ORIGINAL ARTICLE

Foveal Hypoplasia Detection by Optical Coherence Tomography

Bušányová B., Porubanová M., Gerinec A.

Clinic of Pediatric Ophthalmology, Medical Faculty, Comenius University, Bratislava,
Head: prof. MUDr. Anton Gerinec, CSc.

SUMMARY

Purpose: To evaluate the contribution of optical coherence tomography (OCT) in the diagnosis of foveal hypoplasia in children.
Material and methods: Children with foveal hypoplasia (FH) were examined with device RTVue Fourier – domain (FD) – OCT, software – version 6.8 (Optovue Inc., Fremont, USA). A qualitative examination of the macular area was performed with single horizontal scan (1024 A-scans/frame). Macular thickness was measured and evaluated quantitatively with an automatic fast macular area protocol MM5 (Macular Map 5x5 mm). A control group of children was used for comparison.
Results: The quality was assessed with OCT image of the macula and quantitatively evaluated macular thickness and configuration in children with foveal hypoplasia. It was subsequently realized the comparison of macular OCT findings in healthy children. The OCT showed a reduction of foveal depression, continuous extension of the inner retinal layers through the area in which should be normally found fovea. Patients with foveal hypoplasia had thicker central macula and fovea than children in the control group.
Conclusion: OCT in our group of patients confirmed the final diagnosis of foveal hypoplasia. FDOCT is a noninvasive and quick method helpful in identifying retinal abnormalities in the diagnosis of foveal hypoplasia in children and may be useful in diagnosing patients with unexplained decrease in vision.

Key words: foveal hypoplasia, optical coherence tomography, children

Čes. a slov. Oftal., 70, 2014, No. 1, p. 22-28

First author:
MUDr. Beáta Bušányová
Klinika detskej oftalmológie DFNsP
LF UK
Limbová 1
833 40 Bratislava
e-mail: b.busany@pobox.sk

INTRODUCTION

Foveal hypoplasia, also termed fovea plana or foveal aplasia, is a congenital pathological condition in which the fovea has not developed. It is characterised as the absence of a foveal depression with continued presence of all the neurosensoric retinal layers in the area in which the fovea should normally be found. The disorder may be associated with other ocular or systemic abnormalities such as aniridia, albinism, microphthalmus, achromatopsia, ROP, Prader-Willi syndrome, Heřmanský-Pudlák ´s syndrome, or may concern a rare disease – isolated foveal hypoplasia (3).
In recent years optical coherence tomography has been described as a fast and effective method for stipulating diagnosis of foveal hypoplasia. In this work we focus on the clinical aspects and tomographical findings in paediatric patients with various types of foveal hypoplasia in comparison with the healthy child population.

MATERIAL AND METHOD

We included in the study patients from the Paediatric Ophthalmology Clinic at the Paediatric University Hospital with Clinic of the Faculty of Medicine of Comenius University in Bratislava. The sample comprised 18 children with a diagnosis of foveal hypoplasia, 36 eyes in total, with a composition of 6 girls and 12 boys. Following a complex eye examination, 9 patients were classified with albinism (Fig. 1a, b, c, d, e), 2 patients with aniridia, 4 patients with isolated foveal hypoplasia, 2 patients with retinopathy of prematurity (ROP) and 1 patient with achromatopsia. The average age of the patients was 10 years (Table 1). For comparison we used a control sample of 10 healthy children, 20 eyes, in which the average age of the patients was 11.8 years (5-15 years).
The patients were completely examined, in each of them we determined monocular best corrected central visual acuity (CCVA) and presence of nystagmus. We measured refractive error in cycloplegia following instillation of 1% tropicamide, the anterior segment was examined biomicroscopically and the fundus ophthalmoscopically. Subsequently each patient was examined by optical coherence tomography, using the instrument RTVue FD-OCT, software – version 6.8 (Optovue Inc., Fremont, USA). For a qualitative examination of the macular area we used an individual horizontal scan (1024 A--scan/image). The thickness of the macula was measured and quantitatively evaluated by an automatic fast macular area protocol MM5 (macular map 5x5 mm). It displays a “cross-sectional” retinal image of the macula and a map of the width of the retina in the macular area, the width is measured from the vitreoretinal interface to the anterior surface of the pigment epithelium and is calculated automatically by an algorithm. As the instrument has the function of automatic segmentation of the macula into the internal and external retinal layer with evaluation of the thickness of these layers, we also evaluated these parameters in our study. For a comparison we examined the control group of healthy children on OCT (Fig. 2, 3), on whom we used the same scans for the

macular area as for the group of children with diagnosis of FH.

