



OPTIC NERVE TUMOUR



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Dr. Krati Gupta
Dr. Saurabh Deshmukh

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What are the common tumors of optic nerve in adults? Give clinical features to differentiate them clinically and give salient pathologic features of these tumors. (3+2+5)

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Tumors may affect the ONH	Retrobulbar portion of the optic nerve
1. Melanocytoma 2. Peripapillary choroidal melanoma 3. Retinal pigment epithelial proliferation 4. Hemangioma 5. Metastasis	6. Glioma 7. Meningioma

Intraorbital or intracanalicular compressive optic neuropathy

- Patients with intraorbital or intracanalicular compressive lesions typically present with
 - ✓ Slowly progressive vision loss
 - ✓ Monocular visual field loss (usually central or diffuse).
 - ✓ RAPD
- There may be subtle associated signs of orbital disease such
 - ✓ As eyelid edema
 - ✓ Retraction, or lag
 - ✓ Ptosis
 - ✓ Proptosis
 - ✓ Or ophthalmoplegia
- The optic disc may be
 - ✓ Normal
 - ✓ Or mildly atrophic at presentation
 - ✓ Anterior orbital lesions may produce optic disc edema.
- The lesions that most commonly produce optic neuropathy include
 - ✓ Optic nerve sheath meningioma
 - ✓ Glioma.
- Optociliary shunt vessels (retinochoroidal collaterals) or choroidal folds may also be present.
- Cavernous hemangioma, although common in the orbit, produces compressive optic neuropathy only occasionally.
- If an orbital compressive lesion is suspected, neuroimaging is indicated.
 - ✓ MRI is best for evaluating soft-tissue abnormalities in the orbit, particularly in differentiating meningioma from Glioma.
 - ✓ Thin-section CT scan remains a highly satisfactory option and is preferred for evaluation of calcification and bony abnormalities.

1. Optic nerve sheath meningioma

- i. Optic nerve sheath meningioma (ONSM) arises from proliferations of the meningoepithelial cells lining the sheath of the intraorbital or intracanalicular optic nerve.
- ii. Primary optic nerve sheath meningiomas arise from the arachnoid sheath of the optic nerve.



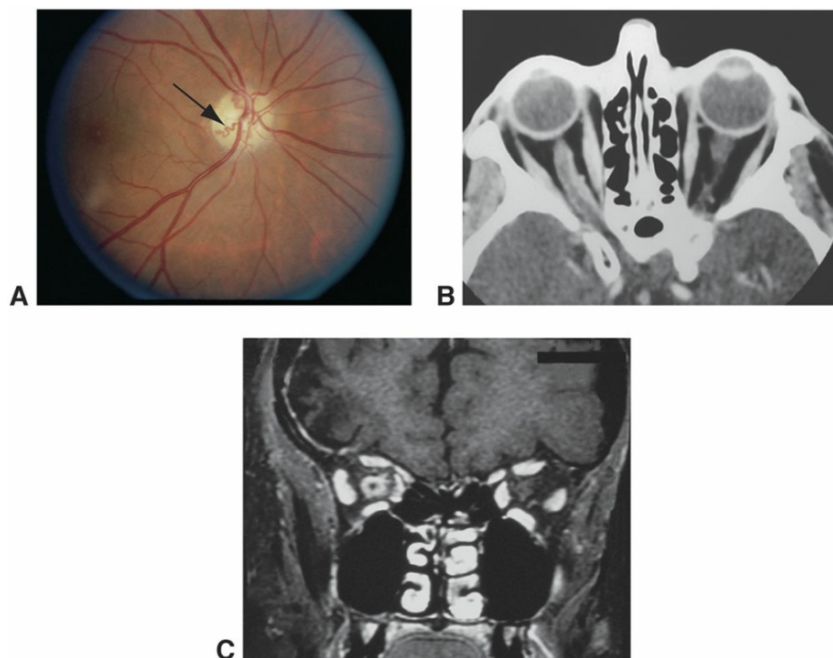
- iii. Although these tumors are uncommon (1%–2% of all meningioma), they account for one-third of primary optic nerve tumors, second only to optic nerve glioma.
- iv. They are usually detected in adults aged 40–50 years.
- v. Affect women 3 times as often as men
- vi. 4%–7% of optic nerve sheath meningiomas occur in children.
- vii. Although meningioma may, in rare instances, be associated with neurofibromatosis (NF1) in younger patients, optic nerve glioma is a more frequent hallmark of NF1 than meningioma.
- viii. They are less frequent than secondary orbital meningiomas, which extend into the orbit from an intracranial primary site.
- ix. Primary optic nerve sheath meningiomas may invade the nerve and the eye; rarely, they may also extend through the dura mater to invade the extraocular muscles.

