(32)

Exudative age-related macular degeneration or Best vitelliform macular dystrophy? – a case report

Wysiękowe AMD czy żółtkowata dystrofia dołkowo-plamkowa dorosłych Besta – opis przypadku

Agnieszka Kubicka-Trząska, Agnieszka Filemonowicz-Skoczek, Izabella Karska-Basta, Bożena Romanowska-Dixon

Department of Ophthalmology, Clinic of Ophthalmology and Ocular Oncology,
Medical College, Jagiellonian University, Kraków, Poland
Head: Ass. Prof. Bożena Romanowska-Dixon, MD, PhD

Summary:

Purpose: To report a case of Best vitelliform macular dystrophy referred to the Department of Ophthalmology in Krakow with a diagnosis of exudative age-related macular degeneration (AMD).

Materials and methods: 70-years old man was diagnosed in our clinic because of a two years history of slow, progressive visual acuity worsening in both eyes with the presence of metamorphopsia. The basic ophthalmic examination was performed with additional diagnostic methods including: colour vision test (Panel D-15), Amsler grid test, contrast sensitivity test (Pelli-Robson chart), fluorescein angiography (FA), indocyanine green angiography (ICGA), electroretinogram (ERG), electrooculogram (EOG) and optical coherence tomography (OCT).

Results: Visual acuity in the right eye was: 0.16 and in the left: 0.25. Amsler grid test revealed the presence of bilateral mild metamorphopsia with the relative central scotoma. Pelli-Robson test showed decreased contrast sensitivity perception in both eyes; PO>LO. On fundoscopy in macula of both eyes the symmetrical round, elevated lesions of 1.5 dd with the meniscus of subretinal creamy-yellow masses were present. The early frames of FA showed the presence of round lesions with distinct borders, unchanged in size and shape throught the examination, hypofluorescent in the lower and hyperfluorescent in the upper half of the lesions. Late frames of FA revealed the irregular hyperfluorescence also in lower aspects of the lesions. ICGA showed: round hypofluorescent lesions with isofluorescence in the upper part of the lesions. ERG – revealed no pathology, EOG – showed decreased light response and depressed Arden ratio in both eyes. OCT demonstrated hiperreflectivity of the retinal pigment epithelium with elevation of retina and deletion of the foveolar depression in both eyes.

Conclusions: Based on the results of performed tests the diagnosis of the Best vitelliform macular dystrophy was established. In some cases various pathologies involving the macula may mimic the exudative AMD. The basic ophthalmic examination supported by additional diagnostic methods allow to establish the definitive diagnosis in most cases of macular disorders.

Słowa klucze: wysiękowe zwyrodnienie plamki żółtej związane z wiekiem (AMD), żółtkowata dystrofia dołkowo-plamkowa dorosłych Besta, angiografia fluoresceinowa, angiografia indocyjaninowa, ERG, EOG, OCT.

Key words: exudative-age related macular degeneration, Best vitelliform macular dystrophy, fluorescein angiography, indocyanine green angiography, ERG, EOG, OCT.

Best disease, also known as Best vitelliform macular dystrophy, is an autosomal dominant form of progressive macular dystrophy first described by Frederich Best in 1905. This disease occurring primarily in European Caucasians is characterized by an accumulation of lipofuscin-like material in the macula that results in an "egg-yolk-like appearance (1,2). Best disease is caused by mutations in the VMD2 gene that encodes a chloride channel in the basolateral membrane of the retinal pigment epithelium (RPE), resulting in lipofuscin deposits in the RPE layer (3,4). The defective chloride channels result also in an abnormal electrooculogram (EOG); depressed Arden ratio, which can be used to diagnose patients without classic macular lesions, as well as identifying patients that are unlikely to have the disease (1,2). Individuals with Best disease generally show a gradual loss of central vision, although the frequency with which an affected person may show symptoms and the severity of those symptoms are highly variable (5).

There are two forms of vitelliform macular dystrophy with similar features. The early-onset form usually appears in childhood. However, the onset of symptoms and the severity of vision loss vary widely. The adult-onset form begins later, usually in middle age, and tends to cause relatively mild vision loss (2,6). The aim of the study is to report a case of Best vitelliform macular dystrophy referred to the Department of Ophthalmology in Krakow with a presumptive diagnosis of exudative age-related macular degeneration (AMD).

