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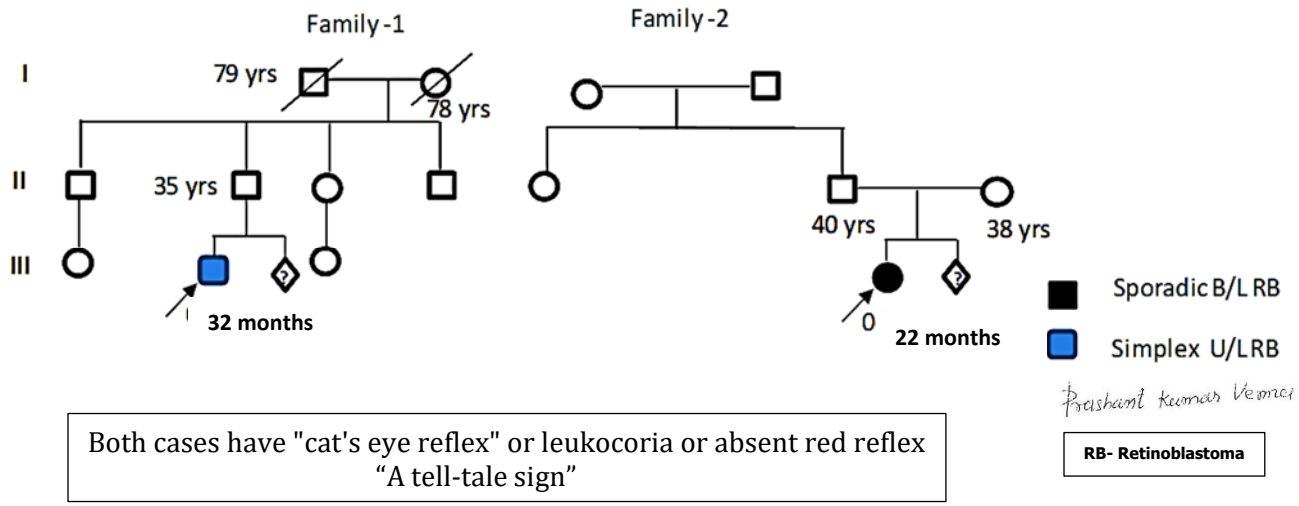
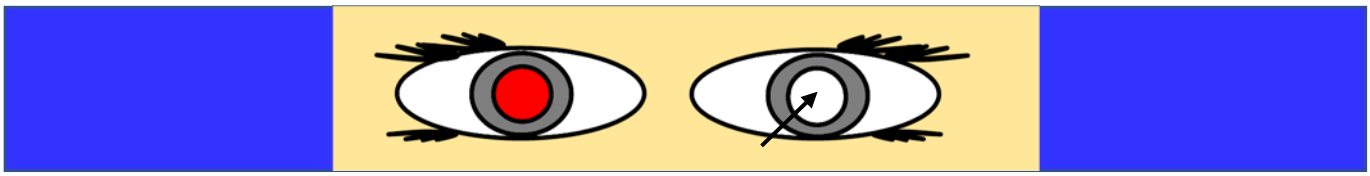
From the desk of Editor

The Department of Paediatrics is publishing a monthly newsletter for faculty and residents. The newsletter is related to genealogical parlance and deliberate attempt to enhance awareness for genetic disorders with recent updates.

RB Genetic Facts



Both cases have "cat's eye reflex" or leukocoria or absent red reflex
"A tell-tale sign"



Insight:

1. **What is the importance of genetic testing of a proband in each family?**
2. **What is the recurrence risk and the phenotypes expected in their offspring and in siblings?**
3. **Will the tumor genotype help in predicting the recurrence risk?**
4. **What will karyotype add to the diagnosis?**
5. **What is the role of MYCN gene testing?**

Plausible tenets:

- RB Transcriptional Corepressor 1(RB1 gene): The first tumor suppressor gene
  - Locus identified by Dryja et al.(1984), on chr. 13q
  - A negative regulator for the cell division and gene expression
  - Autosomal Dominant pattern of inheritance
- **2** complementary mutational events are required for the development of retinoblastoma (TWO HIT HYPOTHESIS)
  - First "hit," is a germline/somatic mutation
  - Second mutation usually occurs in multiple retinal progenitor cells
- Unilateral (U/L) RB - 60 % and Mean age of diagnosis – 24 months
- Bilateral (B/L) RB - 40 % and Mean age of diagnosis – 15 months

RB Recurrence risk (RR) in offspring and sibling				
RR	**Offspring**		**Sibling**	**Mutation Detection Rate (Gene study- Sequencing & deletion/ duplication analysis)**
Peripheral Blood sample	**Negative**	**Positive**	**Empirical**	
Sporadic B/L RB	**< 45 %**	**45 – 50 %**	**2%**	**90-97 %**
Simplex U/L RB	**5 -14 %**	**45 -50 %**	**1%**	**8 -14 %**

U/l –Unilateral B/l – Bilateral ▭ *Germline Mosaicism* (*more than one set of genetic information is found specifically within the gamete cells)*

Penetrance and recurrence risk:

- High penetrance-90 to 99 % complete loss of protein(pRB) function (germline mutations) (30% U/L RB and rest develop B/L retinoblastoma) families have diseased-eye ratios 1.5 or greater
- Low penetrance –reduced level of expression of pRB /partially inactivated pRB (mutation other than germline and mosaicism) families have diseased-eye ratios less than 1.5

Syndromic presentation: **3** % RB have interstitial chromosomal deletion in 13q14 in **karyotype**

High-level **MYCN** copy number amplification present in around 1.5% of sporadic U/L RB with both alleles of the RB1 gene being normal.

Thought Riveting:

With the loss of RB function (tumor suppressor protein), why predominantly it is the retinal cells that develop cancer?

Are there any treatment options ensuring cure without the need for radical surgery?

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