Signs and symptoms

- Patients may present with the **classic diagnostic triad**:
 1. Painless, slowly progressive monocular vision loss
 2. Optic atrophy
 3. Optociliary shunt vessels
- Optociliary shunt vessels are preexisting optic disc channels that dilate in response to chronic obstruction of outflow through the central retinal vein.
- These vessels shunt retinal venous outflow to the choroidal circulation and may be more correctly termed retinochoroidal collaterals.
- They occur in approximately 30% of patients with ONSM but are nonspecific; they are also present in
 - ✓ Sphenoid wing meningioma,
 - ✓ Optic glioma,
 - ✓ CRVO,
 - ✓ And chronic papilledema.
- Patients with ONSM also demonstrate an RAPD
- Optic nerve-related visual field defect.
- Minimal to mild proptosis
- Mild ocular motility defects can also occur.
- Disc edema may be present, especially if the tumor extends anteriorly.

Diagnosis

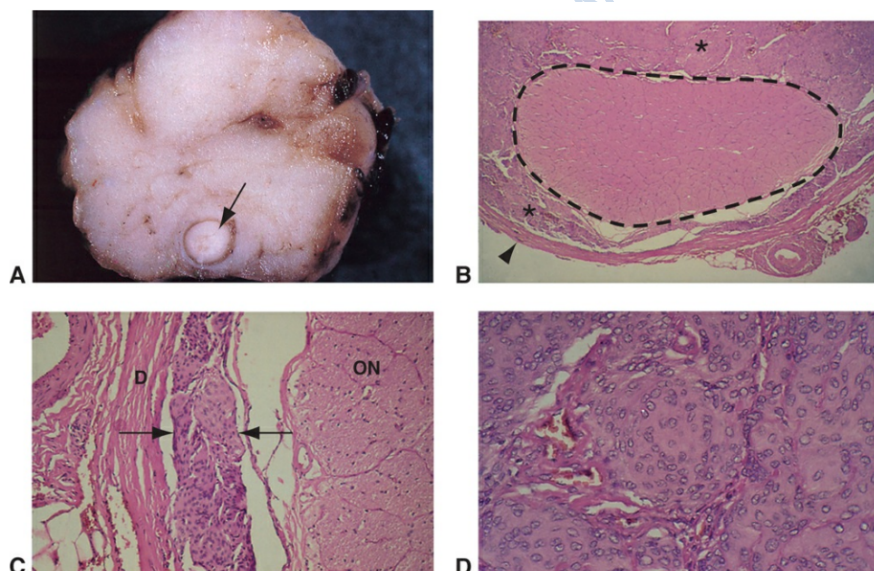
- Diagnosis is confirmed by neuroimaging findings.



- A. Fundus photograph shows optic disc atrophy, with Optociliary shunt vessels (retinochoroidal collaterals, arrow) visible at the 8 and 12 o'clock positions.
- B. CT scans reveals "tram track sign"; diffuse enlargement of the right intraorbital optic nerve extending anteriorly to the globe, with enhancement of the optic nerve sheath.
- C. "Ring sign" in meningioma. Coronal orbital MRI scan shows similar optic nerve sheath enhancement surrounding relatively normal, darker optic nerve on

Pathology

- Histologically, the tumor (primary or secondary)
 - ✓ Is usually meningotheial,
 - ✓ Composed of plump cells with indistinct cytoplasmic margins (also called a syncytial growth pattern) arranged in whorls.
 - ✓ Psammoma bodies, extracellular rounded calcifications surrounded by a cluster of meningioma cells, tend to be sparse.



