Solitary Idiopathic Choroiditis

The Richard B. Weaver Lecture

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Objective: To report the clinical characteristics of solitary idiopathic choroiditis and the features that differentiate it from tumors and other inflammatory lesions.

Design: Retrospective medical record review.

Patients: Sixty consecutive patients with solitary idiopathic choroiditis.

Main Outcome Measures: Clinical features, natural course, and follow-up.

Results: The mean and median ages of the patients were 35 and 36 years, respectively, 56 (93%) of the 60 patients were white, 38 (63%) were female, and 22 (37%) were male. No patient had a history, clinical findings, or laboratory study results to support a specific cause of uveitis. All were referred to us because of a suspected intraocular tumor. The patient was asymptomatic in 21 cases (35%); the patient had mild visual loss in 36 cases (60%). The lesion was posterior to the equator in 56 cases (93%), was yellow in 58 cases (97%), and had distinct margins in 38 cases (63%). The lesion showed signs of active inflammation in 20 cases (33%) and no inflammation in 40 cases (67%). Fluorescein angiography disclosed that all lesions had early hypofluorescence and late hyperfluorescence. In the late-phase angiograms inactive lesions had distinct margins and active lesions had ill-defined margins. Lesions with active inflammation appeared to show a favorable response to the administration of systemic corticosteroids but generally improved with or without treatment. Most of the inactive lesions remained stable on long-term follow-up. Overall, the condition remained stable in 36 patients (60%), improved in 22 (37%), and recurred in 2 (3%). The clinical and angiographic features and clinical course of solitary idiopathic choroiditis were generally different from known intraocular tumors.

Conclusions: Solitary idiopathic choroiditis is a distinct clinical entity that can simulate an intraocular neoplasm. Recognition of its typical clinical features can assist in differentiating it from tumors and other inflammatory lesions of the ocular fundus.

Arch Ophthalmol. 2002;120:311-319

CHOROIDITIS USUALLY occurs as multifocal lesions, often with signs of generalized ocular inflammation.1 Sometimes, however, choroiditis can manifest as a solitary lesion. Conditions known to manifest as a solitary choroidal granuloma include sarcoidosis, tuberculosis, toxocariasis, or several other diseases.1 In many instances, however, solitary choroiditis remains idiopathic, in spite of extensive systemic evaluation.2,3 Even when uveal granulomas are subjected to detailed histopathologic studies, no cause can be determined in many cases.2 Such solitary idiopathic choroiditis (SIC) can simulate clinically an amelanotic choroidal tumor, like nevus, melanoma, metastasis, or osteoma, or a retinal tumor like retinoblastoma or astrocytic hamartoma.4,6 We describe our experience with 60 patients with SIC, who were referred because of a suspected tumor, and we elucidate the features that differentiate SIC from tumors and other type of inflammations.

RESULTS

Sixty consecutive patients had SIC. Demographic information for these patients is given in Table 1. No patient had a history of intraocular inflammation, ocular trauma, or ocular surgery. No patient had systemic findings of sarcoidosis, tuberculosis, histoplasmosis, syphilis, toxoplasmosis, toxocariasis, Lyme disease, cat-scratch disease, pneumocystosis, blastomycosis, coccidioidomycosis, aspergillosis, herpes simplex, herpes zoster, or human immunodeficiency virus infection. Other than symptoms related to the choroidal lesion, no patient had prior ocular problems.
PATIENTS AND METHODS

A medical record review was performed for patients clinically or by mail consultation seen on the Ocular Oncology Service, Wills Eye Hospital, Philadelphia, Pa, who were diagnosed as having unifocal choroiditis, for which no apparent cause was determined. General data collected included age at diagnosis, race, sex, eye involved, and medical and ocular histories. Prior treatment for the ocular lesion and the referral diagnoses were listed. The manifesting symptoms, visual acuities, intraocular pressures (IOPs), and results of slitlamp biomicroscopy were tabulated. The results of studies for specific causes of intraocular inflammation were reviewed when available. These included physical and ocular findings, chest x-ray film, and conventional methods to rule out sarcoidosis, tuberculosis, histoplasmosis, syphilis, toxoplasmosis, toxocariasis, Lyme disease, cat-scratch disease, and other conditions when indicated. Since the results of these studies were uniformly negative in all of the early patients, most asymptomatic patients with inactive lesions were subsequently not subjected to the time and expense of extensive systemic evaluation.

