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Atypical peripapillary location of choroidal neovascularization – cases report

Nietypowa przytarczowa lokalizacja neowaskularyzacji podsiatkówkowej – opis przypadków

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Summary: Choroidal neovascularization (CNV) is one of the main reasons for sight loss in adults. CNV located at the border of the optic disc or adherent atrophy is described as peripapillary choroidal neovascularisation (PPCNV).
The aim of the work is to present a course of changes and the effects of treatment with intravitreal ranibizumab injections for peripapillary subretinal neovascularization, its consequences and accompanying other CNV foci in two patients. The diagnosis and monitoring of the therapeutic effects were based on the results of fluorescein angiography and OCT. In a 53-year-old female patient three injections of ranibizumab at a dose of 0.05 mg were administered according to a saturation regimen. Visual improvement of 5 lines on an ETDRS board (25 letters) was obtained, as well as withdrawal of the subretinal fluid from the area of the macula in OCT and limitation of the peripapillary exudate visible in 12 months follow-up angiography. In a 70-year-old female patient bilateral development of symmetric peripapillary CNV foci was observed accompanied by a occult CNV focus in the left eye macula. Spontaneous CNV limitation without macular lesions was visible in the right eye. Intravitreal ranibizumab injections were given into the left eye. A 12 months follow-up revealed vision stabilisation in both eyes at the baseline level.
Conclusions: Intravitreal injections can be used in the treatment of atypical extramacular CNV, responsible for secondary damage to the fovea. Ranibizumab, a non-selective VEGF-A inhibitor, allows the elimination of changes in the central retina, closure or significant limitation of the exudates and vision improvement. Spontaneous limitation of lesions may also be frequently expected in the eyes with peripapillary CNV foci.
Key words: peripapillary choroidal neovascularization, intravitreal injections, ranibizumab.
Słowa kluczowe: przytarczowa odnaczyniówkowa neowaskularyzacja, iniekcje doszklistkowe, ranibizumab.

Choroidal neovascularization (CNV) is one of the main reasons for sight loss in adults. CNV located at the border of the optic disc or adherent atrophy is described as peripapillary choroidal neovascularization (PPCNV). Changes of this type are usually classified as extrafoveal CNV foci. Clinical trials have demonstrated that in the majority of cases this is occult CNV (1). A natural history of PPCNV is various: starting from stable, asymptomatic foci found in an ophthalmoscopic examination to conditions of a progressive course, where CNV is located in the papillo-macular bundle, fovea, and is accompanied by haemorrhages and exudates as well as progressive vision impairment (2).

The aim of the work is to present a course of changes and the effects of treatment with intravitreal injections of ranibizumab (Lucentis) for peripapillary subretinal neovascularization, its consequences and other accompanying CNV foci in two patients during 12 months follow-up.

Case 1.

A 53-year-old female patient reported herself at the Retinal Clinic due to visual acuity impairment in the left eye lasting for 4 months and blurring in the centre of the field of vision and image distortion. A full ophthalmic examination was performed, together with the visual acuity evaluation using Snellen and ETDRS charts (Vod 0.80 sc – 82 letters), Vos 0.10 sc – 36 letters), the evaluation of the anterior and posterior segment using a slit lamp, retinoscopy, aplanation tonometry, ultrasound examination, fluorescein angiography and OCT (SOCT Copernicus). Drusen typical of dry degenerative lesions were observed in the macula in the fundus of the right eye. In the left eye at the superior and temporal edge of the optic disc a greyish, elevated lesion with border exudates was visible, and a focus of the subretinal fluid with a round border in the macula. Fluorescein angiography (FA) of the right eye revealed retinal pigment epithelial window defects typical of drusen. In the left eye at the optic disc FA revealed hyperfluorescence increasing in time, typical of CNV with fluorescein retention in later study phases in accompanying fluid compartments in the papillo-macular bundle and in the macula (Fig. 1). OCT of the right eye revealed wavy distortion of the reflection line from the pigment epithelium layer confirming the presence of drusen. OCT of the left eye above the optic disc revealed