- A, The shaggy border of this gross specimen emphasizes the tendency of the perioptic meningioma to invade surrounding orbital tissues. Note the size of the optic nerve (arrow) in relation to the tumor.
- B, This meningioma (asterisks) has grown circumferentially around the optic nerve (outlined by dashed line) and has compressed the nerve (arrowhead = dura mater).
- C, Meningioma (between arrows) of the optic nerve (ON) originates from the arachnoid.
- D, Note the whorls of tumor cells, characteristic of meningotheial meningioma, which are the most common histologic variant arising from the optic nerve.

Treatment

1. Fractionated radiation therapy is the treatment of choice for ONSM and has been reported to produce stability or vision improvement in up to 94.3% of patients.
2. However, it remains unclear whether radiation should be administered immediately upon diagnosis or when tumor growth or progressive vision loss is documented because patients with ONSM may have minimal loss of vision for several years.



3. Radiation retinopathy and pituitary dysfunction are reported as late radiation complications.
4. Surgery for biopsy or excision is typically ill-advised because the potential for significant vision loss is considerable.
5. However, if the tumor extends intracranially or, in very rare cases, across the planum sphenoidale, the risk of contralateral vision loss may warrant surgical excision, particularly when severe ipsilateral vision loss is present.
6. Observation is considered appropriate by many if there is no change in visual function or tumor size.
7. Optic nerve sheath meningiomas in children may be more aggressive, with more rapid vision loss and more frequent recurrence after therapy.
8. Therefore, children must be monitored with increased frequency and decisions made accordingly.

Optic Nerve Sheath Meningioma	Optic Nerve Glioma
Adjacent bony hyperostosis on CT scan	No calcification or hyperostosis on CT scan
Apical expansion of the tumor	Kinking or buckling of the optic nerve
Calcification of the nerve sheath on CT scan	Smooth sheath margins (no extradural extension)
Diffuse, tubular enlargement of the optic nerve	Fusiform or globular enlargement of the optic nerve
Extradural tumor extension	Regions of low intensity within the nerve (cystic spaces)
Isointense or mildly hyperintense to brain on T1- and T2-weighted MRI scan	Isointense or mildly hypointense to brain on T1-weighted MRI scan
Prominent contrast enhancement on CT and MRI scans	Hyperintense on T2-weighted MRI scan Variable-contrast (CT scan) and gadolinium (MRI scan) enhancement
Sheath thickening and enhancement, with relative sparing of optic nerve substance ("tram track" or "railroad track" signs)	Thickening of both nerve and sheath by tumor

2. Optic pathway glioma

- i. Although optic pathway gliomas (OPGs, or pilocytic astrocytomas) are generally uncommon (accounting for only about 1% of intracranial tumors), they are the **most common primary tumor of the optic nerve**.
- ii. A glioma (astrocytoma) may arise in any part of the visual pathway, including the optic nerve head and optic nerve.
- iii. They may involve the optic nerve, the chiasm, or both
- iv. Optic nerve gliomas are frequently associated with neurofibromatosis 1 (NF1).
- v. The tumors most commonly present in the first decade of life and are low-grade juvenile pilocytic astrocytomas.
- vi. High-grade tumors (Grade IV astrocytomas/glioblastoma multiforme) rarely involve the optic nerve.
- vii. When this does occur, the optic nerve is usually involved secondarily from a brain tumor.
- viii. Approximately 70% of OPGs are detected during the first decade of life and 90%, by the second; however, they may occur at any age.
- ix. There is no definite sex predilection.

