Combined hamartoma of the retina and retinal pigment epithelium: OCT images and a case report of a clinical evolution since 1998

Hamartoma combinado de retina e epitélio pigmentar: imagens de OCT e relato de caso clínico com acompanhamento evolutivo desde 1998

João Borges Fortes Filho[1], Paula Gabriela Batista dos Santos[2], Lucas Borges Fortes[2], Isabel Habeyche Cardoso[3], Humberto Lubisco Filho[4]

ABSTRACT

The combined hamartoma of sensorial retina and pigmentary epithelium is a congenital and benign pseudo-tumoral and slightly elevated lesion, located most times at the posterior pole, affecting macula, peripapillary region, but sometimes situated at the peripheral retina. This paper describes a clinical case of a patient who has been followed since 1998 presenting convergent strabismus and severe visual loss in his right eye since born due to a supra papillary lesion and introduces some optical coherence tomography, fluorescein angiography and ecographic images of this lesion. A 9-year-old white boy presented with visual acuity of counting-fingers in the right eye and 20/20 on the left eye since first consultation in 1998. On inspection presented convergent strabismus in the right eye. The biomicroscopic examination and intraocular pressures were normal in both eyes. The ophthalmoscopic examination of the right eye revealed a suprapapillary lesion, slightly elevated with pigmented limits and a white-blue coloration centrally. There was retinal vascular dilation, tortuosity and capillary *telangectasias* over the lesion. The fluorescein angiography showed hyperfluorescence coming from the dilated capillaries and mild leakage at the late phases. This patient had OCT, angiographic and clinical follow-up since then without important changes over the lesion. The combined hamartoma of the retina and retinal pigment epithelium is a benign congenital pseudo-tumoral lesion that can be found at macular area, juxtapapillary or at the peripheral retina. The differential diagnosis with the malignant intraocular tumors has clinical relevance due to the better prognosis.

Keywords: Hamartoma/diagnosis; Pigment epithelium of eye/physiopathology; Eye neoplasms; Diagnosis, differential

[1]Professor de Oftalmologia da Faculdade de Medicina da Universidade Federal do Rio Grande do Sul – UFRGS - Porto Alegre (RS), Brasil; Doutorando em Oftalmologia pela Universidade Federal de São Paulo – UNIFESP - São Paulo (SP), Brasil; Coordenador do Curso de Especialização em Oftalmologia do Hospital Banco de Olhos de Porto Alegre - Porto Alegre (RS), Brasil;
[2]Residentes do Curso de Especialização em Oftalmologia do Hospital Banco de Olhos de Porto Alegre - Porto Alegre (RS), Brasil;
[3]Preceptora do Setor de Retina do Curso de Especialização em Oftalmologia do Hospital Banco de Olhos de Porto Alegre - Porto Alegre (RS), Brasil;
[4]Chefe do Setor de Retina do Curso de Especialização em Oftalmologia do Hospital Banco de Olhos de Porto Alegre - Porto Alegre (RS), Brasil.
Recebido para publicação em: 05/01/2007 - Aceito para publicação em 27/02/2007

Introduction

Tumors of the retinal pigment epithelium (RPE) are uncommon. They are classified into four groups, including congenital hamartoma of the RPE, congenital hypertrophy of the RPE, adenoma or adenocarcinoma of the RPE and combined hamartoma of the retina and RPE. [1]

Combined hamartomas of the RPE and sensory retina are rare congenital abnormalities which may occur anywhere in the fundus. The lesion is a benign pseudo-tumoral and slightly elevated, located most of times at the posterior pole, affecting macula and peripapillary region. Sometimes it can be situated at the peripheral retina.

Usually, the diagnosis is made since childhood and the main reason for consultation is reduction of vision. The combined hamartoma of the RPE is characterized by a proliferation of the retinal pigmentary epithelium and retinal gliosis leading to a disorganization of the retina, the papilla and the vitreous adjacent. [2-3]

This paper describes a clinical case of a patient who has been followed since 1998 due to a suprapapillary combined hamartoma of the RPE and introduces some images of Optical Coherence Tomography (OCT) and fluorescein angiography and ultrasonographic features of this kind of lesion.

