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Foveal hypoplasia in children: own observations

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ABSTRACT

Introduction: Foveal hypoplasia is defined as a developmental disorder of the macula with a relatively preserved neuroretina. The condition may cause reduced visual acuity and other coexisting ocular disorders. On ophthalmoscopic examination, macular reflexes in the eyes with foveal hypoplasia are either absent or diminished. Morphological changes in the fovea can be visualized by optical coherence tomography (OCT). Four grades of foveal hypoplasia have been distinguished.

The aim of the study was to perform an ophthalmoscopic, imaging (OCT), and functional assessment of the retinal macula in children with foveal hypoplasia.

Material and methods: The study group consisted of eight pediatric patients (four boys and four girls), aged between 6 and 18 years, who were diagnosed with foveal hypoplasia. The children underwent ophthalmic examinations including the assessment of visual acuity and eye fundus, and macular OCT.

Results: Visual acuity was impaired in one or both eyes in seven children, ranging from the sense of light (in the eye with coexisting optic nerve pathologies) to 5/6. In the majority of children, macular reflexes were found to be absent or diminished either in one or both eyes. In all the patients, foveal hypoplasia was diagnosed on the basis of OCT findings and graded.

Conclusions: Abnormal ophthalmoscopic appearance of the macula, exhibiting anomalous light reflexes, is an indication for a more detailed diagnostic approach. Our studies show that unexplained reduced visual acuity with preserved macular reflexes also justifies performing a non-invasive OCT examination of the macula. Macular OCT imaging is necessary for making the diagnosis of foveal hypoplasia and grading the severity of the condition. Severe foveal hypoplasia reduces visual acuity and may impair other visual functions.

KEY WORDS: foveal hypoplasia, child, optical coherence tomography of the macula, visual acuity.

INTRODUCTION

The morphological features of the macula of retina, which is a distinct structure comprising the fovea (a depression in the middle of the macula) and the foveola (a pit lying in the center of the fovea), are intrinsically linked to the role of the macula in the process of vision. Foveal hypoplasia is defined as abnormal development of the central part of the macula [1]. The fovea is formed by the migration of internal retinal neurons towards the periphery and the elongation of the underlying photoreceptor protrusions and their nuclei – cones. The macula, especially in its central part, contains the largest cluster of densely packed cones. They are responsible for daylight (photopic) vision, discrimination of details, and color vision. The process of foveal formation is long, linked to the development of the retina during the fetal stage and continuing for many months after birth. Disturbances in this process may inhibit normal foveal development. Foveal hypoplasia may coexist with other developmental anomalies of the organ of vision (aniridia, microphthalmia, vitiligo, achromatopsia) or it may be isolated or genetically determined. Familial foveal hypoplasia is associated with damage to the *PAX6* gene [2]. Heterozygous mutations in the *PAX6* gene may lead to foveal hypoplasia with a near normal ophthalmoscopic appearance of the macula, resulting in diagnostic difficulties.

On ophthalmoscopy of the fundus, the margins of the fovea in pediatric patients appear as a round light reflex. The foveolar depression is due to the thinning of the retina in this area, formed only by cones and Müller's glial cells that create a support layer and have a nourishing function. The region within the fovea, lying around the foveola, is referred to as the foveal avascular zone. On ophthalmoscopic examination, in a normal macula, the fovea is visualized as a central reflex from the central depression called the umbo of the fovea.

When examining the macula by ophthalmoscopy, there is no possibility to determine its morphology. An opportunity

