Comprehensive Genomic Profiling Case Study : Integrating Somatic and Germline Testing with Counseling Services

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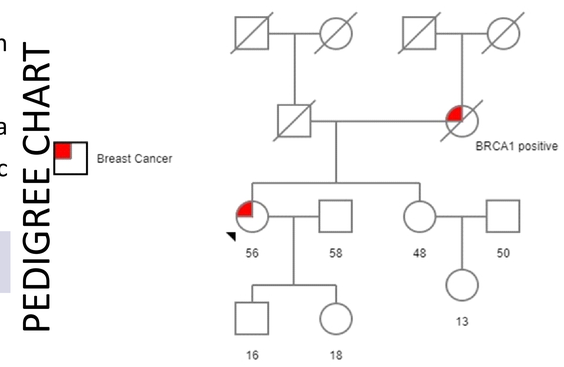
INTRODUCTION

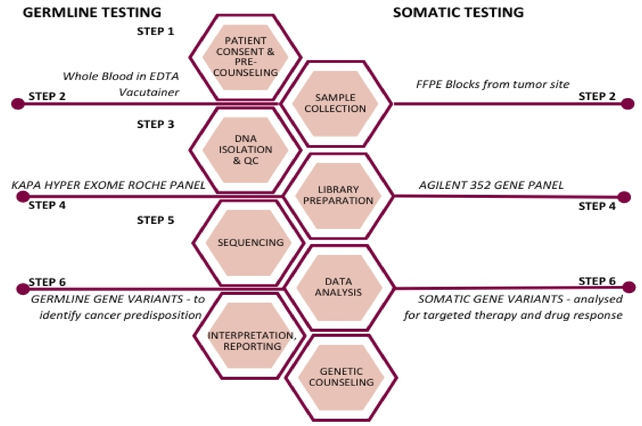
- Precise cancer diagnosis often hinges on identifying both somatic and germline mutations.
- This case report illustrates how comprehensive screening, encompassing both types of genetic analysis, can provide essential insights for clinical decision-making and patient management.
- This analysis allows clinicians to not only target specific driver mutations within a tumor but also assess a patient's inherited susceptibility to cancer recurrence and familial risk. Information about tumor - specific mutations also aids in tracking minimal residual disease and predicting recurrence.

Germline Variants	Micro-Satellite instability (MSI)	Anti-Cancer Pharmacogenomics	PD-L1
Response to FDA Approved Targeted Therapies	Tumor Mutation Burden (TMB)	Homologous Recombination Repair	

PEDIGREE CHART



MATERIALS & METHODS



RESULTS

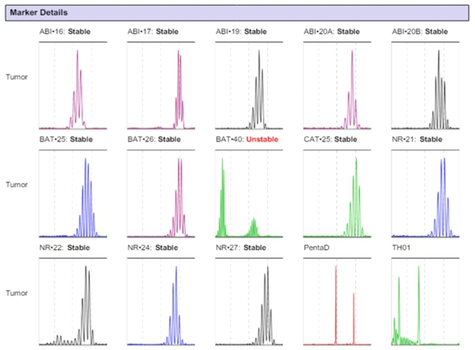
GERMLINE VAIRANTS

Name	State	Impact	Size	Classification
CHEK2 ex7-8 del	Het Deletion; CN:1,	Loss of function	6.6 Kb	Likely pathogenic
BRCA2 ex5 del	Het Deletion; CN:1,	Loss Of Function	944 bp	Likely pathogenic

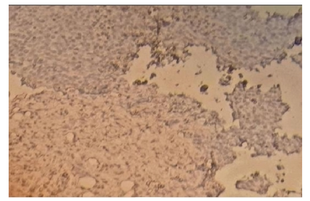
GENOMIC FINDINGS WITH EVIDENCE OF CLINICAL SIGNIFICANCE

GENOMIC FINDING	BENEFIT FROM FDA-APPROVED THERAPIES (LEVEL OF EVIDENCE)	RESISTANCE TO LAROTRECTINIB, DRUG	POTENTIAL CLINICAL TRIALS
BRCA1 G1801Afs*33 BRCA1 Truncation	Olaparib, Talazoparib tosylate (1A)	None	No
PTEN Q298* PTEN R335* PTEN W274* PTEN c.634+2T>G	Capivasertib+ Fulvestrant (1A)	None	No

MSI



PD-L1



IHC Marker	RESULT
PDL1	NEGATIVE in lymphocytes

TMB STATUS

TMB – LOW
5.76 Mutations per Mb
Average Coverage 3262x

- Somatic testing identified oncogenic mutations in the BRCA1 gene, including single nucleotide variants (SNVs) and copy number variants (CNVs), suggesting potential benefit from PARP inhibitor (PARPi) therapy.
- MSI was Low with Unstable BAT-40 marker. TMB was Low with 5.76 mutations/Mb.
- No clinically relevant rearrangements in the NTRK1, NTRK3, RET, ALK, or ROS genes. Unlikely to benefit from TRK inhibitors such as Larotrectinib or Entrectinib.
- **These findings correlate with better survival outcomes and improved response predictions to targeted therapy. Especially to PARPi in particular.**
- Additionally, Anti-cancer PGx suggested a poor response and high side effects to previously administered chemotherapy drugs, potentially explaining severe adverse reactions. It also helped in identifying thr right drugs with minimal side effects.

GENETIC COUNSELING

- Genetic counselling assisted the clinician develop a better treatment protocol, tailored to the patient's genetic profile.
- Detailed pedigree analysis identified at-risk individuals who were advised to undergo germline testing, enabling early implementation of appropriate screening protocols.
- This dual approach of comprehensive genetic screening empowers informed treatment decisions, potentially including targeted therapies and prophylactic measures for at-risk relatives.
- This case report underscores the benefits of comprehensive screening strategies in optimizing personalized cancer care.

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