Signs and symptoms

- The most common presenting findings are

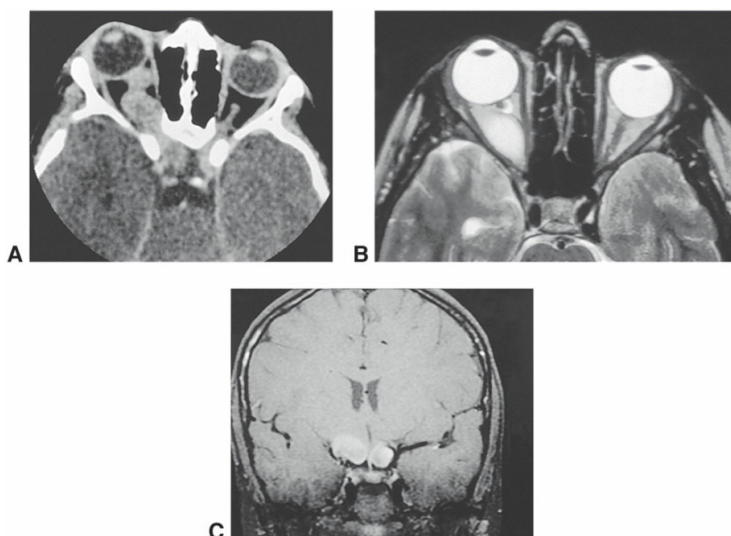
- ✓ Proptosis (94%),
- ✓ Vision loss (87.5%),
- ✓ Optic disc pallor (59%),
- ✓ Disc edema (35%),
- ✓ Strabismus (27%).
- Patients infrequently present with asymptomatic isolated optic atrophy.
- An RAPD is usually present in unilateral or asymmetric cases,
- Retinochoroidal collaterals may be present on the affected disc, although they are observed less commonly than with meningiomas.
- A typical optic nerve-related visual field defects (if the patient is cooperative enough for visual field testing).
- OPG involving the chiasm may show bitemporal or bilateral optic nerve-related visual field defects.
- Involvement of the chiasm may produce see-saw nystagmus or a monocular shimmering nystagmoid oscillation (pseudo-spasmus nutans).
- Large tumors may cause obstructive hydrocephalus with elevated ICP, headache, and papilledema.
- Involvement of the hypothalamus may result in precocious puberty or the diencephalic syndrome.

Association

- The association of OPG to neurofibromatosis type 1 (NF1) is incompletely understood.
- In patients with NF1, the incidence of OPG is 7.8%–21%; in patients with OPG, the incidence of NF1 is 10%–70%.
- The wide variance probably relates to referral bias, differences in neuroimaging detection rates, and criteria for diagnosis.
- Similarly, the relationship between NF1 and the behavior of the glioma is unclear.
- Several investigators suggest that optic nerve gliomas in patients with NF1 have a more benign prognosis, but this issue is unresolved.

Diagnosis

- Diagnosis is confirmed by neuroradiologic findings.

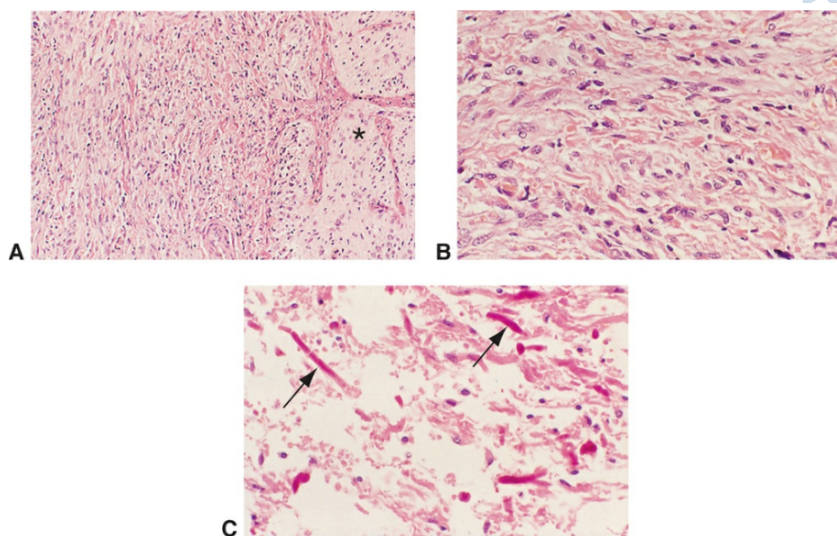


- A. Axial contrast-enhanced orbital CT scan shows a right optic nerve glioma. The optic nerve is enlarged and kinked and demonstrates mild hypodense cystic change centrally. The tumor extends intracranially.
- B. Axial T2-weighted MRI scan (non-contrast enhanced) of the orbits shows an enlarged, hyperintense, globular glioma of the right optic nerve.
- C. Coronal T1-weighted MRI scan shows prominent enlargement at the junction of the



