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Multimodal Imaging of Retinal Astrocytic Hamartoma Associated with Congenital Hypertrophy of Retinal Pigment Epithelium

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KEYWORDS

retinal astrocytic hamartoma, congenital hypertrophy of retinal pigment epithelium

INTRODUCTION

Hamartoma is a nodular malformation, with a single or multiple malformations, it is a recognized prenatal developmental abnormality. This benign tumor lesion has the same histological components of normal parenchyma, but these components are arranged haphazardly which disrupts normal function. Hamartomas usually remain connected with the tissue of origin; as is the case with pulmonary hamartoma or the splenic hamartoma. The exact incidence of retinal astrocytic hamartoma (RAH) is not well known, but it is estimated at one case per 100 000 births per year [1]. The astrocytic hamartoma is neuroglial tissue and produces astrocytes within the optic nerve, [2] and consequently is often appears within papillary region.

Congenital hypertrophy of retinal pigment epithelium (CHRPE) is also a developmental anomaly occurring during differentiation of the retina from the ectoderm. This lesion can be observed in 1 - 4.4 % of the general population regardless of gender and age [3].

The difference between these congenital lesions is the site of differentiation; glial cells in AH, and retinal pigment epithelium in CHRPE. AH is more often observed in patients with tuberous sclerosis [4], and maybe a precursor to central nervous system hamartomas. CHRPE can be isolated to the retina or present with familial adenomatous polyposis (FAP), especially when CHRPE lesions are multiple, grouped and bilateral. The coexistence of these two lesions types in the same patient is rare [5], within this article, we present the case of a 25-year old female who presented with AH in the right eye and CHRPE in the left eye.

CASE REPORT

A previously healthy, 25 year old female, presented with a central scotoma in her right eye, 3 days later this scotoma resolved spontaneously. Visual acuity at presentation was 0.9 decimal scales in both eyes. Examination of the anterior segment in both eyes was normal.

Right eye - RAH

The fundus examination revealed in the right eye a juxta-papillary lesion in the temporal area. The lesion was white-yellowish, semi-translucent, non-calcified and mildly protruding into the vitreous (Fig. 1A and Fig. 1B). Optical coherence tomography (OCT) of the right eye lesion showed a nodular lesion extending from optic nerve temporally to perifoveal area, and was 2468 μm x 3015 μm x 1099 μm (horizontal diameter x vertical diameter x thickness) (Fig. 1C, Fig 1D). A continuous transition from an abnormal retina towards a normal retina was observed on OCT images (thicker, with posterior shadowing, with no "moth-eaten spaces") (Fig. 2A). The outer plexiform layer showed distinct cystic spaces. Ultrasonography (US) of the right eye lesion showed a nodular hyper-reflective lesion with no posterior shadowing, nor intra-tumor calcifications, and was useful to rule out a possible retinoma /retinoblastoma (Fig. 5B). OCT-RNFL (OCT-retinal nerve fiber layer) thickness showed an abnormal thickness in temporal fibers and was correlated to visual field defect (enlarged blind spot) detected on visual field examination with Octopus 30 degree (Fig. 6).

At a later visit, Fluorescein angiography (FA) confirmed the vascularized nature of the lesion in the right eye (Fig. 3A 3B), another

hyper fluorescent nodular lesion was detected superonasally in the juxta-papillary area, and that lesion was not previously identified on fundus examination (Fig.3C Fig.3D). This second lesion was also confirmed by OCT (Fig. 2B) and angio OCT (Fig. 2C). Indocyanine green angiography (ICGA) did not show hyper-cyanescence in later images (Fig.3). Blue auto-fluorescence (BAF) showed a masking effect at the location of the tumor lesion (Fig. 5A).

Left eye - CHRPE

In the left eye, fundus examination revealed in the temporal periphery a CHRPE, a hyper-pigmented, round, flat lesion surrounded by a hypo-pigmented halo (Fig. 1E and Fig. 1F). OCT of the CHRPE in the left eye showed atrophy of the outer retina with thinning of outer nuclear layer (Fig. 1G). Fluorescein angiography (FA) showed a peri-papillary leakage due to dilated juxta-papillary vessels within the lesion.

