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ORIGINAL PAPER

Low-grade "benign" birdshot retinochoroiditis: prevalence and characteristics

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Abstract

Purpose To establish the prevalence, morphologic and functional characteristics and evolution of mild birdshot retinochoroiditis (BRC).

Methods Retrospective review of all BRC cases treated at the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland, with at least 3 years of follow-up since the initial symptoms. Sub-Tenon's injection of triamcinolone was the first line of treatment if visual field changes were unilateral, with no additional treatment if visual field returned to normal. The percentage of patients who did not need systemic therapy was established, and the following parameters were evaluated: demographic characteristics, best-corrected visual acuity (BCVA), fundus photographs, fluorescein angiography (FA) and indocyanine green (ICGA) angiography frames and perimetry evaluation from initial visit to last follow-up.

Results Twenty cases of BRC were included in this study. Three of these patients (15%) received only local periocular therapy and qualified as mild BRC, with a mean follow-up of 9.3 years. The BCVA was 0.89 ± 0.25 at presentation and 1.0 ± 0.39 at last follow-up. Average visual field mean defect was 5.05 ± 3.27 at presentation and 1.78 ± 0.95 at last follow-up. Depigmented fundus lesions remained stable from presentation to last follow-up. Choroidal inflammatory activity monitored by ICGA decreased from 11.66 ± 3.44 at presentation to 4.25 ± 2.87 at last follow-up. FA revealed mild retinal vasculitis (2.25 ± 3.20) which remained stable (2.00 ± 4.00).

Conclusions In our setting, 15% of BRC cases had a benign course, controlled with periocular treatment. It is important to identify such cases in order not to overtreat, exposing patients needlessly to potential side effects of aggressive and prolonged immunosuppressive treatment.

Keywords Birdshot retinochoroiditis · Immunosuppressive therapy · Sub-Tenon's triamcinolone · Stromal choroiditis

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Introduction

Birdshot retinochoroiditis (BRC), described for the first time in 1980 [1, 2], is a bilateral autoimmune uveitis, with no extra-ocular involvement, that predominantly affects Caucasians [3]. Clinically, it presents with subclinical anterior segment inflammation, vitritis, retinal vasculitis of large veins and small retinal capillaries [4] and rice-shaped hypopigmented choroidal fundus lesions (BCR lesions) [5]. Two findings have changed our appraisal of BRC: HLA-A29 antigen is present in quasi 100% of cases when PCR is used for detection [6–10], and indocyanine green angiography (ICGA) allows detection of disease activity in the choroid before the visible BRC lesions appear in the fundus [11]. Due to these findings, new diagnostic criteria were established to allow an early diagnosis of BRC [12]: "presence of vitritis and retinal vasculitis in one or both eyes, visual field anomalies in one or both eyes, stromal choroiditis as evidenced by ICGA in both eyes (required), HLA-A29 antigen positivity (required), and the absence of extra-ocular inflammation sites" [12, 13].

In BRC, inflammatory involvement of the choroid and the retina is independent, and the inflammatory damage to the retina is the main culprit responsible for the functional impairment these patients experience [3, 14]. Fluorescein angiography (FA) and optical coherence tomography (OCT) have been used to study the retinal involvement in BRC. In BRC early exudative phase, FA shows massive and diffuse retinal capillary leakage, diffuse macular edema with an often spared fovea, leakage along large veins and disk hyperfluorescence [3]. In the later stages of the disease, diffuse thinning of arteries and veins is evident in FA and OCT shows extensive atrophic retinal thinning [15]. In the long run, there is also thinning of the choroid as shown by enhanced depth imaging OCT (EDI-OCT) [16].

For many years after BRC was first discovered, it was considered a benign disease which did not necessarily require aggressive inflammation suppressive therapy (IST) or any treatment at all [17–19], mainly for two reasons: (1) in early reports, IST was not successful and (2) visual acuity was used to evaluate progression but, currently, we know visual acuity is an inadequate parameter as it can remain excellent in a considerable group of patients even after years of disease progression [20]. In the last decades, increasing evidence became available that the majority of patients needs aggressive and prolonged IST [21, 22]; only 10–15% of patients present a more benign course [23]. It has also become clear that the most appropriate functional parameter to support treatment initiation and to follow evolution is visual field testing rather than visual acuity [3, 12, 24, 25]. Early treatment can lead to an improvement of visual field and sparing of central vision, in parallel with disappearance of ICGA signs and amelioration of FA signs [12]. Prompt treatment was shown to avoid complications such as retinal and choroidal atrophy, as evidenced by OCT and EDI-OCT [15, 16].

The primary goal of this study was to determine the percentage of mild BRC cases in our collective of patients, based on our treatment paradigm. The secondary goals were to characterize the treatment regimen required to attain disease control in these patients and the evolution of clinical characteristics from presentation to the last evaluation.

Methods

Study design

Retrospective case series.

Patients

From the 1917 uveitis cases treated at Centre for Ophthalmic Specialized Care, Lausanne, Switzerland, from 1995 to 2017, we retrieved all charts with the diagnosis of BRC.

