

Idiopathic Choroidal Neovascularization in a 10 Year-Old Child Treated with Intravitreal Bevacizumab Injections

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ABSTRACT

Purpose: to report a case of idiopathic choroidal neovascularization (CNV) in a pediatric patient successfully treated with intravitreal bevacizumab injections.

Methods: case report of a 10 year-old patient, who presented with reduced unilateral visual acuity during a visual screening. Complete ophthalmological examination was performed, along with fluorescein angiography, spectral domain optic coherence tomography (SD-OCT), fundus autofluorescence, ocular ultrasound, magnetic resonance imaging (MRI) of the brain and orbits and infectious serologies.

Results: visual acuity was 20/400 in the left eye (OS) and 20/20 in the right eye (OD). No significant refractive error was detected. Fundoscopy in OS revealed a subretinal macular lesion associated with subretinal hemorrhage and fluid. Fluorescein angiography and SD-OCT confirmed the presence of NVC. Retinal hereditary dystrophies, along with infectious and neoplastic causes were excluded. The patient underwent two intravitreal bevacizumab injections in OS with a 3 months interval. Treatment resulted in progressive fibrosis of NVC, resolution of subretinal fluid and improvement of visual acuity in OS to 20/125, which remained stable 4 years after treatment.

Conclusions: In the case of pediatric NVC, retinal hereditary dystrophies along with infectious and neoplastic causes should be excluded after a thorough investigation. No standard treatment for CNV in children has yet been validated. In our patient anti-vascular endothelial growth factor (VEGF) treatment induced regression of the CNV and resolution of subretinal fluid with a modest recovery in visual acuity and no reported ocular or systemic side effects.

Keywords: idiopathic choroidal neovascularization; pediatric vision impairment, anti-VEGF treatment in children

RESUMO

Objetivo: descrição de um caso de neovascularização coroideia (NVC) idiopática em doente pediátrico, submetido com sucesso a tratamento intravítreo com bevacizumab.

Métodos: caso clínico de um doente de 10 anos, do sexo masculino, com redução unilateral da acuidade visual (AV) detetada durante um rastreio visual. Foram realizados exame oftalmológico completo, angiografia fluoresceínica, tomografia de coerência ótica de domínio espectral (SD-OCT) com autofluorescência, ecografia oftálmica, ressonância magnética crânio-encefálica e órbitas e serologias virais.

Resultados: A AV do olho esquerdo (OE) era de 20/400 e do olho direito (OD) era de 20/20, sem erro refrativo significativo. À fundoscopia do OE foi detetada uma lesão macular subretiniana associada a hemorragia e líquido subretinianos. A angiografia fluoresceínica e o SD-OCT confirmaram a presença de NVC. Foi excluída a existência de distrofia retiniana hereditária, assim como causas infecciosas e neoplásicas. O doente foi submetido a duas injeções intravítreas no OE com intervalo de 3 meses. O tratamento resultou na fibrose progressiva da NVC, com resolução do líquido subretiniano e melhoria da AV OE para 20/125, permanecendo estável 4 anos após o tratamento.

Conclusões: Em casos de NVC em idade pediátrica deve ser realizada uma investigação etiológica exaustiva, de forma a excluir a presença de distrofias retinianas hereditárias, assim como causas infecciosas e neoplásicas. Não existe tratamento consensual estabelecido para o tratamento de NVC em idade pediátrica. No caso clínico descrito, o tratamento com anti-VEGF permitiu a regressão da NVC com melhoria modesta da AV e sem evidência de efeitos secundários locais ou sistémicos.

Palavras-Chave: Neovascularização coroideia idiopática, compromisso visual na criança, tratamento anti-VEGF em idade pediátrica

INTRODUCTION

Choroidal neovascularization (CNV) is a rare but sight-threatening disease in the pediatric age group^{1,2}. The most common causes of CNV in children and adolescents are inflammatory CNV and Best Disease³, however idiopathic CNV is relatively frequent when these etiologies have been excluded. Subfoveal location is the most common site³ and treatment is associated with better visual outcomes when compared to spontaneous regression of CNV, which is not infrequent.³ Several treatment strategies have been used for CNV in the pediatric population, including anti-VEGF and photodynamic

therapy^{1,4} although no standard treatment has yet been established.