The combination of clinical and imaging findings confirmed the diagnosis of juxtapapillary astrocytic hamartomas in the right eye and CHRPE in the left eye. A detailed clinical examination and imaging studies were done to rule out a possible tuberous sclerosis. The patient did not have any abnormal skin lesion (adenoma sebaceous, ash leaf spots or café-au-lait spots). Cardiac and pulmonary auscultation was normal. Brain MRI was normal and did not show any astrocytic nodule. The patient has no past medical history of epileptic seizure and no family history of phacomatosis, familial adenomatous polyposis or retinal tumors.

DISCUSSION

Lesions associated with RAH are often located outside the macula and remain asymptomatic; therefore detection is more likely to occur during routine fundus examination or during the workup of a patient with tuberous sclerosis. In the case reported here, the patient did not have any extra-ocular lesion, classically found in those with tuberous sclerosis. However, a secondary smaller RAH located in the superonasal juxtapapillary area (with confirmation on FA and OCT Fig. 2B, Fig. 3C, Fig. 3D) was observed close to the main temporally located astrocytic hamartoma. According to Roach et al. [6], the presence of this secondary lesion is a strong indication of the diagnosis of tuberous sclerosis. Moreover, the presence of a CHRPE in contralateral eye is also a minor indication of the diagnosis of tuberous sclerosis. Combined these criteria suggest the diagnosis of tuberous sclerosis in this patient, however as there was no extra-ocular involvement, the diagnosis was not confirmed, and we choose not to test for TSC1 and TSC2 mutations.

In tuberous sclerosis, RAH has been associated with, unilateral or bilateral, decreased visual acuity, metamorphopsias or scotoma(e) especially in cases with macular edema[7]. Isolated retinal RAH is usually asymptomatic [8]. In this case, the patient had a central scotoma in her right eye (Fig. 6), however this later resolved. In a study by Schields et al [9] in 15 cases of RAH, retinal alterations were observed in all retinal layers except outer retina (from ONL to RPE). In the present case, OCT revealed the presence of microcystic changes in outer plexiform layer in perimacular area (Fig. 2A).

Juxta-papillary highly vascularized RAH have been associated with self-limited episodes of exudation, with transitory symptomatic discomfort, as was case in the patient described herein who complained of central scotoma lasting 3-days. Microcystic changes in outer plexiform layer can occur with episodes of exudation. In general, when RAH presents in isolation it is not associated with exudation, which is in contrast with RAH presenting with concomitant tuberous sclerosis has been associated with exudative retinal detachment in extreme cases [10].

A thorough exam should include several imaging modalities including fluorescein angiography, as many retinal lesions may go undiagnosed with simple fundus examination. Patients elevated risk of tuberous sclerosis be seen more frequently. For example the case presented here, since the symptoms were transitory and since there is no treatment for RAH, this patients is being observed on an annual basis with a combination of clinical and imaging examination. To the best of our knowledge this is the second case of the RAH and CHRPE simultaneously presenting in contralateral eyes [5]. This combination could be a part of the larger tuberous sclerosis syndrome.

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Conflict of interest

The authors declare that they have no conflict of interest to the publication of this article.

