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Idiopathic choroidal neovascularization (ICNV) in subfoveal, parafoveal, and perifoveal localization

Małgorzata Woś, Magdalena Obtułowicz

Departament of Ophthalmology, Stefan Żeromski Specialist Hospital in Krakow, Krakow, Poland

ABSTRACT

BACKGROUND: Idiopathic choroidal neovascularization (ICNV) is a disease entity occurring in people under 50 years of age, not associated with any ophthalmic or systemic diseases. The course of ICNV and the prognosis depend on the location of the neovascular membrane in relation to the yellow spot, while treatment in some cases requires anti-vascular endothelial growth factor (anti-VEGF) therapy.

CASE PRESENTATION: The article presents cases of idiopathic neovascular membrane in three different locations.

CONCLUSION: Idiopathic neovascular membrane is a rare condition that can lead to a significant deterioration of vision in young people, which can be safely and effectively treated with anti-VEGF injections. The final visual acuity depends on the location of the neovascular membrane.

KEY WORDS: ICNV; subfovea; parafovea; perifovea

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INTRODUCTION

Choroidal neovascularization (CNV) in young people may occur in the course of high myopia (62%), uveitis, ocular histoplasmosis, toxocarosis, sarcoidosis, angioid streaks, perifoveal telangiectasia, choroid ruptures, pigmented epithelial dysgenesis, retinal dystrophy (Best disease, Stargardt disease), optic nerve anomaly (disc drusen, developmental fossa, disc fissure) and after injuries of the eyeball with choroid rupture [1–3].

In young patients, if the cause (primary ophthalmological or systemic diseases) is not found, we consider an idiopathic neovascular membrane [4, 5]. They account for 17% of patients with active CNV [6]. The pathogenesis of the disease is still unknown [1].

Idiopathic choroidal neovascularization (ICNV) is a disease that appears suddenly in people under 50 years of age, more often affecting females, and the symptoms depend on the location of the neovascular membrane [4, 7].

ICNV occurs in most cases (86–100%) unilaterally, most often in the subfovea, rarely perifovea and parafovea [5, 8]. Therefore, subfovea changes are more often described [2, 7, 8]. ICNV presages better than other types of CNV; in 95% of cases, there is spontaneous stabilization or improvement of visual acuity, and in 5% of patients a permanent decrease in visual acuity is observed [7].

CASE PRESENTATION

Subfoveal location

A 31-year-old female patient presented to the ophthalmologist due to deterioration of the right

CORRESPONDING AUTHOR:
Małgorzata Woś, Departament of Ophthalmology Stefan Żeromski Specialist Hospital in Cracow, Os. Na Skarpie 66, 31–913 Krakow, Poland, tel: (+48) 12 622 95 11; email: mwos@zeromski-szpital.pl

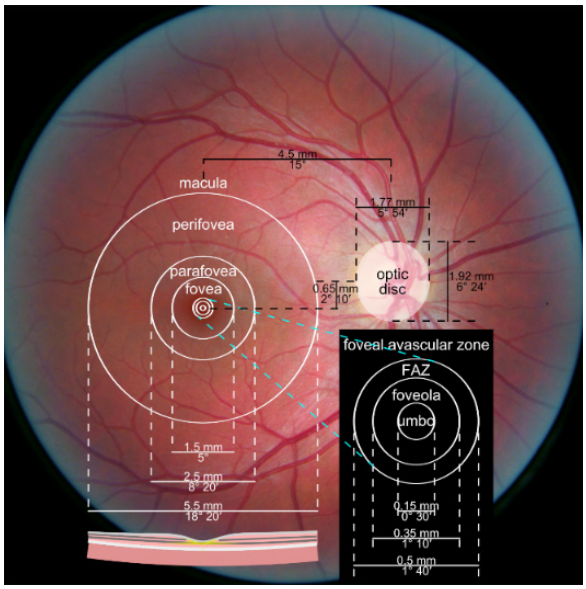

FIGURE 1. Anatomical structure of the posterior pole of the fundus

eye's (RE) vision with central fogging. Th patient associated the symptoms with a workload.