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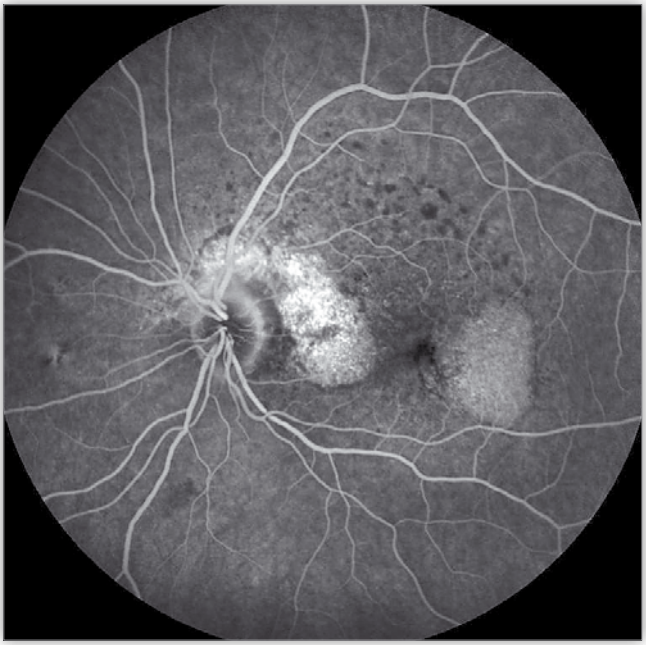

Fig. 1. Case 1. Baseline fluorescein angiography of the left eye. At the optic disc increasing in time hyperfluorescence typical of CNV with fluorescein retention in later study phases in accompanying fluid compartments in the papillo-macular bundle and the macula.

Ryc. 1. Przypadek 1. Wyjściowa angiografia fluoresceinowa oka lewego. Przy tarczy nerwu wzrokowego narastająca w czasie hiperfluorescencja typowa dla CNV z zastojem fluoresceiny w późnych fazach badania w towarzyszących przestrzeniach płynowych w pęczku plamkowo-tarczowym i w plamce.

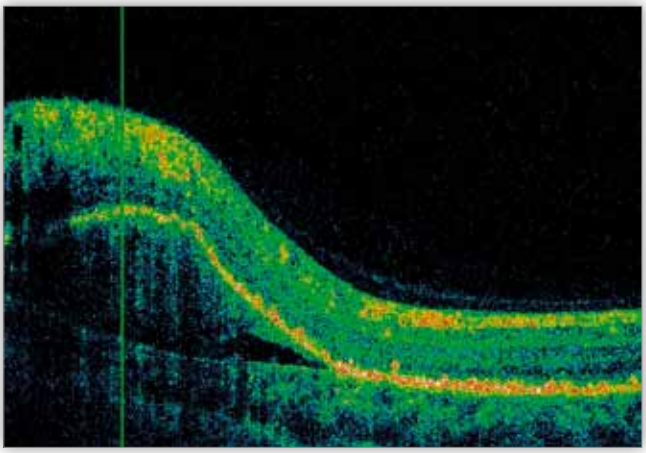

Fig. 2. Case 1. Baseline OCT of the left eye. Above the optic disc the subretinal fluid and retinal oedema.

Ryc. 2. Przypadek 1. Wyjściowe OCT oka lewego. Powyżej tarczy nerwu II płyn podsiatkówkowy oraz obrzęk siatkówki.

the subretinal fluid and retinal oedema (Fig. 2). The subretinal fluid was also visible in foveal tomograms (Fig. 3). A decision was made to administer ranibizumab at a dose of 0.5 mg in a saturation regimen into the vitreous body – three doses at one month intervals. As early as after the first injection vision improvement in the left eye up to 56 letters – 0.25 on an ETDRS chart was observed what correlated with a complete removal of the subretinal fluid visible in macular tomograms and with restoration of a foveal contour (Fig. 4). Above the

