CASE STUDY

Keeping Tabs on Cancer: The Liquid Biopsy Way

Quick Summary

- Ms. Preet Jhurani*, a 65-year-old homemaker, was diagnosed with breast cancer.
- Genetic analysis of the tumor biopsy revealed the presence of a mutation in the TP53 gene.
- The identification of the genetic profile of the tumor is crucial for tracking the progression of the disease in response to administered therapy.
- Surgical excision of the tumor was performed and adjuvant chemotherapy was provided to the patient.
- The tumor marker was not detected in a liquid biopsy sample, drawn at three months post-surgery.
- The patient is well as of September 2017 and is under medical observation.
- Additional liquid biopsies can be performed at 3-4 month intervals to ascertain recurrence of breast cancer, prior to the emergence of other clinical symptoms.

Introduction

Breast cancer is now the number one lethal cancer in women, in India. It has overtaken cervical cancer to be the most frequent cancer in India (1–3). Treatment of metastatic breast cancer with chemotherapy is the standard of care, in practice.

The results of chemotherapy are assessed by clinical symptoms and imaging techniques such as PET-CT scans, ultrasound imaging and mammograms (4). Another useful technique that can be leveraged for monitoring the response of cancer to given therapies, is Liquid Biopsy.

The significant advantage of liquid biopsy tests is that there is no exposure to radioactive probes (PET-CT scan) and the results are obtained within 5 working days. A blood sample for liquid biopsy can be obtained in settings where a patient is comfortable and the frequency of these tests can be set by the doctor.

One can perform two liquid biopsy tests in the time interval that is mandatory between two PET-CT scans.

Liquid Biopsy

Liquid Biopsy is essentially a blood sample from a cancer patient. Blood naturally contains DNA shed by cancer cells as well as normal cells when they die. Scientists can then extract tumor-specific DNA from this blood sample and understand the genetic profile of the cancer as well as estimate tumor burden.
Patient Profile

Preet Jhurani, age 65 years, was looking forward to visiting her son in Australia and spending 6 months with him. She was also a bit apprehensive about the upcoming trip because some nagging health issues bothered her. She hoped that her breast pain and discharge would not bother her during her stay with her son. She had also recently noticed a small lump on her right breast and dimpling in the areola.

Eventually, she decided to consult a physician and lay her doubts to rest before departing for Australia.

Preet’s gynecologist suspected the incidence of breast cancer and referred her to a prominent oncologist in Bangalore, India. Medical investigations, including a mammogram and a tissue biopsy, led to the diagnosis of breast cancer.

Results of Genetic Testing

Preet’s oncologist recommended genetic testing of the breast biopsy sample, with two objectives in mind:

A. Choice of targeted therapies
B. Tracking the progression of cancer using liquid biopsies

The StrandAdvantage 56-gene test was prescribed for the molecular diagnosis of Preet’s breast cancer, in January 2017.

<table>
<thead>
<tr>
<th>Sample Collection Date</th>
<th>Test</th>
<th>Gene</th>
<th>Mutation</th>
<th>Result</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-Jan-2017</td>
<td>Strand Advantage</td>
<td>TP53</td>
<td>R273H</td>
<td>Detected</td>
<td>9.80%</td>
</tr>
</tbody>
</table>

A mutation in the TP53 gene - TP53\(^{R273H}\) - was detected in the breast tissue biopsy.

Treatment Options

A lumpectomy with wide margins was performed on Preet to curtail the growth and spread of cancer, in March 2017. Adjuvant chemotherapy was prescribed to her to ensure that remnant cancer cells, if any, would be eliminated.

Follow-up Liquid Biopsy

A liquid biopsy sample was drawn from Preet to understand the progression of her breast cancer, in June 2017. A highly sensitive detection assay was used on cell-free DNA (cfDNA) isolated from the blood sample. The detection test is designed to identify the precise gene variant - TP53\(^{R273H}\) - in cfDNA.

<table>
<thead>
<tr>
<th>Sample Collection Date</th>
<th>Test</th>
<th>Gene</th>
<th>Mutation</th>
<th>Result</th>
<th>Copies/ml plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>27-Jun-2017</td>
<td>Strand Liquid Biopsy*</td>
<td>TP53</td>
<td>R273H</td>
<td>Not detected</td>
<td>N/A</td>
</tr>
</tbody>
</table>

The tumor marker mutation - TP53\(^{R273H}\) - was not detected in the blood sample within 3 months of the surgical excision of the parent tumor.

The parameter marked with an * are not accredited by NABL and CAP.
Conclusions

- Preet Jhurani, age 65 years, was diagnosed with breast cancer.
- A mutation in the TP53 gene was identified from the breast tissue biopsy.
- Surgery and adjuvant chemotherapy were administered to Preet.
- A liquid biopsy was performed, 3 months post-surgery, to ascertain the tumor burden in the patient.
- The tumor marker mutation was not present in cell-free DNA isolated from blood plasma.
- At this time-point, the combinatorial therapy of surgery and chemotherapy seems to have limited the growth of breast cancer cells. The patient is in remission and is under medical surveillance as of September 2017.
- Follow-up liquid biopsies can be performed at 3-4 month intervals to gain insights about the progression of cancer before clinical symptoms of recurrence are evident.
- Detection of the tumor-specific TP53 mutation in cfDNA from subsequent liquid biopsies, will indicate proliferation of remnant breast cancer cells.

StrandAdvantage 56-gene Test

StrandAdvantage 56-gene test is a pan-cancer test designed to identify mutations that are frequently found in most solid tumors. The 56-gene test has the advantage of being applicable for analysis of solid tumors as well as NGS analysis of cell-free DNA obtained from a liquid biopsy.
References


