Intraocular tumors

Tumors of the choroid

Choroidal naevus

Choroidal naevi are present in 5–10% of Caucasians but are very rare in dark-skinned races. Although they are probably present at birth, growth occurs mainly during the pre-pubertal years and is extremely rare in adulthood. For this reason clinically detectable growth should arouse suspicion of malignancy. The lifetime risk of malignant transformation is up to 1%

Histology

The tumour is composed of a proliferation of spindle cell melanocytes.

Symptoms.

The vast majority of naevi are asymptomatic and detected by routine examination.

Signs

- Usually post-equatorial, oval or circular, brown to slate-grey lesion with indistinct feathery margins.
- Overlying drusen is typical.
- Dimensions are <5 mm in basal diameter (i.e. 3 disc diameters) and <1 mm thickness.
- ***Features suspicious of early melanoma:***

  1- Documented growth.

  2- Symptoms such as blurred vision, metamorphopsia, field loss and photopsia.

  3- Dimensions >5 mm in diameter and >1 mm in thickness.

  4- Absence of drusen.

  5- The presence of overlying orange pigment (lipofuscin).

  6- Margin of the lesion at or near the optic disc.

  7- The presence of associated subretinal fluid.

  - The greater the number of these features, the higher the chance that the lesion is a melanoma.

Management

Involves baseline fundus photography and ultrasonography, and then indefinite follow-up. If growth has been documented, the lesion should be reclassified as a melanoma and managed accordingly

Choroidal melanoma

Choroidal melanoma is the most common primary intraocular malignancy in adults.

Presentation peaks at around the age of 60 years and occurs in one of the following ways.

- An asymptomatic tumor, usually in the periphery, is detected by chance on routine fundus examination performed for other reasons.
- A symptomatic tumor causes decreased visual acuity, blurring, metamorphopsia, visual field loss, floaters or photopsia.

Signs

- A solitary elevated subretinal grey-brown or rarely amelanotic dome-shaped mass; diffuse infiltration is uncommon.
- About 60% are located within 3 mm of the optic disc or fovea.
- Clumps of orange pigment are frequently seen overlying the tumour .
- If the tumour breaks through the Bruch membrane it acquires a **'collar stud' appearance.**
- Exudative retinal detachment, initially confined to the surface of the tumour and which later shifts inferiorly and becomes bullous.
- Other signs can include haemorrhag ,choroidal folds, inflammation, rubeosis iridis, secondary glaucoma and cataract.

Special investigations

Although binocular indirect ophthalmoscopy combined with indirect slit-lamp biomicroscopy is sufficient for diagnosis in the vast majority of cases the following may be useful;

1-Ultrasonogrphy is used to measure lesion dimensions and to detect tumors through opaque media and exudative retinal detachment; it may also demonstrate extraocular extension. The characteristic findings are internal homogeneity with low to medium reflectivity, choroidal excavation and orbital shadowing and acoustic hollowing. **A 'collar stud' configuration is almost pathognomonic when present.**

2- Fluorescein angiography (FA) is of limited diagnostic value because there is no pathognomonic pattern.

3- Indocyanine green angiography (ICGA) is superior to flourescein angiography.

4- Magnetic resonance imaging (MRI). is useful to demonstrate extraocular extension and may be of some help in differential diagnosis.

5- Colour-coded Doppler imaging may be helpful in differentiating pigmented tumors from intraocular haemorrhage, particularly in eyes with opaque media.

6- Biopsy is useful when the diagnosis cannot be established by less invasive methods.

Systemic investigations

Systemic investigation is aimed at the following:

1- Excluding a metastasis to the choroid, most frequently from the lung in both sexes and from the breast in women.

2- Detecting possible metastatic spread from the choroid, Mainly to the liver and lung.

Principles of treatment

Management should be tailored to the individual patient taking the following factors into consideration:

1- Size, location and extent of the tumor together with effects on vision.

2- State of the fellow eye.

3- General health and age of the patient.

Treatment may not be required in the following cases:

- If the tumor is slow-growing and present in the only seeing eye of a very elderly or chronically ill patient.
- If it is not possible to determine clinically whether a tumor is a small melanoma or a large naevus. In this case the lesion is observed and treatment is administered only if growth is documented by sequential ultrasonography or photography.

1-Brachytherapy (episcleral plaque radiotherapy) .

Is usually the treatment of first choice. **Survival** is similar to that following enucleation for comparable tumours.

2- External beam radiotherapy.

Suitable for tumors of large size or posterior location. **Survival results** are similar to those following brachytherapy or enucleation.

3- Stereotactic radiotherapy

Uses multiple collimated beams from different directions, that only the tumour receives a high dose of radiation.

4- Transpupillary thermotherapy (TTT) uses an infrared laser beam to induce tumour cell death by hyperthermia rather than coagulation.

5- **Trans-scleral choroidectomy.** This is a technically difficult procedure that may be used for carefully selected tumours that are too thick for radiotherapy but less than about 16 mm in diameter.

6- Enucleation (excision of the globe). Indications for are large tumor size, optic disc invasion, extensive involvement of the ciliary body or angle & irreversible loss of useful vision.

7- Exentration is indicated for melanomas with extensive extraocular extension.

8- Systemic chemotherapy in cases where there is evidence of metastatic spread.

Differential diagnosis

1. A choroidal naevus.
2. Melanocytoma.
3. Congenital hypertrophy of the RPE.
4. Subretinal or suprachoroidal haemorrhage.
5. Metastatic cutaneous melanoma.

Retinoblastoma

Retinoblastoma is the most common primary intraocular malignancy of childhood and accounts for about 3% of all childhood cancers. Even so, it is rare, occurring in about 1 : 18 000 live births.

