Presumed Solitary Circumscribed Retinal Astrocytic Proliferation

The 2010 Jonathan W. Wirtschafter Lecture

Jerry A. Shields, MD; Carlos G. Bianciotto, MD; Tero Kivela, MD; Carol L. Shields, MD

Objective: To report the clinical features and differential diagnosis of an unusual entity termed presumed solitary circumscribed retinal astrocytic proliferation (PSCRAP).

Methods: Retrospective review of medical records.

Results: All patients with PSCRAP were asymptomatic, and the lesion was found during routine examination. There were 5 men and 2 women with a median age of 53 years. No patient had a history or clinical findings of tuberous sclerosis complex. Each PSCRAP lesion was circumscribed, abruptly elevated, and opaque white to yellow and mostly obscured the underlying retinal vessels. The lesions had no associated subretinal fluid, hemorrhage, calcification, or retinal traction. Fluorescein angiography disclosed mild hyperfluorescence in the venous phase and moderate late staining of the lesions. Autofluorescence showed mild hyperautofluorescence of the lesions. Ultrasoundography revealed no calcification. Optical coherence tomography showed an abruptly elevated retinal mass with optical shadowing posterior to the lesion. Six lesions were stable after a median follow-up of 6 years, and 1 lesion gradually disappeared. The pathogenesis and pathologic features of PSCRAP are unknown.

Conclusion: Presumed solitary circumscribed retinal astrocytic proliferation appears to be a unique retinal lesion of adulthood that resembles astrocytic hamartoma or retinoblastoma but displays distinctive ophthalmoscopic features.

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RETINAL GLIAL CELLS (ASTROCYTES AND MÜLLER CELLS) can spawn nonneoplastic proliferations, known as gliosis. Gliosis can develop after a variety of retinal insults, including inflammation, hemorrhage, vitreous traction, retinal detachment, retinal vein obstruction, and others. Such reactive gliosis is generally small and rarely enters into the differential diagnosis of neoplasms. On occasion, however, reactive gliosis can be extensive and assume tumorous proportions, a condition called massive gliosis. True tumors of astrocytic derivation are uncommon and include astrocytic hamartoma of tuberous sclerosis complex (TSC) and acquired retinal astrocytoma. We herein report the fundus findings in 7 patients each with a solitary white or yellow retinal mass that differs clinically from other retinal tumors and reactive gliosis. We have chosen the term presumed solitary circumscribed retinal astrocytic proliferation (PSCRAP) for this entity.

METHODS

This study was approved by the institutional review board of Wills Eye Institute. We reviewed the medical records of 7 adult patients, each of whom had a small, well-circumscribed, white or yellow mass in the sensory retina that differed from astrocytic hamartoma and retinoblastoma. Patient age at presentation; sex; visual acuity; ocular symptoms; tumor characteristics, including the tumor base diameter in millimeters (estimated ophthalmoscopically) and tumor elevation (estimated by ultrasonography); and fundus location, color, and configuration were recorded. The detailed fundus drawings and photographs were scrutinized for subretinal fluid, exudation, vitreous seeding, hemorrhage, feeding retinal vessels, and retinal traction. Ocular imaging features were reviewed using fundus photography, intravenous fluorescein angiography (FA), autofluorescence (AF), and optical coherence tomography (OCT). Data were recorded at the initial examination and on follow-up visits.

RESULTS

All 7 patients were referred for a small asymptomatic fundus lesion found on routine examination that met our diagnostic criteria for PSCRAP as described in the “Methods” section. The examination results are given in Table 1. No patient had a history or signs of TSC or any associated ocular findings that seemed related to the fundus lesion.
The mean age at referral was 60 (median, 53; range, 37-85) years (Table 1). The lesion was located within 3 mm of the optic disc in 3 cases and in the equatorial region in 4 cases. No patients had symptoms related to the lesions, and visual acuity was 20/40 or better in all cases. The lesions ranged from 1 to 2 mm in diameter and 1 to 2 mm in thickness (Figure 1). They were opaque, usually preventing a clear view of retinal blood vessels; 5 were white and 2 were yellow. The adjacent retinal blood vessels traversed through or around the lesion, were not dilated or tortuous, and did not have the appearance of feeder vessels. There was no appreciable traction on the retinal blood vessels, suggesting the absence of adjacent gliosis. There was no ophthalmoscopic or ultrasonographic evidence of calcification in any case. Three of the patients had subtle proliferation of the retinal pigment epithelium adjacent to the lesion (Figure 1A, G, and H). On follow-up, 6 lesions remained stable and 1 spontaneously resolved within 1 year (Figure 1C and D).

