Unilateral retinoblastoma – genetic implications

Unilateral retinoblastoma is the commoner form of the disease, usually occurring sporadically with no family history, and accounting for 60% to 70% of cases. Although the tumour cells in what is a unifocal tumour may show loss of the chromosome 13 carrying the normal copy of the retinoblastoma susceptibility gene (RB1) in 50% to 70% of cases, with a mutation in the remaining chromosome 13, there is no abnormality of chromosome 13 outside these somatic cells and so no risk of transmission of the tumour to any offspring.

Around 10% of patients with unilateral retinoblastoma, however, have a germinal mutation of RB1, the tumour being unilateral and unifocal rather than the more usual bilateral, multifocal form possibly because of mutation occurring later in embryogenesis. Such individuals are at risk of transmitting the loss of function genetic defect to their children, who are thus at risk of developing retinoblastoma and other primary malignancies, especially sarcomas.

It is customary, therefore, at present to examine all the children of all unilaterally affected individuals in the same way that one would follow those born to bilaterally affected parents, in the absence of an inexpensive, high yielding, readily available technique to pick up germline mutations. Is this the correct approach? We lack information on which to base an answer.

Notis et al from the Ellsworth Center, New York, address this matter in their important paper published in this issue of the BJO (p 197). They have identified 54 children, including nine pairs of sibs, each with one unilaterally affected parent. Their findings that the affected children of patients with unilateral retinoblastoma behave in a similar fashion to those born to a bilaterally affected parent (91% bilateral, more than one tumour per eye, and a mean age at diagnosis of 10.5 months), is perhaps what is to be expected in the presence of a germinal mutation but this is the first time that the case has been convincingly established.

The message that all children born to a retinoblastoma patient, including those with unilateral retinoblastoma, must have their whole retina examined soon after birth and at regular intervals thereafter is re-emphasised. For how long? Until what age? Lacking the information to answer these questions with confidence we err on the side of caution, a point made by these authors who found no new tumours after the age of 3 years, but advise continuing observation beyond this age in view of the small numbers studied.

Among other interesting points to emerge from this study is the observation of five children with unilateral retinoblastoma born to a unilaterally affected parent. We still have much to discover about the genetics of retinoblastoma.

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