CASE REPORT

A 10 year-old male patient presented with reduced visual acuity in the left eye (OS) during a school visual screening. He had a personal history of alpha-thalassemia, but was otherwise a healthy child. There was no personal history of eye trauma nor documented family history of eye or retinal disease.

On observation, his best corrected visual acuity was 20/400 in OS and 20/20 in the right eye (OD). No

significant refractive error was detected and anterior segment was unremarkable bilaterally (OU) on biomicroscopy. Fundoscopy (figure 1) revealed a subretinal macular lesion in OS, associated with subretinal hemorrhage and fluid but no vitreous inflammation. No changes were detected on fundoscopy in OD.

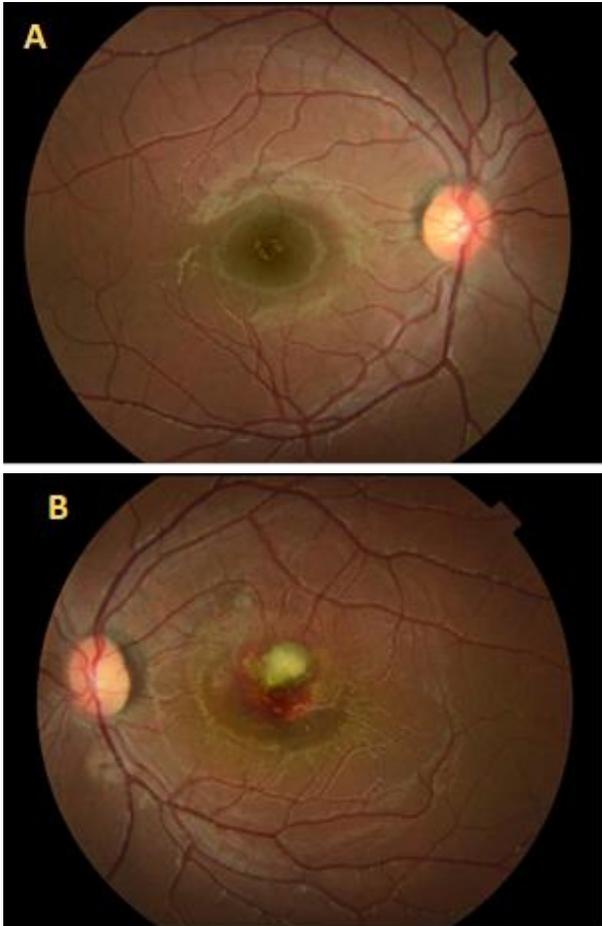


Figure 1 - Fundus photographs - A) In OD no macular or optic disc changes are visible. B) OS showing a subretinal macular lesion, associated with retinal hemorrhage and fluid

Fluorescein angiography of OS (figure 2) revealed late hyperfluorescence due to staining of the subretinal macular lesion and scarce leakage.

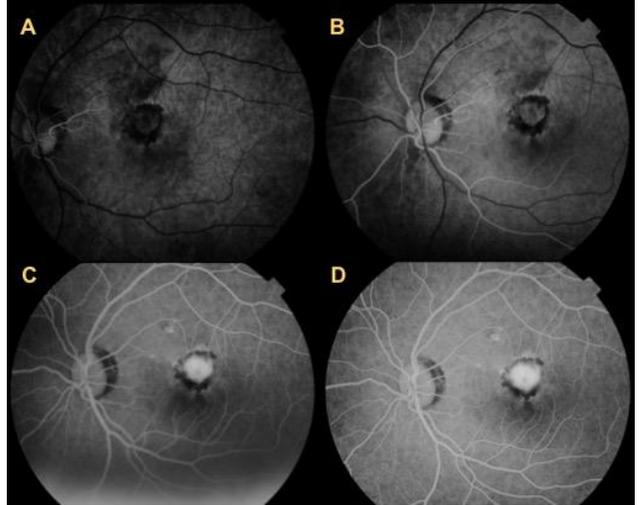


Figure 2 - Fluorescein angiography of OS – Early frames (A, B) revealed blockade of choroidal fluorescence due to the presence of a subretinal macular lesion surrounded by hemorrhage; Late frames (C and D) showed hyperfluorescence due to staining of the subretinal macular lesion and scarce leakage.