In the observed sample of children with FH we qualitatively assessed the OCT image of the macula (Fig. 4) and evaluated central macular thickness (CMT), the thickness of the internal retinal layer (IRL) and outer retinal layer (ORL) (see Table 1). We subsequently conducted a comparison of the OCT findings of the macula with the healthy children in the control group. According to the current classification criteria for FH we attributed a degree of FH to patients on the basis of to the OCT finding, and we searched for a correlation with central visual acuity (CVA).

RESULTS

In all of our patients, OCT examination determined a reduction to absence of foveal depression, continuous extension of the internal retinal layers across the central macular area in which the fovea should ordinarily be located, absence of extension of the outer segment (OS) of cone cells and slight constriction of the outer nuclear layer (ONL) (Fig. 5 a-d). In the patient with achromatopsia, disruption of the junction of the internal and outer segment (IS-OS) of cone cells was determined.

On average, the patients with foveal hypoplasia had a level of central macular thickness of 290 μm in the right eye and 294.2 μm in the left eye in comparison with the control group of children, who had an average of 249 μm in the right eye and 250.3 μm in the left eye. The average thickness of the IRL was also higher in children with FH – 103.8 μm in the right eye and 107.8 μm in the left eye in comparison with the healthy children, who had an average of 77.7 μm in the right eye and 81.8 μm in the left eye. No pronounced divergence was determined in the thickness of the ORL in the observed and control group of children (Table 2). We did not find a