Clinical Case

A 9-year-old white boy, presented with visual acuity of counting-fingers and convergent strabismus in the right eye since first consultation in 1998. The left eye was unremarkable and biomicroscopic examination and intraocular pressures were normal in both eyes. The ophthalmoscopic examination of the right eye revealed the existence of a suprapapillary and slightly elevated lesion with pigmented limits and a white-gray color centrally. There was retinal vascular dilation, tortuosity and capillary *telangectasias* over the lesion, some subretinal fluid and a mild radial macular traction. There was no macular edema or exudation. (Figure 1)

Fluorescein angiography revealed striking vascular change over the lesion, hyperfluorescence coming from the dilated capillaries and mild leakage of dye at the late phases. Part of the pigment epithelium obscured the upper temporal retina. (Figure 2)

Echography disclosed only a slight elevated juxtapapillary lesion and some vitreous alterations. The retinal peak was separated from the choroido-scleral peak by an acoustically silent space suggested of thick and minimally detached retina. The echographically silent subretinal space would correspond to a serous detachment of the retina. (Figure 3)

OCT findings at the site of the combined hamartoma disclosed no posterior vitreous detachment, vitreous tractions and nor epiretinal membrane, but showed retinal disorganization, retinal thickening, retinal edema, subretinal fluid and retinal pigmentary epithelium irregularities. The thickened retina showed a hyperreflective surface and a deep shadowing. The retina separated from the mass and the macular region appeared to be normal despite the low visual acuity in this eye and also the choroidal space showed no abnormalities (Figure 4).

This patient had OCT, fluorescein angiography, ultrasonography and clinical follow-up since then without any remarkable changes over the lesion.

Discussion

Combined hamartoma of the sensory retina and RPE is a supposed rare benign tumor. It is probably a congenital unilateral tumor whose pathogenesis has not yet been elucidated. The fact that many cases are diagnosed in young children and infants lends support to the hypothesis that the lesion is congenital. [4-5] The combined hamartoma are usually asymptomatic and are often discovered coincidentally if the patient has no strabismus or visual impairment.

In 1984, Schachat et al. published 60 cases collected from the members of the Macula Society (USA) and described the clinical features and natural course of this benign lesion. They noted that the lesion was typically pigmented, elevated, had vascular tortuosity, vitreoretinal changes in around more than 80% of the cases and exudation in around 7% of the patients observed. [6]

The diagnosis is clinical and the patient can be thoroughly examined by retinal angiography, ocular ultrasonography and OCT. The clinical features and the ophthalmoscopic appearance of the combined hamartoma vary according to whether the lesion is in a juxtapapillary or a peripheral location. The juxtapapillary lesions seem to be more common in males and appear as a solitary mass adjacent to or overlying the optic disc, with variable amounts of pigmentation, vascularity, and typical gray-white tissue. Some larger lesions surround the entire disc margin and extend temporally to produce elevation of the fovea. The larger retinal vessels within and overlying the lesion are often stretched or tortuous and are obscured by white fibroglial tissue at the