Pathology

- Histologic examination of juvenile pilocytic astrocytomas shows proliferation of spindle-shaped astrocytes with delicate, hairlike (pilocytic) cytoplasmic processes that expand the optic nerve parenchyma.
- Enlarged, deeply eosinophilic filaments known as Rosenthal fibers, which represent degenerating cell processes, may be found in these low-grade tumors.
- In addition, calcification and foci of microcystic degeneration may occur, and the pial septa are thickened.
- The meninges show a reactive hyperplasia and astrocyte infiltration.
- Because the dura mater remains intact, the nerve demonstrates fusiform or sausage-shaped enlargement.
- Primary malignant gliomas of the anterior visual pathways occur mainly in adults and are characterized histologically by nuclear pleomorphism, high mitotic activity, necrosis, and hemorrhage
- As with optic nerve sheath meningiomas, biopsy of the mass is generally not required because
 - ✓ The advent of high-resolution neuroimaging has improved diagnostic accuracy
 - ✓ Biopsy of the sheath alone may be inaccurate, with reactive meningeal hyperplasia in gliomas falsely suggesting meningioma
 - ✓ Biopsy of the optic nerve substance may cause additional vision loss
 - ✓ The histologic appearance of the tumor is not necessarily predictive of biological behavior



Astrocytoma of the optic nerve.

- A. The right side of this photomicrograph demonstrates a normal optic nerve (asterisk); the left side shows a pilocytic astrocytoma.
- B. The neoplastic glial cells are elongated to resemble hairs (hence the term pilocytic).
- C. Degenerating eosinophilic filaments, which are known as Rosenthal fibers (arrows), may be observed in these tumors

Treatment

- i. Occasionally, surgery may relieve external compression on the chiasm, but otherwise surgical excision of the tumor is not indicated.
- ii. Hydrocephalus may require surgical shunting.
- iii. There is no universally accepted management for OPG. Observation is indicated for patients with relatively good vision and stable radiographic appearance.
- iv. Most patients show stability or very slow progression over years and sometimes show spontaneous regression.
- v. Chemotherapy is emerging as initial treatment for patients with severe vision loss at presentation or evidence of progression.



- vi. Combination therapy with carboplatin and vincristine is the most accepted regimen, but other chemotherapeutic drugs are used as well.
- vii. Radiotherapy is controversial because of inconclusive results and potential complications, including panhypopituitarism and cognitive disabilities.
- viii. Fractionated stereotactic radiotherapy was used successfully for optic nerve gliomas in 1 study without secondary adverse effects after a median follow-up period of 97 months.
- ix. Surgical excision may be indicated in patients with severe vision loss associated with disfiguring proptosis.
- x. Surgery has been advocated to prevent advancement into the chiasm; however, extension to the chiasm is rare.

Malignant astrocytomas

- Malignant astrocytomas are rare neoplasms involving the anterior visual pathway that almost always occur in adulthood.
- The mean age is in the 60s, and there is no sex predilection.
- Patients present with acute onset pain and either unilateral or bilateral vision loss.
- With unilateral lesions, the second eye invariably becomes involved within weeks.
- The optic disc appears normal or pale at presentation in most cases, but disc edema and retinal obstruction can also occur.
- An MRI scan most often shows diffuse intrinsic enlargement and enhancement of the affected optic nerves, chiasm, and optic tracts, with inhomogeneity due to cystic spaces within the tumor.
- Occasionally, a large exophytic component may encroach on the suprasellar cistern.
- Histologically, malignant optic nerve gliomas are classified as anaplastic astrocytomas or glioblastoma multiforme.
- Vision loss is severe and rapidly progressive.
- Treatment is rarely successful, although radiotherapy and chemotherapy have been attempted, with blindness usually developing 2–4 months after onset of vision loss.
- The tumor is aggressively infiltrative, and death from hypothalamic and brainstem involvement usually occurs within 6–12 months.