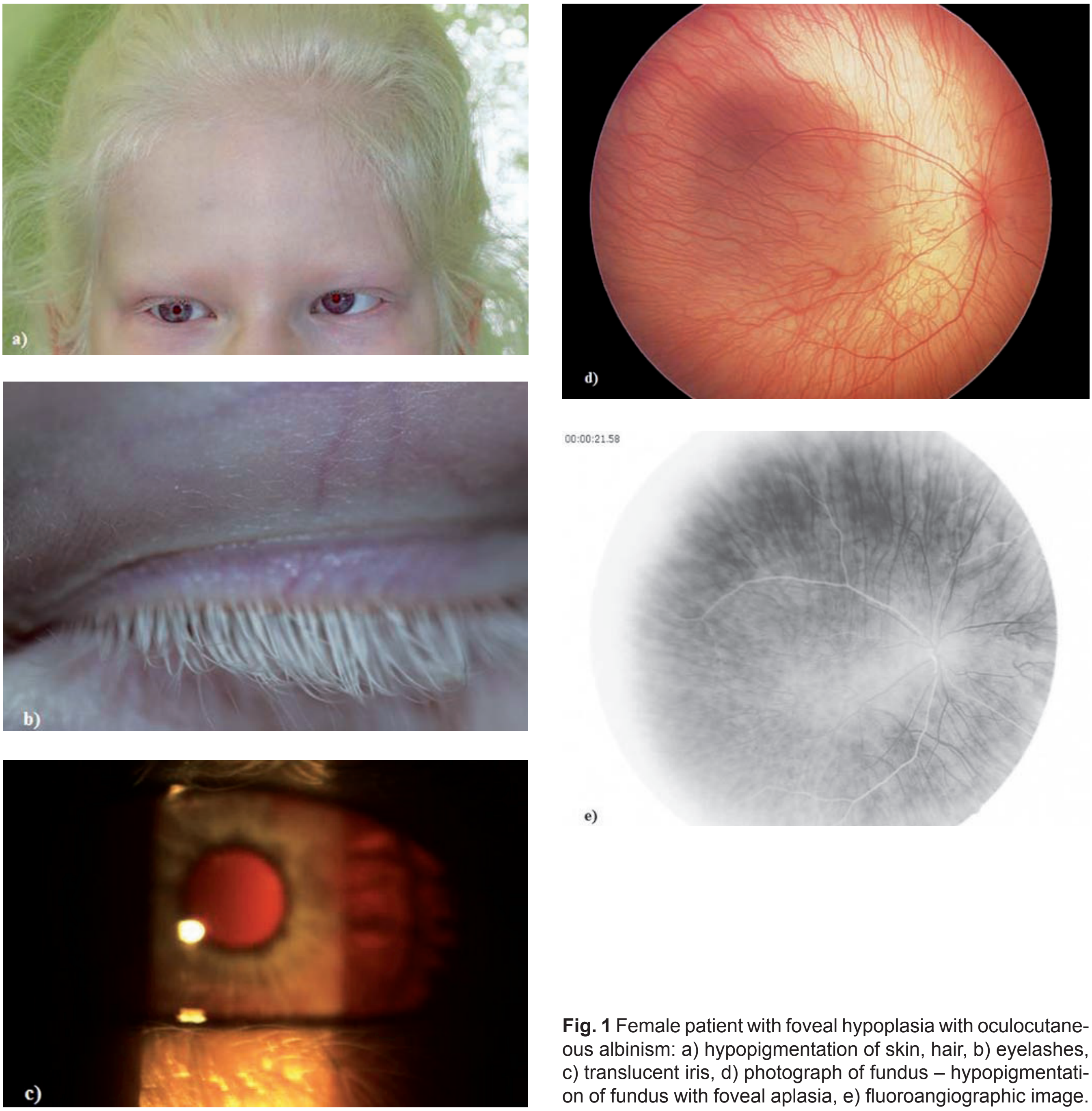
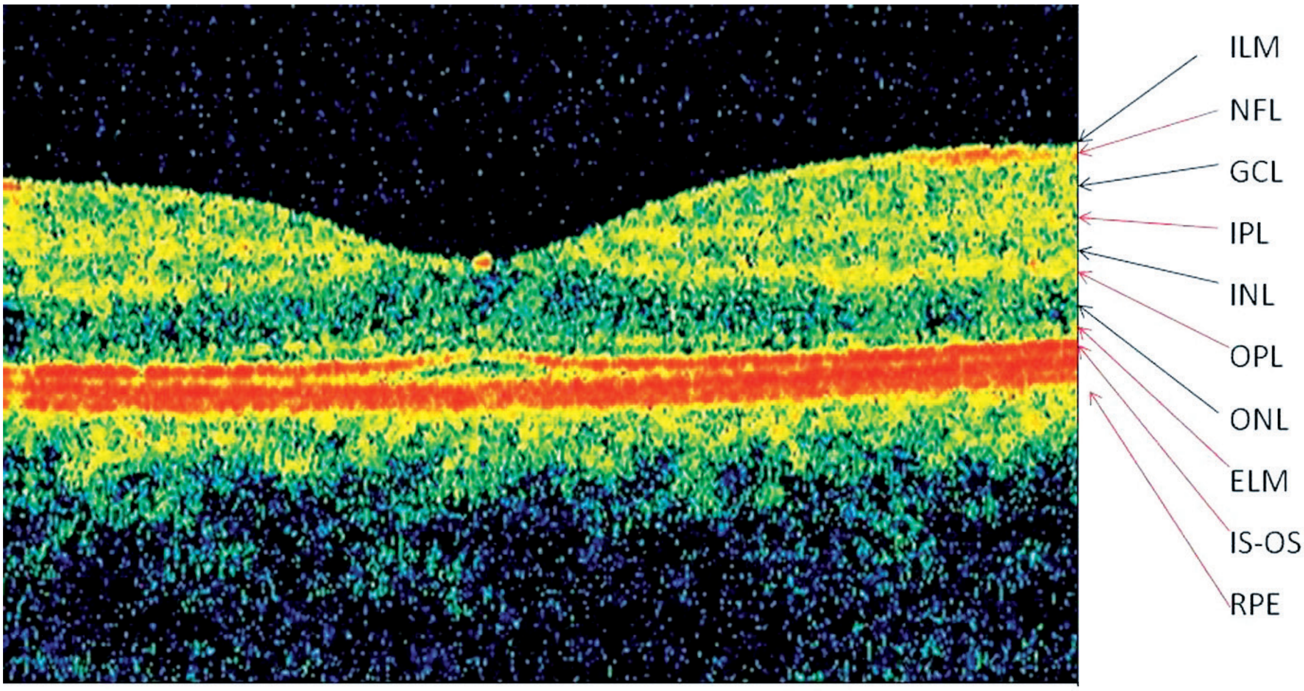