Fundus drawings and photographs, done for all patients, were reviewed. We determined the ocular zone in which the main portion of the lesion was located (macular, juxtapapillary, between the macular area and the equator, or between the equator and the ora serrata). Macular was defined as the area extending for 2 disc diameters (3.0 mm) from the foveola in any direction. A juxtapapillary lesion was defined as one that touched or covered the margin of the optic disc. If a lesion touched the optic disc on the temporal side, it was classified as juxtapapillary, rather than macular, in this study. The main retinal sector affected by the lesion was determined (inferior, nasal, superior, and temporal).

Data related to the fundus lesion itself included the basal size, distance of the margin of the lesion from foveola and optic nerve, signs of active inflammation (vitreous cells and hazy margins of the lesion), color (yellow, yellow-white, or orange), characteristics of the margins (distinct, indistinct, or surrounded by an orange halo), and associated changes in the retinal pigment epithelium. The presence and extent of exudation, hemorrhage, subretinal fluid, retinal or vitreal inflammation, and the presence of a choroidal neovascular membrane and retinochoroidal vascular anastomoses were determined. The method of management was reviewed. Follow-up information included visual acuity; IOP; size, color, and margins of the lesion; signs of recurrent inflammation; presence of an orange halo; retinal pigment epithelial changes; presence of exudation, hemorrhage, or subretinal fluid; presence of a choroidal neovascular membrane; status of the optic disc; and final status of the globe with regard to visual acuity and appearance of the lesion (stable, improved, or worse). Since most patients were referred to us for suspicion of an intraocular neoplasm, we specifically reviewed the features that were helpful in differentiating SIC from intraocular tumors such as choroidal metastasis, choroidal hemangioma, amelanotic nevus, amelanotic melanoma, osteoma, and other ocular tumors and pseudotumors.

Table 1. Demographic Findings in 60 Consecutive Patients With Solitary Idiopathic Choroiditis

<table>
<thead>
<tr>
<th>Demographic Findings</th>
<th>No. (%) of Patients</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>35 (36 [3-70])</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>56 (93)</td>
</tr>
<tr>
<td>African American</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (5)</td>
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<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>38 (63)</td>
</tr>
<tr>
<td>Male</td>
<td>22 (37)</td>
</tr>
<tr>
<td>Eye</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Left</td>
<td>31 (52)</td>
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Of the 60 patients, 16 (27%) had received prior treatment elsewhere for the fundus lesion, including systemic corticosteroids in 7 patients (12%), topical corticosteroids in 3 patients (5%), both systemic and topical corticosteroids in 3 patients (5%), periocular corticosteroids in 1 patient (2%), systemic corticosteroids and laser treatment in 1 patient (2%), and vitreous biopsy and laser treatment in 1 patient (2%). The other 32 patients were referred directly to us or had no prior treatment. The main referral diagnoses are given in Table 2. In every case, there was consideration of an intraocular tumor, prompting referral to the Ocular Oncology Service. Patient symptoms are listed in Table 3. Mild visual symptoms were present in 39 patients (65%) and 21 patients (35%) were asymptomatic, with the lesion discovered on routine ophthalmic examination.

The visual acuity in the affected eye was 20/20 in 24 patients (40%), 20/25 to 20/40 in 15 (25%), 20/50 to 20/100 in 9 (15%), and 20/400 to finger counting in 10 (17%). A visual acuity of hand motions was recorded in 1 patient and no light perception in 1 patient (advanced optic disc granuloma). The mean IOP was 17 mm Hg, with a median of 16 mm Hg, and a range of 5 to 31 mm Hg. An IOP greater than 22 mm Hg was recorded in 6 patients; in no case was the elevated IOP believed to be due to the choroidal lesion. The anterior segment findings as noted with slitlamp biomicroscopy are summarized in Table 4. Only 5 (8%) of 60 patients had inflammatory cells in the anterior chamber and the 3 cataracts did not seem to be directly related to the choroidal inflammation.