A case report

A 70-years old man was admitted to our clinic with a two years history of slow, progressive visual acuity worsening in both eyes with the presence of bilateral metamorphopsia. The basic ophthalmic examination was performed with additional diagnostic methods including: colour vision test (Panel D-15), Amsler grid test, contrast sensitivity test (Pelli-Robson chart), fluorescein angiography (FA), indocyanine green angiography (ICGA), electroretinogram (ERG), electrooculogram (EOG) and optical coherence tomography (OCT).

The patient was complaining of blurred and distorted vision affecting near and far vision. The colour vision in both eyes was affected in blue-yellow axis, more in the right eye compared with the left. The symptoms affected activities of his daily life. No ocular disorders run in patient's family. Best corrected visual acuity of the right eye was: 0.16 and 0.25 in the left eye. Amsler grid test revealed the presence of bilateral mild metamorphopsia with the relative central scotoma in both eyes. Pelli-Robson contrast sensitivity test showed decreased contrast sensitivity perception in both eyes; in the right eye it was worse as compared to the left. Intraocular pressure in both eyes was normal; right eye – 14 mmHg, left eye – 16 mmHg. Anterior segment examination revealed the presence of senile arcus in the periphery of the cornea and early stages of cortical cataract in both eyes. On fundoscopy in macula of both eyes the symmetrical round, elevated lesions (cysts) of 1.5 disc diameter (dd) with the meniscus of subretinal creamy-yellow masses were present (Fig. 1a, 1b). The early frames of FA showed the presence of round lesions with distinct borders, unchanged in size and shape throught the examination, hypofluorescent in the lower and hyperfluorescent in the upper half of the lesions (Fig. 2a, 2b). Late frames of FA revealed the irregular hyperfluorescence also in lower aspects of the lesions (Fig. 3a, 3b). ICGA showed round hypofluorescent lesions with isofluorescence in the upper part of the lesions (Fig 4a, 4b and Fig. 5a, 5b). ERG revealed normal scotopic and photopic a and b waves. EOG showed decreased light response and depressed Arden ratio in both eyes which was: 0.97 in the right eye and 0.92 in the left eye. OCT demonstrated in both macular regions hyperreflectivity of the retinal

Fig. 1a. Fundus of the right eye.
Ryc. 1a. Dno oka prawego.

Fig. 1b. Fundus of the left eye.
Ryc. 1b. Dno oka lewego.

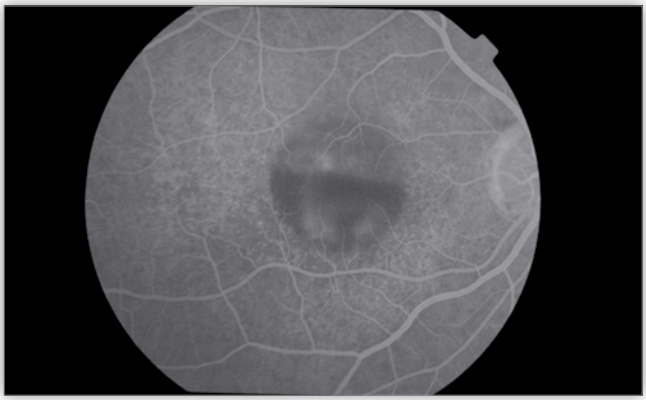

Fig. 2a. Early phase of the FA of the right eye.
Ryc. 2a. AF – wczesna faza oka prawego.

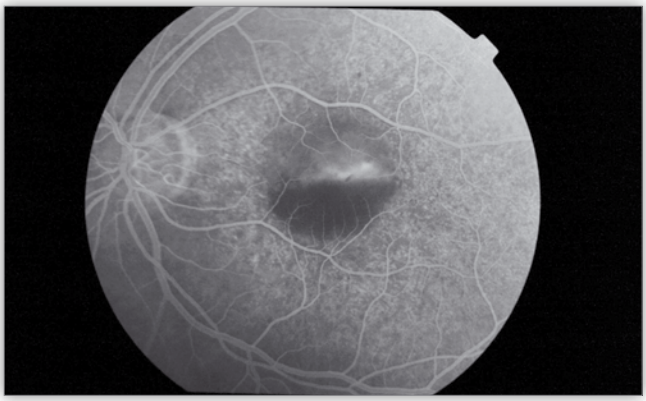

Fig. 2b. Early phase of the FA of the left eye.
Ryc. 2b. AF – wczesna faza oka lewego.