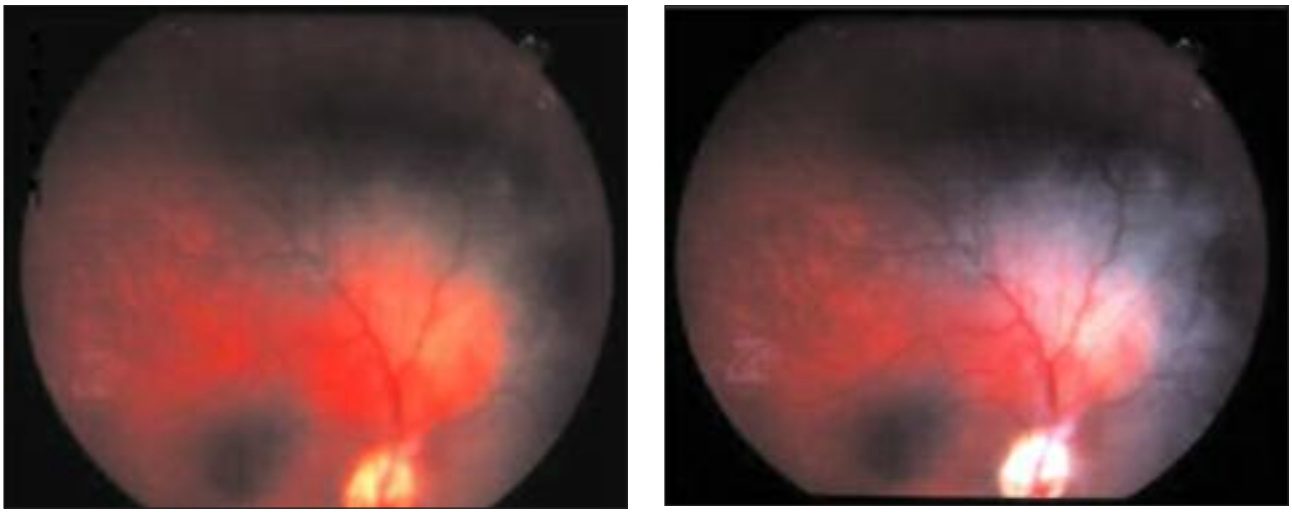

Figure 1: The ophthalmoscopic examination of the right eye revealed the existence of a suprapapillary and slightly elevated lesion with pigmented limits and a typical gray-white tissue over the lesion. There was retinal vascular dilation, tortuosity and capillary *telangectasias.* There was no macular edema or exudation. (left image: year 1998, right image: year 2006)

vitreoretinal interface. This surface glial tissue tends to gradually contract, leading to further stretching of the blood vessels and retinal striae, which may distort the fovea. [5] (Figures 1 and 2)

In this disorder, it is important to eliminate retinoblastoma, choroidal melanoma and also other malignancies because confusion of pigmented lesions is possible despite combined hamartoma of retina and RPE typically presents with a history of reduced acuity or the onset of strabismus. Some patients, especially those with lightly pigmented lesion, may be mistaken for *Toxocara canis*. [7]

Clinically, the lesion is elevated, with a variably pigmented outer portion and a lighter central core of dilated tortuous vessels, and gliosis like an epiretinal membrane. \

The ophthalmoscopic and fluorescein angiographic features of the combined hamartoma are widely described in the literature, while ultrasonographic and OCT findings are very rarely reported.

Giuffre, in 1986, described about the echographic findings in these lesions. The combined hamartoma is a developmental tumor characterized by a plaque of thickened retinal pigment epithelium, gliotic and disorganized retina, tortuous retinal and disc vessels, preretinal fibrosis. A-scan echography showed that, in the tumor area, the retinal peak was separated from the choroido-scleral peak by an acoustically silent space. B-scan echography revealed a thick and detached retina. The echographically silent subretinal space corresponds to a serous detachment of the macular retina. This lesion, infrequently reported in association with the combined hamartoma, probably depends on the exudation of the retinal vessels and the traction of the hamartoma on the macula. In addition, the echography allows to exclude an extension of the lesion to the choroid and the sclera. [8] In the patient here related, the echography showed no extension of the lesion to the external part of the eye-globe but slightly vitreous alterations over the suprapapillary region. (Figure 3)

Recently, OCT has assumed an important role in the management of numerous ocular conditions. With regard to ocular oncology, OCT can illustrate retinal changes overlying choroidal tumors and contributing to the differential diagnosis. Some of these features include photoreceptor loss, intraretinal edema, and retinal thinning overlying choroidal nevus; fresh subretinal fluid with preservation of photoreceptors overlying choroidal melanoma; and intraretinal edema, retinoschisis, and retinal thinning overlying irradiated choroidal melanoma. The OCT features of tumors of the retinal pigment epithelium include typical findings of peaked vitreoretinal traction and retinal disorganization with combined hamartoma of the RPE, full-thickness retinal shadowing with congenital simple hamartoma, and photoreceptor loss and retinal thinning overlying congenital hypertrophy of the retinal pigment epithelium.

For combined hamartoma of retina and RPE, OCT provides valuable information regarding the status of the retina and the retinal pigment epithelium and can be useful in ascertaining reasons for visual loss. [9] OCT can show a thickened retina, a hyperreflective surface and a