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to evaluate the successive retinal layers that make up this area, known to play a critical role in the process of vision, emerged with the introduction of optical coherence tomography (OCT) into the diagnostic process. Based on OCT assessment, Thomas *et al.* in their 2011 paper distinguished four grades of foveal hypoplasia associated with different stages of arrested development of the fovea [1]. According to the authors, their grading system offers three advantages. It defines the stage of foveal development, provides a prognostic indicator based on morphologic findings obtained by OCT, and can be used to determine the majority of disorders associated with foveal hypoplasia. The classification is now widely used [3, 4]. Every grade of foveal hypoplasia is characterized by the presence of plexiform layers that are absent in the normally developed fovea. Consequently, this feature can be used as a pathological hallmark of foveal hypoplasia. Grade 1 foveal hypoplasia is characterized by the presence of plexiform layers together with shallow foveal pit, preserved normal widening of the outer nuclear layer (ONL) and lengthening of the outer cone elements – outer segments (OS) of photoreceptors. Grade 2 is marked by the absence of foveal pit and the presence of all other characteristics of grade 1 foveal hypoplasia. Grade 3 comprises the same changes as in grade 2, except for the absence of OS lengthening. The diagnosis of grade 4 foveal hypoplasia is made on the basis of the same changes as in grade 3 but without ONL widening. There is a fundamental difference in visual acuity associated with the grade of foveal hypoplasia. It is the best in patients with grade 1 hypoplasia, and it gradually decreases in more severe grades [4]. Foveal hypoplasia, as already mentioned, can be isolated, similarly to isolated optic nerve hypoplasia, or associated with systemic abnormalities and preterm birth [4-7]. The OCT examination is conclusive in establishing the diagnosis of developmental anomalies of the macula, which can result in visual dysfunction and other ocular abnormalities, such as nystagmus.

The aim of this study was to perform an ophthalmoscopic, imaging (OCT), and functional assessment of the retinal macula in children with foveal hypoplasia.

MATERIAL AND METHODS

The study group consisted of eight pediatric patients (four boys and four girls), aged 6-18 years, who were diagnosed with foveal hypoplasia. The follow-up included children that presented in 2019-2021 to the Ophthalmology Outpatient Clinic at the University Pediatrics Center for ophthalmic examinations because of visual dysfunction. Based on collected medical history, it was determined that four of the children were born preterm, with features of extreme immaturity, at a gestational age of 24-26 weeks and with an extraordinarily low birth weight of 550-620 g. Three preterm infants developed retinopathy of prematurity (ROP). One had a neurosurgical procedure. The study group also included one female patient treated for recurrent uveitis in both eyes. Three other patients had a history of ophthalmic surgery.

All the children studied underwent an ophthalmic examination including evaluation of visual acuity using the Snellen chart, assessment of ocular motility and alignment with a synoptophore, autorefractometry, measurement of intraocular pressure, biomicroscopic evaluation of the anterior segment and ophthalmoscopic assessment of the fundus, as well as OCT scan of the macula and, if indicated, OCT of the optic disc and magnetic resonance imaging (MRI) of the head and orbits. Examinations of the macula and optic nerve were carried out using Topcon's DRI OCT Triton (3D Optical Coherence Tomography) system.

Measurements of the analyzed parameters were taken by hand on a linear central OCT scan of the macula, by means of a caliper integrated into the software. The following measurements were performed in every patient: central retinal thickness (CRT), i.e. distance between the inner limiting membrane and the interface between photoreceptors and the retinal pigment epithelium; width of the outer nuclear layer (ONL), i.e. distance between the outer plexiform layer and the outer limiting membrane; length of photoreceptor outer segments (OS), i.e. distance between the ellipsoidal hyperreflective photoreceptor zone and the interface between photoreceptors and the retinal pigment epithelium; and length of photoreceptors (PR), i.e. distance between the outer limiting membrane and the retinal pigment epithelium interface.

RESULTS

Visual acuity was impaired in one or both eyes in seven children, ranging from the sense of light (in the eye with coexisting optic nerve pathologies) to 5/6. One child was found to have low-amplitude horizontal nystagmus persisting since infancy. Another child had undergone nystagmus surgery at another medical center. Monocular esotropia developed in a child with macular and optic nerve hypoplasia and severe visual acuity impairment. Esotropia was also present in two other patients who were born prematurely. Another child, also born preterm, had undergone strabismus surgery. Refractive assessment revealed hyperopic astigmatism ranging from 1 Dcyl to 1.75 Dcyl, binocularly in three patients; myopic astigmatism of –3.5 Dcyl and 5 Dcyl in one patient; and minor hyperopia ranging from 0.5 Dsph to 1 Dsph binocularly in four patients.

Examination of the anterior segment of the eye revealed no abnormalities, with the exception of one patient, born prematurely, who had leucoma in one eye, present from birth. Intraocular pressure was normal in all the children.