Fig. 1

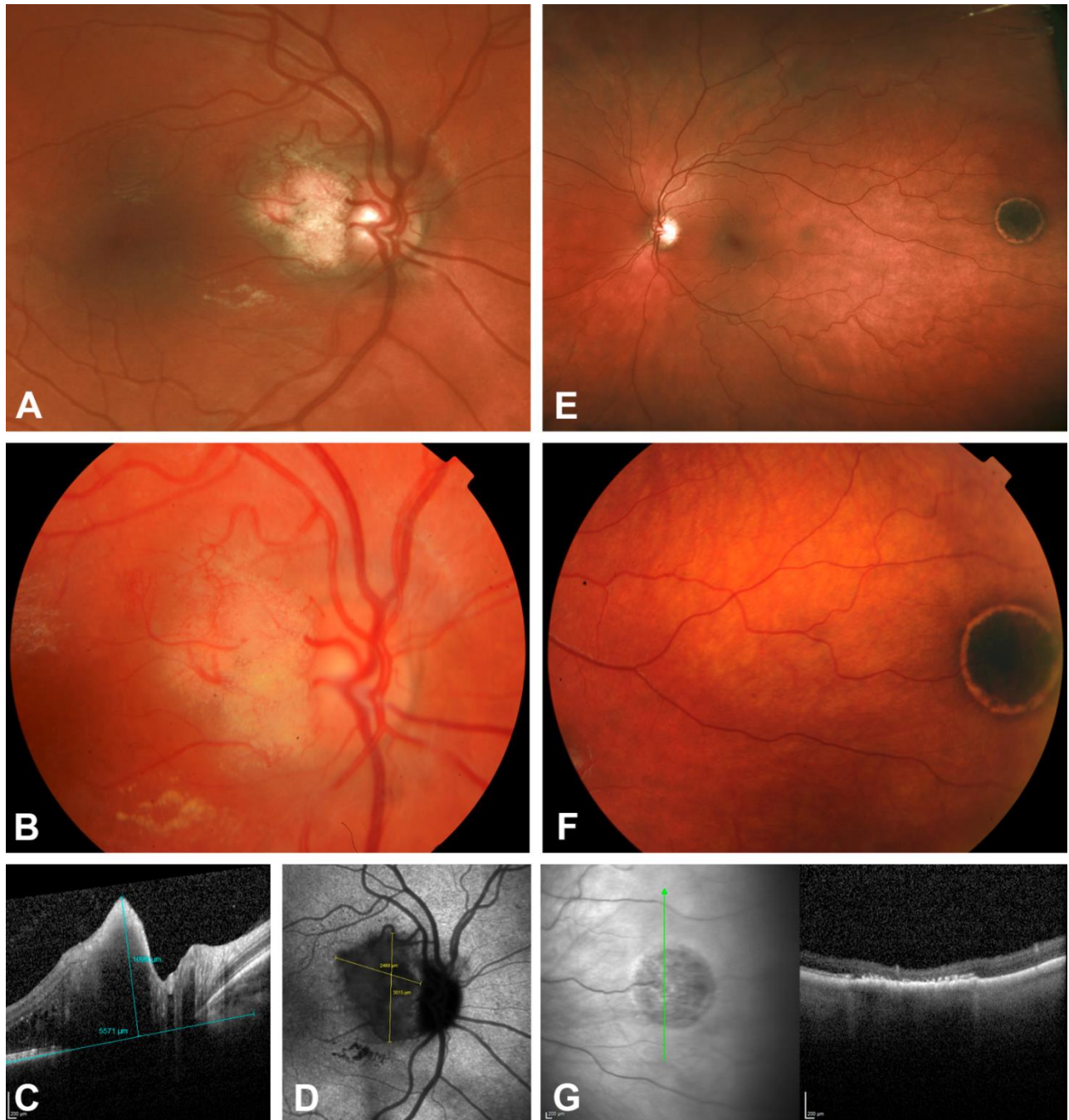


Fig. 1A Optos Photo of fundus of right eye showing an astrocytic hamartoma in the temporal juxtapapillary area. The astrocytic hamartoma appears as a white yellowish, poorly delimited lesion protruding toward the vitreous, with poorly visible cilioretinal artery within the tumour. Lipid exudations could also be seen in macular area. **Fig. 1B** Topcon Photo of the fundus of the right eye. **Fig. 1C** OCT images of the right optic nerve showing the astrocytic hamartoma. **Fig. 1D** ICG angiography at 30 minutes showing the astrocytic hamartoma as a hypocyanescent lesion. **Fig. 1E** Optos Photo of the fundus of the left eye showing the CHRPE in the temporal periphery. **Fig. 1F** Topcon Photo of the fundus of the left eye showing the CHRPE in the temporal periphery: hyperpigmented lesion of 2 disc diameters, surrounded by a clear hypopigmented halo. **Fig. 1G** OCT image centered at the CHRPE showing retinal thinning at the level of outer nuclear layer.