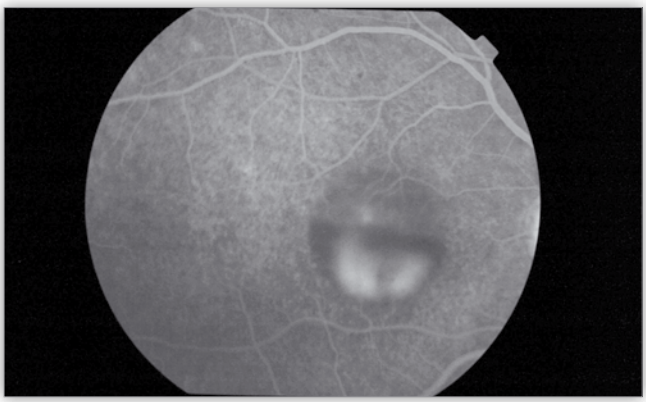

Fig. 3a. Late phase of the FA of the right eye.
Ryc. 3a. AF – późna faza oka prawego.

ISSN 0023-2157 Index 362646

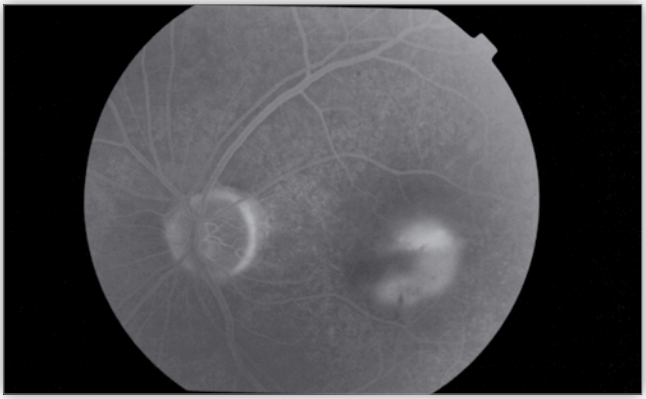

Fig. 3b. Late phase of the FA of the left eye.
Ryc. 3b. AF – późna faza oka lewego.

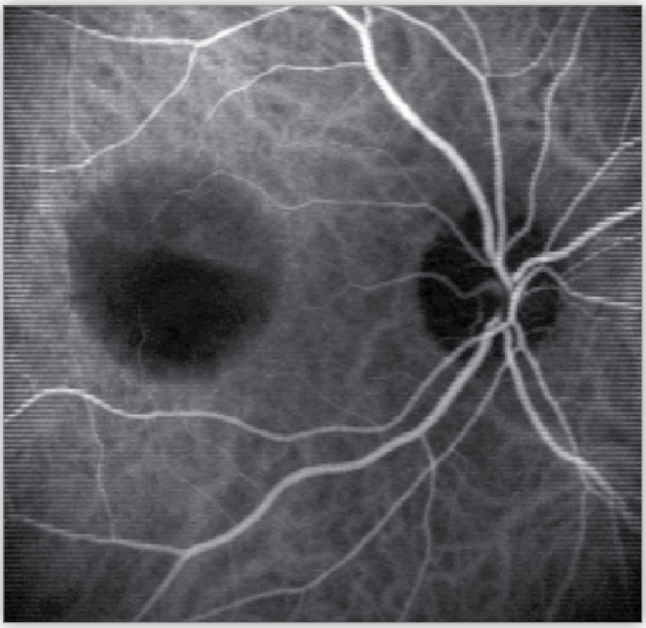

Fig. 4a. Early phase of the ICGA of the right eye.
Ryc. 4a. ICA – wczesna faza oka prawego.

