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Melanocytoma of the optic nerve head: a review*

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Abstract

The melanocytoma of the optic disc is a deeply-pigmented tumor located on the optic nerve head. In contrast to malignant melanoma, it appears to occur in equal frequency in whites and non-whites. Histologically, it consists of deeply-pigmented plump nevus cells with benign characteristics. No treatment is usually necessary and the prognosis is excellent.

Introduction

The term melanocytoma has come to designate a rather specific intraocular tumor which usually appears ophthalmoscopically as a black lesion of variable size and shape located over the optic disc (Fig. 1). There has been considerable confusion as to the clinical and pathologic nature of this lesion and how it fits into the classification of pigmented ocular tumors. This article will review the historical aspects, clinical features, diagnostic approaches, differential diagnosis, racial incidence, histopathology, pathogenesis, treatment, and prognosis of this intriguing intraocular tumor. The information is derived partly from the literature and partly from observations on fifteen patients personally evaluated by the author on the Oncology Unit of the Retina Service of Wills Eye Hospital.

History

From a historical point of view, the melanocytoma of the optic nerve is a good example of the changing concepts regarding the malignancy of certain intraocular tumors (23). Until a few years ago, this pigmented tumor was considered by many authorities to be a juxtapapillary malignant melanoma which had invaded the optic nerve head (22, 25). With few exceptions (3, 14) eyes containing melanocytomas were enucleated because of suspected malignancy and even after histologic examination were still classified as malignant melanomas (5, 9, 10).

The question as to the malignancy of the melanocytoma was gradually resolved as more cases were submitted to the Registry of Opththalmic Pathology at the Armed Forces Institute of Pathology (22). By 1962, enough data had accumulated to permit Zimmerman & Garron (25) to document the extremely benign nature of the melanocytoma. They reported 35 cases of melanocytoma, 20 of which were enuclated, 14 were followed without enucleation, and one was obtained at autopsy. Of the 20 cases which were enucleated because of suspected malignancy, follow-up examination revealed no tumor-related deaths. At first, one might suspect that enucleation was a life-saving measure in these patients. A review of the 14 cases which were not enucleated, however, also revealed no tumor-related deaths. In fact, these cases showed little or no ophthalmoscopic change during a follow-up period ranging from one to 34 years. It became apparent that the melanocytoma of the optic disc is a benign lesion which requires no treatment.

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Confusion also exists as to the correct nomenclature of the tumor. Cogan, noting the large plump to polyhedral cells comprising the melanocytoma, believed the term *magnocellular nevus* was most appropriate (4). Reese, stating that the melanocytoma is probably a congenital tumor, prefers to call it a *benign melanoma* of the optic nerve head (15). Zimmerman was impressed by the similarity of the tumor cells to the melanocytes found in the uveal tract in patients with ocular melanocytosis. Consequently, he proposed the term *melanocytoma,* which has become widely accepted among clinicians and ophthalmic pathologists (22).

The melanocytoma is traditionally recognized to be ophthalmoscopically stable with no tendency to grow. If one carefully records its appearance with drawings or photographs, however, subtle enlargement may occasionally be detected over several years. In one case which showed enlargement over six years, the eye was enucleated and a low grade malignant melanoma was found (24). For the most part, however, these lesions remain stationary, with minimal or no tendency to enlarge.

Clinical features

Symptoms

Patients with melanocytomas of the optic nerve head usually have normal vision and are asymptomatic. If the tumor is fairly large, the observant patient may notice slightly blurred vision or a scotoma due to an enlarged blind spot. On rare occasions, progressive but reversible loss of visual acuity has occurred in the involved eye (21). Whether the visual loss in such cases is secondary to necrosis of the tumor, obstruction of adjacent blood vessels, or an incidental optic neuritis, is uncertain.

Signs

Visual acuity and intraocular pressures are usually normal. On occasion, an afferent pupillary defect (Marcus-Gunn pupil) has been noted, probably due to compression of nerve fibers by the melanocytoma cells (12). External ocular examination is usually normal and the vitreous is clear. There may be hyperpigmentation of the uveal tract, identical to that which occurs in ocular melanocytosis, but this is usually overlooked clinically. We have noted other pigmented ocular lesions such as uveal nevi and hypertrophy of the retinal pigment epithelium to be slightly more common in eyes with melanocytomas (8).