By performing an ophthalmoscopic examination, six children were found to have bilateral abnormalities in macular appearance including absent or diminished central and peripheral reflexes manifesting as blurring, loss of clarity, and discontinuity. In one patient, the absence of the macular reflex was shown in the eye with macular and optic nerve hypoplasia. The patient's other eye was healthy, and MR scan of the head and orbits revealed no other anomalies in the central

Table I. Grades of foveal hypoplasia and coexisting ocular and systemic abnormalities

No.	Age years	Eye	Hypoplasia grade	Macular reflexes	Best corrected distance visual acuity	Best corrected near visual acuity	Other abnormalities
1	6	RE	1	Absent	5/5	0.5/30	None
		LE	1	Absent	5/5	0.5/30	
2	9	RE	2	Absent	5/7	0.5/30	Born prematurely, stage 3 ROP, history of retinal laser coagulation and nystagmus surgery
		LE	2	Absent	5/10	0.5/30	
3	12	RE	3	Reduced	5/8	0.5/30	None
		LE	3	Reduced	5/8	0.5/30	
4	14	RE	3	Absent	5/16	0.5/30	Born prematurely, spontaneous regression of ROP, esotropia, hydrocephalus – VP shunt
		LE	3	Absent	5/6	0.5/30	
5	15	RE	1	Normal	5/16	1.0/30	Recurrent bilateral uveitis
		LE	1	Normal	5/6	0.5/30	
6	16	RE	3	Reduced	5/16	0.5/30	Born prematurely, spontaneous regression of ROP, congenital horizontal nystagmus, history of surgery to correct esotropia in the left eye
		LE	4	Absent	5/50	1.0/30	
7	17	RE	4	Absent	Sense of light	0	Hypoplasia of the right optic nerve, esotropia in the right eye
		LE	none	Normal	5/5	0.5/30	
8	18	RE	1	Normal	5/10	0.5/30	Born prematurely, spontaneous regression of ROP, leucoma in the left eye, esotropia in the left eye
		LE	1	Normal	5/32	2.5/30	

LE – left eye; RE – right eye

Table II. Grades of foveal hypoplasia and mean values of retinal layer measurements

Hypoplasia grade	Number of eyes	Mean CRT (μm)	Mean ONL (μm)	Mean PR (μm)	Mean OS (μm)
1.	6/15	255.8	120.8	70.0	31.7
2.	2/15	299.5	132.5	73.0	32.5
3.	5/15	276.4	114.0	75.4	22.6
4.	2/15	293.0	88.0	62.5	19.0

nervous system. In the other two children, normal macular reflexes were preserved in both eyes.

Evaluation of the remaining part of the retina also revealed the following findings in two prematurely born children: pigment scars after laser photocoagulation due to ROP in one, and chorioretinal atrophy together with pigment rearrangement on the periphery of the retina following spontaneous regression of ROP in the other.

Other characteristics of the children included in the study group are listed in Table I.

With OCT of the macula, it was possible to determine the degree of arrest of foveal development and to classify detected lesions in all the children studied. Six out of 15 eyes with foveal hypoplasia (6/15 eyes) showed grade 1 hypoplasia. These children had full visual acuity or it was decreased because of other ocular conditions (uveitis, leucoma). Grade 1 hypoplasia was associated with the lowest CRT values. Grade 2 foveal hypoplasia was diagnosed in two eyes (2/15 eyes). Grade 1 and 2 foveal hypoplasia were found to have the greatest mean OS length (31.7 μm and 32.5 μm, respectively). Grade 3 and 4 hypoplasia was observed in five (5/15 eyes) and two eyes (2/15 eyes), respectively, with an accompanying reduction in mean OS length (22.6 μm and 19.0 μm, respectively). Higher grades of hypoplasia were correlated with increasing CRT values and deceasing OS values. ONL was the thinnest in the eyes with grade 3 and 4 hypoplasia (114 μm and 88 μm, respectively). PR length was similar (70-75.4 μm) in patients with grades 1-3 hypoplasia, but it became shorter (62.5 μm) in the patient diagnosed with grade 4 hypoplasia. Detailed data are shown in Table II.