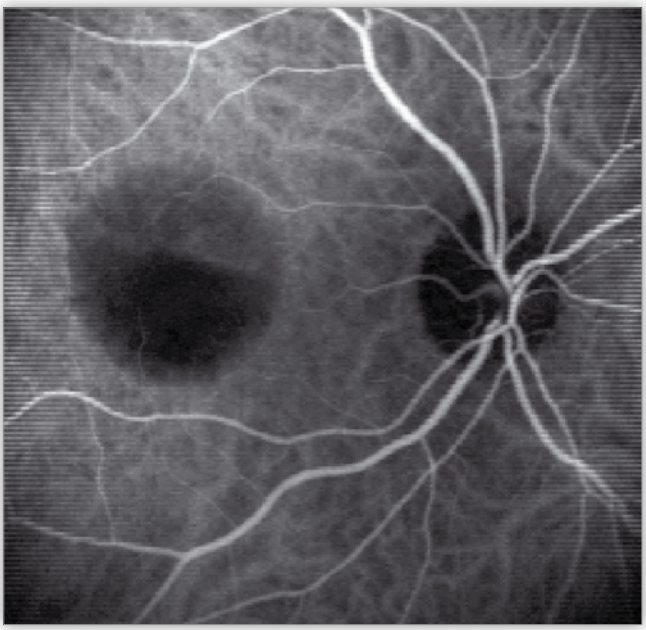

Fig. 4b. Early phase of the ICGA of the left eye.
Ryc. 4b. ICA – wczesna faza oka lewego.

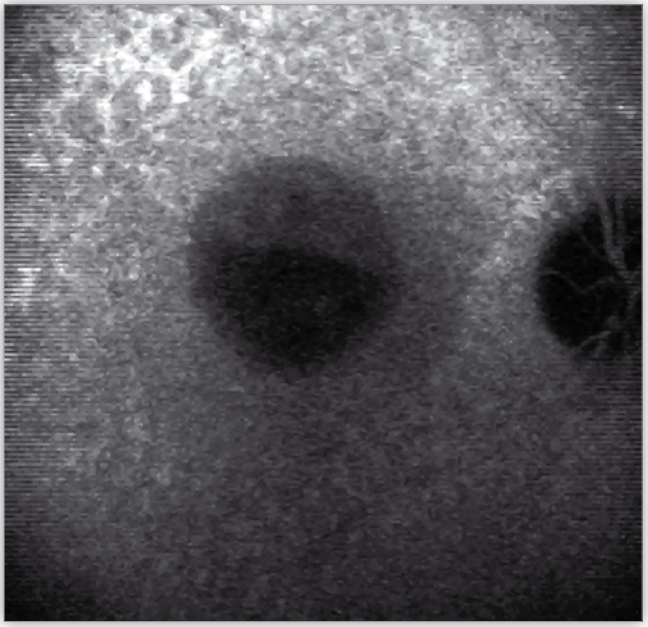

Fig. 5a. Late phase of the ICGA of the right eye.
Ryc. 5a. ICA – późna faza oka prawego.

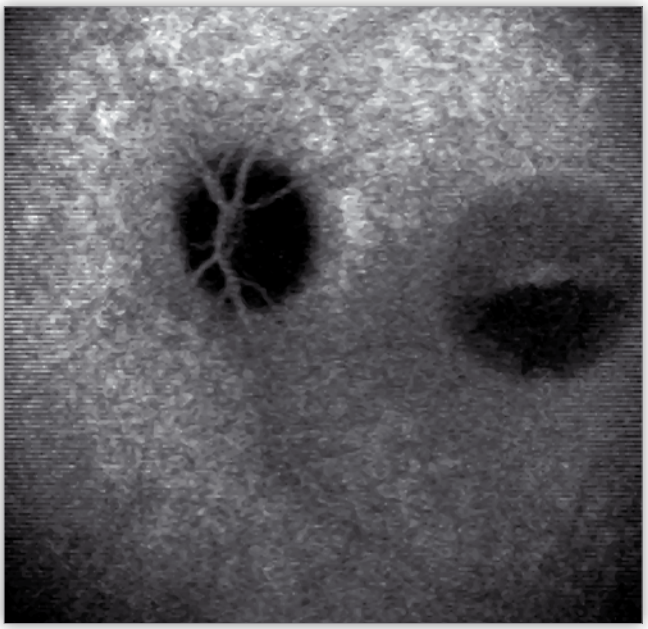

Fig. 5b. Late phase of the ICGA of the left eye.
Ryc. 5b. ICA – późna faza oka lewego.

