

CASE STUDY

Genetic Analysis Confirms Hereditary Retinoblastoma in a Young Patient

Introduction

Retinoblastoma is a frequently occurring cancer evident in very young kids, worldwide. In fact, it represents 3% of all the pediatric cancers, globally (1,2). Retinoblastoma is highly treatable if a confirmed diagnosis is obtained early enough. There exists a huge disparity between the outcomes of retinoblastoma in developed and developing countries. The success rate in treating retinoblastoma cases is 93% (5-year survival rate) in European countries and is as high as 96.5 % in the US. In contrast, the mean survival rate for retinoblastoma is 40-79% in the developing world (3). Confirmed diagnoses of retinoblastoma, aided by genetic analyses, can go a long way in increasing the survival rate of retinoblastoma patients.

Patient Profile

Sujay* was an active, cheerful child born to Amrita* and Sukrut Jaishanker*, a young couple who ran a local chain of coaching classes in Chennai. They were naturally overjoyed and were following their child's progress keenly. Photographing each stage of Sujay's development had become their daily habit. As the kid turned one, Amrita noticed that some of Sujay's photos showed a white spot on the right eye. For some time, she ignored it as an artifact of the camera settings but gradually, she started noticing that Sujay developed a preference for things on his left. The white spot in his pupil was becoming more and more prominent.

Her concern prompted her to take Sujay to a pediatrician. Suspecting a case of retinoblastoma, the pediatrician referred her to an ophthalmologist as well as to a well-known geneticist in Chennai. Sujay's ophthalmologist diagnosed his condition as retinoblastoma and in concurrence with the geneticist, advised a genetic test to confirm the diagnosis.

* Names of individuals changed to protect their identity



-Gender: Male

-Age: 2 years

-Location: Chennai, Tamilnadu

-Diagnosis: Retinoblastoma

-Strand Test: Germline Cancer

-Conclusions:

#Likely Pathogenic mutation in the *RB1* gene identified

#Hereditary retinoblastoma confirmed

#Therapeutic options explained to child's parents

Results of Genetic Testing

Sujay was advised the Strand Germline Cancer Test to establish the genetic basis of his retinoblastoma. This is a lab-developed test that looks for mutations in the *RB1* gene, known to be involved in hereditary predisposition to retinoblastoma.

RESULT



A 'Likely Pathogenic' variant in exon 1 of the *RB1* gene was identified

Key Findings

Gene	Variation	Zygoty	Clinical significance
<i>RB1</i>	chr13:48878094_48878116delGCCGC CGCGGAACCCCGGCACC c.46_68delGCCGCCGCGGAACCCCGCACC p.Glu19AlafsTer4	Heterozygous	Likely Pathogenic

Key Interpretations

- Sujay's retinoblastoma resulted from the likely pathogenic variant of the *RB1* gene.
- He is heterozygous for this mutation indicating that he has one normal and one mutant copy of the *RB1* gene. His parents should be tested to ascertain, whether, the mutations is inherited or *de novo* in nature.
- Mutations in the *RB1* are inherited in an autosomal dominant manner and hence one copy of the likely pathogenic variant is sufficient to result in the development of this cancer.

Conclusions

- Sujay, a 2-year-old-child, was diagnosed with retinoblastoma.
- Genetic testing was advised in order to confirm the diagnosis of retinoblastoma and arrive at a differential diagnosis of the vision problems, quickly.
- The Strand Germline Cancer Test helped to identify a 'likely pathogenic' variant of the *RB1* gene in Sujay's case.
- Diagnosis of retinoblastoma was confirmed with this genetic analysis.

- Sujay’s parents were advised to undergo mutation-specific testing in order to understand whether the mutation is inherited via either of the parents or *de novo* in nature.
- Mutation-specific testing would also allow them to understand their risks for having a second child bearing the same gene variant.
- Therapeutic options like enucleation, brachytherapy, external beam radiation, chemotherapy, photocoagulation, and cryotherapy were explained to Sujay’s parents.
- Early identification of the mutation status of *RB1* is essential because a deficiency of this gene also increases a person’s risk for developing bladder cancer, lung cancer, melanoma, breast cancer and osteosarcoma ([Genetics Home Reference](#)). The chances of developing retinoblastoma in the contralateral eye are also high, owing to the presence of the inherited mutation.
- Sujay’s parents have now been alerted to the presence of the *RB1* mutation and can adopt preventive health measures like regular medical examinations to look for signs of other cancers.

References

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2. Yun J, Li Y, Xu C-T, Pan B-R. Epidemiology and Rb1 gene of retinoblastoma. *Int J Ophthalmol* [Internet]. 2011 [cited 2017 Sep 1];4(1):103–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22553621>
3. Naseripour M. “Retinoblastoma survival disparity”: The expanding horizon in developing countries. *Saudi J Ophthalmol* [Internet]. 2012 Apr [cited 2017 Sep 1];26(2):157–61. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1319453412000306>

Strand Germline Cancer Test

The Strand Germline Cancer Test is a lab-developed test, designed to identify mutations that increases an individual’s risk predisposition for developing hereditary cancer. The test screens for 86 genes, and has been leveraged across several types of cancer cases.