Visual acuity (Snellen test) during the first examination was in RE count finger up to 1.0 m, with full visual acuity (1.0) in the left eye (LE) (both eyes in correction –2.0 D in relation to myopia).

Optical coherence tomography (OCT) and angio-OCT (OCTA) revealed the presence of subfoveal CNV with partial scarring (Fig. 2). In the ophthalmological examination no other pathologies were found. Taking into account the possibility of systemic infection, laboratory tests were done, and obtained the following results: test results for Epstein-Barr virus (EBV) were positive (IgG), for *Borrelia* — negative (IgG and IgM), for cytomegalovirus (CMV) — positive (IgG), for *Toxoplasma gondii* — negative (IgM and IgG).

Based on the performed exams, idiopathic subfoveal neovascularization with partial scarring was diagnosed, and it was decided to administer anti-vascular endothelial growth factor (anti-VEGF) therapy. The patient received 3 doses of anti-VEGF at monthly intervals: 1 dose of aflibercept and 2 doses of ranibizumab (in another center due to proximity to the place of residence). The visual acuity of the right eye after 3 injections was 0.16 c.c.- 2.0 Dsph (Snellen test). Due to the presence of scar tissue at the CNV site, further treatment was discontinued. The patient is being monitored at the oph-

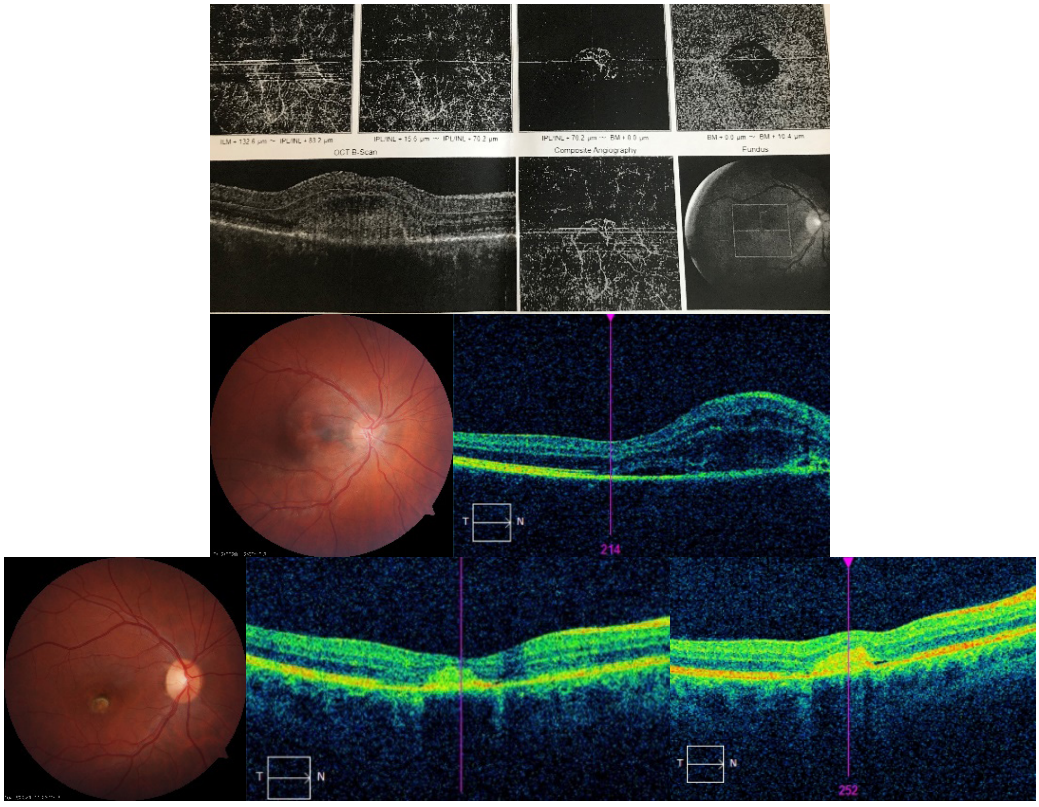

FIGURE 2. Patient's right eye (RE) with choroidal neovascularization (CNV) subfoveal localisation at the time of diagnosis (top), after three anti-vascular endothelial growth factor (anti-VEGF) injections (middle) and after two years (bottom)