Red-free fundus photograph (figure 3A) and macular SD-OCT (figure 3B) confirmed the presence of a unilateral subretinal lesion associated with subretinal fluid and fundus autofluorescence (figure 3C) revealed macular hypoautofluorescence due to the presence of blood and a subretinal lesion. These findings suggested the presence of a neovascular choroidal membrane in OS.

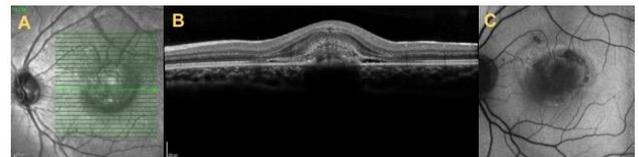


Figure 3 – Red-free fundus photograph (A) and macular SD-OCT (B) confirmed the presence of a subretinal lesion and subretinal fluid. Fundus autofluorescence (C) revealed macular hypoautofluorescence due to the presence of blood and a subretinal lesion.

Ocular ultrasound and MRI of the brain and orbit were performed, excluding the possibility of retinoblastoma or other malignancies of the central nervous system. Infectious causes were also excluded through blood serologies and PCR, particularly toxoplasmosis, toxocariasis, syphilis, cat-scratch disease, Lyme's disease, leptospirosis, brucellosis, Rickettsia, CMV and HIV infections. Sickle cell test was also negative and abdominal ultrasound was normal. Chest x-ray and angiotensin conversion enzyme levels were not suggestive of sarcoidosis.

During the course of the etiological investigation, SD-OCT revealed a slight increase in subretinal fluid

suggesting CNV activity. The patient was immediately submitted to an intravitreal bevacizumab injection in OS with resolution of subretinal fluid. However, 3 months later there was recurrence of subretinal fluid and a second intravitreal bevacizumab injection was performed. This resulted in definitive resolution of subretinal fluid with progressive fibrosis of the subretinal neovascular membrane (figure 4). Best corrected visual acuity in OS improved from 20/400 to 20/125, remaining stable at the last follow-up, 4 years after the last injection.

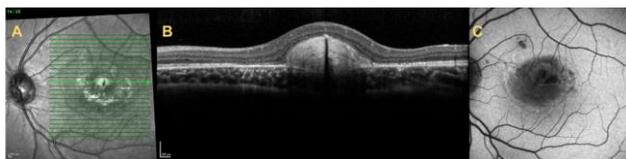


Figure 4 - Red-free fundus photograph (A) and macular SD-OCT (B) confirmed resolution of subretinal fluid and fibrosis of the subretinal neovascular membrane, resulting in macular hypofluorescence in fundus autofluorescence (C).

DISCUSSION

The diagnosis and management of CNV in children is considered challenging for several reasons – its infrequency, the usual delay in presentation, the limited data on natural history and the lack of randomized or controlled clinical trials regarding treatment options⁵. Besides hereditary macular dystrophies and inflammation, idiopathic CNV is a relatively common subtype in younger patients^{1,6}. These patients usually do not have a significant refractive error and CNV is usually unilateral, which was the case with our patient⁶.

The main differential diagnosis considered in this case were infectious causes (toxoplasma and toxocara being the most suspected agents) and also neoplastic causes. However infectious serologies were negative and ocular ultrasound along with MRI of the brain and orbits were uncharacteristic for retinoblastoma or other malignancies of the central nervous system.