Fig. 2

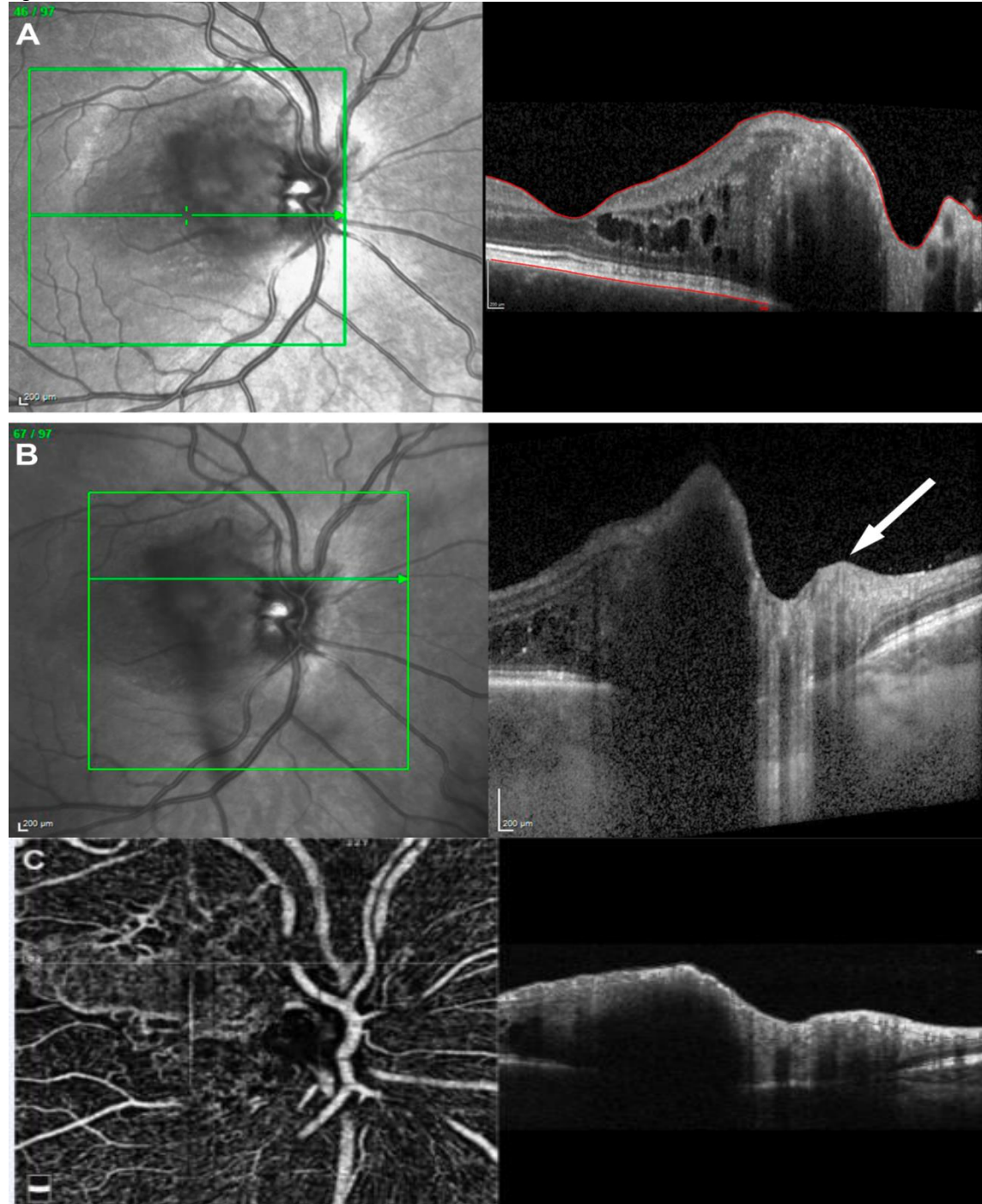


Fig. 2A OCT of the astrocytic hamartoma showing microcystic changes at the level of the outer plexiform layer. **Fig. 2B** OCT of the optic nerve in the right eye showing the second astrocytic hamartoma located superonasally, which was not seen on fundus examination. **Fig. 2C** Angio OCT compatible with a vascularized lesion in the ganglion cell layer