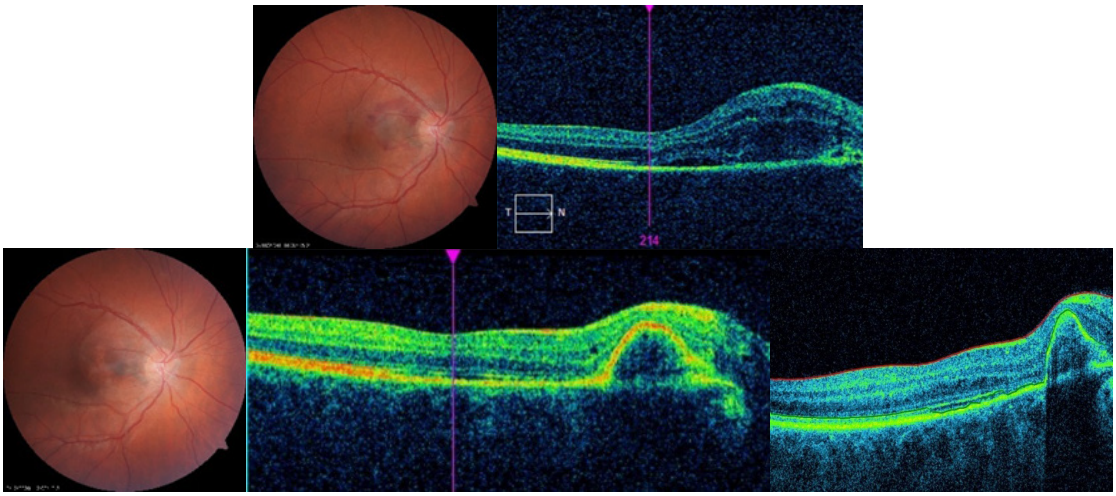

FIGURE 3. Patient's right eye (RE) with parafoveal choroidal neovascularization (CNV) at diagnosis (top), after three anti-vascular endothelial growth factor (anti-VEGF) injections and after two years (bottom)

thalmology outpatient clinic. Visual acuity (Snellen: RE 0.2) and the OCT image of the macula during the 2 years of observation remain stable.

Parafoveal location

A 34-years-old female patient, generally healthy, during breastfeeding for 15 months, presented to the emergency room with blurred vision in the previously better-seeing RE (LE visually impaired due to amblyopia).

Visual acuity to the distance (Snellen test) was: RE — 0.4 without correction (sc), LE — 0,4 c. sph + 2.5 cyl-3, 5ax175. The anterior segment of both eyes and ocular pressure were within normal limits.

OCT, OCTA, and fluorescein angiography (FA) were performed, and a neovascular membrane located at the parafoveal was found (Fig. 3). As in the previous case, in the absence of ophthalmic causes of CNV, diagnostics for infectious diseases were performed.

The following test results were obtained: *Borrelia* (Elisa test) — IgG- and IgM-negative, Coxsackie virus A7,B1 — IgM-negative, IgG-positive, *Toxoplasma gondii* — IgG- and IgM-negative, *Toxocara* — IgG-negative, CMV — IgG- and IgM-negative.

Based on the performed tests, a diagnosis of idiopathic parafoveal CNV was made, and treatment with anti-VEGF injections was implemented. Three doses of aflibercept were given at monthly intervals. RE visual acuity after 3 doses was 0.8 sc and remains stable over 2 years of follow-up (last exam RE 0,9 sc).

Perifoveal location

A 45-year-old male patient was diagnosed in the outpatient clinic due to deterioration of vision in the form of a "spot" and metamorphosia of LE; RE is visually impaired due to amblyopia.