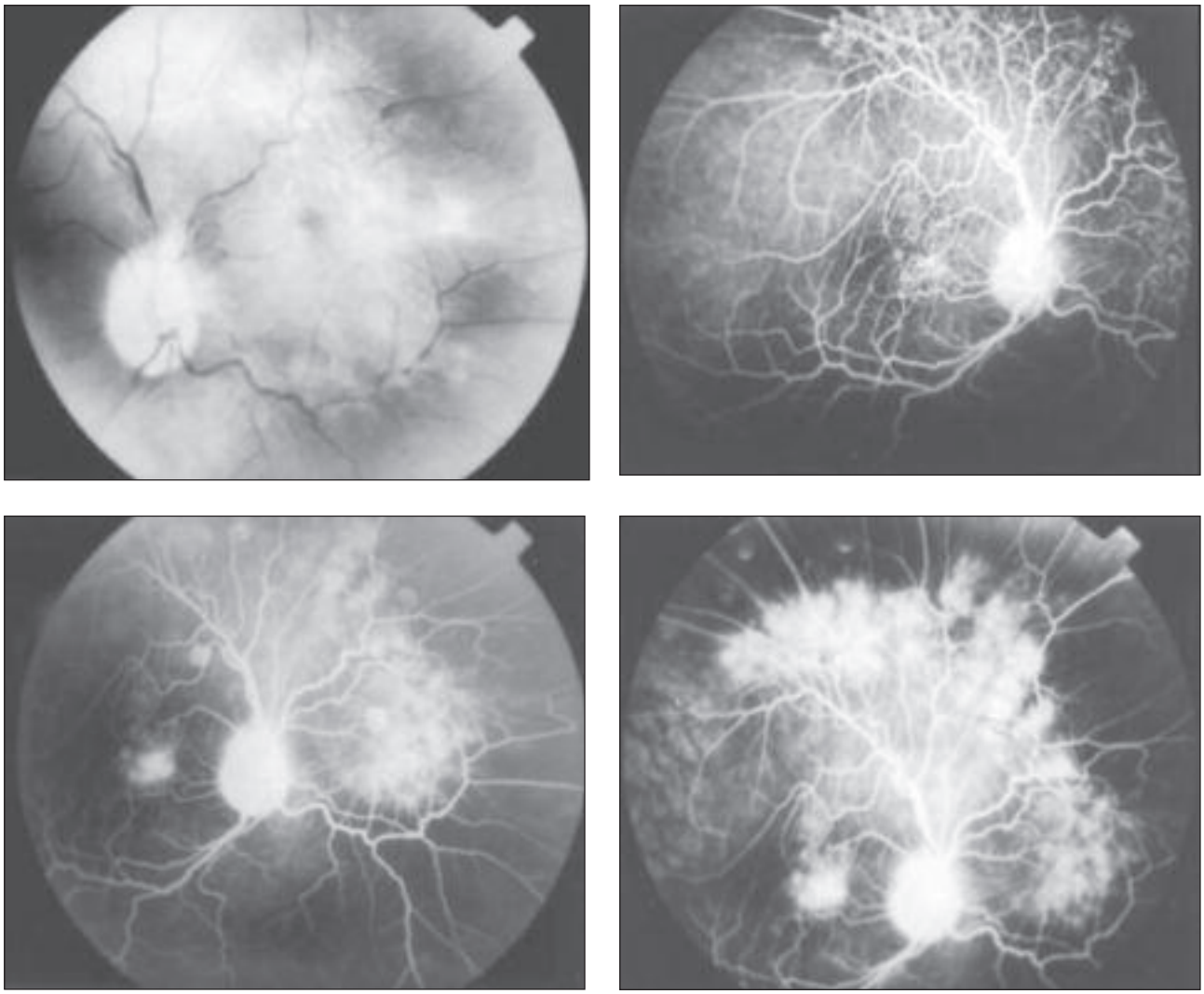

Figure 2: Black and white image of the typical gray-white tissue overlying the optic disc and superior retina (superior left image). Fluorescein angiography showing striking vascular change over the lesion (right superior image), hyperfluorescence coming from the dilated capillaries and mild leakage at the late phases (both inferior images). Part of the pigment epithelium obscured the upper temporal retina (inferior right image).

deep hyporreflective shadowing. The choroidal layer with the coriocapillary looking intact can make dif\ferential diagnosis with choroidal melanomas. [10] In the patient here described, the OCT did not showed peaked vitreoretinal traction, but only the retinal thickening, pigment epithelium disorganization and the hyporreflective deep shadowing. (Figure 4)

There is no established treatment for the combined hamartoma. In those cases that produce visual loss because of retinal traction in the fovea, vitrectomy and membrane peeling have been used in an attempt to improve the visual acuity. [5,11,12] Shields, presented in 2005, eleven cases of patients with combined hamartoma of the RPE studied by OCT and concluded that OCT can provide important information regarding the vitreoretinal interface of this abnormalities and could influence surgical decision. [13]

Combined hamartomas of the retina and RPE are also described in patients with neurofibromatosis type 1 (NF-1) and type 2 (NF-2). Vianna et al., in 2001, reported this association on a child with NF-1, who presented lesions in both eyes. The diagnosis of bilateral combined hamartoma was performed on the basis of the ophthalmoscopic appearance and NF-1 was diagnosed following the current international clinical criterion, supplemented by neuroimaging findings and concluded that despite the extreme rarity, this association was not coincidental, as the presence of a hamartomatous retinal lesion in a patient with a systemic hamartomatous neuroectodermic disease would be, at least, rational.