Fluorescein angiography generally showed mild hyperfluorescence of the lesions beginning in the venous phase and moderate, well-defined, late staining perfluorescence of the lesions beginning in the venous phase (Figure 1C and D). Autofluorescence revealed moderate hyperautofluorescence of the mass (Figure 2A). The OCT findings suggested that each lesion was located in the sensory retina with optical shadowing of deeper structures (Figure 2E-H).

A brief history of each case is summarized in Table 1.

### Table 1. Clinical Findings in 7 Patients With Presumed Solitary Circumscribed Retinal Astrocytic Proliferation

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>DFS VA</th>
<th>Ocular Complaints</th>
<th>Diameter/ Thickness, mm</th>
<th>Location</th>
<th>Color</th>
<th>Associated Ocular Conditions</th>
<th>Associated Systemic Conditions</th>
<th>Tumor Status (Follow-up, mo)</th>
<th>Tumor Characteristic</th>
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<tr>
<td>1/M/46 02/23/95 20/20</td>
<td>None</td>
<td>2.0/1.8</td>
<td>Temporal equator</td>
<td>Yellow</td>
<td>None</td>
<td>Optic disc drusen both eyes</td>
<td>None</td>
<td>Stable (173)</td>
<td>2/M/53 05/04/98 20/30</td>
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<td>2/M/53 05/04/98 20/30</td>
<td>None</td>
<td>1.5/1.7</td>
<td>Inferotemporal postequatorial</td>
<td>White</td>
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<td>T2DM, psoriasis, peripheral neurophy</td>
<td>Rheumatoid arthritis, arrhythmia</td>
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<td>3/F/76 01/11/99 20/25</td>
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<td>1.5/1.4</td>
<td>Inferior to optic disc</td>
<td>Yellow</td>
<td>None</td>
<td>None</td>
<td>Completey regressed (114)</td>
<td>Stable (12)</td>
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<tr>
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<tr>
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<td>None</td>
<td>CAD</td>
<td>Stable (10)</td>
<td>Stable (20)</td>
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</table>

### Case 1

A 46-year-old man had an elevated, superficial, yellow retinal lesion near the equator temporally with mild hyperplasia of the retinal pigment epithelium near its margin. It measured 2.0 mm in diameter and 1.8 mm thick (Figure 1A). After 14 years of observation, visual acuity and the tumor remained stable.

### Case 2

A 53-year-old man with bilateral optic disc drusen had a white retinal lesion with abrupt inferotemporal elevation in the left eye. The lesion obscured the underlying vessels and measured 1.5 mm in diameter and 1.7 mm thick (Figure 1B). Intravenous FA showed mild early hyperfluorescence in the late venous phase with intense late fluorescence (Figure 2A and B). Autofluorescence disclosed moderate hyperautofluorescence of the mass, and ultrasonography showed no calcification. When viewed with OCT, the lesion was abruptly elevated with optical shadowing (Figure 2G). The lesion was stable after 10 years of follow-up.

### Case 3

A 76-year-old woman had an opaque yellow retinal lesion located inferonasal to the optic disc, measuring 1.0 mm in diameter and 1.4 mm thick (Figure 1C). Intravenous FA disclosed a fine vascular pattern in the venous phase and diffuse late staining of the mass. The patient was followed up at 4-month intervals and the lesion gradually resolved. One year later, the lesion had resolved completely, leaving normal-appearing retina at the site (Figure 1D). This case was previously reported as spontaneous disappearance of astrocytic hyperplasia before our coining of the term PSCRAP.

### Case 4

A 37-year-old man had a solitary opaque white juxta-papillary retinal lesion located superotemporal to the optic disc, measuring 1.0 mm in diameter and 1.0 mm thick (Figure 1E and Table 1). Findings of intravenous FA, AF, ultrasonography, and OCT (Figure 2E) were similar to those of the previous cases (Figure 2G). On follow-up 6 years later, visual acuity and the fundus lesion were stable.
CASE 5

An 85-year-old woman had an opaque white retinal lesion superior to the right optic disc, measuring 1.5 mm in diameter and 2.0 mm thick (Figure 1F). The ultrasonographic and OCT findings were similar to those of previous cases (Figure 2F). One year later, the lesion was unchanged.

CASE 6

A 43-year-old man had a white equatorial retinal lesion superior to the equator in the right eye, measuring 2.0 mm in diameter and 1.9 mm thick (Figure 1G). There were nonspecific pigment alterations adjacent to the lesion. Fluorescein angiography, ultrasonography, and OCT revealed findings similar to the other cases. Visual acuity and the lesion were unchanged at 10 months.