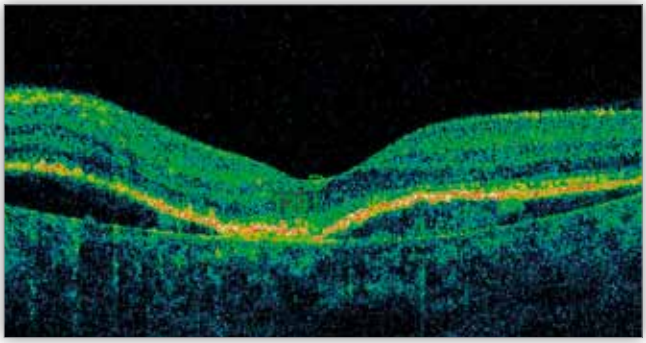

Fig. 3. Case 1. Baseline OCT of the left eye – macular tomograms. The subretinal fluid, a distorted foveal contour.

Ryc. 3. Przypadek 1. Wyjściowe OCT oka lewego – tomogramy plamkowe. Płyn podsiatkówkowy, zniekształcony kontur dołka.

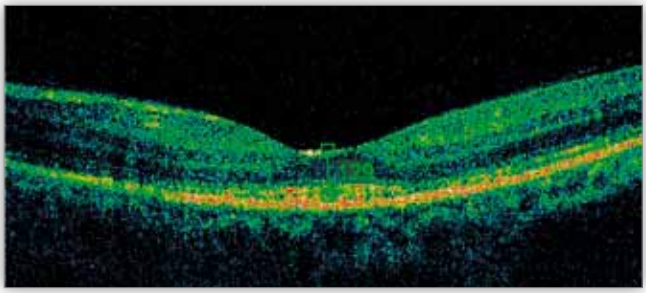

Fig. 4. Case 1. OCT of the left eye following the first intravitreal ranibizumab injection. Complete removal of the subretinal fluid visible in macular tomograms and restoration of a foveal contour.

Ryc. 4. Przypadek 1. OCT oka lewego po pierwszej iniekcji doszklistkowej ranibizumabu. Całkowite wycofanie się płynu podsiatkówkowego w tomogramach plamkowych i odtworzenie konturu dołka ze zmniejszeniem grubości siatkówki dołeczkowej do 129 μm.

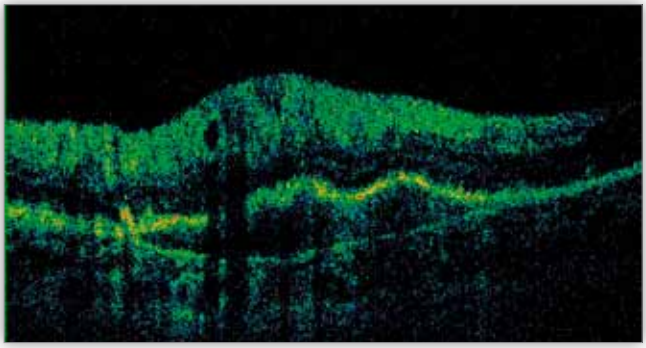

Fig. 5. Case 1. OCT of the left eye following the first intravitreal ranibizumab injection. The amount of the subretinal fluid has decreased above the optic disc, the retinal oedema persists.

Ryc. 5. Przypadek 1. OCT oka lewego po pierwszej iniekcji doszklistkowej ranibizumabu. Powyżej tarczy nerwu wzrokowego zmniejszyła się ilość płynu podsiatkówkowego, utrzymuje się obrzęk siatkówki.

optic disc in the left eye OCT revealed the retention of the subretinal fluid and retinal oedema (Fig. 5). FA of the left eye performed one month after the injection of Lucentis revealed a complete withdrawal of fluid from the macula and the papillo-macular bundle and a significant limitation of the exudates