Figures 1-4 illustrate the grades of foveal hypoplasia seen on macular OCT, with the marking of the retinal layers analyzed (green caliper) in the studied children.

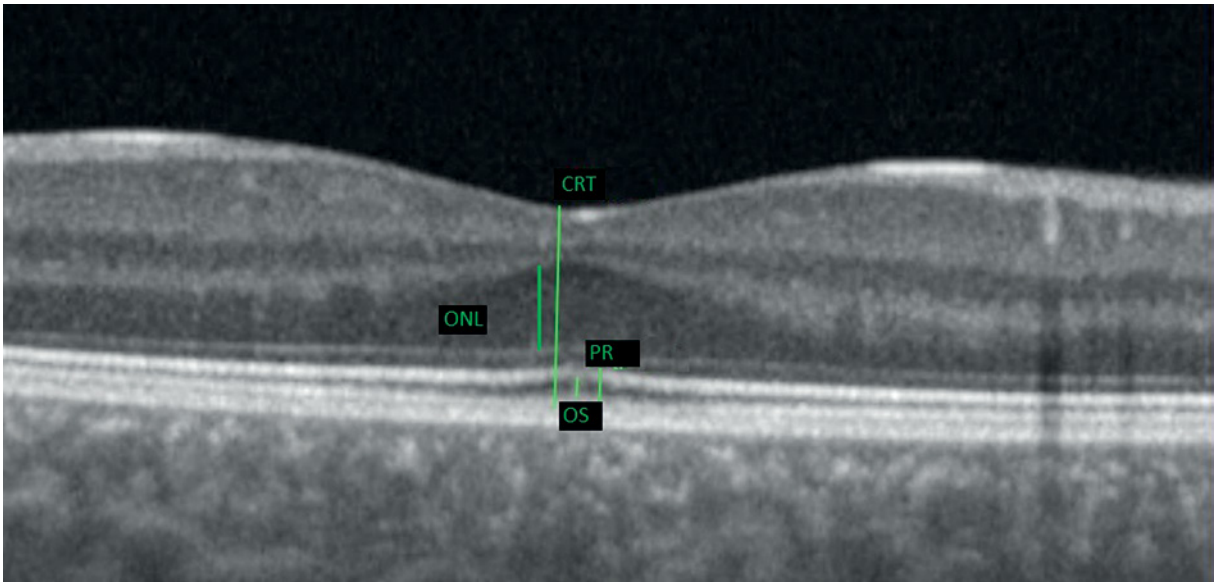

Figure 1. Grade 1 foveal hypoplasia; shallow foveal pit, CRT widening, OS lengthening, ONL widening, normal PR length