We included all patients which had a follow-up of 3 years or more since the beginning of the symptoms. Patients were divided into two groups: (1) the ones who received systemic treatment and (2) the ones that received solely periocular treatment. This latter group was defined as having mild BRC. The percentage of patients who did not need systemic therapy was established, and their characteristics and evolution were analyzed. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Diagnosis and treatment protocol

Every patient included fulfilled the previously published BRC diagnostic criteria: "retinal vasculitis in large or small veins in one or both eyes; vitritis in one or both eyes; ICGA lesions in both eyes (required); and the presence of HLA-A29 antigen (required), with or without oval, depigmented, BRC lesions" [12, 13].

Patients were treated if visual field defects were present, using the following protocol: if visual field changes were unilateral, introduction of systemic immunosuppressive therapy was deferred and first step treatment consisted of sub-Tenon's injection of triamcinolone (40 mg per injection) with no additional treatment if visual field returned to normal. Sub-Tenon's injection could be repeated in case visual field disturbances reappeared. If there was a bilateral decreased in visual function (visual field or visual acuity), systemic therapy was decided. Once systemic treatment was decided, our regimen combined systemic steroids with non-steroidal immunosuppressants, mostly mycophenolic acid. Steroids were subsequently tapered to < 7.5 mg per day. In case of insufficient recovery of visual fields and/or persistence of retina and/or inflammatory signs (mainly monitored by FA/ICGA dual angiography), a second immunosuppressant or biologic agent was added (e.g., anti-TNF-α agents) [3, 12].

Clinical data

The following data were retrieved: Snellen best-corrected visual acuity (BCVA) test, slit-lamp examination, applanation tonometry and fundoscopy, laser flare photometry (Kowa FM-500 or FM-700 laser flaremeter, Kowa Co, Tokyo, Japan) computerized visual field testing, OCT and EDI-OCT (when available) (Spectralis HRA-2 OCT, Heidelberg Engineering Inc., Heidelberg, Germany) and dual FA and ICGA angiography (Heidelberg Retina Angiograph HRA 2, Heidelberg Engineering Inc., Germany).

Visual field testing

Visual field assessment was performed with the G1 Program of the OCTOPUS 900 (Octopus 900, G Standard; Haag-Streit, Bern, Switzerland), and the parameter analyzed was mean defect (VFMD).

BRC fundus lesions

BRC fundus lesions were evaluated, using a fundus score (0–4) based on distinctness and number of "cream-colored" oval depigmented birdshot lesions as described previously [14].

FA/ICGA scoring

Evaluation of choroidal and retinal inflammatory involvement was performed using dual FA/ICGA according to a well-established scoring system for retina and choroid described previously [26]. Briefly, "a total maximum score of 40 was assigned to the FA signs including, macular edema, optic disc hyperfluorescence, retinal vascular staining and leakage, capillary leakage, retinal capillary non-perfusion, neovascularization of the optic disk or elsewhere, pinpoints leaks, retinal staining and/or subretinal pooling. Similarly, a total maximum score of 40 was assigned to the ICGA signs, including choroidal vasculitis (fuzzy vessels), early stromal vessel hyperfluorescence, hypofluorescent dark dots (HDD) or areas (excluding atrophy) and hyperfluorescence of the optic disc". In order to compensate for the fact that ICGA scoring items were half as numerous as FA items, each ICGA item was given a coefficient of 2 to be able to compare the scores in the retinal and choroidal compartments [27, 28].

OCT and EDI-OCT

All OCT measurements were taken using a Heidelberg Spectralis HRA-2 OCT instrument (Heidelberg Engineering Inc., Heidelberg, Germany). Retinal OCT was described, and EDI-OCT choroidal thickness measurement was taken as described previously [16]. Briefly, "choroidal thickness was measured manually on EDI scans under the foveola and 1500 μm temporal (T), nasal (N), superior (S), and inferior (I) to the foveola. Choroidal thickness measurements were performed perpendicular to the retinal pigmentary epithelium (RPE), going from the posterior RPE edge to the choroid–scleral junction. The mean choroidal thickness of each eye was established by calculating the mean of six measurements (under the foveola and at 1500 μm T, N for the horizontal three scans and under the foveola and at 1500 μm I, S for the vertical three scans)". Evaluation of OCT scans and

measurements of choroidal thickness were conducted by the same experienced observer (AG) and checked in a blinded fashion by an additional trained observer (CPH).

Vitritis (SUN scoring)

Fundal views of all involved eyes were evaluated using the SUN (standardization of uveitis nomenclature) grading scheme ranging from 0 to 4 [29].

Statistical analysis

The descriptive statistics used were the mean and standard deviation. Analysis was performed using the Statistical Package for the Social Sciences version 23 (IBM SPSS Statistics, Chicago, IL).

Results

Demographics

Of the 1917 new cases of uveitis seen at the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland, from 1995 to 2017, 30 (1.56%) had the diagnosis of BRC. Among those patients, 20 (11 women and 9 men) had sufficient data and follow-up to be included in the study. In all 20 patients (100%), the human leukocyte histocompatibility antigen HLA-A29 was present. Based on our treatment criteria, 17/20 patients needed systemic therapy, whereas 3/20 patients (15%) received only local periocular therapy. Of these 17 patients, initial treatment consisted of sub-Tenon's injections of triamcinolone in five patients. In the eight patients where treatment started with sub-Tenon's injections of triamcinolone, periocular treatment did not halt progression in 5 and systemic treatment had to be introduced within a mean of 22.80 ± 21.01 months. The outcomes of the systemic treatment group have been previously reported and extensively commented [3, 12]. Mean follow-up of the mild group was 9.3 ± 4.6 years.