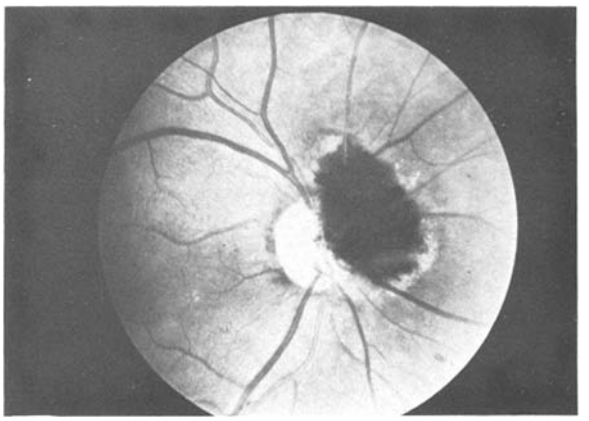

Fig. 1. Typical melanocytoma of optic nerve head.

Ophthalmoscopically, the melanocytoma has typical but somewhat variable clinical features. It is usually an elevated jetblack epipapillary mass located eccentrically over the edge of the optic disc (Fig. 1). The tumor may involved the nerve fiber layer of the retina, producing a fibrillated margin (Fig. 2). In a number of cases, a peripapillary choroidal nevus appears to be continuous with the epipapillary tumor (Fig. 3). The uninvolved portion of the optic disc is

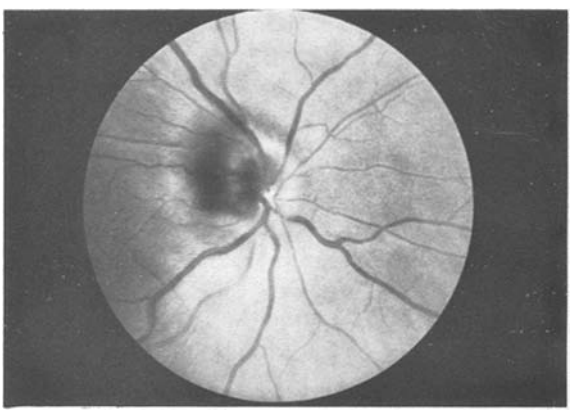

Fig. 2. Melanocytoma on temporal side of disc, showing fibrillated margin to tumor.

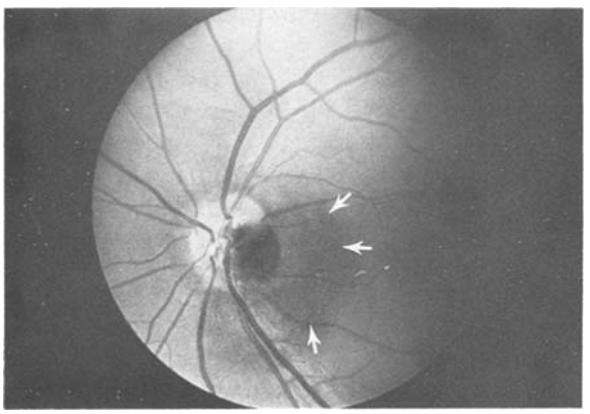

Fig. 3. Melanocytoma of optic disc with peripapillary choroidal nevus (Arrows).

often normal, but may occasionally be edematous (Fig. 4). In some instances, the lesion may be small, flat, and confined to the optic disc (Fig. 5). In older patients, there may be chronic degenerative changes in the RPE around melanocytomas. Although the melanocytoma usually occurs unilaterally, in rare instances bilateral lesions have occured (20).

Diagnostic approaches

With regard to the diagnosis of melanocytoma, it is most important that the clinician be aware of its typical features and recognize its benign nature. The lesion can usually be recognized by ophthalmoscopy alone, and further studies add little to the diagnosis. Certain ancillary procedures such as serial fundus photographs, fluorescein angiography, and visual fields are helpful in follow-up evaluation.

Fundus photography

Serial fundus photographs are helpful in ascertaining whether the lesion is showing evidence of growth. Although most melanocytomas show no evidence of enlargement, occasionally progressive growth may be noted (24).