Genetics

- Retinoblastoma results from malignant transformation of primitive retinal cells before final differentiation.
- Retinoblastoma may be heritable or non-heritable.

***Heritable (hereditary, germline) retinoblastoma*.**

Accounts for 40%, these children develop early onset bilateral and multifocal tumours and also have a predisposition to nonocular cancers, including pinealoblastoma (trilateral retinoblastoma), Second malignant neoplasms include osteosarcoma, melanoma, and malignancies of the brain and lung. The risk of second malignancy increases five-fold if external beam irradiation has been used to treat the original tumour.

- Patients wih heritable retinoblastoma have 50% risk of transmitting the disease to their offspring (autosomal dominant). The gene predisposing to retinoblastoma is located on long arm of chromosome 13.
- If a child has heritable retinoblastoma, the risk to siblings is 5% if the parents are healthy, and 45% if a parent is affected.

Non-heritable (non-hereditary, somatic) retinoblastoma

Accounts for 60% of cases, the tumor is unilateral, not transmissible and does not predispose the patient to second nonocular cancers.

- If a patient has a solitary retinoblastoma and no positive family history, this is probably but not definitely non-heritable so that the risk in each sibling and offspring is about 1%.

✓ **Siblings at risk of retinoblastoma should be screened by prenatal ultrasonography, and by ophthalmoscopy soon after birth and then regularly until the age of 4 or 5 years.**

Presentation

Presentation is within the first year of life in bilateral cases and around 2 years of age if the tumour is unilateral.

1- Leukocoria (white pupillary reflex) is the commonest presentation (60%) and may first be noticed in family photographs.

2-Strabismus is the second most common (20%); fundus examination is therefore mandatory in all cases of childhood strabismus.

3- Secondary glaucoma which is occasionally associated with buphthalmos.

4- Pseudouveitis with painful red eye associated with pseudohypopyon and hyphaema due to invasion of retinoblastoma to the anterior segment and tends to present in older children. It is therefore important to consider retinoblastoma in the differential diagnosis of unusual chronic uveitis in children.

5- Poor vision.

6- Orbital inflammation mimicking orbital or preseptal cellulitis may occur with necrotic tumors.

7- Proptosis as the result of orbital involvement may occur in neglected cases.

8- Metastatic disease involving regional lymph nodes and brain before the detection of ocular involvement is rare.

9- Routine examination of a patient known to be at risk may reveal the presence of the tumor.

Examination

- **Red reflex testing** with a direct ophthalmoscope is a simple screening test for leukocoria that is easily employed in the community.
- **Examination under anaesthesia** includes the following;

1- Anterior segment examination. Including tonometry and measurement of the corneal diameter

2- Indirect ophthalmoscopy with scleral indentation must be performed on both eyes after full mydriasis. This is because without indentation pre-equatorial tumours may be missed and one eye may harbour multiple tumours. The following fundus appearance may be seen;

- ✓ An intraretinal tumour is a homogeneous, dome-shaped white lesion which becomes irregular, often with white flecks of calcification.
- ✓ An endophytic tumour projects into the vitreous as a white mass, that may 'seed' into the vitreous.
- ✓ An exophytic tumour forms subretinal, multilobular white masses and causes overlying retinal detachment.

Investigation

1- Ultrasonography is used mainly to assess tumour size. It also detects calcification.

2- MRI does not detect calcification but is useful for optic nerve evaluation, detection of extraocular extension and pinealoblastoma.

3- CT also detects calcification but entails a significant dose of radiation so is **avoided** by many practitioners.

4- Systemic assessment. For metastatic disease.

Treatment

1-Small tumors;

Chemotherapy, Trans-pupillary thermotherapy (TTT) or Cryotherapy.

2-medium-size tumors;

Brachytherapy , chemotherapy with (TTT or Cryotherapy).

3- large tumors;

- Chemotherapy.
- Enucleation, is generally indicated if there is neovascular glaucoma, anterior chamber infiltration, optic nerve invasion or if a tumour occupies more than half the vitreous volume. It is also considered if chemoreduction fails and is useful for diffuse retinoblastoma because of a poor visual prognosis and a high risk of recurrence with other modalities.

4-Extraocular extension;

Enucleation followed by chemotherapy with or without external beam radiotherapy.

Review. Careful review at frequent intervals is generally required following treatment, in order to detect recurrence or the development of a new tumor, particularly in heritable disease.

Differential diagnosis of childhood leukocoria

1- Retinoblastoma.

2- Congenital cataract, which may be unilateral or bilateral , present without diagnostic problems.

3- Persistent anterior fetal vasculature (persistent hyperplasic primary vitreous), is caused by a failure of regression of the primary vitreous and can be divided into anterior and posterior types.

4- Coats disease. is almost always unilateral, more common in boys and tends to present later than retinoblastoma.

5- Retinopathy of prematurity. Diagnosis is usually straightforward because of the history of prematurity and low birth weight.

6- Toxocariasis. A granuloma at the posterior pole may resemble an endophytic retinoblastoma.

7- Uveitis may mimic the diffuse infiltrating type of retinoblastoma seen in older children. Conversely, retinoblastoma may be mistaken for uveitis, endophthalmitis or orbital cellulitis.

8- Vitreoretinal dysplasia is caused by faulty differentiation of the retina and vitreous that results in a detached dysplastic retina forming a retrolental mass with leukocoria.

9- Other tumors.

- **Retinoma** (retinocytoma) is a benign variant of retinoblastoma.
- **Retinal astrocytoma.**