Characteristics of mild BRC patients (Table 1)

Three of twenty BRC patients (15%, 2 men and 1 woman) did not need to get systemic therapy and were termed as mild BRC cases. The mean age of this group at disease onset was 53.5 ± 14.5 years (range 39–68 years). HLA-A29 was positive in all three patients. Anterior inflammation was minimal at presentation in all three patients with a mean laser flare photometry value of 7.43 ± 2.64 ph/ms.

Table 1 Mild birdshot retinochoroiditis: functional and morphological parameters at presentation and upon follow-up

N (%)		3 (100.0%)
Male (*n*, %)		2 (66.7%)
Age (mean ± SD, years)		53.5 ± 14.5
Follow-up (mean ± SD, years)		9.3 ± 4.6
	Presentation	Last follow-up
BCVA (mean ± SD, decimal)	0.89 ± 0.25	1.0 ± 0.39
Visual field mean defect (mean ± SD, dB)	5.05 ± 3.27	1.78 ± 0.95
BRC fundus lesion score (mean ± SD)	1.66 ± 1.61	1.66 ± 1.15
ICGA score (mean ± SD)	11.66 ± 3.44	4.25 ± 2.87
FA score (mean ± SD)	2.25 ± 3.20	2.00 ± 4.00
EDI-OCT thickness (mean ± SD)	–	230.57 ± 65.10

SD standard deviation, *BCVA* best-corrected visual acuity, *dB* decibel, *BRC* birdshot retinochoroiditis, *ICGA* indocyanine green angiography, *FA* fluorescein angiography, *EDI-OCT* enhanced depth imaging optical coherence tomography

Treatment

The eye principally involved was the left eye in patients 1 and 2 and the right eye in patient 3. Patient 1 also had minimal involvement of the right eye at presentation and received a bilateral sub-Tenon's injection of 40 mg of triamcinolone. Patient 2 received two sub-Tenon's injections OS, one at presentation and another 2 months later. Patient 3 received three sub-Tenon's injections OD, one at presentation, one after 12 and another 18 months later.

Functional data

BCVA was 0.89 ± 0.25 at presentation and 1.0 ± 0.39 at last follow-up. If considering only the principally involved eye, BCVA was 0.83 ± 0.21 at presentation and 0.88 ± 0.44 at last follow-up, indicating stability of BCVA.

Average VFMD was 5.05 ± 3.27 at presentation and 1.78 ± 0.95 at last follow-up. When considering only the principally involved eye, average VFMD was 7.10 ± 3.57 at presentation and 1.93 ± 0.55 at last follow-up, indicating that treatment improved the visual field values in both eyes (Fig. 1).

BRC fundus lesions

Depigmented BRC fundus lesions were present faintly in patient 1 and 2, and numerous and bilaterally present in patient 3. Fundus score was 1.66 ± 1.61 (out of a possible maximal score of 4) at presentation and 1.66 ± 1.15 at last follow-up, indicating that there was no evolution of BRC lesions during the mean follow-up of 9 years (Fig. 2).

FA and ICGA

At presentation, choroiditis was present in both eyes of all patients at a substantial degree with a mean ICGA score of 11.66 ± 3.44 (out of a maximal score of 40) which decreased to 4.25 ± 2.87 at last follow-up, indicating absence of progression. Retinal involvement was less pronounced amounting to a score of 2.25 ± 3.20 (out of a maximal possible score of 40) at presentation and decreasing to 2.00 ± 4.00 at last follow-up, indicating that retinal vasculitis was less responsive to periocular therapy (Fig. 3).

OCT and EDI-OCT

Only OCTs from examinations at the end of follow-up were available for two of the patients with mild BRC patients. In patient 1, who had bilateral macular edema on FA at presentation, retinal OCT showed bilateral macular changes, moderate bilateral epiretinal membranes, areas of retinal thinning and thinning of the choroid (Fig. 4). In patient 2, retinal OCT showed discreet epiretinal membranes bilaterally and normal retinal and choroidal thickness values. Patient 3 had retinal OCTs from presentation and from the last follow-up. At presentation, both eyes (OD > OS) showed retinal and choroidal thickening, as described during the exudative phase of BRC [15], as well as a moderate epiretinal membrane on OD with normalization after three sub-Tenon's injections OD (Fig. 5). Mean choroidal thickness at the end of follow-up for the whole group was 230.57 ± 65.10 µm, which was less when compared to a subgroup of three patients with disease of less than 1 year duration (374.6 ± 141.1) reported in a previous study [16], comparable to a subgroup of seven patients that had received early, adequate and sustained therapy (288.3 ± 76.9), reported in a previous study [16], but much less atrophy/thinning of the choroid than a subgroup of six patients having received late or insufficient treatment (161.4 ± 39.2 µm) reported in a previous study [16]. Mean follow-up of this latter group of 7 + 6 patients published earlier was 13.7 ± 3.7 years [16].