Fig. 1 Female patient with foveal hypoplasia with oculocutaneous albinism: a) hypopigmentation of skin, hair, b) eyelashes, c) translucent iris, d) photograph of fundus – hypopigmentation of fundus with foveal aplasia, e) fluoroangiographic image.



ILM – internal limiting membrane, NFL – nerve fibre layer, GCL – ganglion cell layer, IPL – internal plexiform layer, INL – internal nuclear layer, OPL – outer plexiform layer, ONL – outer nuclear layer, ELM – external limiting membrane, IS--OS – junction of internal and outer segment of photoreceptor, RPE – retinal pigment epithelium

Fig. 2 Normal stratification of retina in a child from the control sample of healthy children

Table 1 Demographic data and measured parameters of 18 children in study

Patient	Diagnosis	Sex	Age/year	Nystagmus	CCVA RE	CCVA LE	CMT RE μm	CMT LE μm	IRLT RE μm	IRLT LE μm	ORLT RE μm	ORLT LE μm	Degree of FH
1.	Albinism	F	9	No	0.50	0.5	282	288	82	109	200	179	2nd
2.	Albinism	M	10	Yes	0.1	0.1	296	346	113	101	183	245	4th
3.	Albinism	F	8	Yes	0.1	0.1	330	309	84	97	246	212	4th
4.	Albinism	M	7	Yes	0.1	0.16	291	299	98	98	194	201	4th
5.	Albinism	M	10	Yes	0.16	0.16	283	264	105	92	179	172	3rd
6.	Albinism	M	7	Yes	0.1	0.1	305	263	111	103	194	160	3rd
7.	Albinism	M	12	Yes	0.1	0.1	297	286	116	108	181	177	4th
8.	Albinism	M	10	Yes	0.1	0.1	298	279	110	109	188	170	4th
9.	Albinism	M	11	Yes	0.16	0.16	295	282	102	97	193	185	4th
10.	Albinism	M	18	Yes	0.1	0.1	290	294	113	110	177	184	4th
11.	Albinism	M	9	No	0.5	0.5	308	302	106	112	202	190	1st
12.	Aniridia	F	17	Yes	0.5	0.32	303	316	108	125	196	191	1st
13.	Aniridia	F	7	Yes	0.16	0.16	310	307	124	105	186	202	3rd
14.	Is. FH	M	6	Yes	0.5	0.5	240	292	70	123	171	170	1st
15.	Is. FH	F	5	Yes	0.25	0.25	250	250	91	91	160	160	3rd
16.	Is. FH	M	8	No	0.8	0.80	311	311	123	122	188	189	1st
17.	Is. FH	M	15	No	0.8	0.5	304	330	127	120	177	210	1st
18.	Achromatopsia	F	11	No	0.25	0.2	236	278	85	118	151	160	-
Average			10		0.29	0.27	290.5	294.2	103.8	107.8	187	186.5	

[1]CCVA – Corrected central visual acuity, RE – right eye, LE – left eye, CMT – central macular thickness, IRLT – internal retinal layer thickness, ORLT – outer retinal layer thickness, Is. FH – isolated foveal hypoplasia