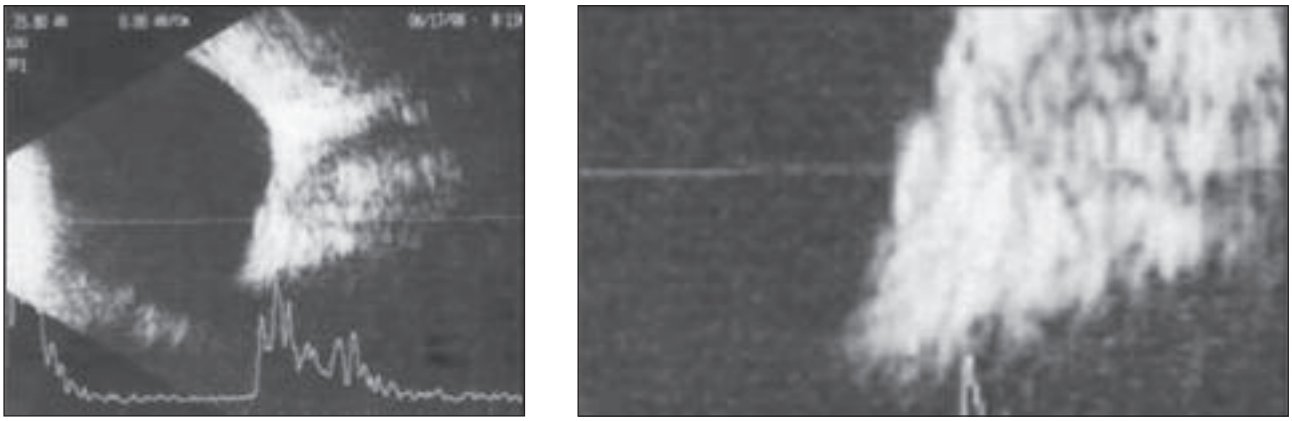

Figure 3: Echography disclosed a slight elevated juxtapapillary lesion with mild vitreous alterations (left image). The retinal peak was separated from the choroido-scleral peak by an acoustically silent space suggested of thick and minimally detached retina. The echographically silent subretinal space would correspond to a serous detachment of the retina (right image).