The retinal zones and the fundus sectors in which the lesion was mainly located are listed in Table 4. The lesion was located posterior to the equator in 56 cases (93%), specifically in the macular area in 17 cases (28%), in a juxtapapillary location in 8 cases (13%), and between the macular area and the equator in 31 cases (52%).

Other ophthalmoscopic findings are listed in Table 4. They varied depending on whether the lesion was dormant (Figure 1) or had signs of active inflammation (Figure 2). Of the 60 lesions, 40 (67%) had minimal or no inflammatory signs and we categorized them as inac-
tive. The other 20 active lesions (33%) had ill-defined margins (Figure 2) and had caused mild visual symptoms and contained vitreous cells, fresh exudation, and localized subretinal fluid.

The results of fluorescein angiography (37 patients), indocyanine green angiography (6 patients), and ultrasonography (36 patients) are given in Table 5. With fluorescein angiography, the inactive lesions generally showed early hypofluorescence, progressive hyperfluorescence, and a distinct margin in the later angiograms (Figure 1). Active lesions displayed early hypofluorescence followed by late leakage from the lesion into the subretinal fluid or the vitreous cavity (Figure 2). Indocyanine green angiography showed findings that paralleled the fluorescein angiography, with early hypofluorescence and late mild hyperfluorescence. No retinal or choroidal neovascularization was identified, but 3 lesions showed mild retinochoroidal anastomosis (Figure 1H). Ultrasonography showed no diagnostic features and the lesions generally had medium to high internal reflectivity.

Because of the variations in treatment in our case series, it was impossible to determine the overall response to treatment. However, it was our impression that lesions with active inflammation generally had a favorable response to therapeutic systemic corticosteroids; no patient’s condition became worse while receiving corticosteroids.

Follow-up data for the patients in this study ranged from 6 months to 25 years (mean, 24 months). The systemic, ocular, and visual outcomes are listed in Table 6. Most lesions remained stable or improved. There was recurrence of the activity of the lesion in 4 cases (12%), but only 2 patients (6%) had worsening of visual acuity during follow-up.

In the evaluation of these patients and in the medical record review, particular attention was paid to the clinical features that help to differentiate SIC from other in-
traocular tumors and pseudotumors. These differential features are covered in the subsequent discussion.

Most cases of posterior segment intraocular inflammation have cells in the anterior chamber and vitreous and multifocal or bilateral lesions of the choroid or retina. In such cases, a clinical evaluation is usually undertaken to detect a specific cause and treatment is directed toward the underlying cause(s). There is little in the literature about the condition described in this study. Our 60 consecutive patients had SIC lesions for which intraocular tumor was a diagnostic consideration. The origin was unknown in all cases despite systemic evaluation for causes of uveitis in many cases.

A series of 6 cases of unifocal choroiditis was reported in 1997 by Hong et al, who used the term “unifocal helioid choroiditis” because of the sunlike appearance of the yellow lesion. Their patients were all symptomatic, having blurred vision, metamorphopsia, or scotoma. In our case series, 39 patients (65%) were symptomatic and 21 (35%) were asymptomatic (ie, the lesion was found on routine ophthalmic examination). All were referred to us to exclude the possibility of an intraocular tumor. We chose the descriptive term “solitary idiopathic choroiditis” to define this entity.

Solitary idiopathic choroiditis can occur at any age, but most patients are between 20 and 50 years old at the time of diagnosis. There seems to be no predilection for sex, race, or laterality. The medical history, ocular history, and systemic study results fail to reveal a specific cause. This is not surprising, since Margo and Zimmerman performed detailed histopathologic studies on 11 enucleated eyes with solitary granulomas, in which no cause could be determined.