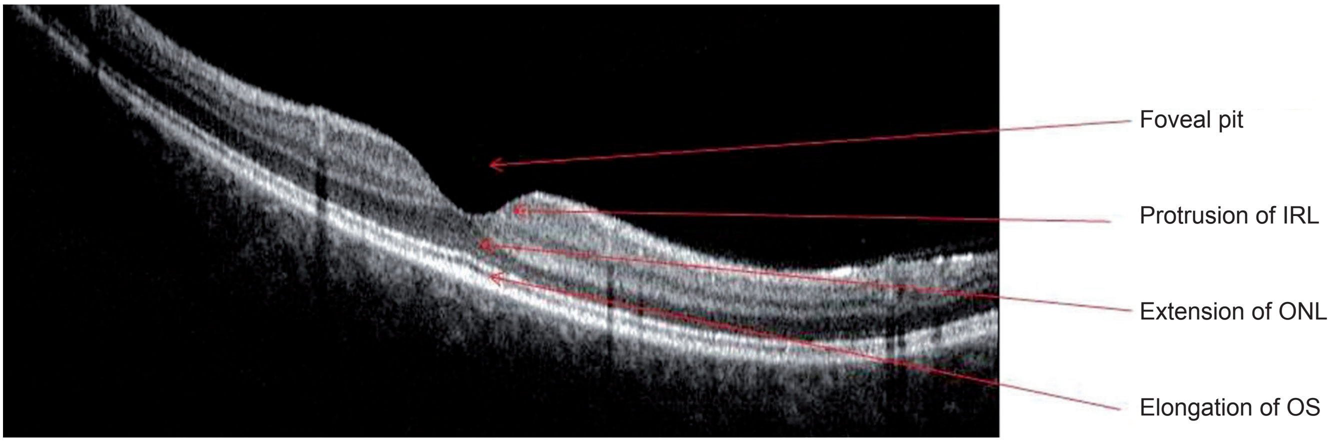


Fig. 3 Normal foveal configuration in child from control group of healthy children

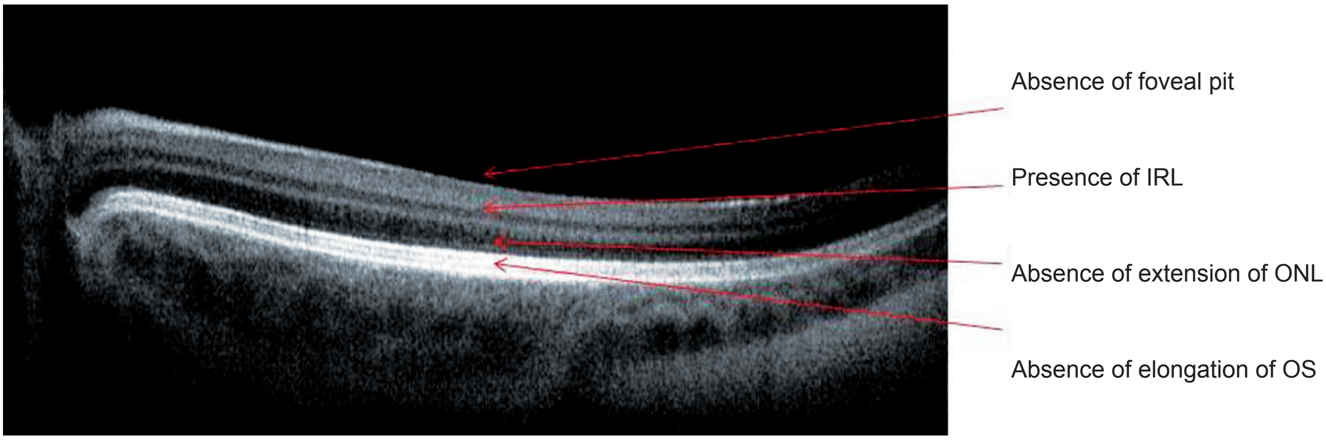
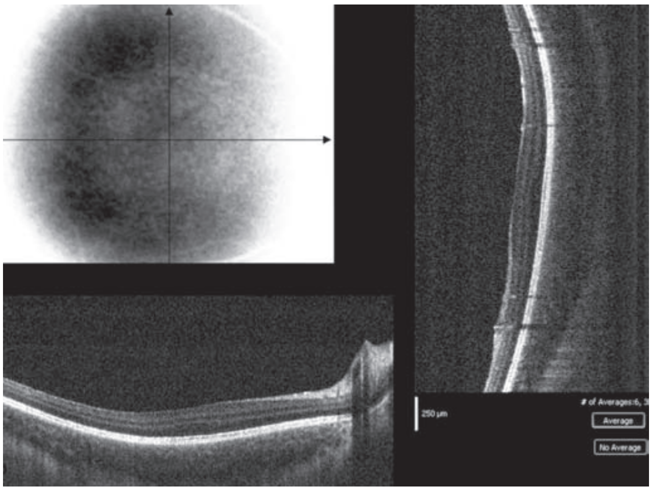
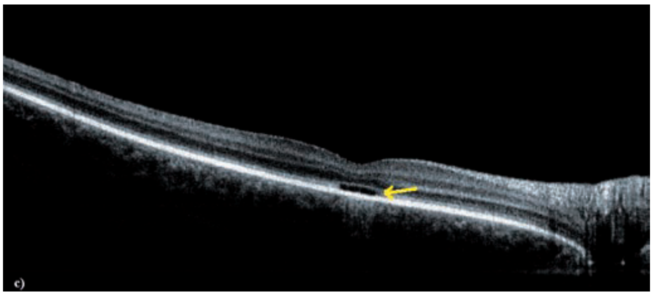


