Polypoidal choroidal vasculopathy causing cystoid macular edema and the response to ranibizumab intravitreal treatment

Vasculopatia Coroidiana Polipoideal causando Edema Macular Cistóide e a resposta ao tratamento com Ranibizumab

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ABSTRACT

Purpose: To report a polypoidal vascular choroidopathy clinical case causing cystoid macular edema and the response to Ranibizumab intravitreal treatment. Methods: A 62-year old caucasian woman was referred by her comprehensive ophthalmologist for retinal evaluation. On presentation best corrected visual acuity was 20/100 in the left eye and 20/20 in right eye. Anterior segment examination was unremarkable in both eyes. Clinical examination and FA on the left eye demonstrated numerous small drusen and a cystoid macular edema due leakage from any polips in justapapilar region and from polips in the superior arcade vascular region and subretinal fluid and cystic change in the OCT. The right eye had FA normal. The patient refused to submit a ICGV angiography. The patient was treated by intravitreal ranibizumab injections in the left eye every 4 weeks, 3 injections, three months. Results: The patient showed resolution both of cystic change and subretinal fluid in the OCT, and the visual acuity in the six months follow-up improved to 20/25. The patient was followed by 18 months at this time and the visual acuity remained stable 20/25. Conclusion: We reported a patient case of cystoid macular edema from a polypoidal choroidal vasculopathy that responded well to ranibizumab intravitreal injection as monotherapy with disappearance of the initial subretinal fluid and cystic change in OCT follow-up and stop the polips.

Keywords: Choroid diseases/drug therapy; Polypoidal choroidal vasculopathy /drug therapy; Macular edema/etiology; Injections; Antibodies, monoclonal/therapeutic use; Case report

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Study carried out with Vitreous Retina Ophthalmology Department of the Iowa University-USA

The authors received no public or private financial support


Rev Bras Oftalmol. 2011; 70 (4): 252-6
**RESUMO**

**Objetivo:** Relatar um caso de paciente com Vasculopatia coroidiana polipoidal com edema macular cistóide e a resposta ao tratamento com Ranibizumab intravitrea como monoterapia. **Métodos:** Uma paciente com 62 anos foi referida por seu oftalmologista para avaliação retiniana. Presentava acuidade visual com correção de 20/100 no olho esquerdo e 20/20 no olho direito. A avaliação do segmento anterior era normal em ambos os olhos. No exame de fundo de olho e retinografia fluoresceina apresentava numerosas drussas pequenas e edema macular cistóide devido à vazamentos de alguns pólipos vasculares coroidianos na arcada vascular superior e ainda fluido sub-retiniano e alteração cística no OCT. O olho direito apresentava angiografia fluoresceina da retina e OCT normais. A paciente recusou-se a se submeter a videoangiografia com indocianina verde. A paciente foi tratada com injeção intravitrea de Ranibizumab como monoterapia, sendo uma injeção a cada quatro semanas, três injeções em três meses. **Resultados:** A paciente apresentou resolução da alteração cística e do fluido sub-retiniano, ambos presentes no OCT prévio ao tratamento no olho esquerdo. A acuidade visual melhorou para 20/25 após 6 meses de tratamento. A paciente permanece com acuidade visual estável de 20/25 após 18 meses de acompanhamento. **Conclusão:** Reportamos um caso de paciente com edema macular cistóide que respondeu ao tratamento com Ranibizumab intravitrea, como monoterapia, e desaparecimento do fluido sub-retiniano e da alteração cística no OCT tendo cessado o vazamento dos pólipos que eram a causa do edema macular cistóide.

**Descritores:** Doenças da coróide/quimioterapia; Vasculopatia polipoidal coroidiana/quimioterapia; Edema macular/etiologia; Injeções; Anticorpos monoclonais/uso terapêutico; Relato de caso

**INTRODUÇÃO**

Polypoidal choroidal vasculopathy (PCV) is a designation coined by Yannuzzi to describe a distinct exudative macular disorder causing recurrent and multiple detachments of the retinal pigment epithelium. These are typically serosanguineous and neurosensory retinal detachments, secondary to bleeding and leakage from polypoidal choroidal vascular lesions. PCV is characterized by an inner choroidal vascular network of vessels, ending in an aneurysmal bulge or outward projection, visible clinically as a reddish-orange, spheroid, polyp-like.

PCV lesions have been seen in patients of many different racial backgrounds, but are known to selectively affect patients of more pigmented races. PCV lesions are found in 23-55% of patients with presumed neovascular age-related macular degeneration (AMD) in Asian countries; in patients of Caucasian origin, PCV lesions have been found in roughly 8-13% of patients with presumed neovascular AMD. Initially, this disease was described as “posterior uveal bleeding syndrome” and later as “multiple recurrent retinal pigment epithelium detachment.”

It has been proposed that PCV is a variant of type 1 neovascular AMD; true type 2 choroidal neovascularization (CNV) is not a rare complication of PCV, and the eyes often show what appears to be classic CNV on fluorescein angiography. However, it is difficult to discriminate type 2 CNV from pure fibrinous tissue deposition before treatment, even with a detailed examination by optical coherence tomography (OCT). PCV has also been reported in association with dry AMD.