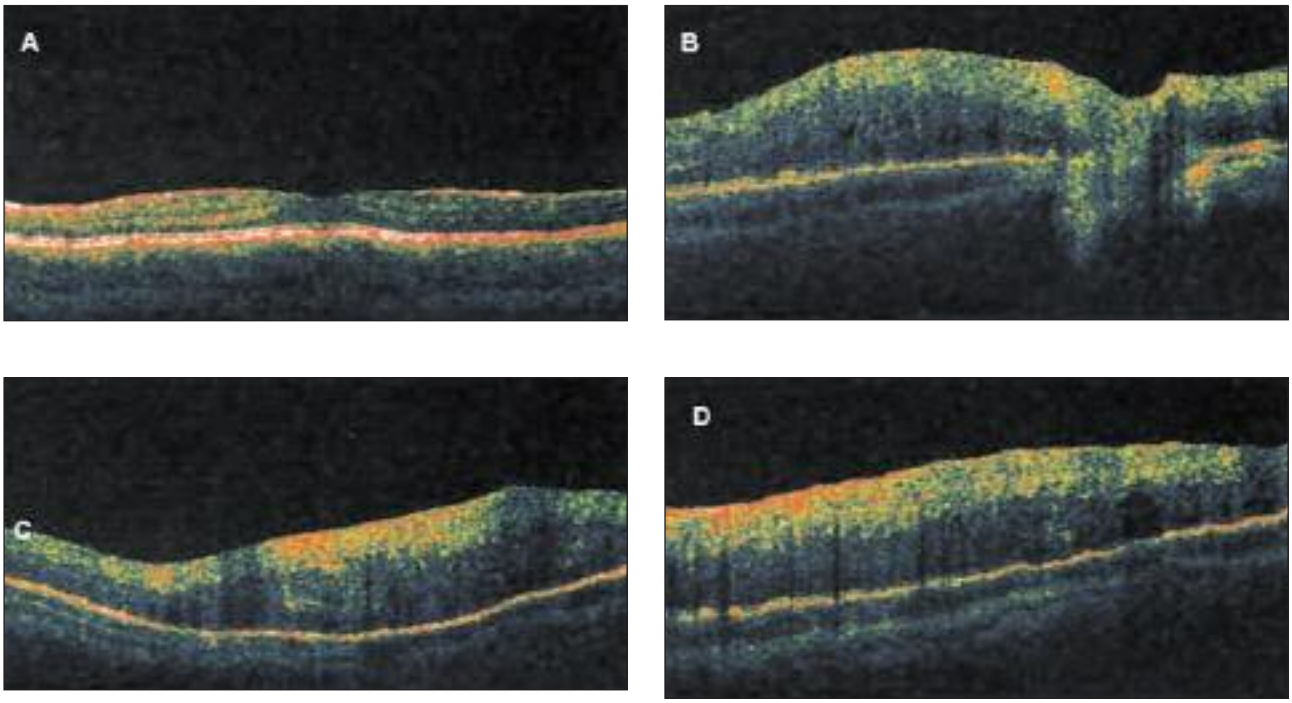

Figure 4 A: OCT image over the retina separated from the mass showing the macular region appearing to be normal and also the choroidal space without abnormalities. There are no posterior vitreous detachment, vitreous tractions and nor epiretinal membrane. **B:** At the site of the combined hamartoma, OCT disclosed retinal thickening, retinal edema, subretinal fluid and retinal pigmentary epithelium irregularities. **C and D:** The thickened retina showed a hyperreflective surface and a deep shadowing.

Thus, NF-1 must be excluded in patients with combined hamartomas of the RPE. [14] Tsai et al. also reported a combined hamartoma of RPE in a 6-year-old child as the presenting sign of NF-1. The patient was followed closely for three years but received no treatment. Observation over these years revealed no significant change in the patient's visual acuity. A referral to the specialized neurofibromatosis clinic resulted in a diagnosis of NF-1, and the patient continues to be observed for further systemic manifestations of this disease. [15]

Sivalingam et al., in 1991, described a young patient with combined hamartoma of the RPE who developed bilateral acoustic neuromas and meningiomas of the cervical-medullary junction and fifth cranial nerve. This case illustrates the association between these lesions and NF-2 and the authors recommended that children with a combined hamartomas should be

screened for NF-2. [16]

Combined hamartoma present in most times as an isolated and a unilateral lesion. Blumenthal, in 1998, related a bilateral presentation of this developmental abnormality. [17]

Progression is stationary; nevertheless a reduction in visual acuity can be related to an epiretinal membrane, a neovascular subretinal membrane or a macular dragging as occurred in the patient here described. This case-report presents a young, otherwise healthy boy with a unilateral example of combined hamartoma of the retina and RPE located in the juxtapapillary area, affecting visual function by macular indirect damage and causing strabismus and amblyopia secondarily.

Laghmari, also described a case of combined hamartoma of the RPE in an 8-year-old girl with strabismus and amblyopia. The fluorescein angiography and the echography allowed excluding a malignant tumor of the retina or the choroid. The clinical follow-up confirmed that the lesion was stationary. [18]

Despite combined hamartomas of the RPE are benign lesions, some eyes have been enucleated for melanoma or retinoblastoma suspicion. [19] Font et al. reported two cases in which apparent growth of the lesion was observed. In case 1, the eye was enucleated with a presumed diagnosis of juxtapapillary malignant melanoma. Histopathologically, the enucleated globe showed an elevated peripapillary mass containing disorganized retinal tissue intermixed with vascular and glial elements as well as tubules of proliferating retinal pigment epithelium. The authors also have summarized the clinical features of 53 patients with combined hamartoma between 1952 and 1988 excluding the cases compiled by Schachat in the Macular Society Collaborative Study. While the latter study found an equal sex predilection among their cases, the authors found a 70% male preponderance among the 53 patients. Of the 54 lesions observed in 53 patients, 76% were juxtapapillary, 17% were macular, and 7% were peripheral. Furthermore, periodic follow-up examination disclosed apparent enlargement of the mass in six patients, five of whom underwent enucleation of the globe for suspected melanoma. [20]

Hayasaka, related a clinical case of an 11-year-old japanese girl who had a greenish-gray, slightly elevated lesion at the optic disc and juxtapapillary retina of the right eye that was diagnosed as a combined hamartoma of RPE. A gliotic epiretinal membrane partially covered the lesion. Tortuous retinal vessels, which leaked fluorescein dye, were noted ophthalmoscopically. The lesion remained stable during a follow-up period of 1 year. After reviewing the japanese literature, the author concluded that these abnormalities may not be as rare in Japan, as previously thought. [21] Maybe this same situation could also to happen in Brazil, once we could not found many articles published in the Brazilian literature on this subject.