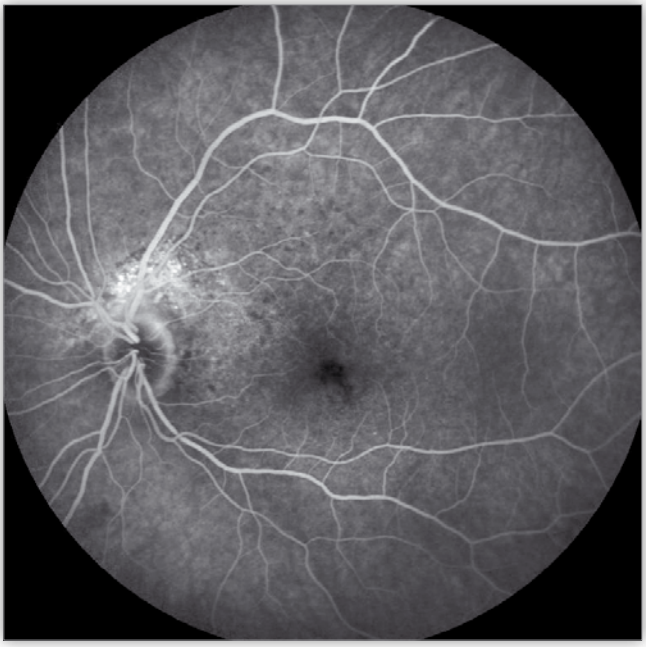

Fig. 6. Case 1. Fluorescein angiography of the left eye one month after the first injection. Complete removal of the fluid in the macula and the papillo-macular bundle and a significant limitation of the exudate above the optic disc.

Ryc. 6. Przypadek 1. Angiografia fluoresceinowa oka lewego miesiąc po pierwszej iniekcji. Całkowite wycofanie się ognisk płynowych w plamce i w pęczku plamkowo-tarczowym oraz znaczne ograniczenie przecieku powyżej tarczy nerwu II.

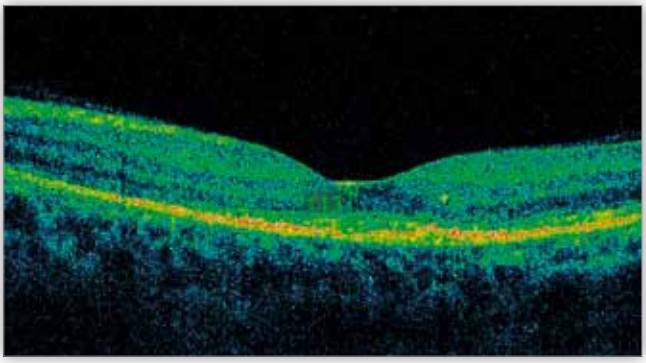

Fig. 7. Case 1. OCT of the left eye in 12 months follow-up. The recurrence of the subretinal fluid is not observed, a foveal contour is maintained, the retinal foveal thickness is 113 μm.

Ryc. 7. Przypadek 1. OCT oka lewego w obserwacji 12-miesięcznej. Nie obserwuje się nawrotu płynu podsiatkówkowego, kontur dołka zachowany, grubość siatkówki w dołeczku – 113 μm.

above the optic disc (Fig. 6). In a 12 months follow-up we do not observe recurrence of the subretinal fluid into the foveal area and the foveal retina is 113 μm thick (Fig. 7). The visual acuity in the left eye is stable and maintained at the level of 0.32 (61 letter ETDRS) what constitutes the improvement of 25 letters when compared to the baseline. Follow-up fluorescein angiography revealed persistent but limited exudates typical of occult CNV above the optic disc in the left eye (Fig. 8) what correlates with the presence of persistent fluid and a distorted reflection line from the RPE/choriocapillaries in OCT (Fig. 9). The patient is still being monitored. The visual acuity and the OCT image are checked every 5-6 weeks.