Vascular changes typical of PCV are evident with slit-lamp biomicroscopy unless blood or exudate overly the lesions.

Fluorescein angiography (FA) can be useful in making the diagnosis if there is no serosanguineous leakage overlying the polyps, but indocyanine green videoangiography (ICGV) is the gold standard method for visualizing polyps and the vessel network.

The treatment strategies now available for PCV include verteporfin photodynamic therapy (PDT) and anti-VEGF therapy with ranibizumab as a monotherapy. Results with this smaller molecular weight compound are promising, showing regression of polypoidal changes and anti-VEGF therapy with ranibizumab as a monotherapy. A combination of PDT therapy and ranibizumab could provide a good alternative, by reducing the number of injections needed relative to that used in other anti-VEGF monotherapy. There are also reports of phototrombosis of neovessels, mediated by indocyanine green.

Cystoid macular edema (CME) can have a variety of causes, including diabetic maculopathy, age-related macular degeneration, retinal vein occlusions, chronic uveitis, epiretinal membranes, choroidal tumors, radiation retinopathy, perifoveal retinal telangiectasis, retinitis pigmentosa, dominantly inherited CME, foveal X-linked retinoschisis, and others.

We describe in this report a case in which PCV led to cystoid macular edema and the response to Ranibizumab intravitreal treatment.

**CASE REPORT**

A 62-year old Caucasian woman was referred by her ophthalmologist for retinal evaluation. Upon
presentation, the best corrected visual acuity was 20/100 in her left eye and 20/20 in her right eye. Anterior segment examination was unremarkable in both eyes. Clinical examination and FA of the left eye demonstrated numerous small drusen and cystoid macular edema, due to leakage from polyps in the juxtapapillary region and in the superior arcade region (figures 1 and 2). Subretinal fluid and cystic change were noted by OCT (figure 3). The right eye was normal by FA. The patient refused to submit to ICGV.

The patient was treated by intravitreal ranibizumab injections in the left eye every four weeks. After three injections and six months of follow-up, the patient showed resolution of both cystic changes and subretinal fluid by OCT (figure 4), and visual acuity during the six-month follow-up improved to 20/25.

The patient has been followed for 18 months at the time of writing, and her visual acuity has remained stable at 20/25.

**DISCUSSION**

Improved visual acuity has been found in many cases to be correlated with anatomic improvement and with restoration of a more normal macular architecture; this has been confirmed by advanced imaging techniques\(^{(19)}\).

An association between VEGF and PCV has been suggested by histopathological evidence of increased VEGF concentration in the aqueous humor in patients with PCV\(^{(20)}\).

The PrONTO study\(^{(21)}\) recommended that
patients treated for exudative macular degeneration from subfoveal CNV be followed by OCT monthly, together with visual acuity testing and possible fluorescein angiography. Our patient was followed by visual acuity testing and by OCT, and improvement in her clinical presentation and in visual acuity was noted.

Verteporfin photodynamic therapy has been shown to be effective in the treatment of symptomatic patients with PCV, although the incidence of retinal pigment epithelium atrophy and of recurrence suggest the need for additional treatment options[14,15].

A study of intravitreal bevacizumab in PCV showed vascular abnormalities persisting in 10 of out 11 eyes after three months[22]. This therapy might be less efficacious for PCV due to the limited retinal penetration expected for a molecule of bevacizumab’s molecular mass. With a molecular weight of 48 kD, ranibizumab is much smaller than the full-length RhuMab VEGF antibody (bevacizumab), which has a molecular weight of 148 kD. Additional studies have reported similar poor results with the larger antibody[23,24].

Results after six months of the EVEREST study were presented during a scientific review by Novartis in Basel, Switzerland. EVEREST is the first multi-center, double-blind, indocyanine green angiography (ICGA)-guided, randomized controlled trial with an angiographic treatment outcome, designed to assess the effect of Visudyne(R) (verteporfin photodynamic therapy) alone or in combination with Lucentis(R) (ranibizumab), as compared to that of Lucentis alone, in patients with symptomatic macular polypoidal choroidal vasculopathy (PCV). A total of 61 PCV patients of Asian ethnicity from five countries (China, Hong Kong), Taiwan, Korea, Thailand and Singapore participated in the study; long-term results are not yet available.

There have been recent reports of studies using ranibizumab monotherapy in PCV cases. Monthly intravitreal injections of ranibizumab for three months had a short-term beneficial anatomic effect, with polyps disappearing on ICG angiography in nine out of 13 lesions (69.2%); retinal thickness had diminished significantly by OCT (p=0.02)[14]. Another report of continuous anti-VEGF treatment with ranibizumab over six months for polypoidal choroidal vasculopathy[17] stimulated us to use this model of treatment in the case discussed here.

In conclusion, we report the case of a patient with cystoid macular edema from polypoidal choroidal vasculopathy who responded well to ranibizumab intravitreal injection as monotherapy. Treatment led to disappearance of the initial subretinal fluid and cystic change by OCT at follow-up, having halted polyp leakage.

Acknowledgements

We thank Professor James Folk, Judith Gardner and Donald Beisner, Professor of Vitreoretinal Diseases and Surgery at Iowa University, for analyzing this case with us.
REFERENCES


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