
Retinoblastoma: Evaluation and Differential Diagnosis

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Abstract

In developed nations, the common presenting features of intraocular retinoblastoma are leukocoria and strabismus. Abnormal pupil reflex is also frequently observed in several pediatric ocular conditions, including cataracts, and it is important to clinically differentiate retinoblastoma from simulating diagnoses. For several reasons, retinoblastoma tends to be more advanced at presentation in developing nations. Misdiagnosis rates ranging from 16 to 53% in referral practices may be attributed to the rarity of retinoblastoma, the multiple conditions that simulate retinoblastoma, and the difficulty of examining children. As the diagnosis of retinoblastoma is clinical, careful evaluation of a child suspected to have retinoblastoma necessarily has to be thorough and conclusive so as to exclude simulating entities such as Coats' disease, persistent hyperplastic primary vitreous/persistent fetal vasculature, astrocytic hamartoma, toxocara, retinopathy of prematurity, and hereditary retinal disorders are common simulating conditions. Both eyes should be examined with an indirect ophthalmoscope after pupillary dilation to confirm a suspicion of retinoblastoma. Scleral depression may be withheld until examination under anesthesia (EUA). Ultrasonography can be attempted primarily to detect a retinal mass with calcification and neuroimaging (MRI of the brain and orbit with and without contrast) is performed to assess the orbital segment of the optic nerve and to detect pinealoblastoma (trilateral retinoblastoma). Fundus photos taken during the EUA with a wide-angle handheld fundus camera aids in assessing the response to treatment. Fluorescein angiography is particularly useful in differentiating retinoblastoma from Coats' disease.

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In the United States and other developed nations, the common presenting features of intraocular retinoblastoma are leukocoria and strabismus (fig. 1) [1]. Abnormal pupil reflex is also frequently observed in several pediatric ocular conditions, including cataracts, and it is important to clinically differentiate retinoblastoma from simulating diagnoses. For several reasons, retinoblastoma tends to be more advanced at presentation in developing nations. Misdiagnosis rates ranging from 16 to 53% in referral practices may be attributed to the rarity of retinoblastoma, the multiple conditions that simulate retinoblastoma, and the difficulty of examining children [2]. As the diagnosis of retinoblastoma is clinical, careful evaluation of a child suspected to have retinoblastoma necessarily has to be thorough and conclusive so as to exclude simulating entities (table 1).

Followed by detailed history taking and initial office examination, focused ophthalmic ultrasonography is performed. Final diagnosis is established by a detailed examination under anesthesia and neuroimaging, if necessary. This stepwise approach for evaluation is merely a guide that can be modified based upon the clinical setting (fig. 2).

History

The gestational age at birth; the type of delivery; the birth weight; and complications, including infections or use of oxygen, are noted. It is also important to inquire if there are any unusual birthmarks, malformations, seizures or developmental delays. A family history suggestive of retinoblastoma or enucleation in childhood should be recorded. Both parents should be questioned about their ocular health and examined if no recent dilation examination has been performed (to exclude retinoma/retinocytoma) [3, 4].

Initial Examination

Observe for leukocoria, strabismus or periorbital swelling and visual behavior before initiating a detailed examination. Use a direct ophthalmoscope to assess the pupillary light reflex in each eye. Both eyes should be examined, including examination with an indirect ophthalmoscope after pupillary dilation to confirm a suspicion of retinoblastoma and determine whether further evaluation with an examination under anesthesia (EUA) is necessary. Scleral depression may be withheld until the EUA. Ultrasonography can be attempted primarily to detect a retinal mass with calcification.

If retinoblastoma is suspected, the child is scheduled for an EUA, and neuroimaging is ordered (MRI of the brain and orbit with and without contrast) to visualize the orbit, the orbital segment of the optic nerve, and pinealoblastoma (trilateral retinoblastoma) [5, 6].



Fig. 1. Leukocoria due to retinoblastoma.