Fig. 3

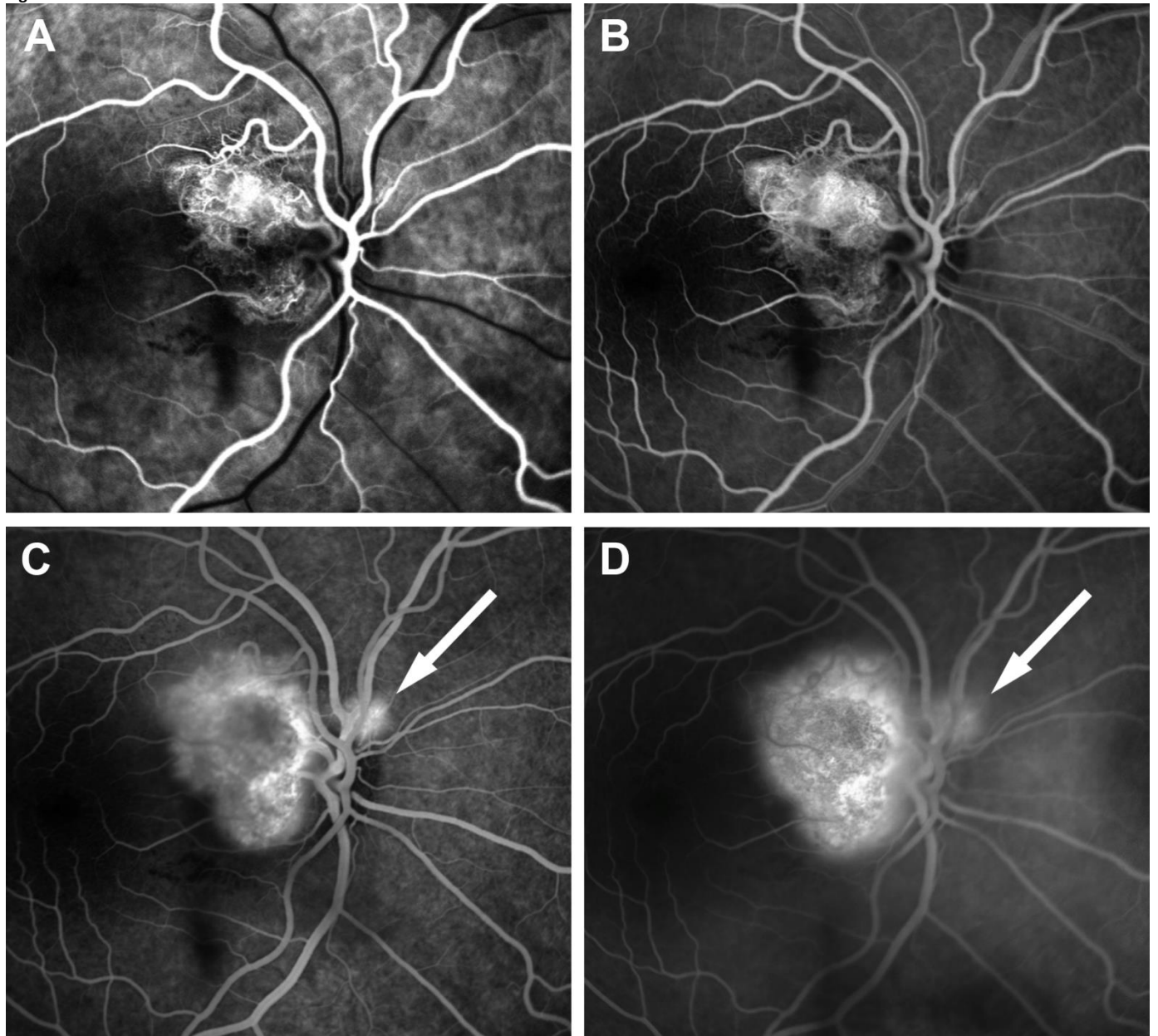


Fig. 3A, 3B, 3C, 3D Fluorescein angiography showing highly vascularised tumoral lesion in the temporal juxtapapillary area at different times respectively: 13 seconds, 18 seconds, 2 minutes and 11 minutes. **Fig 3C and Fig. 3D** show also the second astrocytic hamartoma (white arrow).