The visual acuity is generally good, unless the lesion occurs in a juxtapapillary or foveal location. The IOPs are normal and there usually are no signs of anterior segment inflammation. Most lesions occur posterior to the equator.

Solitary idiopathic choroiditis has typical ophthalmoscopic features that vary depending on whether the lesion is inactive or active.

In the inactive stage, SIC appears as a discrete, nummular, yellow-white lesion. A highly characteristic sign, seen in some cases, is an ill-defined red-orange halo that surrounds the lesion (Figure 3C). Retinal pigment epithelial abnormalities are usually minimal. Retinochori-
dal shunt vessels are occasionally present (Figure 3G). In the active stage, SIC usually appears as a dull-yellow choroidal lesion with an ill-defined margin, yellow intraretinal exudation, localized subretinal fluid and occasional retinal vascular dilation, and focal retinal hemorrhages (Figure 4). The exudation sometimes can assume a stellate configuration in the foveal area often separate from the main lesion (Figure 2A). As the inflammation subsides, the margins become better defined and exudation, hemorrhage, subretinal fluid, and vascular abnormalities disappear. Margo and Zimmerman2 speculated that the advanced findings seen in their case series represented the more severe form of the disease and that the clinical features of the less severe cases were unknown. It is possible that our cases represent this less severe form of what they described.

Fluorescein angiography of SIC varies with the activity of the lesion (Table 5). An inactive lesion shows early relative hypofluorescence and intense late staining, with a clearly defined margin (Figure 1). An active lesion also shows hypofluorescence in the vascular-filling phases and progressive hyperfluorescence in the later angiograms, with a poorly defined margin due to leakage into adjacent subretinal fluid and vitreous (Figure 4). The SIC is usually a small lesion and ultrasonography is of little diagnostic value.

The etiology of SIC is unknown. A choroidal granuloma secondary to sarcoidosis,7-10 tuberculosis,4,5,11-15 ocular toxocariasis,16 cat-scratch disease,17 and other conditions can assume a similar clinical appearance and clinical course. Most of these entities can be diagnosed by history, clinical findings, and laboratory test results. None of the patients in our case series had findings suggestive of the aforementioned diseases. Inflammatory conditions like ocular histoplasmosis, retinal toxoplasmosis, nodular posterior scleritis, intraocular abscess, and syphilis usually have a different clinical appearance1 and are usually not serious considerations in the differential diagnosis of SIC.

It is tempting to speculate that the condition described herein represents a focal granuloma. However, multifocal choroiditis, often considered to be a granulomatous process, has been shown histopathologically in one case to represent a nongranulomatous inflammation.18 Since we have no histopathologic confirmation on our case series, we have chosen to call this condition SIC and to avoid the term "granuloma" at this time. It is tempting to speculate that SIC is in the spectrum of other ocular inflammations like nodular posterior scleritis or orbital inflammatory pseudotumor, where a specific etiologic agent is not demonstrable.