Fluorescein angiography

In most cases, this deeply pigmented tumor is hypofluorescent throughout the angiogram (Fig. 6). This is presumably because of the deeply pigmented, densely packed cells with little vascularity. Occasionally there may be rather intense staining of the optic disc adjacent to the tumor. This is probably due to staining of the secondary disc edema.

Visual Fields

The visual fields of eyes with melanocytomas may be variable. Enlargement of the blind spot is most frequent, but nerve fiber bundle defects and nasal step have been observed (12). If the lesion is small and confined to the superficial portion of the optic disc, the visual field may be normal.

Other diagnostic tests

Since the diagnosis of melanocytoma of the optic disc can usually be made by ophthalmoscopy alone, other

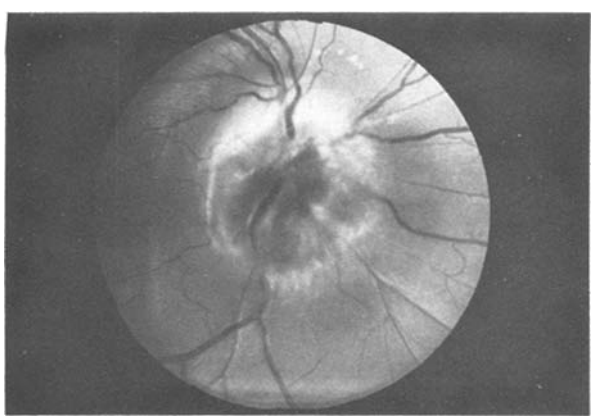

Fig. 4. Melanocytoma of inferior portion of optic disc with edema of superior portion of disc.

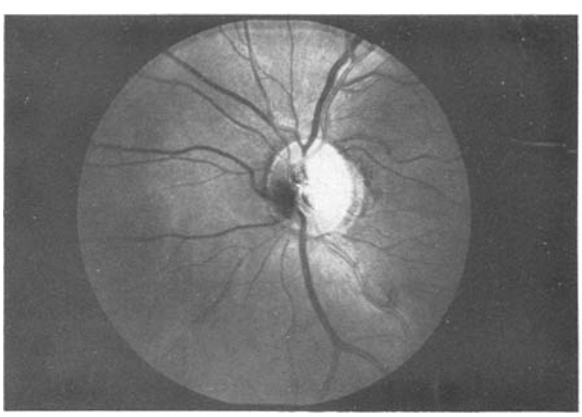

Fig. 5. Small melanocytoma confined to prepapillary portion of disc.