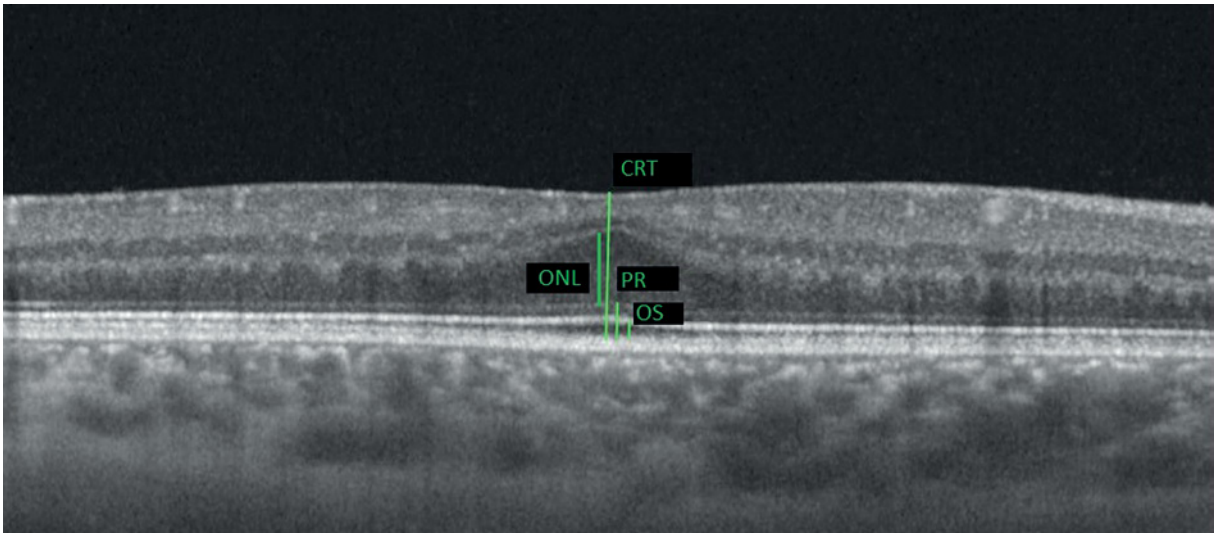

Figure 2. Grade 2 foveal hypoplasia; absence of foveal pit, other layers as in grade 1

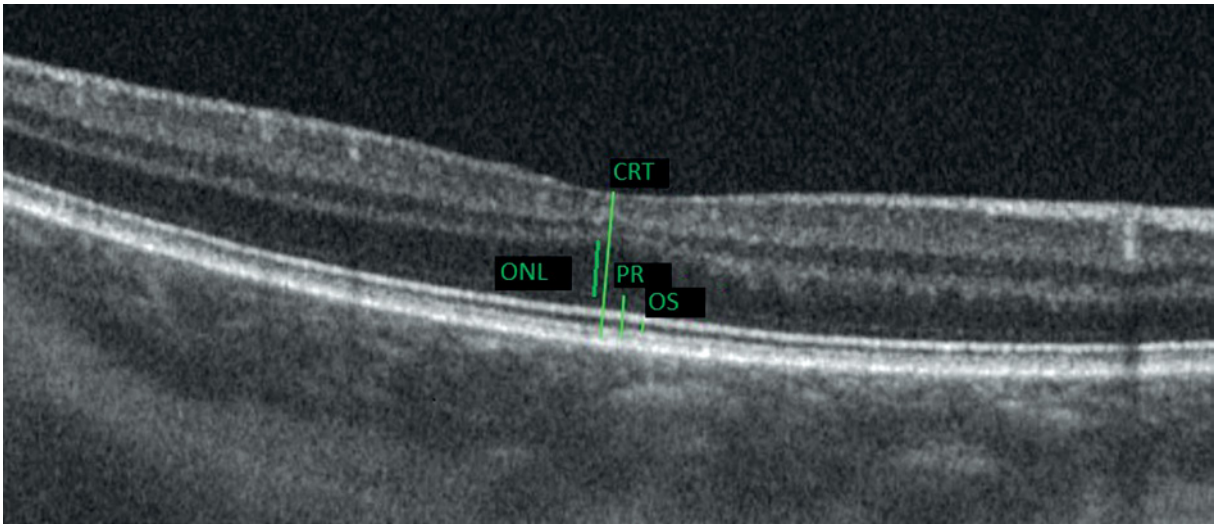

Figure 3. Grade 3 foveal hypoplasia; absence of OS lengthening, otherwise the retinal layers as in grade 2

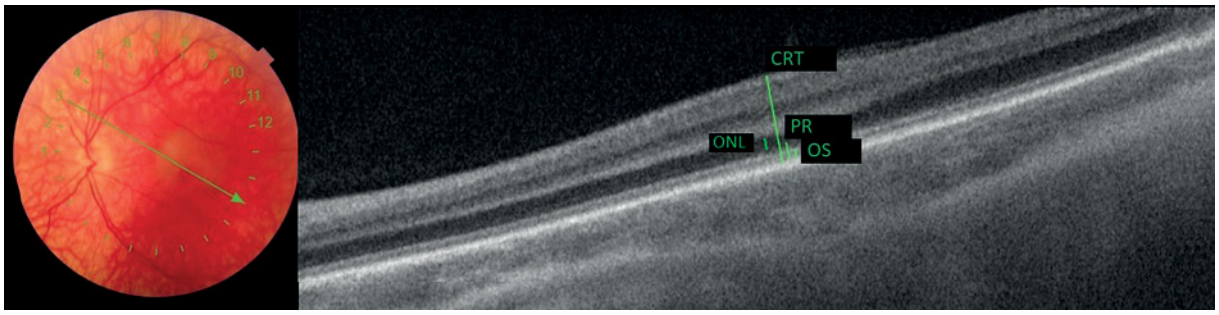

Figure 4. Grade 4 foveal hypoplasia; scan through the macula (green arrow) with no features differentiating the macula from the remaining retina. All retinal layers present in the fovea, no ONL widening, PR shortening, otherwise as in grade 3