3. Melanocytoma

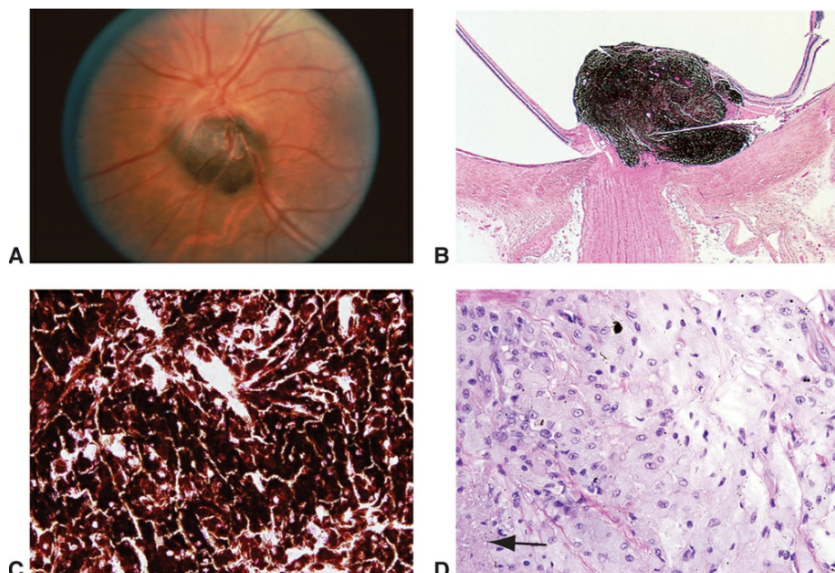
- Melanocytoma is a rare benign pigmented neoplasm, that usually affects anywhere in the uvea and can affect the optic nerve head, even involves the adjacent retina and choroid in some cases.
- A Melanocytoma is a benign, deeply pigmented melanocytic tumor situated eccentrically on the ONH.
- It may be elevated, and it typically extends into the adjacent retina as well as posteriorly into the optic nerve.
- Melanocytomas may grow slowly; however, malignant transformation to melanoma rarely occurs.

Pathology

- Histopathologically is composed of highly pigmented round cells with a cytoplasmic melanosomes and deficit of lipofuscin deposits.
- Histologically, a melanocytoma is a magnocellular nevus, composed of closely packed, heavily pigmented, plump, polyhedral melanocytes.
- The dense pigment obscures nuclear detail (B,C).
- Thus, bleached preparations (D) are necessary to demonstrate the bland cytologic features:



- ✓ Abundant cytoplasm,
- ✓ Small nuclei with finely dispersed chromatin,
- ✓ Inconspicuous nucleoli.
- Necrosis and melanophagic infiltration within melanocytoma are sometimes observed but are not necessarily indicative of aggressive behavior.



A, Fundus photograph shows melanocytoma of the ONH.

B, Low-magnification photomicrograph of melanocytoma shows a dome-shaped, jet-black mass involving the prelaminar optic nerve. The tumor also involves the juxtapapillary choroid and retina.

C, Higher magnification photomicrograph shows darkly pigmented polyhedral melanocytes with dense intracytoplasmic pigment, obscuring nuclear detail.

D, Bleached preparation displays the bland nuclear morphology of Melanocytoma cells. Note the area of necrosis within the

Demographics

- Age- The diagnosis mean age is 50 years, with a range of 1 year to 91 years, (similar to the age at diagnosis of uveal melanoma); is possible to find an amelanotic lesion not clinically evident at birth, that becomes pigmented in the next years.
- Race -It has no predilection for races, nevertheless, the demographic features found in the some studies revealed a preponderance for Caucasians (65%). Otherwise, uveal melanoma is infrequent in Asians and African Americans.
- Gender-Is slightly more frequent in women in 63% of cases