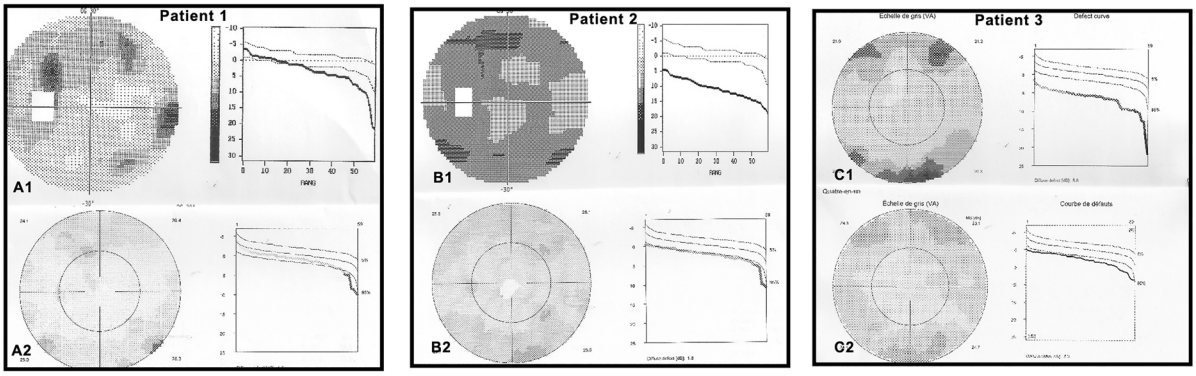

Fig. 1 Visual fields of mild birdshot retinochoroiditis patients not having needed systemic therapy. The top row of visual fields (A1, B1 and C1) shows disturbance of visual fields at presentation, and the bottom row (A2, B2 and C2) shows the visual fields obtained at the last follow-up. These patients responded to simple periocular injections of triamcinolone acetonide allowing to avoid systemic therapy with an improvement of the visual field mean defect from 5.05 ± 3.27 to 1.78 ± 0.95 ($p = 0.02$) after a mean follow-up of 9.3 ± 4.6 years

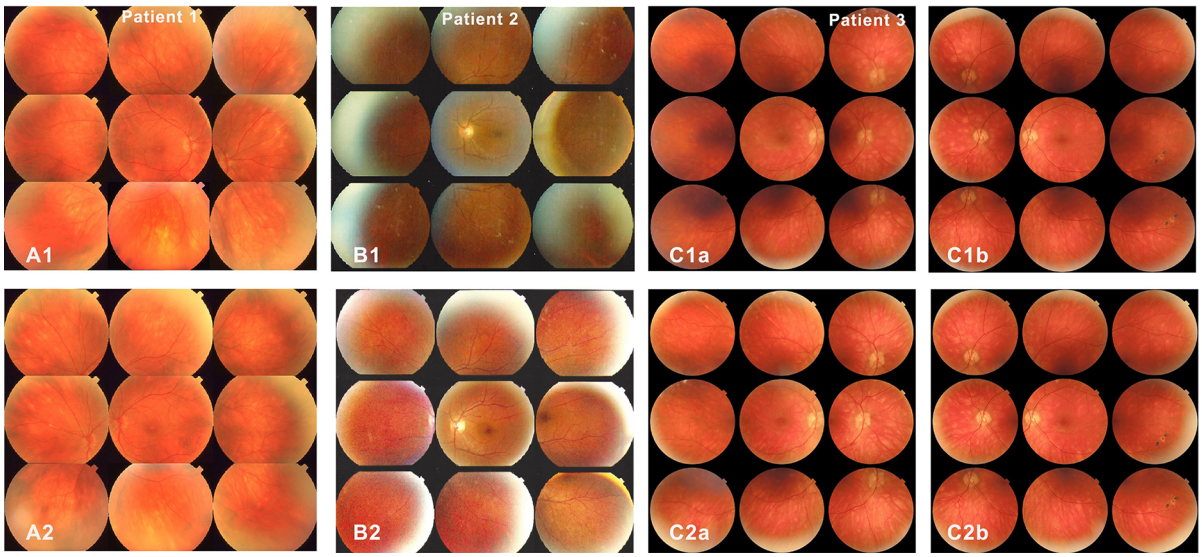

Fig. 2 Evolution of BRC fundus lesions in mild retinochoroiditis patients not having needed systemic treatment. In total, 2/3 patients showed moderate presence of BRC fundus lesions in the principally affected eye (A1 and B1) and one patient showed a substantial grade of lesions in both eyes (C1a and C1b). There was no evolution of the grade of BRC fundus lesions after a mean follow-up of 9.3 ± 4.6 years (A2, B2, C2a and C2b) with a stable mean score at presentation and on last follow-up (1.66 ± 1.6 vs. 1.66 ± 1.15)

Vitritis

Detectable vitritis was observed at presentation in only 2/6 eyes with a mean score of 0.5 ± 0.83 out of a maximal score of 4 [following the criteria from the Standardization of Uveitis Nomenclature (SUN)] [29].