Fig. 4

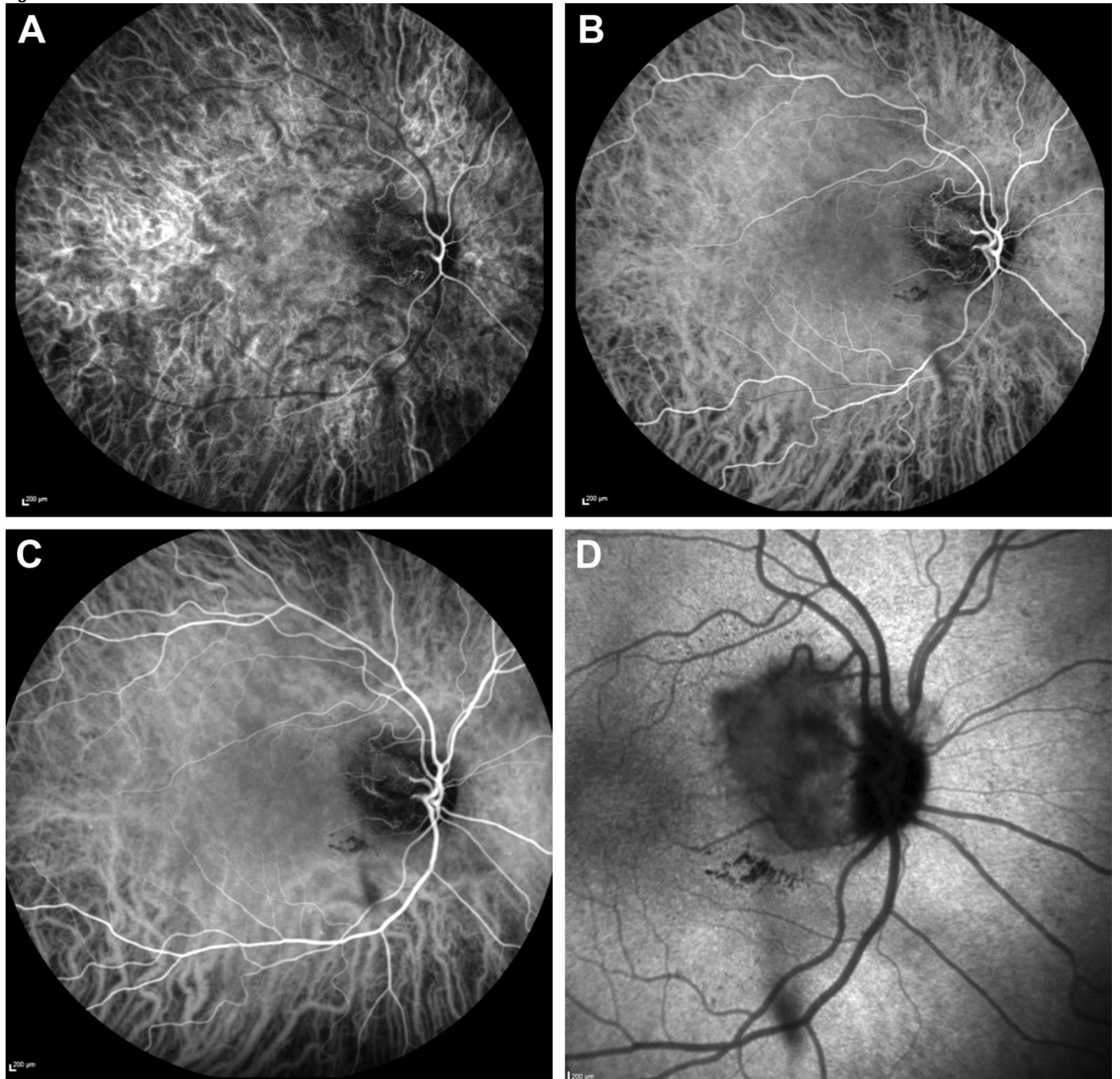


Fig. 4A, 4B, 4C, 4D Indocyanine green angiography of the right eye showing the retinal astrocytic hamartoma at different time (13 seconds, 18 seconds, 2 minutes and 30 minutes, respectively)

