Primitive tumor of lamina fusca
Original findings

Tumor primitivo de lámina fusca
Achados originais

Carlos Oswaldo Degrazia

RESUMO


UNITERMOS: Lâmina Fusca, Tumor Indiferenciado, Lofoneurogonioma, Crista Neural, Lofoneuroepitélio de Masson.

ABSTRACT

In a meeting of the Pan-American Association of Ophthalmic Pathology, held in Los Angeles, CA, on October 10, 1991, at the Doheny Eye Institute, C.O. Degrazia proposed the name LOFONEUROGONIOMA for a single undifferentiated intraocular tumor originated in the cells of lamina fusca, with undifferentiated cells of expressive differentiation into Schwann cell, melanoblast and neuroendocrine cell lineages. In view of trimorphism, a pathologist may be led to a diagnosis of malignant melanoma, schwannoma or endocrine cell tumor. After this date, an article was published in Revista da AMRIGS, Porto Alegre, 52 (4): 261-272, oct-dez 2008, with collaboration of experts from the fields of Immunohistochemistry and electron microscopy. The current publication is the third one and its main purpose is to highlight the original characteristics of such a tumor.

KEYWORDS: Lámina Fusca, Undifferentiated Tumor, Lofoneurogonioma, Neural Crest, Masson’s Lofoneuroepithelium.

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INTRODUCTION

The present work is the third publication on a tumor that affects a structure of the eyeball, the lamina fusca, a site where no pathology has been described and is very unlikely to give rise to a neoplasm. This publication is being brought to scientific literature again due to the desire to underscore the original aspects of the case. The list of original characteristics that I will make should be carefully accompanied with the figures, as they are the authentic documents on which readers should rely.

The case was first presented by me under the title of Choroidal Tumor, in the meeting of the Pan-American Association of Ophthalmic Pathology, held in Los Angeles, CA, on October 10, 1991, at the Doheny Eye Institute.

Having observed the progressive thickening of the lamina fusca (LF), in connection with the tumor, I showed images of its structure and proposed the name Lofoneurogonioma for the neoplasm. The word has a Greek origin, lofos = crest, neuro = nerve, gonos = origin, and oma = tumor, meaning: tumor of cells originated in the neural crest.

The second presentation was an article published in Revista da Associação Médica do Rio Grande do Sul (1), which includes the history, discussion, details related to the case, and names of the collaborators, both clinicians and experts in Immunohistochemistry, Pathology and Electron Microscopy.

The name lamina fusca originates from Latin, since fuscus means dark, due to the greater or lower amount of melanin present on its path, which may be evidenced by special stains, such as picrosirius, a dye that highlights collagen in intense red, as shown in figure 1.

![](image)

**FIGURE 1** – Lamina fusca evidenced by picrosirius stain, measuring around 6 micra in thickness.

In view of its diminutive thickness, measuring around 6 or 7 micra, it can only be seen with a light microscope, with some difficulty though, as it is confused with the choroid, which encloses it on the inner side of the eye.

This difficulty is sometimes overcome because the paraffin impregnation techniques used for preparing histological sections separate it from the choroid and the sclera that encloses it externally, causing an artificial detachment. This is seen in figure 2.

![](image)

**FIGURE 2** – artificial detachment of Lamina fusca. The LF is seen between the sclera and the uvea which maintains the retinal epithelium. The retina is not seen because it was also artificially detached, as shown in figure 4.

The figure 3, marked with letter C, viewed at low magnification, shows the beginning of the LF hyperplasia, located between the two arrows.

![](image)

**FIGURE 3** – The two arrows signal the beginning of hyperplasia. Picrosirius staining.

**1st Original Aspect: Tumor Shape**

Choroidal tumors that reach a certain size, from a few millimeters, show a convex inner surface. I have never seen, under these conditions, a melanoma with a different shape. They should not be mistaken with nevi, which may have a flat surface.

When they disrupt the Bruch's membrane, the mushroom-shaped ones always show a convex surface.

In the photograph of the specimen, figure 4, the white arrow points to the tumor concavity. The tumor mass is whitish and has a very wide base.

![](image)

**FIGURE 4** – Section of the specimen showing wide neoplasm with concave internal surface (marked by the arrow) with rugged aspect indicative of rupture of the Bruch's membrane, artificial detachment of retina, and uveal staining in the background.
On the fluorescein angiographic report, I highlight the following findings:

**Scarcely pigmented tumor, rupture of the Bruch’s membrane, intraretinal invasion, no nourishing vessels are seen. The conclusion is amelanotic melanoma.**

The expression with intraretinal invasion, used on the report, should not be understood as having the same meaning as in pathological anatomy, in which the word invasion means the penetration of malignant cells into a tissue, the retina is never invaded by cells of a choroidal melanoma.

The findings mentioned are all supported by the histological study and may serve to differentiate it from choroidal melanoma.

The echography report is brief, showing a tumor with a wide base – confirmed by the anatomopathological study – and arriving at the conclusion that it is a choroidal melanoma. By observing the figure, an expert could describe other characteristics, such as the concave aspect and retinal detachment.

### 2nd Original Aspect: Nerve/Tumor Relationship.

The three photomicrographies of figure 5 were included to show the differences of LF with a nerve extending alongside. In the first image, the LF is observed to be already thickened, so it is easy to differentiate it from the smaller, light-colored Schwann cells of the nerve.