Discussion

The appraisal of BRC, after its first reports [1, 2] in the early nineteen–eighties, has evolved over the years. The first two reports indicated that systemic corticosteroid therapy was not very efficient [1, 2] and BRC became to be perceived as a relatively benign disease probably not needing aggressive treatment [5, 19, 30, 31]. This opinion also prevailed because visual acuity remained conserved for long periods. This is explained by the fact that, although profuse macular and retinal edema was present, peculiarly the fovea was relatively spared in a large proportion of cases [3]. When longer follow-up data became available, it was shown that morbidity and complications were in fact of substantial importance, including severe visual field impairment, retinal thinning and atrophy with pseudo-retinitis pigmentosa evolution in some cases [32], epiretinal membranes as well as choroidal atrophy [16]. Numerous reports began to demonstrate that steroidal and non-steroidal immunosuppression was needed to improve the outcome of BRC in the long run and this became the standard of care [21, 22, 33]. It was further shown that, when considering visual field as the functional parameter to decide upon treatment for BRC cases, treatment was started earlier [23]. The grade of early activity could also be determined clearly thanks to ICGA showing choroidal foci and choroidal vasculitis, two signs of activity [34–38]. On the other hand, it became clear that oval depigmented birdshot fundus lesions, representing stromal scars, were not influenced by therapy and were not a sign of disease activity [12]. ICGA signs and the presence of visual field disturbances allowed both an early diagnosis and an early treatment, before oval depigmented BRC fundus lesions were noted [23]. It was even shown that, when treated early and before appearance of oval depigmented BRC lesions, those lesions never developed [23]. The belief, in the nineteen–eighties, that BRC was a benign disease was possibly also based on the fact that early reports certainly included benign cases. Such mild cases certainly exist and are important to identify such cases in order not to overtreat patients who do not need

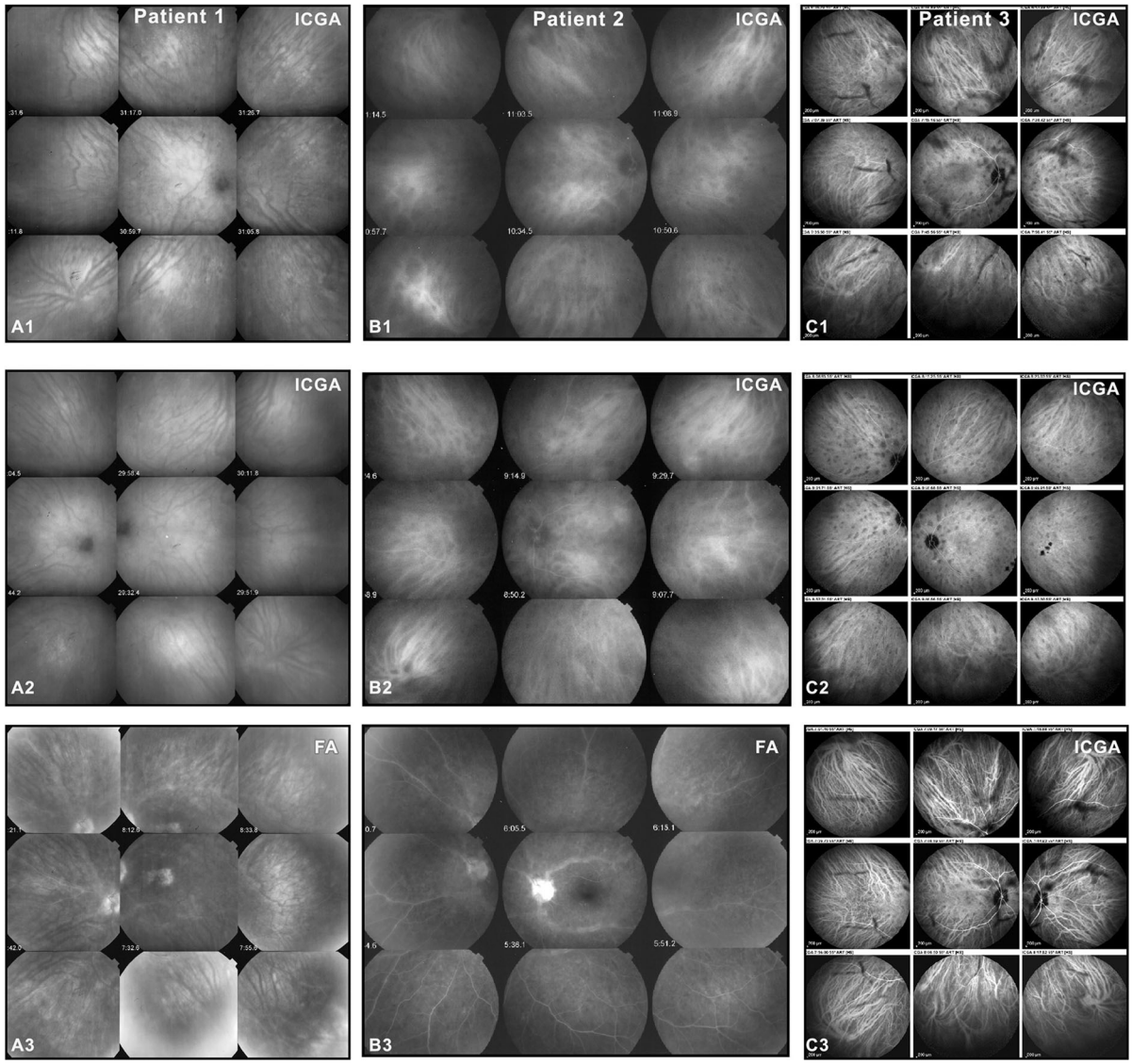

Fig. 3 ICGA/FA angiographic signs in mild retinochoroiditis patients not having needed systemic treatment. Patient 1 (A), ICGA frames show substantial choroiditis with fuzzy choroidal vessels and hypofluorescent dark dots (HDDs) OD (A1—ICGA score 8) and OS (A2—ICGA score 10). FA shows minimal retinal involvement with cystoid macular edema (A3). Patient 2 (B), with substantial choroiditis, OD (B1—ICGA score 10) and OS (B2—ICGA score 12). B3: FA showing typical vascular sheathing. Patient 3 (C), substantial choroiditis OD (C1—ICGA score 12) and OS (C2—ICGA score 18). C3 shows OD with resolution of most choroiditis at the end of follow-up (ICGA score 4)