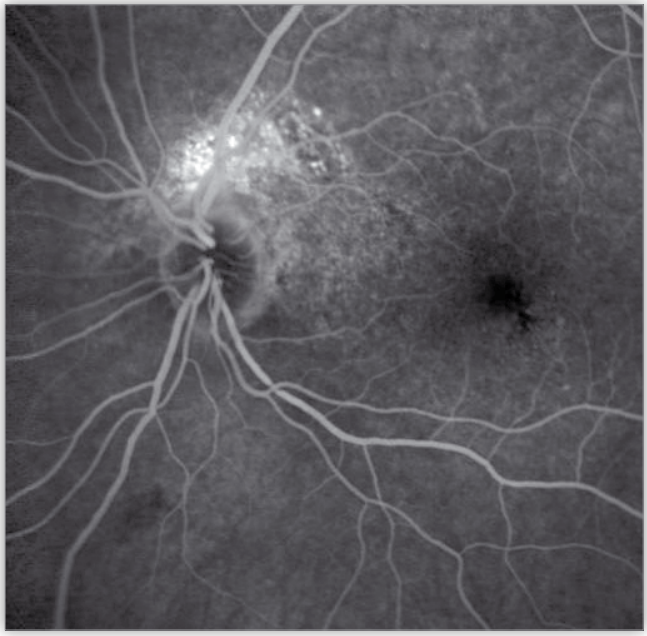

Fig. 8. Case 1. Fluorescein angiography of the left eye in 12-month follow-up. A decreased exudate typical of occult CNV persists above the optic disc.

Ryc. 8. Przypadek 1. Angiografia fluoresceinowa oka lewego w obserwacji 12-miesięcznej. Powyżej tarczy nerwu II utrzymuje się zmniejszony przeciek typowy dla ukrytej CNV.

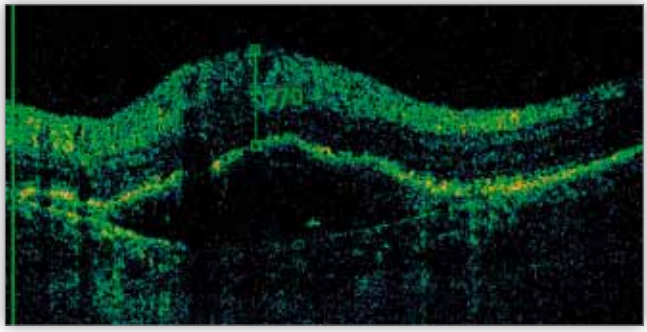

Fig. 9. Case 1. OCT of the left eye in 12-month follow-up. The subretinal fluid, a distorted reflection line from the RPE/ choriocapillaries, retinal oedema persist above the optic disc.

Ryc. 9. Przypadek 1. OCT oka lewego w obserwacji 12-miesięcznej. Powyżej tarczy nerwu II utrzymuje się płyn podsiatkówkowy, zniekształcony prążek odbić linii RPE/ choriokapilary, obrzęk siatkówki.

Case 2.

A 70-year-old female patient was referred to the Retinal Clinic with suspected central retinal vein thrombosis in the right eye with the aim of further diagnostics. She did not report visual acuity impairment in her medical history. A full ophthalmic examination was performed, together with the visual acuity evaluation using Snellen and ETDRS charts (Vod 1.00 cc +4.0 Dsph – 84 letters, Vos 0.80 cc +4.5 Dsph – 79 letters), the evaluation of the anterior and posterior segment using a slit lamp, retinoscopy, aplanation tonometry, ultrasound examination, fluorescein angiography and OCT (SOCT Copernicus). The ophthalmoscopic examination revealed oedema and a greyish elevated lesion with subretinal haemorrhage at the nasal edge of the optic disc in the right eye. Fluorescein angiography of the

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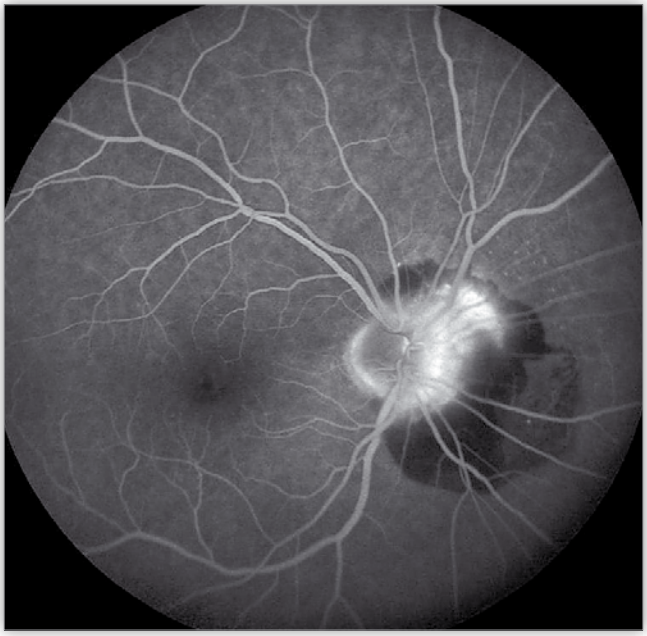

Fig. 10. Case 2. Fluorescein angiography of the right eye. A peripapillary focus of increasing hyperfluorescence typical of CNV, surrounded by constant hypofluorescence – fluorescence blockage by blood.