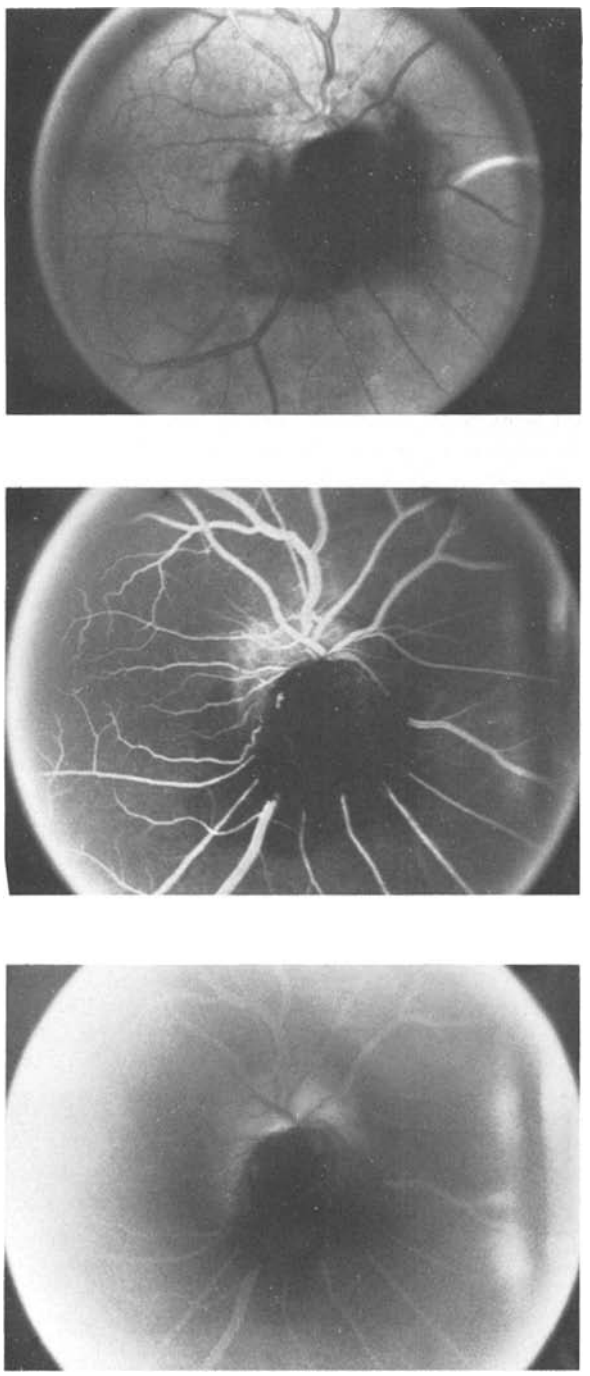

Fig. 6. A. Large melanocytoma of inferior portion of optic disc in 50 year-old black male referred with diagnosis of malignant melanoma. B. Fluorescein angiogram of same lesion during anteriovenous phase, showing hypofluorescence of the lesion. C. Angiogram in late phase about 15 minutes after injection, showing continued hypofluorescence of the lesion.

steps are not essential. If the lesion is greater than 0.5 mm in elevation, it may be demonstrated with ultrasonography, but this technique will not easily differentiate melanocytoma from other lesions of the optic disc. Ultrasonography is not particularly helpful in determining the extent of optic nerve involvement behind the globe. The ^{32}P test is not usually helpful because the location of the lesion usually renders it inaccessible to the counting probe.

Differential diagnosis

Several lesions may clinically simulate melanocytomas of the optic nerve. These include malignant melanoma, peripapillary choroidal nevus, hyperplasia of the retinal pigment epithelium (RPE), congenital hypertrophy of the RPE, and so-called 'combined hamartoma' of the RPE and sensory retina.

On occasion, a choroidal melanoma may be located in the peripapillary region. Such a tumor may grow around the termination of Bruch's membrane at the disc margin and extend anteriorly into the vitreous cavity. In contrast to melanocytoma, they do not usually invade the nerve fiber layer producing the fibrillated appearance that is characteristic of melanocytoma. They are more likely to have a mushroom shape due to their growing from the choroid and tuning abruptly around the termination of Bruch's membrane at the disc margin.

A choroidal nevus, when located adjacent to the optic disc, may occasionally be confused with melanocytoma. Choroidal nevi, however, are usually delineated by the disc margin corresponding to the termination of the choroid and do not overlie the optic disc itself. They do not extend superficially into the nerve fiber layer of the retina.

Hyperplasia of the RPE may occur in the region of the optic disc and produce a black, elevated mass resembling a melanocytoma (Fig. 7). In contrast to melanocytoma, its margins are often irregular and there may be associated gliosis. The eye may show similar areas elsewhere or signs of previous inflammation or trauma.

Congenital hypertrophy of the RPE may occur in the region of the optic disc and be confused with melanocytoma (Fig. 8). It is usually flat and delineated by the disc margin at the termination of the

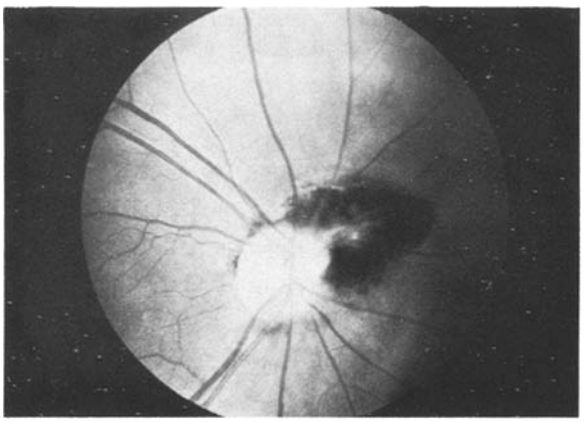

Fig. 7. Hyperplasia of RPE simulating a melanocytoma. Note the gliosis in the center of the lesion. There were also focal chorioretinal scars in the periphery, compatible with a previous inflammatory process.

