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REVIEW ARTICLE

Glial tumors of the retina. The 2009 King Khaled Memorial Lecture

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Abstract Retinal glial tumors and pseudotumors can be classified into astrocytic hamartoma, acquired retinal astrocytoma, massive gliosis, and focal nodular gliosis. Each has different clinical manifestations. Astrocytic hamartoma is usually seen patients who have some manifestations of tuberous sclerosis complex (TSC). It can occur as a noncalcified or calcified variety, and often a combination of the two, and has fairly typical features with fluorescein angiography, ultrasonography, and optical coherence tomography. Although it is generally a stationary lesion, an aggressive variant seen in very young children with TSC can lead to exudative retinopathy, retinal detachment, and neovascular glaucoma. Acquired astrocytoma general occurs in somewhat older individuals who do not have TSC. Like the aggressive form of astrocytic hamartoma it can lead to exudative retinopathy and exudative retinal detachment. Pseudoneoplastic diffuse retinal gliosis can occur as massive glial proliferation in eyes with prior trauma, Coats disease, retinal angiomatosis and other conditions and often occurs in blind eyes. Pseudoneoplastic focal retinal gliosis is characterized by a very superficial, white, noncalcified lesion in otherwise normal eye in somewhat older individuals. Recognition of these glial lesions is important because they can resemble malignant tumors and have different clinical courses and complications.

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1. Introduction

Like the central nervous system, the retina contains supportive glial cells known as astrocytes. These cells spawn several reactive processes that can assume clinical importance. The most common ones include surface wrinkling retinopathy, the gliosis that follows retinal hemorrhage, trauma, or tumors like combined retina hamartoma and retinal hemangioblastoma. In such cases the gliosis itself does not assume tumorous proportions and is not usually considered in the differential diagnosis of glial tumors. This review describes the clinical features of selected tumors and pseudotumors presumed to be of retinal glial cell origin. These include astrocytic hamartoma, acquired retinal astrocytoma, massive gliosis, and idiopathic focal pseudoneoplastic gliosis of the retina (Shields and Shields, 2009; Nyboer et al., 1976; Margo et al., 1993; Mullaney et al., 1997; Shields et al., 2004a,b, 2005, 1995, 1996; Zimmer-Galler and Robertson, 1995; Mennel et al., 2005; Jost and Olk, 1986; Drewe et al., 1985; Ulbright et al., 1984; Coppeto et al., 1982; Kroll et al., 1981; Reeser et al., 1978; Eagle et al., 2000; Gunduz et al., 1999; Cohen et al., 2008; Ramsay et al., 1979; Reeser et al., 1978; Bornfeld et al., 1987; Yanoff et al., 1971; Nowinski et al., 1984; Gelisken et al., 2004; Berger et al., 1979; Green, 1967; Ryan, 1954; Demirci et al., 2002; Khawly et al., 1999).

2. Retinal astrocytic hamartoma

Retinal astrocytic hamartoma is a benign tumor that is composed of a proliferation of well differentiated astrocytes (Shields and Shields, 2005, 2009; Nyboer et al., 1976; Margo et al., 1993; Mullaney et al., 1997; Shields et al., 2004a, 1996, 2005; Zimmer-Galler and Robertson, 1995; Mennel et al., 2005; Jost and Olk, 1986; Drewe et al., 1985; Ulbright et al., 1984; Coppeto et al., 1982; Kroll et al., 1981; Reeser et al., 1978; Eagle et al., 2000; Gunduz et al., 1999; Cohen et al., 2008). It is believed to be congenital in most cases but it can become clinically apparent sometime after birth. It is frequently associated with tuberous sclerosis complex (TSC), a syndrome that includes various combinations brain astrocytoma, cutaneous angiofibromas (“adenoma sebaceum”), cutaneous depigmented macules (ash-leaf sign), cardiac rhabdomyoma, renal angiomyolipoma, and other hamartomas (Shields and Shields, 2005, 2009; Nyboer et al., 1976). In those cases that are part of TSC, various genetic alterations have been identified on chromosomes 9 and 16. Some patients have only the retinal tumor without additional findings of TSC. It is still undetermined whether they represent a separate entity or a forme fruste, or partial expression, of TSC. An identical fundus tumor is occasionally seen in patients with neurofibromatosis type 1.

2.1. Clinical features

Ophthalmoscopically, retinal astrocytic hamartoma can show considerable variation from case to case. The two most common variations are the noncalcified tumor, the calcified tumor or, more commonly, a combination of the two. The noncalcified variant appears as a small gray-yellow, sessile of slightly elevated lesion in the inner aspect of the sensory retina. It can occasionally be transparent and fairly flat, sometimes suggesting reactive gliosis. Slightly larger lesions have a gray-yellow color and may cause adjacent retinal traction. The calcified variant may have minimal calcification or may be totally calcified. The characteristic feature is glistening yellow spherules of calcification.

In contrast to retinoblastoma, astrocytic hamartoma show glistening yellow calcification that differs from the more dull, chalky calcification that characterizes retinoblastoma. It does not usually develop prominent retinal feeding and draining blood vessels, and often causes retinal traction, a finding not usually seen with untreated retinoblastoma. Vitreous seeding of the tumor and hemorrhage can sometimes occur (Kroll et al., 1981; Cohen et al., 2008).

Although astrocytic hamartoma was historically considered to be a relatively stable lesion, there are recent reports of progressive growth and locally malignant behavior (Shields et al., 2005; Gunduz et al., 1999). These aggressive astrocytic hamartomas can cause exudative retinal detachment and neovascular glaucoma, ultimately requiring enucleation. Extraocular extension into the orbital and epibulbar tissues has been recognized in these cases (Shields et al., 2005; Gunduz et al., 1999).