Most of our patients with SIC were referred to us because of diagnostic uncertainty and because intraocular tumor was a consideration. Therefore, the main goal
Figure 3. Clinical spectrum of presumed inactive solitary idiopathic choroiditis. A, Well-defined, yellow, inactive lesion inferior to the optic disc in a 23-year-old woman. The patient experienced recurrent bouts of inflammation for 26 years after this photograph was taken. B, Well-defined, inactive juxtapapillary lesion, touching superior margin of optic disc in a 43-year-old man. C, Juxtapapillary lesion inferonasal to the optic disc in a 30-year-old woman shows a characteristic red-orange halo. D, Discrete lesion superior to the optic disc in a 37-year-old man. E, Same lesion (Figure 1D) shown in 3-dimension after 2 years. Note that it is stable in size but has developed mild pigmentary mottling on the surface. F, Lesion inferior to the optic disc with mild overlying proliferation of the retinal pigment epithelium in a 30-year-old man. G, Small juxtafoveal lesion with a superficial retinal arteriovenous communication in a 13-year-old girl. H, Juxtafoveal lesion with retinal arteriovenous communication in a 47-year-old woman. There is a small amount of residual intraretinal exudation inferior to the lesion. Prior subretinal fluid has resolved.
Figure 4. Clinical spectrum of active lesions of solitary idiopathic choroiditis showing a response to treatment and resultant complications. A, Juxtafoveal lesion in a 12-year-old boy with blurred vision. The active lesion has an ill-defined border and subretinal fluid is present in the entire macular region. Consultation with infectious disease experts and exhaustive laboratory studies failed to uncover a cause. The patient was treated with oral corticosteroids. B, Lesion shown in Figure 2A after 3 weeks of oral corticosteroid therapy. The lesion is smaller and more discrete, the subretinal fluid has resolved, and the visual acuity has dramatically improved to 20/20. C, Juxtapapillary lesion in a 25-year-old woman. There is partially resolved exudation and subretinal fluid in the foveal area. Note the peculiar retinal vascular tortuosity on the surface of the lesion. The patient was treated with oral corticosteroids. D, Lesion shown in Figure 2C after 2 years. The exudation and subretinal fluid have subsided. E, Juxtafoveal lesion in a 12-year-old girl with sudden onset of blurred vision. The lesion responded to oral corticosteroid therapy. F, Lesion shown in Figure 2E after 2 years. The lesion is larger and associated with continued inflammatory signs. G, Typical lesion inferior to the optic disc in a 60-year-old woman. The patient was asymptomatic. H, Lesion shown in Figure 2G 6 years later when patient had floaters. There is a superficial hemorrhage along the course of a retinal artery that passes over the lesion.
of this study was to clarify the clinical manifestations of SIC and to review the clinical features that serve to differentiate it from specific inflammatory processes, fundus tumors, choroidal neovascular membranes, organized hemorrhage, and other conditions that may have a similar clinical appearance.

Concerning inflammatory conditions, SIC may be similar clinically to a choroidal granuloma of sarcoidosis, tuberculosis, or other related entities. None of our patients had a history, clinical findings, or positive laboratory study results to suggest known granulomatous disease. However, we cannot absolutely exclude these conditions since it is possible that they could produce a solitary granuloma as the only manifestation of the disease. As a rule, however, these conditions produce more severe inflammatory disease, with anterior uveitis and vitreous inflammatory cells. In our case series, anterior segment and vitreous inflammation was usually absent or very subtle.

Other ocular inflammatory conditions that may superficially resemble SIC include ocular histoplasmosis, ocular toxoplasmosis, nodular posterior scleritis, syphilis, and cat-scratch disease, but there are features that should assist in differentiating them from SIC.1 Ocular histoplasmosis most often affects the eye as a classic triad of juxtapapillary choroidal atrophy, peripheral discrete lesions, and a macular neovascular membrane. Ocular toxoplasmosis primarily affects the retina and not the choroid, usually produces more vitreous cellular reaction, is likely to have satellite lesions, and heals as a flat or punched-out scar with more pigment proliferation than seen in our patients.10 Nodular posterior scleritis has a faint orange-red color similar to the background fundus, is often associated with choroidal folds, and shows characteristic multiple hyperfluorescent spots on angiography.20 Syphilis can rarely produce a posterior choroidal granuloma. However, it more often appears as a solitary, placoid, pale-yellow lesion that lacks the yellow-white color and distinct margins that characterize SIC.21 Cat-scratch disease is recognized to produce a variety of intraocular inflammatory signs. Usually it occurs as an optic papillitis with a stellate macular exudation. One reported case of presumed cat-scratch disease was seen as a solitary mass that was identical to the cases reported herein.17 Some of our patients were seen prior to the widespread recognition of cat-scratch disease as a cause of intraocular inflammation. Therefore, they did not undergo serologic studies for Bartonella. However, none of our patients had a history of excessive contact with cats.