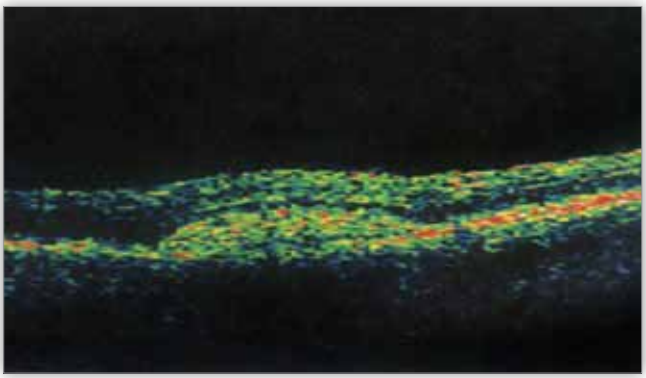

Fig. 6a. OCT of the right eye.
Ryc. 6a. OCT – oko prawe.

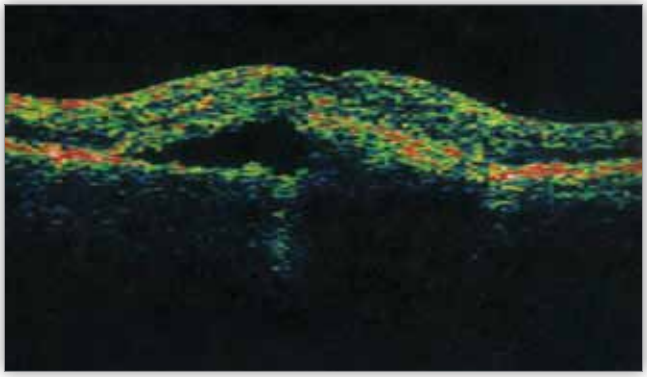

Fig. 6b. OCT of the left eye.
Ryc. 6b. OCT – oko lewe.

pigment epithelium with elevation of retina and deletion of the foveolar depression (Fig. 6a, 6b).

Discussion

Clinical expression of Best vitelliform dystrophy vary from one individual to another, thus in some cases it may cause problems in differential diagnosis. Onset of the disease may occur in childhood or decades later. Within 5 identifiable stages, examination of the eye discloses a distinct progression (2,6). At first and second stages, there may be little or no effect on sight. At the second stage (usually between 10-25 years of age), typical yellow spots, sometimes accompanied by material leaking into a space by the retina, can be observed; a pathology called "egg-yolk" lesion. When part of this lesion becomes absorbed a pseudohypopyon (aqueous-lipid fluid level) is identified as stage three. Even at this stage there may be little affect on vision. At the fourth stage, when the "egg-yolk" breaks up, in a process referred to as "scrambled-egg", sight will be affected. The fifth and final stage is when the condition causes the most severe sight loss due to choroidal neovascularization (CNV) and RPE atrophy. In typical Best disease the EOG is usually abnormal even in asymptomatic patients. However there are some data about the normal EOG in patients suffering from this disease and also in adult onset of Best disease the EOG is normal (5). Other tests such as FA, ICGA and OCT might add information for the correct diagnosis (7-10). In our patient based on the results of EOG we diagnosed the Best vitelliform dystrophy and the results of FA, ICGA and OCT were consistent with the third stage of this disease. Differential diagnosis of Best vitelliform dystrophy includes: pattern macular dystrophies, Stargardt disease, fundus flavimaculatus, central serous retinopathy, pigment epithelial detachment (PED), North Carolina macular dystrophy, age-related macular degeneration (6). Best disease is genetically passed through families by the autosomal dominant pattern of inheritance. Many affected people, however, have no history of the disorder in their family and the disease develops as a result of a new mutation in an affected person. Without a family history, only 25% of patients will have a mutation (3). In our patient we did not perform the genetic tests because they are not available on a routine way. Currently, there is no treatment for Best disease but scientific research, both traditional and genetic, may provide useful treatments for the future. In cases complicated with subfoveal CNV photodynamic therapy with verteporfirin may be a useful method of treatment (11).