Ryc. 10. Przypadek 2. Angiografia fluoresceinowa oka prawego. Przytarczowe ognisko narastającej hiperfluorescencji charakterystycznej dla CNV otoczonej stałą hipofluorescencją – blokada fluorescencji przez krew.

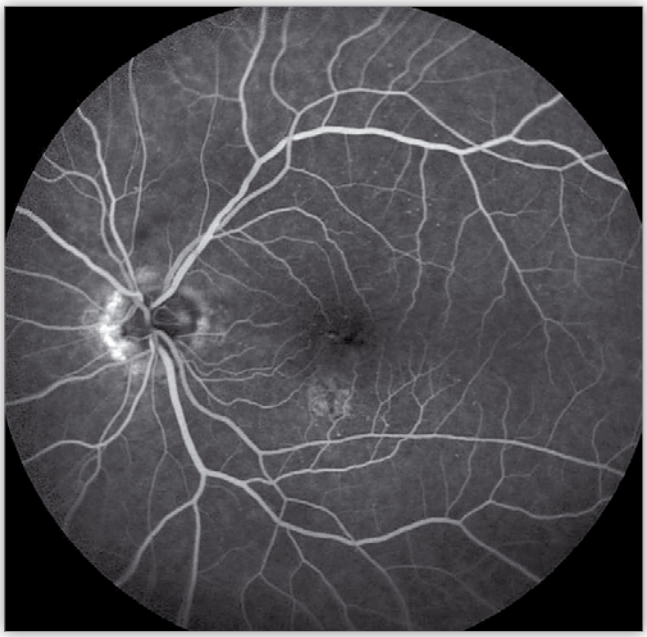

Fig. 11. Case 2. Fluorescein angiography of the left eye. Heterogenous hyperfluorescence in the macula.

Ryc. 11. Przypadek 2. Angiografia fluoresceinowa oka lewego. W plamce niejednorodna hiperfluorescencja.

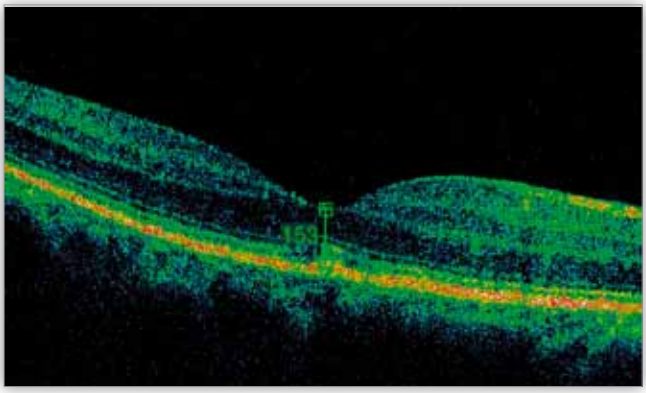

Fig. 12. Case 2. OCT of the right eye. Normal macular tomograms, retinal foveal thickness of 153 μm.

Ryc. 12. Przypadek 2. OCT oka prawego. Tomogramy plamkowe prawidłowe, grubość siatkówki w dołeczku – 153 μm.

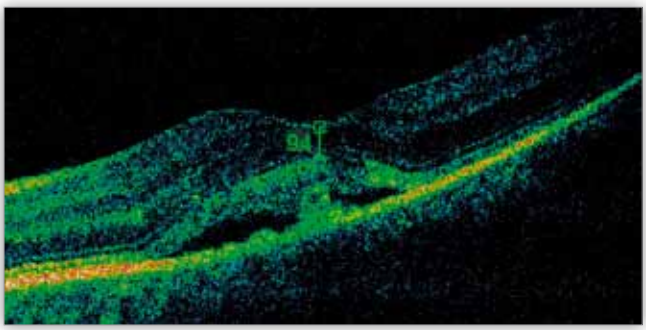

Fig. 13. Case 2. OCT of the left eye. The subfoveal fluid, a distorted reflection line from RPE/ choriocapillaries – occult CNV.

