnormalities, the child was referred for genetic consultation. Molecular examination showed 1966_1967delAT mutation in one allele of the ZEB2 gene. The lesion is presented in the Human Gene Mutation Database as a pathogenic defect, correlated with Mowat-Wilson Syndrome. The child has regularly scheduled appointments at neurology, urology, ENT, genetic, hematolgy and ophthalmology clinics. He also receives speech therapy, general developmental rehabilitation and early developmental support.

On the day of admission to the Division of Pediatric Ophthalmology, the child’s general condition was good. Physical examination revealed facial dysmorphism including hypertelorism, antimongoloid eye slant, deep-set eyes, high and prominent forehead, large eyebrows, open mouth, M-shaped upper lip, micrognathia, and low-set, dysplastic ears. Figure 1.

The ophthalmic examination revealed nystagmus and normal response of pupils to light; the child followed toys with his eyes and tested well on optotypes; visual acuity was 0.05 in both eyes. The mother mentioned the boy did not speak.

The examination was continued under general anaesthesia. Eye optical systems were transparent, corneal diameters were 10.5x11.5 mm, intraocular pressure was normal, i.e., 17mmHg and 18mmHg in the right and left eye, respectively. Corneal thickness was 606 µm in the right and 588 µm in the left eye. Gonioscopy showed a prominent and anteriorly displaced line of Schwalbe in the temporal quadrants (posterior embryotoxon). Fundus examination revealed a pink optic disk with a cup-to-disc ratio of 0.5, macular pigment regrouping and normal blood vessels.

Ocular ultrasonography showed normal posterior segments and axis lengths of 23 and 22.87 mm in the right and left eye, respectively. Refraction of the optical system after accommodation paralysis was +0.75Dsph+0.25Dcyl ax 78° in the right and +0.75Dsph+0.25Dcyl ax 73° in the left eye. Flash VEP - P2 latency was normal. P2 amplitude from the left hemisphere was reduced to 50%, P2 amplitude over the right hemisphere was normal. Alternating divergent strabismus was also found (Figure 4. Ocular ultrasonography).
Following diagnostic testing, the child was discharged home in good general condition. Due to nystagmus, strabismus and changes in the appearance of the optic disc, further diagnostic procedures were scheduled in the Outpatient Department. Regular check-ups with other medical specialists were also recommended.

Discussion

Mowat-Wilson syndrome is a rare genetic congenital malformation syndrome. According to the National Organization for Rare Disorders, the prevalence of MWS is 1 per 50,000-100,000 live births. Coyle et al. [6] analyzed 256 cases of MWS reported worldwide by 2015. However, the prevalence may be higher due to undiagnosed cases, including patients who are not fully symptomatic.

When describing ocular lesions characteristic of MWS, Mowat, Wilson et al [1,7] emphasized hypertelorism and deep-ly-set but large eyes. The eyebrows tend to be broad and horizontal with a wide medial separation. The authors also mention early nystagmus owing to fixation difficulties. Some patients with blue irides were shown to have dark pigment clumps in the irides, described as heterochromia. Garavelli and Mainardi [8] reported that 4.1% of patients with MWS had structural anomalies of the eye. Adam et al. [9] mentioned that 4% of affected individuals had eye anomalies, including microphthalmia, iris and retinal colobomas, Axenfeld anomaly, peripapillary atrophy, ptosis, cataract, retinal aplasia, nystagmus and strabismus. Mowat and Wilson [1] described one case of unilateral eyelid ptosis. Vascular and retinal fissures were also found. Faltin et al. [3] described a 3-month-old girl with unilateral coloboma of the iris and retina and other symptoms typical of MWS. Ariss et al [10] reported a 9-year-old girl with MWS and severe ocular lesions including bilateral microphthalmia, cataract and retinal aplasia. Other authors also pointed out the occurrence of changes in the organ of vision. Hartill et al. [11] described a case of a 41-week-old child with deep-set eyeballs, diagonal wrinkles and strabismus, while Tanteles et al. [12] described two patients with vision defects. In the first patient with poor visual contact, the ophthalmic examination revealed bilateral colobomata of the iris and choroid, and optic nerve involvement. The other patient had a bilateral microphthalmia, right iris coloboma and left partial aniridia.

The presented patient remains under the supervision of several health professionals due to multi-organ structural anomalies and functional disorders in the form of psychomotor and speech delay. The clinical picture prompted the attending physicians to order a genetic test, which revealed ZEB2 gene mutation indicative of Mowat-Wilson syndrome. Ocular anomalies potentially associated with MWS are quite diverse. Our patient exhibited abnormalities reported by the majority of authors, i.e., hypertelorism, deep-set eyeballs, nystagmus and strabismus. Gonioscopy revealed displacement of Schwalbe’s line anterior to the limbus of the cornea (posterior embryotoxon), which is characteristic of Axenfeld anomaly observed in patients with MWS [9]. Due to ocular disorders, the boy is under regular supervision by our ophthalmic clinic.

Conclusions

Although only about 4% of patients diagnosed with Mowat-Wilson syndrome exhibit ocular abnormalities, they should receive regular ophthalmic evaluation to accurately assess the organ of vision and determine the prospects of vision function development.

References