RPE. It may show the typical lacunae of depigmentation (13).

The so-called 'combined hamartoma' involving the RPE and sensory retina may also simulate melanocytoma. It consists, however, of a combined proliferation of RPE and glial and vascular elements of the sensory retina. The vascular elements may give the appearance of angioma and the glial elements may cause retinal traction folds. Such tractional phenomena do not occur with melanocytoma. In addition, the combined hamartoma usually shows leakage and late staining with fluorescein angiography (6).

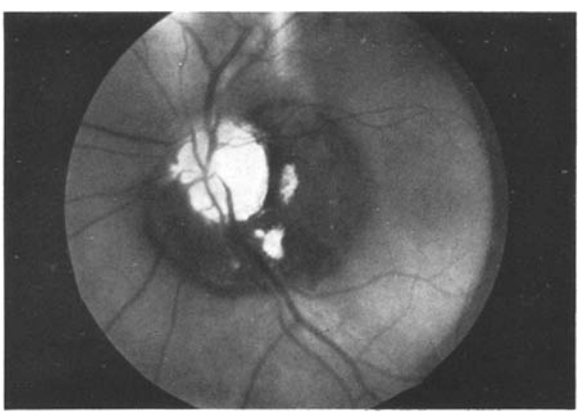

Fig. 8. Peripapillary congenital hypertrophy of RPE simulating a melanocytoma.

Racial incidence

Because melanocytomas have often been confused clinically with malignant melanoma, it is important to consider the racial differences of these two tumors. Approximately 50% of melanocytomas occur in black patients or dark-skinned caucasians (25). Less than 1% of uveal melanomas occur in black patients. When one sees a pigmented, epipapillary lesion in a black patient, therefore, melanocytoma should be strongly considered in the differential diagnosis. The diagnostic problem was best exemplified in the series of Shields & Zimmerman (18), where a 13 year-old black female with 20/20 vision had an enucleation because the melanocytoma was clinically misdiagnosed as a melanoma (Fig. 9).

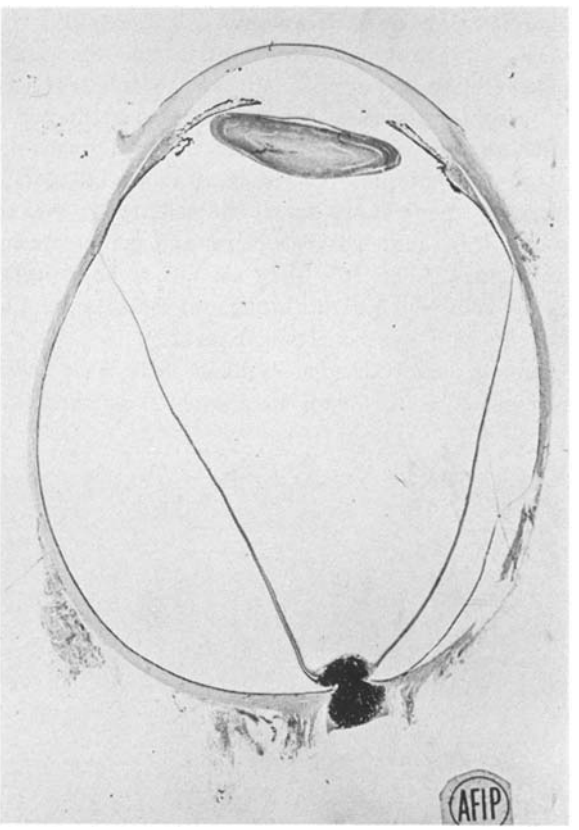

Fig. 9. Lower power photomicrograph of melanocytoma of optic nerve. Eye of a 13 year-old black female with 6/6 vision, enucleated as suspected melanoma. From Shields, J.A. & L.E. Zimmerman. *Arch. Ophthal.* 89: 466–471, 1973 (18).