Ryc. 13. Przypadek 2. OCT oka lewego. Płyn podsiatkówkowy, zniekształcony prążek odbić RPE/ choriokapilary – ukryta CNV.

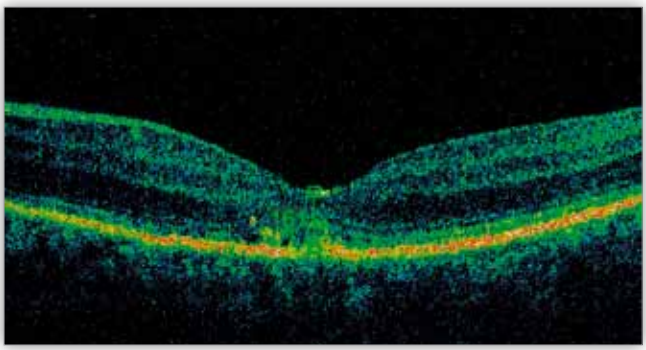

Fig. 14. Case 2. The left eye – withdrawal of the subfoveal fluid and restoration of a foveal contour following two ranibizumab injections.

Ryc. 14. Przypadek 2. Oko lewe – wycofanie się płynu podsiatkówkowego i odtworzenie konturu dołka po dwóch iniekcjach ranibizumabu.

right eye revealed a peripapillary focus of increasing hyperfluorescence typical of CNV, surrounded by constant hypofluorescence – blockage of fluorescence by blood (Fig. 10). The right eye macula was normal on FA. Heterogeneous hyperfluorescence was visible in the left eye macula on FA (Fig. 11). In OCT of the right eye macular tomograms did not demonstrate abnormalities; the retinal foveal thickness was 153 μm (Fig. 12). OCT of the left eye revealed some unexpected subfoveal fluid and a distorted reflection line from the RPE/ choriocapillaries as in occult CNV (Fig. 13). Moreover, NMR CNS was performed in order to eliminate possible optic disc oedema associated with increased intracranial pressure. As OCT of the right eye macula did not reveal abnormalities and the visual acuity was

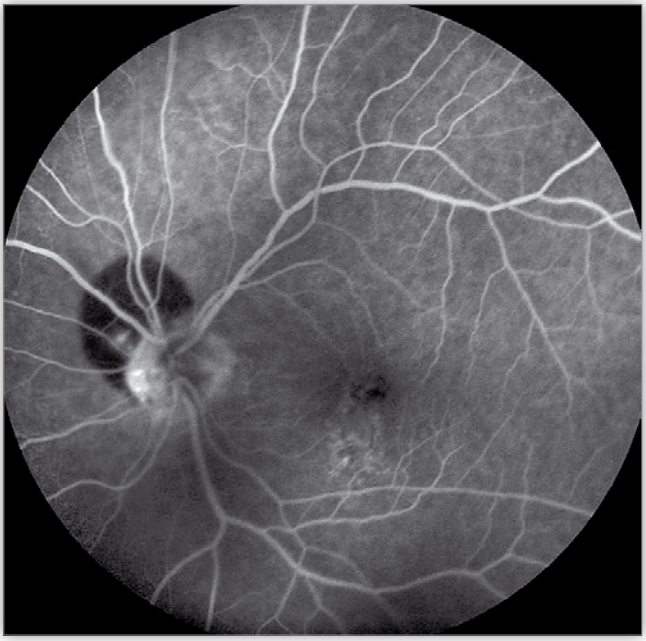

Fig. 15. Case 2. The left eye – appearance of a new focus of peripapillary CNV.
Ryc. 15. Przypadek 2. Oko lewe – pojawienie się nowego ogniska przytarczowej CNV.