Fig. 4 Foveal structure in patient with FH with aniridia





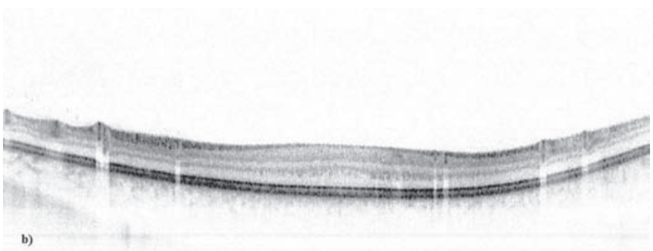


Fig. 5 OCT image of FH in our patients a) albinism b) aniridia c) achromatopsia (→disruption of junction IS-OS) d) ROP

correlation between visual acuity and central macular thickness (Table 3), although we determined a correlation of visual acuity according to the degree of foveal hypoplasia.

Table 2 Comparison of average foveal thickness in patients with FH and in healthy children

	CMT RE µm	CMT LE µm	IRLT RE µm	IRLT LE µm	ORLT RE µm	ORLT LE µm
Patients with FH	290.5	294.2	103.8	107.8	187	186.5
Control group	249	250.3	77.7	81.8	171.1	168.7

[1]FH – foveal hypoplasia, RE – right eye, LE – left eye, CMT – central macular thickness, IRLT – internal retinal layer thickness, ORLT – outer retinal layer thickness

Table 3 Corrected central visual acuity according to degree of foveal hypoplasia in the observed sample

Degree of FH	CCVA	Average CCVA	CMT µm
1st	0.8-0.5	0.57	310
2nd	0.5-0.25	0.5	285
3rd	0.25-0.1	0.17	258
4th	0.1 and less	0.11	308

[1]FH – foveal hypoplasia, CCVA – corrected central visual acuity, CMT – central macular thickness

DISCUSSION

The fovea centralis (FC) is characterised by an avascular zone and increased density of photoreceptors – cone cells with an extension of the outer segments and excavation of the internal retinal layers. In newborns this is not completely differentiated, a certain degree of hypoplasia is physiological and the development continues postnatally (2). Normal foveal development begins in the stage of formation of the pit in the 25th foetal week, and excavation is completed by the 15th month after birth.

Definitive development is not completed until the 45th month after birth (6). Developmental phases of fovea centralis:

1. Centrifugal shift of internal retinal layers (15th month) – displacement of internal retinal layers by fovea.
2. Centripetal migration of cone cells to place of incipient fovea – extension of outer nuclear layer.
3. Specialisation of cone cells to foveal cone cells, reduction of diameter of outer segment of cone cells and increase in length (up to 45th month) – OS elongation.