Table 1. Differential diagnosis of childhood leukocoria

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| 1. Tumors |
| Retinoblastoma |
| Medulloepithelioma |
| Leukemia |
| Combined retinal hamartoma |
| Astrocytic hamartoma (Bourneville's tuberous sclerosis) |
| 2. Congenital malformations |
| Persistent fetal vasculature |
| Posterior coloboma |
| Retinal fold |
| Myelinated nerve fibers |
| Morning glory syndrome |
| Retinal dysplasia |
| Norrie's disease |
| Incontinentia pigmenti |
| Cataract |
| 3. Vascular diseases |
| Retinopathy of prematurity |
| Coats' disease |
| Familial exudative vitreoretinopathy |
| 4. Inflammatory diseases |
| Ocular toxocariasis |
| Congenital toxoplasmosis |
| Congenital cytomegalovirus retinitis |
| Herpes simplex retinitis |
| Other types of fetal iridochoroiditis |
| Endophthalmitis |
| 5. Trauma |
| Intraocular foreign body |
| Vitreous hemorrhage |
| Retinal detachment |

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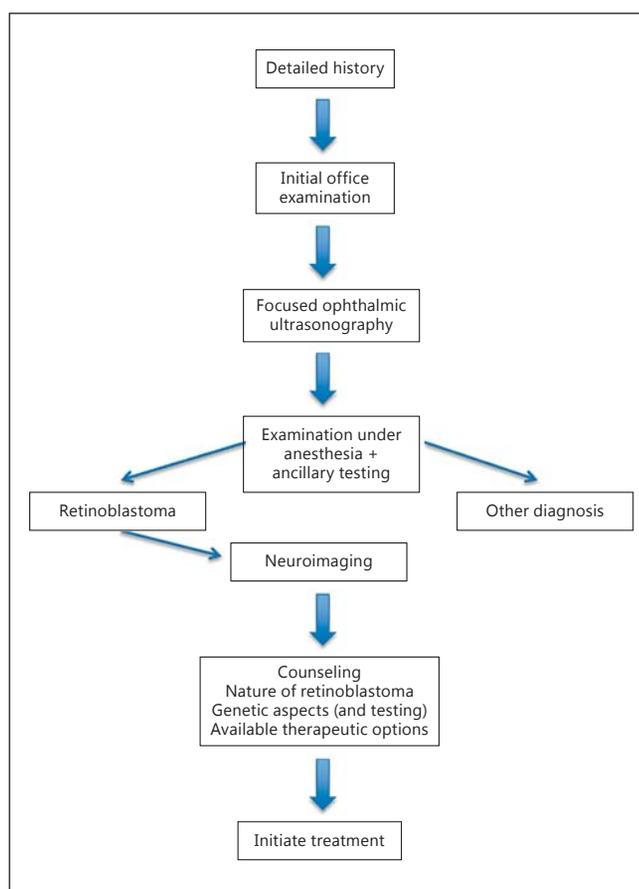


Fig. 2. Stepwise evaluation of retinoblastoma. This approach is merely a guide that can be modified as needed based upon the clinical setting. Reproduced with permission from Marr and Singh [20].

Examination under Anesthesia

Perform a detailed ophthalmic examination that includes all components of the initial office examination and recording of intraocular pressure. Elevated intraocular pressure in retinoblastoma patients suggests the possibility of iris neovascularization, with an associated risk of optic nerve involvement and metastatic disease [7, 8]. Horizontal corneal diameters are also measured to exclude microphthalmos and buphthalmos.

Anterior segment examination can be done either with a handheld slit lamp or an illuminated magnification system to check for a shallow anterior chamber, neovascularization of the iris, cataract, retinoblastoma seeding or hyphema. In addition, check for persistent fetal vasculature and evaluate the anterior vitreous for seeding, hemorrhage or a retrolental mass.

An indirect ophthalmoscope is used to evaluate the posterior segment in a systematic approach to evaluate the vitreous; optic disc; macula; and peripheral retina, in-