As demonstrated from our study, SIC may be clinically similar to ocular tumors like amelanotic choroidal melanoma, amelanotic choroidal nevus, choroidal metastasis, solitary choroidal hemangioma, choroidal osteoma, lymphoma, retinoblastoma, or retinal astrocytic hamartoma.22-26

Amelanotic choroidal melanoma differs from SIC in that it tends to be larger in diameter and thickness, often has visible blood vessels within the mass, usually has a less distinct margin, does not produce yellow exudation, does not have a surrounding red halo, and often has overlying drusen or golden-brown pigment mottingling. Amelanotic choroidal nevus has similar features to amelanotic choroidal melanoma except it is usually smaller.

Choroidal metastasis tends to have a duller, creamy yellow color, usually has less distinct margins, does not produce appreciable inflammation or exudation, causes more extensive retinal detachment, and generally shows less intense late fluorescence on angiography. Solitary choroidal hemangioma tends to have a more red-orange color, has slightly ill-defined margins, usually lacks yellow exudation, and shows diffuse mottled fluorescence by the arterial phase and moderately intense late staining on angiography. Choroidal osteoma has a yellow-orange color and well-defined margins but has more irregular or scalloped borders, lacks inflammatory signs, and produces a highly reflective echo on ultrasonography, a bone density pattern with computed topography, and is more likely to cause choroidal neovascularization. Intraocular lymphoma can sometimes occur as a solitary lesion in the choroid, retina, or beneath the retinal pigment epithelium. It has clinical and angiographic features similar to a choroidal metastasis. It frequently occurs in patients who have concurrent systemic lymphoma.

A small retinoblastoma occurs in younger patients, is located in the retina rather than the choroid, and has retinal feeding and draining blood vessels that are derived from the sensory retina. Chalky white foci of calcification are occasionally seen in retinoblastoma. Retinal astrocytic hamartoma usually has a gray-white rather than yellow-white color, is located in the sensory retina rather than the choroid, and may show glistening yellow foci of calcification; findings not seen with SIC.

The diagnostic evaluation of a patient with ophthalmoscopic findings of SIC should depend on the clinical findings. If the lesion shows signs of active inflammation and the visual acuity is affected, a systemic evaluation for the aforementioned specific inflammatory conditions is justified. In most instances, clinical testing for various causes of uveitis yields negative results. Since many of the inactive lesions are asymptomatic and are unlikely to recur, evaluation should be limited to testing for treatable conditions like sarcoidosis, tuberculosis, and syphilis. If positive results are found, then a course of appropriate treatment should be considered. Negative results would support the diagnosis of SIC.

The management of SIC varies with the clinical findings. If the lesion appears inactive and is discovered on routine ophthalmic examination, periodic observation only is warranted. Active lesions in the region of the optic disc or fovea should be treated with systemic corticosteroids in a traditional manner.

CONCLUSION

We have described the clinical features of 60 cases of a rather distinct clinical entity, which we have called SIC. It has features similar to solitary granulomas that can occur with ocular sarcoidosis, tuberculosis, and toxocariasis, but clinical and laboratory studies fail to reveal a specific cause. Although it can superficially resemble several amelanotic intraocular tumors like choroidal melanoma, metastasis, hemangioma, osteoma, lymphoma, retinoblastoma, and retinal astrocytic hamartoma, it has distinctive clinical and fluorescein angiographic features that should differentiate it from most intraocular tumors. The
patient should have limited systemic and laboratory studies to determine a specific cause, but most cases will remain idiopathic. If vision is threatened, therapeutic systemic or periocular corticosteroids should be administered. In contrast to most malignant tumors, SIC is a self-limited disease, but it may occasionally display recurrent bouts of inflammation. However, it generally stabilizes and usually does not show progressive enlargement. It is important for clinicians to be familiar with SIC and to differentiate SIC from other inflammatory conditions and tumors to avoid misdirected therapy.

Submitted for publication July 12, 2001; final revision received September 25, 2001; accepted December 11, 2001.

This study was supported in part by the Eye Tumor Research Foundation, Philadelphia; the Award of Merit in Retina Research, Houston, Tex (Dr J. A. Shields); and the Macula Foundation, New York, NY (Dr C. L. Shields).

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