Impairment of the developmental process of FC leads to the onset of foveal hypoplasia (Fig. 3).

Characteristic clinical findings in patients with FH are nystagmus of varying degrees, reduction of visual acuity,

Table 4 Degree of FH according to developmental disorder of maturation of foveola and correlation of OCT image.

Development of maturation of foveola	OCT image upon unimpaired development of foveola	Degree of foveal hypoplasia upon impaired development of foveola			
		1st degree	2nd degree	3rd degree	4th degree
Centrifugal shift of internal retinal layers	**Foveal pit and displacement of IRL**	Shallowing of foveal pit, extension of IRL	Absence of foveal pit		
Specialisation of cone cells	**Elongation of oute segment**			Absence of elongation of OS	
Centripetal migration of cone cells	**Extension of outer nuclear layer**				Absence of extension of ONL

Developmental process occurred at least within partial scope (black)

No developmental process occurred (white)

absence or abnormal maculofoveal reflex upon ophthalmoscopy, fovea is indistinctly structured and more difficult to differentiate from the other retina. It has less macular lutein visible ophthalmoscopically (1, 4, 5). Upon fluorescence angiography there is variable and incomplete filtration of choroidal fluorescence in the macular area and the avascular zone is very narrow (8).
Etiologically the PAX6 gene has been identified, indicating the process of differentiation of the fovea, the mutation of which may cause hypoplasia. Heredity is autosomally dominant or recessive, but sporadic cases have also been described.
Determination of a diagnosis of foveal hypoplasia in children is not always easy, since only discrete changes are present on the fundus, and these are frequently more difficult to detect, especially if nystagmus is present. In the past, foveal hypoplasia has been diagnosed on the basis of a fundoscopic and fluoroangiographic image.
OCT confirmed foveal hypoplasia in the majority of our patients. In previous publications, typical abnormalities were determined upon OCT examination of patients with FH, such as absent foveal depression, foveal hyporeflectivity, choroidal transillumination and appearance of a double hyper-reflective layer in the junction of the retina and choroidea (9, 10 ,12, 15), which was also confirmed by our study. With regard to the low resolution in the previous Time-domain OCT instruments, a discussion has arisen concerning the classification of FH described in the previous studies. Grading of FH in the majority of the previous works was focused on patients with albinism (11). Only recently a classification system for foveal hypoplasia has been published according to findings on Fourier-domain optical coherence tomography, which enables faster imaging with higher resolution and also detailed evaluation of the layers of the retina.
The classification is based on the presence or absence of a foveal pit, caused by the presence and extension of the internal retinal layers, which are displaced from the fovea under normal conditions, and also on the extension of the outer nuclear layer and outer segment of cone cells in the fovea. The degree of foveal hypoplasia was defined on the basis of the following criteria proposed by Thomas (14).

4 degrees of FH are differentiated (Table 4):

1. st degree – shallowing of foveal pit, presence and extension of IRL, extension of ONL, elongation of OS,
2. nd degree – same as 1st degree, but absence of foveal pit,
3. rd degree – same as 2nd degree, but absence of OS elongation,
4. th degree – same as 3rd degree, but absence of ONL extension.

On the basis of the above classification, we also identified the stated changes in our sample of patients, which enabled us to attribute a specific degree of FH. The degree of FH is an important prognostic indicator for CVA, applicable within the scope of diseases associated with FH, with the exception of achromatopsia (7, 13). In the published works, the 1st degree has been linked to the best CVA (up to 0.63), the 2nd, 3rd and 4th degrees are linked to progressively worse CVA (0.4, 0.25, 0.16). We discovered similar findings also in our group, where a higher degree of FH corresponded to progressively lower CVA, although we did not determine a correlation between CVA and foveal thickness.

Atypical are symptoms in FH associated with **achromatopsia**, which is characterised by:

- decrease of thickness of retina and ONL,
- deeper foveal pit,
- disruption of junction IS-OS.