During the first study, visual acuity (Snellen test) was: RE — 0.05 sc, LE — 1.0 sc. The front segment of the RLE and ocular pressure were within the norm.

As a result of the diagnostics (OCT, OCTA, and FA), a CNV located at the optic nerve disc was found (Fig. 4). In the examination of the fundus on the periphery of the retina in the left eye, a scar was found as after toxoplasmosis. This is why an assessment in this direction was performed, extending the diagnosis to other zoonotic diseases. The results were as follows: *Toxoplasma gondii* — IgM and IgG non-reactive, *Borrelia* (Elisa test) — IgG-negative, CMV — IgG and IgM non-reactive, *Toxocara* — IgG repetitively slightly elevated (14.186 and 13.51 with normal up to 11).

In addition, tests for thromboembolism were performed: D-dimers and the coagulation system were in the norm.

Treatment included 3 doses of anti-VEGF ranibizumab at monthly intervals. As a result of treatment, there was an improvement in fluid absorption, petechiae, and partial scarring. Visual acuity was still full. There was a subjective improvement and a decrease in metamorphopsia, although they did not go away completely.

Three months after the third injection, the patient came back due to increased metamorphopsia and an increase in the "spot" in the field of vision.

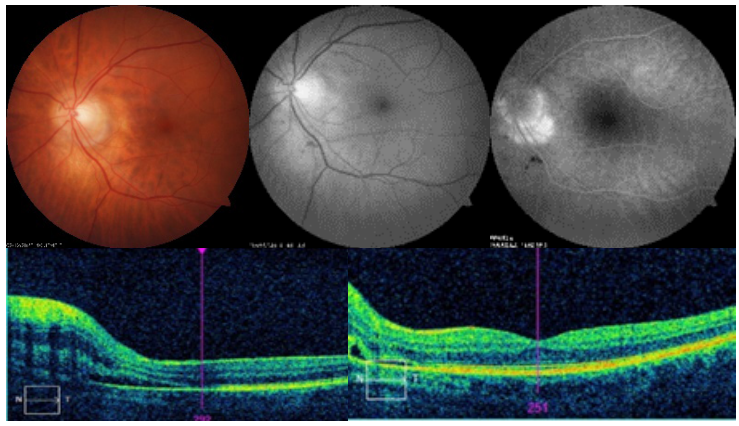

FIGURE 4. Patient's left eye (LE) with perifoveal choroidal neovascularization (CNV) at the time of diagnosis

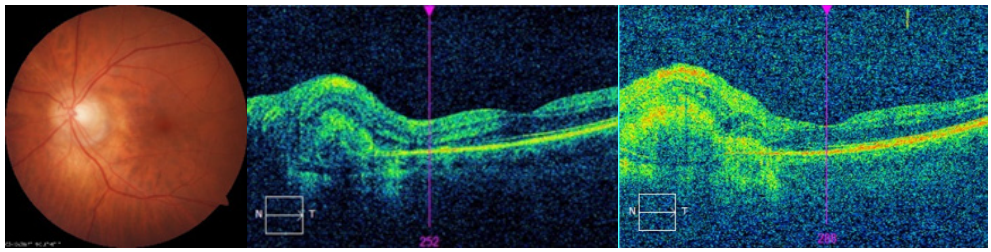

FIGURE 5. Patient's left eye (LE) with perifoveal localization after 3 anti-vascular endothelial growth factor (anti-VEGF) injections and after two years

In the ophthalmological examination, a recurrence of CNV parafoveal was noted. OCT presented fluid under the optic disc's sensory retina and the macula in the examination of the fundus swelling of the retina and petechiae. Visual acuity in LE was still full. It was decided to administer anti-VEGF treatment in LE. Three doses of ranibizumab were administered at monthly intervals until the swelling regressed and petechiae were absorbed (Fig. 5). The patient's follow-up continues. During the disease activity, the next anti-VEGF injections were administered (the patient received 13 injections from the beginning until now). The visual acuity of the LE is still 0.9–1.0 sc with discreet subjective changes in the visual field.