it. Data on such patients are reported in our study. At presentation, in case of unilateral functional involvement, an attempt was made to treat locally, delaying systemic treatment until disease progression was documented. In half of the patients, an attempt was made to start treatment with sub-Tenon's injections of triamcinolone acetonide (40 mg). In 5/8 patients, periocular treatment did not halt progression and systemic treatment had to be introduced. In the 3/20 patients (15%) reported here, progression was halted by periocular therapy and they could be termed mild cases, whereas 85% of patients needed systemic treatment. In our three mild patients, as expected, BRC fundus lesions did not progress nor regress as they are choroidal scars and not active lesions. FA signs were minimal and remained stable. In contrast,

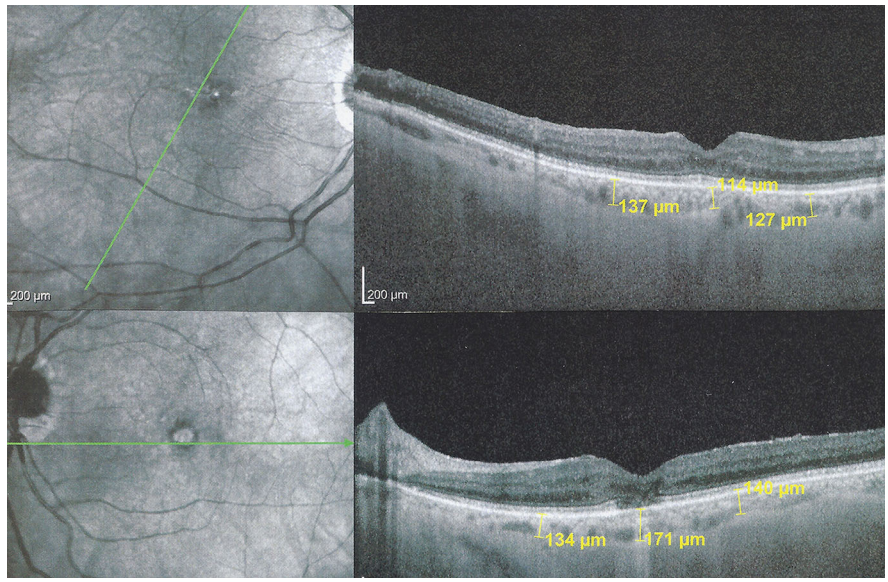

Fig. 4 OCT signs for patient 1 at last follow-up: discreet epiretinal membranes ODS and retinal thinning shown on the left of the top scan, bilateral choroidal thinning and macular changes ODS, a sequel of cystoid macular edema

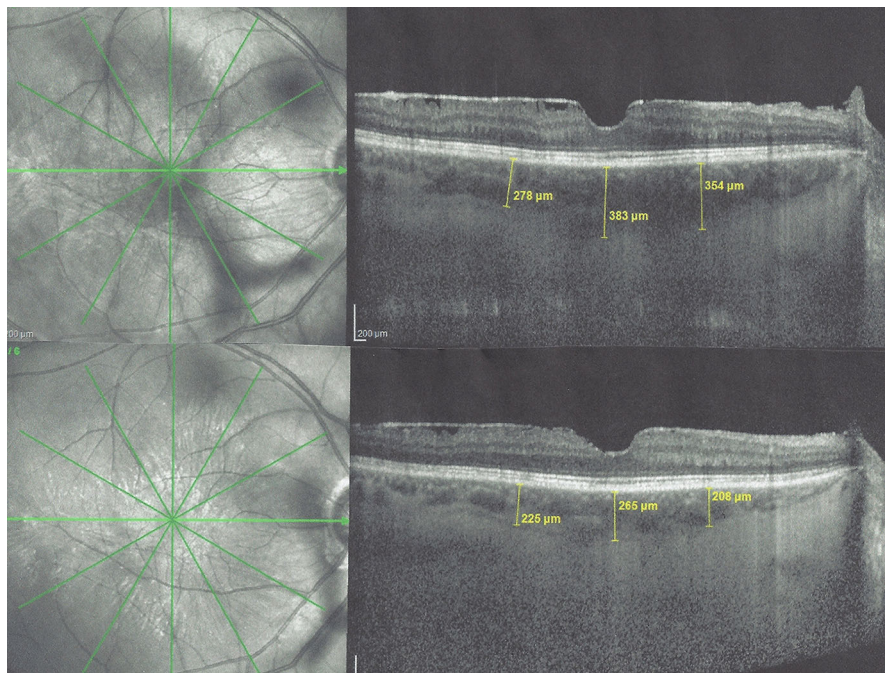

Fig. 5 Evolution of OCT findings in a patient with mild retinochoroiditis (patient 3): Top scan shows an epiretinal membrane, a discreet thickening of retina and choroid at presentation. At last follow-up (bottom scan), the ERM has decreased, retinal and choroidal thickness have decreased and vitreous opacities are substantially less

ICGA lesions, a witness of disease activity, did regress indicating that there was no active disease progression until the last follow-up. In this group, the disease resulted from a minimally aggressive process. OCT and EDI-OCT showed that both retinal and choroidal structures were preserved without significant thinning after a mean follow-up of more than 9 years.