Histopathology

There has been considerable confusion in the ophthalmic literature as to the histologic nature of the melanocytoma and how it fits into the spectrum of pigmented fundus lesions. Apparently, it is not widely recognized that the melanocytoma is merely a variant of a nevus, containing a relatively uniform array of rather specific nevus cells. When Naumann and coworkers (11) classified uveal nevi cytologically, they noted that one type of nevus cell was plump to polyhedral in shape and deeply pigmented. They pointed out that a melanocytoma was composed almost entirely of that particular cell type.

Histologically, the melanocytoma is characteristic even on low power microscopy. It is a deeply pigmented mass occupying the optic nerve head and extending for a variable distance into the optic nerve itself (Fig. 9). Occasionally, the sensory retina and choroid may also be involved. Cytologically, the most distinguishing characteristics are the dense pigmentation and uniform appearance. It is necessary to prepare bleached preparations to satisfactorily visualize the cellular characteristics. Although the dense pigment prevents visualization of cell detail, bleached preparations reveal the cells to be oval or round with abundant cytoplasm and comparatively small nuclei (Fig. 10). They are said to be identical to the cells which occur throughout the uveal tract in patients with ocular melanocytosis (22).

Tumors composed of similar cells have been recognized in the uveal tract away from the optic nerve. There have been well-documented cases in the choroid (17) and ciliary body (2). In one study there were five uveal melanocytomas in a series of 907 histologically proven pigmented intraocular tumors (7). One such lesion located in the choroid has been known to undergo malignant change (1). Tumors composed of typical melanocytoma cells have also been recognized in the iris (16, 19).

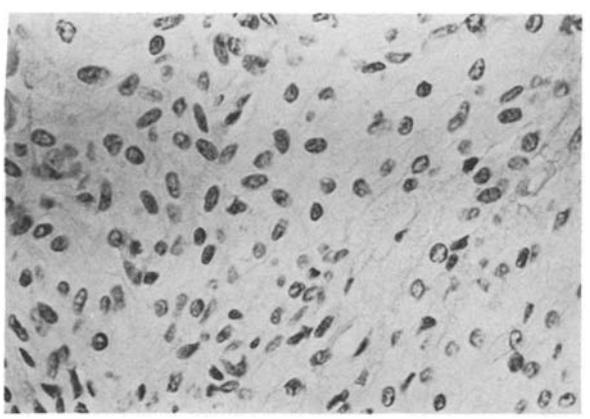

Fig. 10. Cytology of melanocytoma. Hematoxylin-eosin, bleached preparation X 250.

Other histologic observations are occasionally made in eyes containing melanocytomas. There is sometimes extreme hyperpigmentation of the entire uveal tract and episclera resembling ocular melanocytosis. It is evident that melanocytomas, in contrast to malignant melanomas, tend to occur in eyes with a genetic predisposition to be heavily pigmented (22).

Pathogenesis

The pathogenesis of melanocytoma of the optic disc is still unknown. The pigmented cells of the uveal tract, the uveal melanocytes, are believed to be derived from the neural crest during embryologic development. It is believed that they are the cell of origin of the melanocytoma.

Zimmerman has stressed another observation which may cast light on the classification and pathogenesis of melanocytoma. He pointed out that in some lower animals, particularly certain reptiles, the normal optic disc has a rather massive accumulation of deeply pigmented melanocytes. On the basis of these observations, he speculated that the melanocytoma may be a so-called atavistic lesion, representing a phylogenic throwback of a finding which is normal in some species. He proposed the general term 'melanotic progonoma' to characterize the melanocytoma (22).

Management

Once the diagnosis of melanocytoma of the optic disc is established, no treatment is usually indicated. Because the melanocytoma is known to enlarge and undergo malignant change on rare occasions, periodic follow-up examination with fundus photography should be performed.

Prognosis

The prognosis for life in patients with melanocytoma of the optic disc is excellent. There have been no

reported tumor-related deaths in such patients, further supporting the fact that no treatment is necessary.

The visual prognosis for the involved eye is likewise very good. As mentioned, there may be visual field changes of which the patient is often unaware. Acute visual loss has rarely been documented, either due to vascular occlusion or necrosis of the tumor.

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