Summary

Table 1 presents the patient's visual acuity depending on the location of neovascularization during diagnosis and after treatment and the number of anti-VEGF injections.

DISCUSSION

Choroidal neovascular membrane means a pathological growth of abnormal new blood vessels in the subretinal space. Membrane formation is a complex multifactorial process for which many factors are responsible, primarily VEGF, but also mediators produced by macrophages such as monocyte colonization protein (MCP), ma-

Table 1. Patients' visual acuity depending on the location of neovascularization during diagnosis and after treatment

Location	Visual acuity at diagnosis	Visual acuity after treatment	Number of injections anti-VEGF
Subfoveal	cf to 2 m	0.2	3
Parafoveal	0.4 sc	0.9 sc	3
Perifoveal	1.0 sc	0.9 sc	13

anti-VEGF — anti-vascular endothelial growth factor; cf — counting fingers; sc — without correction

trix metalloproteinase (MMPS), tumor necrosis factor (TNF) [9]. The role of inflammatory factors is also important; histological changes and membrane response to immunosuppressive and anti-inflammatory therapy were observed [10]. The problem mainly affects older people and is related to age-related macular disease (AMD). In younger patients, the neovascular membrane is usually secondary to conditions such as high myopia, angioid streaks, trauma, or uveitis [4]. Ophthalmic diagnosis includes ophthalmological examination and complementary examinations, among which OCT, OCTA, FA, and, in unclear cases, indocyanine angiography are important. In the absence of ophthalmic and general causes, the idiopathic neovascular membrane is diagnosed. In our cases, we diagnosed ICNV after eliminating other causes. We carried out detailed diagnostics of our patients, including ophthalmological and laboratory tests, to exclude general disease. The type of research was targeted by anamnesis, ophthalmological examination, and possible causes.

Many treatments have been used to treat ICNV, including photodynamic therapy with vertoporphyrin, transpupil thermotherapy, classical laser therapy, surgical treatment by vitrectomy (macular translocation) [11]. Currently, all these methods have been substituted by intravitreal anti-VEGF injections, which are effective in treating patients with ICNV [9]. Therapy is available, reproducible, and well-tolerated by patients [8, 11]. The treatment results depend on the extent and location of the membrane and the time of entry with treatment from the onset of symptoms [9, 12]. In all our patients, after using anti-VEGF therapy (ranibizumab or aflibercept), we improved the retina's vision and morphology after the first injection. The worst final visual acuity was achieved in a patient with subfoveal CNV localisation, who, after three injections, developed a subfoveal scar and permanent damage to vision. In a patient with parafoveal localisation, there was a gradual improvement in visual acuity and the disappearance of subjective ailments. With perifoveal localisation, visual acuity was still full, but subjective ailments gradually disappeared (slower than in previous cases), which should be associated with high amblyopia in the other eye. The complaints reported by patients depended on the location of the lesion. The fastest deterioration in vision occurred in the subfoveal localisation. Interestingly, the other patients also noticed symptoms relatively quickly (blurring, fog, curvature) associated with visual amblyopia in the healthy eye. Since they did not have ophthalmic factors for the risk of CNV, the diagnostics were extended to laboratory tests for viral and zoonotic diseases. Still, no other cause was found that could explain the occurrence of CNV.

The natural course of idiopathic CNV is better than that of AMD. Despite this, the loss of visual acuity can be significant [11, 12]. The most important prognostic factor for final visual acuity in patients treated with anti-VEGF in ICNV is the location and extent of the resulting neovascular membrane [12].

CONCLUSIONS

Idiopathic neovascular membrane is a rare condition that can lead to a significant deterioration of vision in young people and can be safely and effectively treated with anti-VEGF injections [4]. The final visual acuity depends on the location of the neovascular membrane. Anti-VEGF therapy is the key to success and gives hope for improving visual acuity and stabilizing the process [11].

The neovascular membrane can occur subfoveal, parafoveal, and perifoveal, and this localisation and impact on vision and treatment we have presented.

Conflict of interests

The authors declare no conflict of interests.

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