good, the decision was made to observe a peripapillary CNV focus and blood vessel-tightening agents were recommended. The left eye was qualified for treatment with intravitreal ranibizumab injections at a dose of 0.5 mg. Following two injections we observed withdrawal of the subfoveal fluid and restoration of a foveal contour (Fig. 14). During subsequent follow-up FA a fresh CNV focus with haemorrhages, symmetrical to the right eye appeared at the nasal edge of the optic disc (Fig. 15). A subsequent, third injection of ranibizumab into the left eye was performed. Six weeks later OCT of the left eye macula did not reveal abnormalities, a peripapillary CNV focus stabilised and haemorrhages partly absorbed. In addition, laser barrage on the CNV border at the right eye optic disc was conducted. The fundus of both eyes are monitored. We observe stabilisation of the macular areas in OCT and visual acuity at the baseline level. The ophthalmoscopic examination reveals scarring of the peripapillary foci.

Discussion

Peripapillary subretinal choroidal neovascularization may accompany different optic disc abnormalities such as drusen, pit, slit or oedema. It can be observed in myopic eyes, with angioid streaks, ocular histoplasmosis, following traumas, uveitis, in evanescent white-dot syndrome, with peripapillary choroidal naevus, with the inflammation of the intermediary part of the vitreous body or in the course of sarcoidosis. According to Browning et al. PPCNV most commonly occurs in the course of age-related maculopathy (45%), as idiopathic disease (39%), in the course of multifocal retinochoroidal inflammation (2.6%), ocular histoplasmosis (1.7%), choroidal osteoma (0.9%) or drusen in the optic disc (0.9%) (3). PPCNV etiopathogenesis is suspected to be associated with peripapillary defects in the Bruch's membrane resulting in choroidal neoplasia. Usually the course of PPCNV is slow, asymptomatic until secondary macular changes develop (4). In the material discussed in our report both cases were associated with additional AMD-like degenerative lesions in the foveas of other eyes, and a occult CNV focus appeared in the macula in the second case. In the other eye peripapillary CNV occurs in 20% of patients during 2-year follow-up (3). In our report it developed within a few months in the second case. One of the methods to treat PPCNV is laser ablation of an active lesion and protection of its boundaries. Browning et al. reported CNV relapses in about 20% of patients following laser ablation. Similar relapse rates are demonstrated by Cialdini et al. – between 20 and 28% cases (5). Protective laser coagulation at the border of peripapillary neovascularization was performed in the case of the second patient (right eye).

Another method to treat PPCNV is photodynamic therapy (PDT) with Visudyne. Rosenblatt et al. applied PDT in the eyes with PPCNV, with the following parameters observed: a laser focus at the distance of at least 125 μm from the optic disc edge, duration of a diode laser action 30 seconds, a light energy dose of 18 J/cm^2 (6). No defects in the nerve fibre layer were found; vision improvement and the resolution of subretinal exudates and haemorrhages accompanying CNV were seen.

There is also a report on surgical removal of vast PPCNV lesions using pars plana vitrectomy with retinotomy. Kokame et al. presented the results of such proceedings in six patients with vast lesions with secondary foveal involvement (7). Vision improved or stabilised in 85% of cases and in one patient a CNV relapse occurred within one month which was effectively treated with laser therapy, and a late relapse 3 years post-procedure was observed in two patients. Harshivinderjit et al. do not demonstrate such good effects in a group of 17 patients with vast PPCNV, who underwent surgical treatment (8). Vision stabilisation or improvement was observed in less than half of patients.

As laser therapy, photodynamic therapy or vitreoretinal therapy are not always associated with positive effects of PPCNV treatment, it seems reasonable to use other methods, such as intravitreal injections of VEGF-A inhibitors. In the reported cases pathological processes were limited following intravitreal injections of ranibizumab.

Conclusions

1. Therapy with intravitreal injections of ranibizumab is used to manage atypical, extramacular CNV lesions, which cause secondary foveal damage.
2. Ranibizumab, a non-selective VEGF-A blocker, helps to withdraw lesions in the central retina, to close or limit significantly a primary peripapillary exudates and allows vision improvement.

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