

Retinoblastoma

Key facts

- Retinoblastoma (RB) is an intraocular embryonal tumour of childhood.
- It affects approximately 1 in 20,000 children and is the common eye cancer in children.
- 40% of cases are bilateral and 60% of cases unilateral; 10% of cases have an identifiable family history. In these situations the condition is inherited in an autosomal dominant manner.
- All identified cases of retinoblastoma should have appropriate molecular genetic management with either germline or tumour studies.
- All pregnancies identified at increased risk of retinoblastoma should have appropriate antenatal or perinatal molecular investigations, and ocular surveillance should be instigated in the neonatal period where the child is shown to have a high probability of developing retinoblastoma or the risk cannot be excluded.

Clinical features

- Retinoblastoma is an intraocular tumour typically diagnosed before the age of 5 years.
- Early identification and treatment while the tumour is confined to the eye has a very high cure rate (greater than 99%).
- Individuals and families with an inherited susceptibility have an increased probability of second primary tumours including sarcomas. In adulthood there is an increased probability of several tumours, in particular melanoma, lung, bladder and breast. It is therefore vital to stress the importance of avoidance of overexposure to UV light and cigarette smoke.

Diagnosis

- The diagnosis should always be considered where the normal red reflex of the eye has been replaced by a white reflex.
- Other indications include loss of vision, a painful swollen eye or strabismus in the first few years of life.
- The diagnosis should always be considered if there is a family history of retinoblastoma until this is excluded with molecular investigations.

Genetic basis

- To date almost all cases of retinoblastoma are due to alteration (mutations) in the retinoblastoma gene (RB1).
- A very small proportion, less than 1%, of unilateral cases may be due to *N-myc* amplification.
- 10% of children with retinoblastoma will have an identifiable family history, typically bilateral disease but occasionally unilateral or low-penetrant disease.
- Most unilateral retinoblastoma is associated with genetic alterations in both copies of the *RB1* gene (somatic mutation). These alterations (or mutations) are present in the retinoblastoma tumour tissue, but are not present in the DNA extracted from blood.
- Of the 40% of tumours that are bilateral, there will be an identifiable germline mutation in 95% or more of cases.

Clinical management

- All individuals with retinoblastoma should have their care led by one of two national services (in London and Birmingham). In some instances, shared care is appropriate under the guidance of the units above.
- Clinical genetic input can be provided by local genetic services, although this is often included in the care pathway of the national services as the information may be necessary for the primary management as well as screening advice for the extended family.
- Enucleation is required in up to 80% of new cases identified but would be required much less frequently in known families where gene carriers, or at risk individuals, are followed up from the neonatal period. All children known to be at risk of retinoblastoma should have a follow-up surveillance plan in place by two weeks of age.
- Local treatment of the eye would involve laser or cryotherapy given during assessment by the national services in London or Birmingham.
- In some instances systemic chemotherapy is required.

Transition care should, in all instances, include a clinical genetic review to ensure individuals are aware of the underlying genetic mechanism for their retinoblastoma and the reproductive options available.

Genetic testing

- Indications for genetic testing and genetic counselling include:
- Diagnostic testing in patients with retinoblastoma. Following the identification of retinoblastoma, genetic testing should follow a stepwise progression to try and identify the underlying molecular cause.
- Unilateral cases, where enucleation is undertaken, should have tumour studies followed by germline studies to exclude a heritable cause of retinoblastoma. In the small proportion of cases where genetic testing is not informative, further studies may need to be undertaken to exclude risk in first- and second-degree relatives where feasible.
- In unilateral cases not requiring enucleation, germline mutation studies should be attempted. These will be negative in 85% of cases. Additional studies should be considered in the management of the extended family.
- Germline cases should have genetic testing of blood sample (and if necessary RNA studies).
- All pregnancies identified at increased risk of retinoblastoma (due to an affected parent or sibling) should have antenatal or perinatal molecular investigations.

Genetic testing is available in the UK and usually provided through specialist clinics or regional genetic centres.

This information is intended for educational use and was current in March 2015. For clinical management, it is recommended that local guidelines and protocols are used.

To find out more, visit

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