No standard treatment for CNV in children has yet been validated¹ but several management options have been used over the years, including watchful waiting⁵, submacular surgery^{7,8} and photodynamic therapy (PDT)⁹. In recent years, the use of anti-vascular endothelial growth factor (anti-VEGF) agents has become the most popular treatment modality in pediatric CNV¹⁰. Besides its most frequent use in retinopathy of prematurity (ROP), several reports have proved anti-VEGF (particularly

bevacizumab) efficacy in the treatment of children with secondary CNV related to Best Disease¹¹, optic nerve head drusen¹² and posttraumatic choroidal neovascularization¹³. A 2011 retrospective case series of 4 pediatric patients with CNV also concluded that intravitreal anti-VEGF treatment seemed to be effective, although authors assumed they did not know how these results would have differed from other treatment modalities, including observation⁵. In 2013 a retrospective case series of 36 patients with CNV, under 18 years of age, proved that mean visual acuity in eyes with subfoveal CNV treated with bevacizumab was better than eyes with regressed CNV, highlighting the importance of early diagnosis and treatment, despite the high probability of spontaneous regression³.

The use of anti-VEGF agents in the pediatric population remains controversial due to concerns regarding the safety profile of blocking VEGF in the systemic circulation of a growing child, particularly in premature infants with ROP^{3,14}. The long-term results of inhibiting VEGF function in children needs to be further evaluated before concluding that these agents are safe in children³. However several case reports and case series have not found local or systemic side effects from anti-VEGF use in the pediatric age group^{3,11,12}.

In our patient VEGF blockade induced regression of the CNV and resolution of subretinal fluid with a modest recovery of visual acuity and no reported ocular or systemic side effects.

It remains reasonable that CNV treatment in children should be tailored to each particular case, considering the evidence of CNV activity, visual impairment, child's age and health status. One should keep in mind that although anti-VEGF treatment seems to be more effective than waiting for spontaneous regression of CNV, further prospective studies are needed to fully understand the benefit and safety profile of this treatment in children.

REFERENCES

1. Barth T, Zeman F, Helbig H, Oberacher-Velten. Etiology and treatment of choroidal neovascularization in pediatric patients. *Eur J Ophthalmol*. 2016 Aug 4;26(5):388-93
2. Wilson ME, Mazur DO. Choroidal Neovascularization in children: report of five cases and literature review. *J Pediatric Ophthalmol Strabismus* 1998 Jan-Feb; 25(1):23-9

3. Rishi P et al. Choroidal neovascularization in 36 eyes of children and adolescents. *Eye (Lond)*. 2013 Oct; 27(10): 1158-1168.
4. Giasanti F et al. Photodynamic therapy for choroidal neovascularization in pediatric patients.
5. Kohly RP, Muni RH, Kertes PJ, Lam Wai-Ching. Management of pediatric choroidal neovascular membranes with intravitreal anti-VEGF agents: a retrospective consecutive case series. *Can J Ophthalmol* 2011; 46:46–50
6. Spaide, RF. Choroidal neovascularization in younger patients. *Current Opinion in Ophthalmology* 1999, 10:177–181
7. Jain K, Shafiq AE, Devenyi RG. Surgical outcome for removal of subfoveal choroidal neovascular membranes in children. *Retina* 22:412–417, 2002
8. Daniels AB et al. Idiopathic subfoveal choroidal neovascular membrane in a 21-month-old child: Ultrastructural features and implication for membranogenesis. *J AAPOS* 2010;14:244-250
9. Mimouni KF, Bressler SB, Bressler NM. Photodynamic Therapy With Verteporfin for Subfoveal Choroidal Neovascularization in Children. *Am J Ophthalmol* 2003;135:900–902
10. Avery RL. Extrapolating anti-vascular endothelial growth factor therapy into pediatric ophthalmology: Promise and concern. *J AAPOS* 2009; 13:329-331
11. Leu J, Schrage NF, Degenring RF. Choroidal neovascularisation secondary to Best's disease in a 13-year-old boy treated by intravitreal bevacizumab. *Graefe's Arch Clin Exp Ophthalmol* (2007) 245:1723–1725
12. Knape RM et al. Intravitreal bevacizumab treatment of bilateral peripapillary choroidal neovascularization from optic nerve head drusen. *J AAPOS* 2011;15:87-90
13. Piermarocchi S, Benetti E, Fracasso G. Intravitreal bevacizumab for posttraumatic choroidal neovascularization in a child. *J AAPOS* 2011;15:314-316
14. Avery RL. Are there safety concerns with bevacizumab for ROP? Presented at: Retina World Congress; Feb. 23-26, 2017; Fort Lauderdale

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