Signs and Symptoms

- **Visual acuity**
 - ✓ Commonly is unilateral, asymptomatic and stable, it usually not causes compromise of visual acuity, however, visual symptoms may be present in 26% of cases and these are associated with exudation with foveal involvement or tumor necrosis.
 - ✓ In other cases, is related to central retinal vein obstruction or more rarely malignant transformation.
 - ✓ Other symptoms can be present, such as flashes of light (4 %), floaters (4%) or none (76%).
- **Pupillary changes**
 - ✓ An afferent pupillary defect has been associated in presence of good visual acuity; optic disk melanocytoma; It is probably because of compression of the optic disk fibers by the melanocytoma cells.



- **Visual field**

The visual field is normal in 10% and abnormal in 90% of patients, these include

- i. Temporal islands of vision,
- ii. Enlargement of blind spot related to the amount of tumor extension;
- iii. Arcuate defects associated to compression of axons, other patterns such as,
 - ✓ Nasal step (10%),
 - ✓ Relative nerve fiber bundle defect (20%)
 - ✓ An absolute arcuate defect (20%).

- **Clinical features**

- ✓ It is usually unilateral, but in children may be bilateral.
- ✓ Clinically, the appearance of optic disk melanocytoma consists of a pigmented homogeneous mass with total absence of autofluorescence.
- ✓ However, an amelanotic lesion that becomes a pigmented lesion over time, has been described.

- **Complications-** Optic disk melanocytoma can show

- ✓ Ischemic necrosis,
- ✓ Disk edema (25%),
- ✓ Intraretinal edema (16%),
- ✓ Subretinal fluid (14%),
- ✓ Yellow intraretinal exudation (12%),
- ✓ Focal hemorrhage (5%),
- ✓ Vitreous seeds (4%),
- ✓ Retinal vein obstruction (3%).
- ✓ progressive growth,
- ✓ Neovascularization.

Clinical diagnosis

- Patient without relevant past or familiar history, attended the ophthalmology service for assessment of a pigmented mass on optic nerve head, without documented growth.
- The visual acuity usually is normal, at slit-lamp examination the anterior segment is normal and ocular melanocytosis usually is not observed; fundus examination showed a pigmented dark brown lesion located entirely or partially the optic nerve head, with or not extending over the margin with adjacent retinal or choroidal involvement, a swelling of inferior optic disk margin can be observe.
- At fundus examination can be found the presence of exudation, vitreous seeds or hemorrhages.

Imaging diagnosis

- Melanocytoma usually is diagnosed using ophthalmoscopic features; nevertheless the imaging is necessary to confirm its benign nature and distinguishing it from other lesions and neoplasms.
- Several imaging modalities have been used for optic disk melanocytoma diagnosis and follow-up.

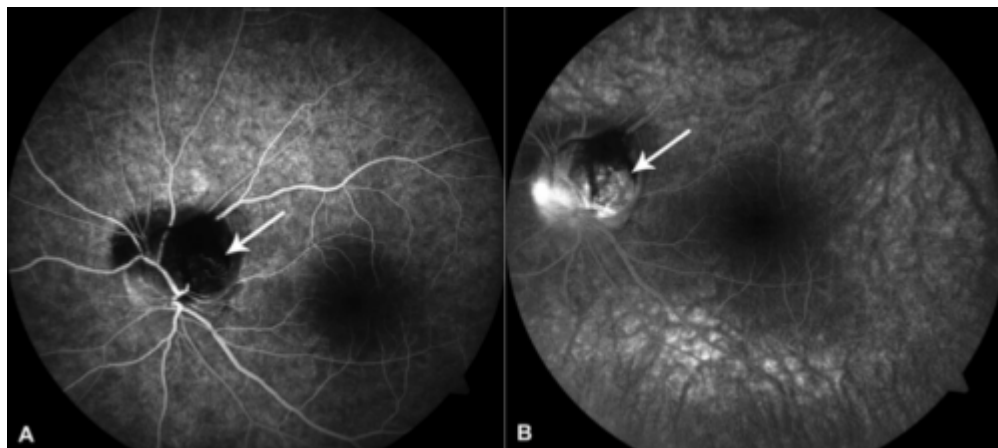
Ultrasonography

- A dome-shaped image is a frequent feature in melanocytoma and its high internal reflectivity indicate a benign lesion; contrarily, if has low internal reflectivity, indicate high-risk for growth and malignant transformation.