Malignant cells begin to invade the nerve, whose thickness increases, as seen in the middle picture, and its fibrils are completely dissociated, as in an explosion (right photo). The finding of nerve fillets sometimes completely isolated within the neoplasm is explained, as they are extensions from the same nerve. The stains employed were: hematoxylin-eosin, S-100 Protein, and luxol, respectively. The insert in the middle figure is the cross-section of an axon, showing the peripheral myelin, which is strongly responsive to S-100 Protein, and the central axis cylinder, aspects that have long been described in scientific literature, but have been seldom shown.

### 3rd Original Aspect: Measurements Of Lamina Fusca

The third original aspect lies exactly on the measurements of LF. These measurements do not appear in the literature on eyeball histology that is typically consulted.

The figures of PLANK 1, from a to b, show progressive thickening. In each of them there are numbers expressing thickness in micra. The thinnest measures 9.29 micra, increasing up to 103.25 micra. Measurements were taken with the LF at a slant position, therefore, they are slightly...
greater. The pigmented epithelium, with melanin grains, may serve as a comparison, as the cell thickness ranges from 6 to 20 micra. The retina cannot be seen because it was artificially detached. The following three pictures, i, j, k, are photos of the histological structure of the tumor. The left one, i, is the LF with an anarchical arrangement of its cells, where a vascular bed is invaded by malignant cells. The two following, j and k, show palisades having the same arrangement as that of the embryonic epiblast from which they derive. Figure m shows cells from a tumor surface smear stained by the Papanicolaou method, with nuclei having the shape of a cufflink. On both sides, two nuclei, figures l and n, viewed by an electron microscope, show deep clefts that account for the nucleus shapes seen under the light microscope.

4th Original Aspect:
Neural Crest And Lofoneurogonia

Usually, neurulation is represented with cross-sections, but we should consider it all along the longitudinal length, from the cephalic region to the caudal region, the neural crest is, therefore, bilateral and rostrocaudal.

— Origin of LF cells in the neural crest

1º - Evidence from the tumor

The same figure 7 from the work mentioned in (1) shows the correlation between tumor cells and embryonic cells. (In this case, a rat embryo was used for comparison.)
The cell palisades, which resemble migrating birds in flight, present evidence of being derived from the embryonic epiblast. Likewise, undifferentiated intermediate cells, which differentiate into Schwann cells, melanoblasts or endocrine cells, derive from the neural crest.

Despite the difficulty establishing these correlations, it is accepted that melanocytes derive from the neural crest. An elucidative approach is made by (2), from which I took the following excerpts:

Currently, it is accepted that, cytogenetically, melanomas are of neuroectodermal origin, from melanocytes derived from the neural crest. This origin is supported by confirming the association of uveal melanomas with abnormalities in the nervous system, such as neurilemomas, (…).

Later it adds: Furthermore, in some cases, there are light tumor areas similar to Schwann cells, adjacent to other areas of evident melanomatous appearance, highly pigmented.

2° Evidence from experimentation

Some elegant evidence is reported in the same book as follows:

If the optic vesicles from a bird are transplanted to the coelom of another, before the cells from the neural crest migrate, only cells of the retinal epithelium are pigmented, but no choroidal melanoblasts appear, which indicates a different origin for both pigments.

If the transplantation is carried out after the emigration of cells from the neural crest, melanocytes appear in the area having characteristics of the donor.

These experiments are attributed to several authors, listed in the Bibliography on page 28 of the same book.

How the neural crest cell migrates, what its initial gene pool is, what influences affect the cell when it crosses different tissues, whether it is always migrating or remains dormant are compelling questions.

In figure 8 and PLANK 2, I try to provide a notion about the links derived from cells originated in the neural crest. A
FIGURE 9 – Typical morphology of a Schwann cell: Lobulated nucleus with clefts, cytoplasm with numerous finger-like structures, incomplete basal membrane (indicated the arrow) and structure viewed at magnification of X34.G0G, comparable with the Luse Body, which was presented by the autor at magnification of X24,000. Letter N is indicating the nucleus. The arrow head in the insert indicates a cell junction.

FIGURE 10 – PLANK 2

Legend: In this plank, three main aspects of the work are included. 1. In the upper portion there is a scheme showing the derivation of neoplastic cells from an undifferentiated cell of the neural crest, which I called lophoneurogonia. From it three arrows depart indicating the differential forms, schwann cells, melanoblasts and endocrine cells. These phenotypical forms were specifically characterized by specific immunohistochemical reactions, PBM, HMB-45, and CHROMOGRANIN A. The neural crest is a proliferation of the epiblast at a slanted angle for formation of the neural tube. II – I named the resulting neoplasm lophoneuropogionioma. In the lower portion, the rectangle resembles a surface with three different ceramic plates, accounting for the word mosaicism for tumor trimorphism. III – Finally, trimorphism may lead to contradictory diagnoses of schwannoma, melanoma and endocrine cell tumor. In the insert with the melanoma picture, a strongly reactive melanoblast is highlighted.
In this paper, I intended to present the several original aspects shown by a tumor that has not been described in scientific literature before. It should be noted that its origin is in the lamina fusca, a site in which no anatomopathological process has been described. In the photomicrographs, the progressive thickening of LF is curious and evident, and being present in the same tumor, are phenotypically different cell lineages. These are tumors with a mosaic-like structure which, according to the technique used by the investigator, show different aspects under different nomenclature, accounting for the substantial diagnostic disagreement.

Hence the designation *lofoneurogonioma* that I assigned to the tumor. The resulting trimorphism, which I call mosaicism – actually, more than three forms are assumed to exist – accounts for the diverging diagnoses among pathologists.

The individuality of LF is documented in figures 1 and 2, which is not found in publications addressing this structure. The artistic quality of the work stands on its own.

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