CASE 7

A 78-year-old man had PSCRAP near the nasal equator in the left eye, measuring 2.0 mm in diameter and 1.9 mm thick (Figure 1H). There was a focus of pigmentation adjacent to the lesion. Fluorescein angiography, AF, ultrasonography, and OCT (Figure 2H) revealed findings similar to the other cases. Visual acuity and the lesion were unchanged at 10 months.

COMMENT

The cases reported herein have specific features that, to our knowledge, have not been clearly defined in the literature. Because the lesions were white and yellow and located in the sensory retina, we coined the term presumed solitary circumscribed retinal astrocytic proliferation, or PSCRAP. In our cohort, PSCRAP lesions occurred in middle-aged to older white patients, and 5 of the 7 were men. The lesions were opaque, preventing a clear view of deeper retinal structures. The adjacent retinal blood vessels passed through or around the lesion, were not dilated or tortuous, and did not have the appearance of feeder vessels. There was no appreciable traction on the normal retinal blood vessels, suggesting that there was no adjacent gliosis. Each lesion was small, solitary, and well defined. All were located in the sensory retina, presumably the nerve fiber layer, and it was not
possible to determine how far they extended into the deeper retinal layers. No lesion showed ophthalmoscopic or ultrasonographic evidence of calcification. None had subretinal fluid or yellow lipoproteinaceous exudate. Three of the lesions (Figure 1A [case 1], G [case 6], and H [case 7]) were associated with minor adjacent pigmentary changes, suggesting a reactive process with mild hyperplasia of the retinal pigment epithelium. One lesion (Figure 1A) had slight visibility of a marginal blood vessel within the lesion, but it was clearly located mostly in the nerve fiber layer.

It is important to differentiate PSCRAP from other similar retinal conditions on the basis of ophthalmoscopic features and ancillary studies. The main lesions in the differential diagnosis include retinal astrocytic hamartoma, acquired retinal astrocytoma, retinoblastoma, myelinated retinal nerve fibers, granuloma, and reactive gliosis. With the exception of astrocytic hamartoma, these conditions are quite different from PSCRAP; the differentiating features are listed in Table 2.

There are subtle but important differences between PSCRAP and astrocytic hamartoma (Table 2). Presumed solitary circumscribed retinal astrocytic proliferation is diagnosed in middle-aged or older people who have no personal or family history of TSC. Astrocytic hamartoma is usually diagnosed in early life, and affected children often have clinical findings of TSC. Presumed solitary circumscribed retinal astrocytic proliferation is unilateral and solitary, whereas astrocytic hamartoma is often multiple and bilateral. Ophthalmoscopically, PSCRAP is opaque and permits no fundus view of the deeper retinal vessels, whereas astrocytic hamartoma is frequently mildly opaque or translucent, and intrinsic vessels are often easily seen. Presumed solitary circumscribed retinal astrocytic proliferation is usually discrete and well defined, whereas astrocytic hamartoma is less well defined and often has a diffuse transparent component, making the margins more difficult to identify. From the cases seen so far, PSCRAP does not show adjacent retinal gliosis and retinal dragging, but astrocytic hamartoma often has adjacent gliosis that pulls on the nearby retinal vessels. Concerning color, PSCRAP tends to be pure white, whereas astrocytic hamartoma is often more yellow to yellow-white. Calcification is not present clinically or ultrasonographically in PSCRAP but is usually demonstrable in astrocytic hamartoma. Presumed soli-

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**Table 2. Comparison of PSCRAP With Other Small Retinal Lesions**

<table>
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<tr>
<th>Variable</th>
<th>PSCRAP</th>
<th>Astrocytic Hamartoma</th>
<th>Acquired Retinal Astrocytoma</th>
<th>Retinoblastoma</th>
<th>Myelinated Retinal Nerve Fibers</th>
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<td>Stable</td>
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Abbreviations: FA, fluorescein angiography; hyper, hyperfluorescence; hypo, hypofluorescence; NF, neurofibromatosis; OCT, optical coherence tomography; PSCRAP, presumed solitary circumscribed retinal astrocytic proliferation; RB, retinoblastoma; RPE, retinal pigment epithelium; TSC, tuberous sclerosis complex.