- Although ultrasonography is a useful guide to suspect a malignant neoplasm, it not detects neovascularization, tumor extension into the retrolaminar portion and other findings as intraretinal edema.

Fluorescein and Indocyanine Green Angiography

- Other studies as fluorescein and indocyanine green angiography show a diffuse hypofluorescent lesion and hyperfluorescent areas related to subretinal fluid and disk edema.



A, Early phase of fluorescein angiogram of melanocytoma of the optic disk. Fine vessels within the tumor can be observed (white arrow). B, Late-phase angiogram showing diffuse leakage through the vessels within the tumor (white arrow).

Optical coherence Tomography (OCT)

- The identification of a nodular elevation with dense posterior shadowing, areas of irregular hyper-reflectivity overlaying the tumor, even, thin hyper-reflective lines delineating the vessels and anterior side of the tumor using spectral-domain OCT, are largely documented in the literature.
- There are few reports of melanocytoma features using swept- source optical coherence tomography.
- At B-scan map are identified multiple irregular hyperreflective dots in anterior surface overlying the tumor, with or without perivascular distribution, these hyper-reflective dots may correspond to melanin-phagocytizing activity of macrophages, this phagocytizing activity induces the formation of subretinal and intraretinal fluid in adjacent retinal tissue.

Swept-source optical coherence tomography angiography (OCT-A)

- OCT–A has increasingly become a noninvasive useful technique in assessment of different ophthalmic diseases.
- Currently, few reports exist regarding the optic disk melanocytoma features using swept-source OCT- A, this new technology will become in a good alternative for follow-up of these lesions, improving the tumor extension detection, identification of progression and finally to differentiate from other neoplasms, including choroidal malignant melanoma.
- OCT-A allows the visualization of vasculature using the motion contrast principle, providing a high definition images of different layers including choroid, thus, theoretically it could shows intrinsically the choroidal involvement and neovascularization.
- OCT-A represent an important advantage, the determination of depth's tumor despite the posterior dense shadowing observed in OCT B- scan.



Differential diagnosis

- Melanocytoma usually is diagnosed using ophthalmoscopic features; nevertheless the imaging is necessary to confirm its benign nature and distinguishing it from other lesions and neoplasms such as malignant melanoma, choroidal nevus, optic nerve glioma, capillary hemangioma or metastases.

DIFFERENTIAL DIAGNOSIS	
CHOROIDAL MELANOMA	A juxtapapillary melanoma has extended around the posterior termination of Bruch's membrane and invaded the sensory retina.
CHOROIDAL NEVUS	It is a flat, or minimally elevated choroidal lesion that lies outside the disk and does not overlie the disk.
HYPERPLASIA OF RETINAL PIGMENT EPITHELIUM (RPE)	There is a history of ocular trauma or inflammation and the lesion is more irregular with evidence of chorioretinal scarring.
COMBINED HAMARTOMA OF RETINA AND RPE	It usually does not involve the disk itself, but may extend from its juxtapapillary location onto the disk margin.
ADENOMA OF RPE	It can also extend onto the disk margin but does not show a feathery margin. It is more likely than melanoma to show adjacent yellow retinal exudation. In contrast to melanocytoma, it can occasionally be clinically amelanotic.
METASTATIC MELANOMA TO OPTIC DISK	It tends to grow more rapidly and to diffusely infiltrate the optic disk, resembling papilledema or acute papillitis.

Management

- This lesion does not require any type of treatment.
- Clinical and imaging follow-up should be performed annually.

Medical follow up- Optic disk melanocytoma requiring a complete clinical and imagenological assessment to characterize the principal features and distinguish it from other pathologies.

Prognosis- Seldom exhibits malignant transformation; 10 % - 15 % of them show subtle enlargement over several years.