Our survey shows indeed that there is a small proportion (15%) of low-grade BRC cases that never go over to a stage where systemic therapy is needed. In contrast, when systemic therapy is needed, an aggressive and quasi-lifelong therapy has to be applied, mostly consisting of a combination of two immunosuppressive agents [3, 12, 21, 22, 32]. Therefore, it is important to identify those cases without massive

involvement at presentation to try to sort out the patients who do not need systemic therapy, as we know that, in that case, treatment is going to be heavy and prolonged.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Ryan SJ, Maumenee AE (1980) Birdshot retinochoroidopathy. Am J Ophthalmol 89:31–45
2. Gass JD (1981) Vitiliginous chorioretinitis. Retina 23:1778–1787
3. Papadia M, Herbort CP (2013) Reappraisal of birdshot retinochoroiditis (BRC): a global approach. Graefe's Arch Clin Exp Ophthalmol 251:861–869. https://doi.org/10.1007/s00417-012-2201-7
4. Guex-Crosier Y, Herbort CP (1997) Prolonged retinal arterio-venous circulation time by fluorescein but not by indocyanine green angiography in birdshot chorioretinopathy. Ocul Immunol Inflamm 5:203–206
5. Gasch AT, Smith JA, Whitcup SM (1999) Birdshot retinochoroidopathy. Br J Ophthalmol 83:241–249
6. Baarsma GS, Priem HA, Kijlstra A (1990) Association of birdshot retinochoroidopathy and HLA-A29 antigen. Curr Eye Res 9(Suppl):63–68
7. Brezin AP, Monnet D, Cohen JH, Levinson RD (2011) HLA-A29 and birdshot chorioretinopathy. Ocul Immunol Inflamm 19:397–400. https://doi.org/10.3109/09273948.2011.619295
8. LeHoang P, Ozdemir N, Benhamou A, Tabary T, Edelson C, Betuel H et al (1992) HLA-A29.2 subtype associated with birdshot retinochoroidopathy. Am J Ophthalmol 113:33–35
9. Nussenblatt RB, Mittal KK, Ryan S, Green WR, Maumenee AE (1982) Birdshot retinochoroidopathy associated with HLA-A29 antigen and immune responsiveness to retinal S-antigen. Am J Ophthalmol 94:147–158
10. Wender JD, Fu AD, Jumper JM, McDonald HR, Johnson RN, Cunningham ET Jr (2008) False negative antibody-based HLA-A29 typing in two patients with birdshot chorioretinopathy. Br J Ophthalmol 92:1153–1154. https://doi.org/10.1136/bjo.2007.125666
11. Herbort CP, Mantovani A, Papadia M (2012) Use of indocyanine green angiography in uveitis. Int Ophthalmol Clin 52:13–31. https://doi.org/10.1097/IIO.0b013e318265d48b
12. Papadia M, Herbort CP Jr (2015) New concepts in the appraisal and management of birdshot retinochoroiditis, a global perspective. Int Ophthalmol 35:287–301. https://doi.org/10.1007/s10792-015-0046-x
13. Herbort CP Jr, Pavesio C, LeHoang P, Bodaghi B, Fardeau C, Kestelyn P et al (2017) Why birdshot retinochoroiditis should rather be called 'HLA-A29 uveitis'? Br J Ophthalmol 101:851–855. https://doi.org/10.1136/bjophthalmol-2016-309764
14. Herbort CP, Probst K, Cimino L, Tran VT (2004) Differential inflammatory involvement in retina and choroid in birdshot chorioretinopathy. Klin Monatsbl Augenheilkd 221:351–356. https://doi.org/10.1055/s-2004-812827
15. Papadia M, Jeannin B, Herbort CP (2012) OCT findings in birdshot chorioretinitis: a glimpse into retinal disease evolution. Ophthalmic Surg Lasers Imaging Off J Int Soc Imaging Eye 43:S25–S31. https://doi.org/10.3928/15428877-20120816-01
16. Skvortsova N, Gasc A, Jeannin B, Herbort CP (2017) Evolution of choroidal thickness over time and effect of early and sustained therapy in birdshot retinochoroiditis. Eye (Lond Engl) 31:1205–1211. https://doi.org/10.1038/eye.2017.54
17. Nussenblatt RBWS, Palestine AG (1996) Birdshot retinochoroidopathy. In: St.-Louis (ed) Uveitis, fundamentals and clinical practice, 2nd edn. Mosby, St. Louis, pp 325–333
18. Ophthalmology TAO (2001) Intraocular inflammation and uveitis. In: 2000–2001 ed. Basic and clinical science course. The Foundation of the American Academy of Ophthalmology, San Francisco
19. Priem HA, Oosterhuis JA (1988) Birdshot chorioretinopathy: clinical characteristics and evolution. Br J Ophthalmol 72:646–659
20. Rothova A, Berendschot TT, Probst K, van Kooij B, Baarsma GS (2004) Birdshot chorioretinopathy: long-term manifestations and visual prognosis. Ophthalmology 111:954–959. https://doi.org/10.1016/j.ophtha.2003.09.031
21. Cervantes-Castaneda RA, Gonzalez-Gonzalez LA, Cordero-Coma M, Yilmaz T, Foster CS (2013) Combined therapy of cyclosporine A and mycophenolate mofetil for the treatment of birdshot retinochoroidopathy: a 12-month follow-up. Br J Ophthalmol 97:637–643. https://doi.org/10.1136/bjophthalmol-2012-302123
22. Kiss S, Ahmed M, Letko E, Foster CS (2005) Long-term follow-up of patients with birdshot retinochoroidopathy treated with corticosteroid-sparing systemic immunomodulatory therapy. Ophthalmology 112:1066–1071. https://doi.org/10.1016/j.ophtha.2004.12.036
23. Knecht PB, Papadia M, Herbort CP Jr (2014) Early and sustained treatment modifies the phenotype of birdshot retinochoroiditis. Int Ophthalmol 34:563–574. https://doi.org/10.1007/s10792-013-9861-0
24. de Courten C, de Herbort CP (1998) Potential role of computerized visual field testing for the appraisal and