Abreu et al., in 1991, described ophthalmoscopic and ultrasonographic aspects of this lesion in two patients. [22]

Biccas Neto, in 2006, revised about the use of the OCT in retinal diseases after macular vitreous-interface complications and concluded that this examination is a new and powerful diagnostic tool that has challenged traditional concepts in retinal diseases, bringing up new paradigms in diagnosis and treatment. [23]

Conclusion

Combined hamartomas of the RPE are of unusual presentation benign tumor that can be easily mistaken for malignant processes such as retinoblastoma or choroidal melanoma depending on the age of the diagnosis. Knowledge of the clinical aspect is essential to differentiate this condition from the malignant retinal processes to prevent unnecessary enucleation. This pseudo tumor can progress despite of its benign character and regular follow-up is essential and can improve the visual prognosis.

Ophthalmologists should also be aware of the association with neurofibromatosis and consider this diagnosis when retinal findings of combined hamartomas are observed in children. Ancillary diagnostic studies can be useful specially OCT and fluorescein angiography images.

Resumo

O hamartoma combinado de retina e epitélio pigmentar é uma lesão pseudotumoral congênita e benigna, de coloração azul-esbranquiçada centralmente, discretamente elevada, que pode acometer as áreas macular, peripapilar ou periférica da retina. Este trabalho descreve o caso de um paciente com acompanhamento periódico desde 1998 por baixa acuidade visual e estrabismo convergente no olho direito desde o nascimento, secundário à presença desta lesão, além de exibir imagens angiográficas, ecográficas e de tomografia de coerência óptica da alteração. Paciente de nove anos de idade, masculino, branco, com acuidade visual de conta dedos no olho direito e 6/6

no olho esquerdo consultou em 1998 por estrabismo convergente e baixa visão no olho direito. A biomicroscopia e a pressão intra-ocular eram normais nos dois olhos, assim como a fundoscopia no olho esquerdo. No olho direito havia uma lesão suprapapilar discretamente elevada com bordas pigmentadas e coloração azul-esbranquiçada centralmente. Havia vasos retinianos tortuosos, dilatados e telangectasias capilares por toda a extensão da lesão. A angiografia fluoresceínica evidenciou hiperfluorescência originada dos capilares dilatados e vazamento discreto nas fases tardias. Este paciente realizou seguimento periódico com tomografia de coerência óptica e ecografia e não mostrou alterações detectáveis em extensão ou em altura na lesão, desde o exame inicial. O hamartoma combinado de retina e epitélio pigmentar pode acometer as áreas macular, peripapilar ou periféricas da retina. O diagnóstico diferencial tem relevância devido ao prognóstico, pois deverão ser afastados tumores malignos da infância com diferentes indicações de tratamento.

Descritores: *Hamartoma/diagnóstico; Epitélio pigmentado ocular/fisiopatologia, Neoplasias oculares; Diagnóstico diferencial*