DISCUSSION

Our follow-up of the children diagnosed with visual problems revealed that OCT provided a considerable benefit in the assessment of disorders associated with abnormal macular morphology, and in children presenting with a decrease in visual acuity without an easily traceable cause.

In the studied children, visual acuity was found to be correlated with refractive errors, coexisting ocular conditions – including foveal hypoplasia – and the children's overall health status.

Evaluation of the eye fundus, combined with a more detailed OCT examination, made it possible to detect different grades of foveal hypoplasia with corresponding structural alterations affecting the central retinal region known to play an important role in visual function. The histological structure of the fovea may exhibit changes that are undetectable by ophthalmoscopy but cause permanent impairment to visual acuity and visual function. Good visual acuity in children with foveal hypoplasia can be explained by the fact that photosensitive elements reach maturity – lengthening of the outer fragments of photoreceptors – independently of the process of foveal development [4]. Since the term foveal hypoplasia often carries negative functional implications, it might be more appropriate in these cases to use the term fovea plana to describe the anatomical absence of the fovea and good visual function [8]. Deterioration of visual acuity in children with foveal hypoplasia is associated with more prominent shortening of the photoreceptor outer segments accompanied by relatively preserved total photoreceptor length. Increased total retinal thickness in the fovea is related to the formation of abnormal additional layers in this area and does not appear to have any prognostic value for visual function. Our observations regarding the increase in total retinal thickness in children with foveal hypoplasia are consistent with the data presented by other authors [3, 9]. OCT is a non-invasive, non-contact, repeatable, painless and fast method. Based on these advantages, OCT is an important basic diagnostic and prognostic examination, though it requires good cooperation with the child being examined. Unfortunately, we do not have an OCT scanner suitable for examining infants and young children. The device greatly facilitates morphological evaluation of the fovea in the youngest patients [6, 9]. As shown by our observations and the cited literature, OCT scan is the first-line procedure, preceding other diagnostic (electrophysiological, fluoroangiographic) assessments that may be necessary and sufficient to detect foveal pathologies in pediatric patients [9]. Children who were born prematurely made up 50% of our study group. Developmental abnormalities, including retinal anomalies, can be the underlying cause of foveal hypoplasia and other associated consequences in these children. They often manifest at school age, typically with reduced visual acuity and impaired contrast vision [10]. In their study, Anwar *et al.* suggest that preterm birth itself rather than the diagnosis of ROP has an impact on retinal thickness and vision [5]. OCT studies of the retina conducted to date indicate that this developmental abnormality may be more common than is currently recognized. In view of advances in the detection of changes by OCT, foveal hypoplasia has been identified as a new feature associated with retinal pathologies, offering a possibility to quantify detected abnormalities [3]. Future studies of large groups of patients will certainly yield more in-depth conclusions based on the results of foveal hypoplasia assessment in children and corroborate the significant benefit of this diagnostic modality in the histological assessment of macular architecture in children and adolescents. The assessment of macular and foveal OCT findings may be affected by artefacts of different origin. This needs to be taken into account in the analysis of retinal images obtained by OCT [11].

CONCLUSIONS

Abnormal ophthalmoscopic appearance of the macula, exhibiting anomalous light reflexes, is an indication for a more detailed diagnostic approach. Unexplained reduction in visual acuity with preserved macular reflexes also justifies a non-invasive OCT-based assessment of the macula as the first-line diagnostic approach. Our observations confirm the validity of this strategy. OCT examination of the macula is necessary for making the diagnosis of foveal hypoplasia and grade the severity of lesions. Severe foveal hypoplasia reduces visual acuity and may impair other visual functions.

DISCLOSURE

The authors declare no conflict of interest.

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