Prognosis for this disease is mixed. Some carriers will never phenotypically express the disorder. Some individuals will never have progression beyond the earliest stages of the disease and will maintain better than 20/40 vision in both eyes. In general, most affected people will maintain reading vision in at least 1 eye throughout life. Almost 90% of patients retained 20/40 or better visual acuity, and only 4% of them had 20/200 or worse visual acuity in the better eye (12). The deterioration of vision usually is very slow and is not significant in most individuals until after age of 40 years.

In some cases the diagnosis of various pathologies involving the macula may be difficult. The basic ophthalmic examination supported by additional diagnostic methods allow to establish the definitive diagnosis in most cases of macular disorders.

Praca została przedstawiona w postaci plakatu na XXVIII Sympozjonie Retinologicznym w Poznaniu w dniach 12-14.04.2007 r.

References:

1. Apushkin MA, Fishman GA, Taylor CM, Stone EM: *Novel de novo mutation in a patient with Best macular dystrophy*. Arch Ophthalmol 2006, 124(6), 887-889.
2. Kański JJ, Milewski SA: *Choroby plamki.* Wyd. I polskie pod red. K. Pecold. Górnicki Wydawnictwo Medyczne, Wrocław 2003, 195-197.
3. Schatz P, Klar J, Andreasson S, Ponjavic V, Dahl N: *Variant phenotype of Best vitelliform macular dystrophy associated with compound heterozygous mutations in VMD2.* Ophthalmic Genet 2006, 27(2), 51-56.
4. Kramer F, White K, Pauleikhoff D, Gehrig A, Passmore L, Rivera A, Rudolph G, Kellner U, Andrassi M, Lorenz B, Rohrschneider K, Blankenagel A, Jurklies B, Schilling H, Schutt F, Holz FG, Weber BH: *Mutations in the VMD2 gene are associated with juvenile-onset vitelliform macular dystrophy (Best disease) and adult vitelliform macular dystrophy but not age-related macular degeneration.* Eur J Hum Genet 2000, 8(4), 286-292.
5. Wabbels B, Preising MN, Kretschmann U, Demmler A, Lorenz B: *Genotype-phenotype correlation and longitudinal course in ten families with Best vitelliform macular dystrophy.* Graefes Arch Clin Exp Ophthalmol 2006, 244(11), 1453-1466.
6. Brecher R, Bird AC: *Adult vitelliform macular dystrophy*. Eye 1990, 4, 210-215.
7. Hayami M, Decock C, Brabant P, Van Kerckhoven W, Lafaut BA, De Laey JJ: *Optical coherence tomography of adult-onset vitelliform dystrophy.* Bull Soc Belge Ophthalmol 2003, 289, 53-61.
8. Sanfilippo P, Troutbeck R, Vandeleur K, Lenton L: *Optical coherence tomography of adult-onset fovemacular vitelliform dystrophy.* Clin Experiment Ophthalmol. 2004, 32(1), 114-118.
9. Pierro L, Tremolade G, Introini U, Calori G, Brancato R: *Optical coherence tomography findings in adult-onset foveomacular vitelliform dystrophy*. Am J Ophthalmol 2002, 134(5), 675-680.
10. Lanzetta P, Virgili G, Menchini U: *Indocyanine green angiography in vitelliform macular lesions*. Ophthalmologica 1996, 210(4), 189-194.
11. Andrade RE, Farah ME, Costa RA: *Photodynamic therapy with verteporfin for subfoveal choroidal neovascularization in Best disease*. Am J Ophthalmol 2003, 136(6), 1179-1181.

ISSN 0023-2157 Index 362646

12. Fishman GA, Baca W, Alexander KR, Derlacki DJ, Glenn AM, Viana M: *Visual acuity in patients with Best vitelliform macular dystrophy*. Ophthalmology 1993, 100(11), 1665-1670.

Praca włynęła do redakcji 20.12.2007 r. (1008)
Zakwalifikowano do druku 26.03.2008 r.

Reprint requests to (adres do korespondencji):
Agnieszka Kubicka-Trząska, MD, PhD
Lea Street 244/7
30-133 Kraków