In our study the patient with achromatopsia had a typical finding of disruption of the IS-OS junction and a deeper foveal excavation.

CONCLUSION

FD-OCT is a non-invasive and quick method which is useful in the diagnosis of foveal hypoplasia, especially in paediatric patients with reduced visual acuity of unknown aetiology. Although the clinical, fluoroangiographic, autofluorescence finding is also important, it is less sensitive for determining of the diagnosis of foveal hypoplasia. The system of evaluation of FH on the basis of FD-OCT findings is objective, precise, widely usable and helpful in the evaluation of paediatric patients with FH, which is confirmed also by our experience.

LITERATURE

1. **Cronin, T.H., Hertle, R.W., Ishikawa, H. et al.:** Spectral domain optical coherence tomography for detection of foveal morphology in patients with nystagmus. J AAPOS, 2009; 13(6): 563–566.
2. **Dubis, A.M., Hansen, B.R., Cooper, R.F. et al.:** Relationship between the Foveal Avascular Zone and Foveal Pit Morphology. Invest Ophthalmol Vis Sci, 2012; 53: 1628–1636.
3. **Gerinec, A.:** Detská oftalmológia. Martin, Osveta, 2005, 593 s.
4. **Holmström, G., Eriksson, U., Hellgren, K. et al.:** Optical coherence tomography is helpful in the diagnosis of foveal hypoplasia. Acta Ophthalmol, 2010; 88(4): 439–442.
5. **Chong, G., Farsiu, S., Freedman, S.F. et al.:** Abnormal Foveal Morphology in Ocular Albinism Imaged With Spectral-Domain Optical Coherence Tomograph. Arch Ophthalmol, 2009; 127(1): 37–44.
6. **McAllistera, J.T., Dubisb, A.M., Taita, D.M. et al.:** Arrested Development: High-Resolution Imaging of Foveal Morphology in Albinism. Vision Res, 2010; 50(8): 810–817.
7. **Mohhamad, S., Gottlob, I., Kumar, A. et al.:** The Functional Significance of Foveal Abnormalities in Albinism Measured Using Spectral-Domain Optical Coherence Tomography. Ophthalmology, 2011; 118:1645–1652.
8. **Mota, A., Fonseca, S., Carneiro, A. et al.:** Isolated Foveal Hypoplasia: Tomographic, Angiographic and Autofluorescence Patterns. Case Reports in Ophthalmological Medicine, 2012; 2012: 864–958.
9. **Pal, S.S., Gella, L., Sharma, T. et al.:** Spectral domain optical coherence tomography and microperimetry in foveal hypoplasia. Indian J Ophthalmol, 2011; 59(6): 503–505.
10. **Park, K.A., Oh, S.Y.:** Clinical characteristics of high grade foveal hypoplasia. Int Ophthalmol, 2013; 33: 9–14.
11. **Rossi, S., Testa, F., Gargiulo, A. et al.:** The Role of Optical Coherence Tomography in an Atypical Case of Oculocutaneous Albinism: A Case Report. Case Rep Ophthalmol, 2012; 3: 113–117.
12. **Saffra, N., Agarwal, S., Chiang, J.P.W. et al.:** Spectral-Domain Optical Coherence Tomographic Characteristics of Autosomal Recessive Isolated Foveal Hypoplasia. Arch Ophthalmol, 2012; 130(10): 1324–1327.
13. **Seo, J.H., Yu, Y.S., Kim, J.H. et al.:** Correlation of visual acuity with foveal hypoplasia grading by optical coherence tomography in albinism. Ophthalmology, 2007; 114(8): 1547–51.
14. **Thomas, M.G., Kumar, A., Mohammad, S. et al.:** Structural Grading of Foveal Hypoplasia Using Spectral-Domain Optical Coherence Tomography. Ophthalmology, 2011; 118: 1653–1660.
15. **Yang, H., Yu, T., Sun, C. et al.:** Spectral-domain optical coherence tomography in patients with congenital nystagmus. Int J Ophthalmol, 2011; 4(6): 627–630.