1. The features listed represent findings in general, but there are exceptions in many instances.
2. Includes sarcoidosis, tuberculosis, cat scratch disease, Lyme disease, toxocariasis, and others.
3. Estimates are for average lesion size, because lesion size can vary.
tary circumscribed retinal astrocytic proliferation appears to remain stable on follow-up, with no tendency to grow or to cause local complications. It is likely that PSCRAP enlarged at one time to attain its observed size. Most astrocytic hamartomas remain stable or demonstrate mild progression, but, on occasion, astrocytic hamartoma can show growth and mild to severe ocular complications, including exudation, vitreous seeding of tumor cells, vitreous hemorrhage, tractional retinal detachment, and proliferative retinopathy. Such ophthalmoscopic features and clinical course did not occur in our patients with PSCRAP.

Another retinal glial tumor is the acquired retinal astrocytoma, which generally occurs in older individuals who have no history or findings of TSC. In contrast to PSCRAP, trocytoma, which generally occurs in older individuals who have no history or findings of TSC. In contrast to PSCRAP, but they appear during childhood and are usually stationary. We believe that acquired retinal astrocytoma is the retinal counterpart of a low-grade astrocytoma that occurs in the brain. A small retinoblastoma differs from PSCRAP by virtue of the fact that it occurs in children and develops retinal feeding and draining vessels when it is still small. Myelinated retinal nerve fibers might superficially resemble PSCRAP, but they appear during childhood and are usually stationary. We believe that acquired retinal astrocytoma is the retinal counterpart of a low-grade astrocytoma that occurs in the brain.

In PSCRAP, ancillary studies, such as FA, AF, ultrasonography, and OCT, show findings that are somewhat similar to astrocytic hamartoma. However, there have not been enough cases studied to make detailed comparisons. It is our impression that FA of PSCRAP shows less early vascularity and less late staining than does astrocytic hamartoma. Ultrasonography does not reveal calcification in PSCRAP; calcification is commonly seen in astrocytic hamartoma, although it may not be apparent ophthalmoscopically. Both lesions can show AF, but not enough cases have been studied to draw conclusions. In both conditions, OCT reveals a dense lesion in the sensory retina with posterior shadowing. However, PSCRAP does not demonstrate the “moth-eaten” appearance that characterizes most calcified astrocytic hamartomas. The further differentiation of PSCRAP from a variety of other conditions, using clinical and imaging studies, is shown in Table 2.

None of the PSCRAP lesions in our series have shown progression. One patient (case 3) experienced spontaneous regression of the lesion more than 1 year after it was detected. The reason for this is unclear.

The histopathologic mechanism of PSCRAP is currently unknown. However, in 1971, Ganley and Streeten reported the histopathologic findings of a retinal lesion that was discovered when sectioning an eye being enucleated for choroidal melanoma. The lesion had not been noted clinically before the enucleation, but the description suggested that the lesion was similar to the PSCRAP lesions described in this report. That lesion was proved histopathologically to be a circumscribed proliferation of benign astrocytes confined to the nerve fiber layer without invasion of the ganglion cell layer. As is often true in such cases, it could not be clearly determined whether the lesion was reactive or neoplastic.

In addition to a pure proliferation of typical astrocytes, one could speculate that PSCRAP might represent a proliferation of oligodendrocytes, as is believed to occur with myelinated retinal nerve fibers. Although oligodendroglioma classically occurs in the central nervous system, we are aware of 2 reports of oligodendrogliomas of the retina. One of these was subsequently reviewed and reclassified as a well-differentiated retinoblastoma. The other case was a progressively enlarging lesion that resembled retinoblastoma. Our term PSCRAP seems appropriate for the condition described in this report. Thus far, all cases have been solitary, unilateral, circumscribed, and located in the sensory retina. Because of the light color and location in the sensory retina, we believe that PSCRAP is most likely composed of a proliferation of astrocytes. However, because the histopathologic features remain uncertain, the words presumed astrocytic proliferation are currently applied to this entity.

In summary, we describe 7 cases of a unique retinal lesion termed PSCRAP. Occurring in adults, PSCRAP is a benign stationary lesion that does not appear to cause visual loss or other complications. The main importance lies in its differentiation from similar lesions (Table 2), such as astrocytic hamartoma, acquired retinal astrocytoma, retinoblastoma, myelinated retinal nerve fibers, granuloma, and other fundus lesions that can have serious ocular and systemic implications. The pathogenesis of PSCRAP remains speculative.

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Correspondence: Jerry A. Shields, MD, Ocular Oncology Service, Wills Eye Institute, 840 Walnut St, Ste 1440, Philadelphia, PA 19107 (jerryshields@comcast.net).
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REFERENCES