REFERENCES

1. Shields CL, Shields JA, Marr BP, Sperber DE, Gass JD. Congenital simple hamartoma of the retinal pigment epithelium: a study of five cases. Ophthalmology. 2003; 110(5):1005-11.
2. Hamdi R, De Korvin H, Speeg-Schatz C, Szwarcberg J. [Combined hamartoma of the retina and retinal pigment epithelium. Four case studies]. J Fr Ophtalmol. 2006;29(3):e6. French.
3. Vandeveer M. Combined hamartoma of the retinal pigment epithelium and sensory retina. J Am Optom Assoc. 1986; 57(11):836-8.
4. Cardell BS, Starbuck MJ. Juxtapapillary hamartoma of the retina. Br J Ophthalmol. 1961; 45:672-7.
5. Shields JA, Shields CL. Tumors and related lesions of the pigment epithium. In: Shields JA, Shields CL, editors. Intraocular tumors: a text and atlas. Philadelphia: WB Saunders; 1992. p. 437-60.
6. Schachat AP, Shields JA, Fine SI, Sanborn GE, Weingeist TA, Valenzuela RE, Brucker AJ. Combined hamartoma of the retina and retinal pigment epithelium. Ophthalmology. 1984; 91(12):1609-15.
7. Gass JD. Combined pigment epithelial and retinal hamartoma. In: Gass JD, editor. Stereoscopic atlas of macular diseases: diagnosis and treatment. 4th ed. St. Louis: Mosby; 1997. p. 824-31.
8. Giuffre G, Cascio G. [Ultrasonic aspects of combined hamartoma of the pigment epithelium and retina]. J Fr Ophtalmol. 1986; 9(4):285-9. French.
9. Shields CL, Materin MA, Shields JA. Review of optical coherence tomography for intraocular tumors. Curr Opin Ophthalmol. 2005; 16(3):141-54.
10. Rodrigues EB, Teixeira LF, Shields CL, Meyer CH, Farah ME. Tumores da coróide, da retina e do nervo óptico. In: Farah ME, organizador. Tomografia de coerência óptica - OCT. Texto e atlas. Rio de Janeiro: Cultura Médica; 2006. p. 305-14.
11. McDonald HR, Abrams GW, Burke JM, Neuwirth J. Clinicopathologic results of vitreous surgery for epiretinal membranes in patients with combined retinal and retinal pigment epithelial hamartomas. Am J Ophthalmol. 1985; 100(6):806-13.
12. Richard G. Retinal and pigment epithelial hamartomas. In: Richard G, editor. Fluorescein and ICG angiography. 2nd ed. New York: Thieme; 1998. p. 306-15.
13. Shields CL, Mashayekhi A, Dai VV, Materin MA, Shields JA. Optical coherence tomographic findings of combined hamartoma of the retina and retinal pigment epithelium in 11 patients. Arch Ophthalmol. 2005; 123(12):1746-50.
14. Vianna RN, Pacheco DF, Vasconcelos MM, de Laey JJ. Combined hamartoma of the retina and retinal pigment epithelium associated with neurofibromatosis type-1. Int Ophthalmol. 2001; 24(2):63-6.
15. Tsai P, O'Brien JM. Combined hamartoma of the retina and retinal pigment epithelium as the presenting sign of neurofibromatosis-1. Ophthalmic Surg Lasers. 2000; 31(2):145-7.
16. Sivalingam A, Augsburger J, Perilongo G, Zimmerman R, Barabas G. Combined hamartoma of the retina and retinal pigment epithelium in a patient with neurofibromatosis type 2. J Pediatr Ophthalmol Strabismus. 1991; 28(6):320-2.
17. Blumenthal EZ, Papamichael G, Merin S. Combined hamartoma of the retina and retinal pigment epithelium: a bilateral presentation. Retina. 1998; 18(6):557-9.
18. Laghmari A, el Moussaif H, Ouazzani B, Boutimzine N, Daoudi R, Mohcine Z. [Hamartoma of the pigment epithelium and retina. Apropos of a case]. J Fr Ophtalmol. 1997; 20(4):297-301. French.
19. Caruso J, Miller KB, Pietrantonio JJ. Combined hamartoma of the retina and retinal pigment epithelium. Optom Vis Sci. 1993; 70(10):860-2.
20. Font RL, Moura RA, Shetlar DJ, Martinez JA, McPherson AR. Combined hamartoma of sensory retina and retinal pigment epithelium. Retina. 1989; 9(4):302-11. Review.
21. Hayasaka S, Kanamori M, Furuse N, Ugomori S, Setogawa T. Combined hamartoma of the retina and retinal pigment epithelium of the juxtapapillary retina and optic disc. Ophthalmologica. 1988; 197(1):42-6.
22. Abreu GB, Toledo Filho MB, Abreu M. Hamartoma combinado de retina e epitélio pigmentar da retina: a propósito de dois casos. Arq Bras Oftalmol. 1991; 54(4 Supl).
23. Biccas Neto L. A tomografia de coerência óptica nas doenças adquiridas da interface vítreo-macular. Rev Bras Oftalmol. 2006; 65(2):124-30.

ENDEREÇO PARA CORRESPONDÊNCIA
Dr. João Borges Fortes Filho
Curso de Especialização em Oftalmologia
Hospital Banco de Olhos de Porto Alegre
Rua Eng. Walter Boehl, 285, Bairro Vila Ipiranga,
CEP 91360-090 - Porto Alegre - RS
Tel: (51) 3344-1972, Fax: (51) 3247-2122
E-mail: jbfortes@cursohbo.com.br