Fig. 5

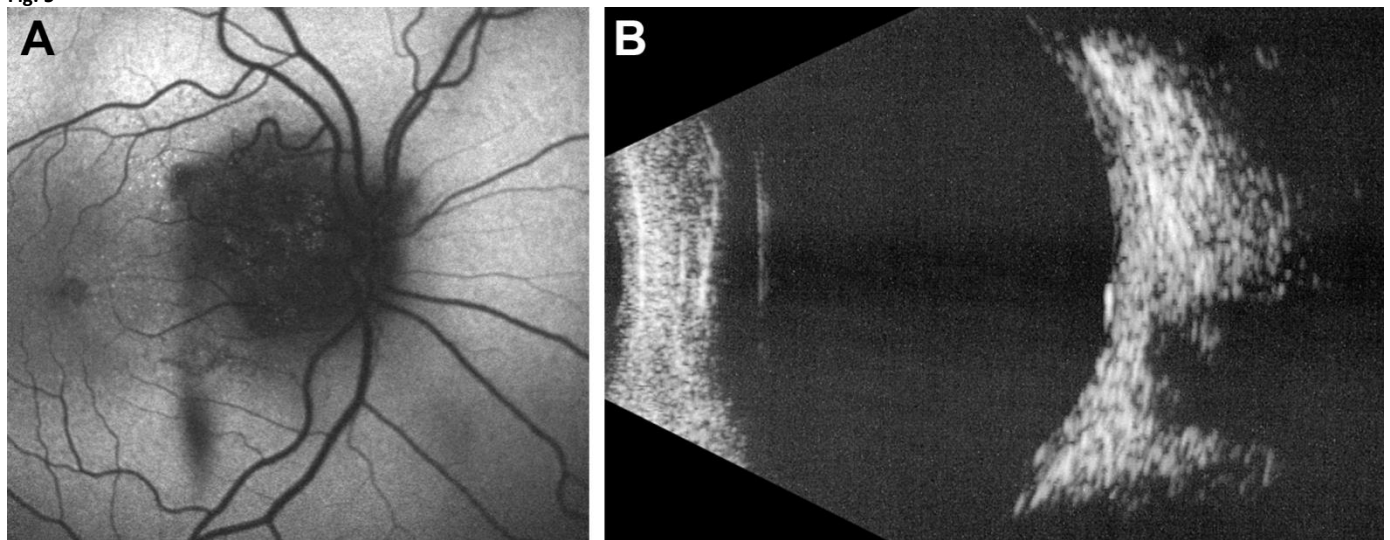


Fig. 5A Blue Autofluorescence of the right eye (30 degree) showing a hypoautofluorescent lesion in the region of the astrocytic hamartoma related to the presence of a richly vascularised network within the tumor.

Fig. 5B Ultrasonography of the right eye showing the astrocytic hamartoma as a hyperreflective lesion with a localized thickening of the retina but with no posterior shadowing.

Fig. 6

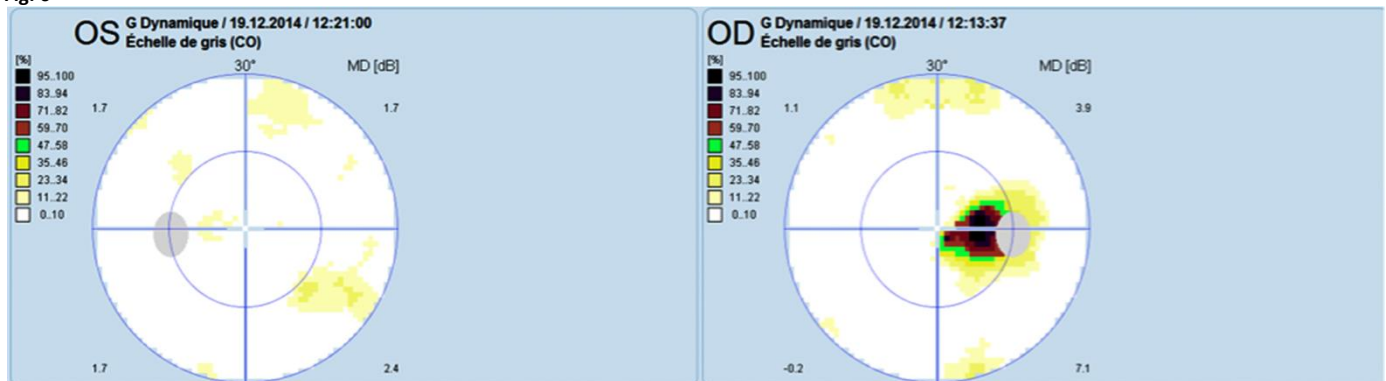


Fig. 6 Visual field (octopus 30 degree) showing an enlargement of the blind spot in the right eye.

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