follow-up of birdshot chorioretinopathy. Arch Ophthalmol (Chic, Ill: 1960 116:1389–1391
25. Thorne JE, Jabs DA, Kedhar SR, Peters GB, Dunn JP (2008) Loss of visual field among patients with birdshot chorioretinopathy. Am J Ophthalmol 145:23–28. https://doi.org/10.1016/j.ajo.2007.08.039
26. Fabro F, Herbort CP (2018) Need for quantitative measurement methods for posterior uveitis: comparison of dual FA/ICGA angiography, EDI-OCT choroidal thickness and SUN vitreous haze evaluation in stromal choroiditis. Klin Monatsbl Augenheilkd 235:424–435. https://doi.org/10.1055/s-0043-124966
27. Tugal-Tutkun I, Herbort CP, Khairallah M (2010) Scoring of dual fluorescein and ICG inflammatory angiographic signs for the grading of posterior segment inflammation (dual fluorescein and ICG angiographic scoring system for uveitis). Int Ophthalmol 30:539–552. https://doi.org/10.1007/s10792-008-9263-x
28. Tugal-Tutkun I, Herbort CP, Khairallah M, Mantovani A (2010) Interobserver agreement in scoring of dual fluorescein and ICG inflammatory angiographic signs for the grading of posterior segment inflammation. Ocul Immunol Inflamm 18:385–389. https://doi.org/10.3109/09273948.2010.489730
29. Trusko B, Thorne J, Jabs D, Belfort R, Dick A, Gangaputra S et al (2013) The standardization of uveitis nomenclature (SUN) project. Development of a clinical evidence base utilizing informatics tools and techniques. Methods Inf Med 52(259–65):s1–s6. https://doi.org/10.3414/me12-01-0063
30. Fuerst DJ, Tessler HH, Fishman GA, Yokoyama MM, Wyhinny GJ, Vygantas CM (1984) Birdshot retinochoroidopathy. Arch Ophthalmol (Chic, Ill: 1960 102:214–219
31. Oh KT, Christmas NJ, Folk JC (2002) Birdshot retinochoroiditis: long term follow-up of a chronically progressive disease. Am J Ophthalmol 133:622–629
32. Willermain F, Greiner K, Forrester JV (2003) Atypical end-stage birdshot retinochoroidopathy. Ocul Immunol Inflamm 11:305–307
33. Artornsombudh P, Gevorgyan O, Payal A, Siddique SS, Foster CS (2013) Infliximab treatment of patients with birdshot retinochoroidopathy. Ophthalmology 120:588–592. https://doi.org/10.1016/j.ophtha.2012.05.048
34. Balci O, Gasc A, Jeannin B, Herbort CP Jr (2017) Enhanced depth imaging is less suited than indocyanine green angiography for close monitoring of primary stromal choroiditis: a pilot report. Int Ophthalmol 37:737–748. https://doi.org/10.1007/s10792-016-0303-7
35. Balci O, Jeannin B, Herbort CP Jr (2018) Contribution of dual fluorescein and indocyanine green angiography to the appraisal of posterior involvement in birdshot retinochoroiditis and Vogt–Koyanagi–Harada disease. Int Ophthalmol 38:527–539. https://doi.org/10.1007/s10792-017-0487-5
36. Cao JH, Silpa-Archa S, Freitas-Neto CA, Foster CS (2016) Birdshot chorioretinitis lesions on indocyanine green angiography as an indicator of disease activity. Retina 36:1751–1757. https://doi.org/10.1097/iae.0000000000000967
37. Fardeau C, Herbort CP, Kullmann N, Quentel G, LeHoang P (1999) Indocyanine green angiography in birdshot chorioretinopathy. Ophthalmology 106:1928–1934. https://doi.org/10.1016/s0161-6420(99)90403-7
38. Papadia M, Herbort CP (2012) Indocyanine green angiography (ICGA) is essential for the early diagnosis of birdshot chorioretinopathy. Klin Monatsbl Augenheilkd 229:348–352. https://doi.org/10.1055/s-0031-1299224