Tackling Rare Cancers: Angiosarcoma of the Breast
Leveraging Genetic Knowledge to Provide Therapeutic Relief

Quick Summary

- A 24- year old woman, Namita, was diagnosed with angiosarcoma of the breast.
- Genetic analysis of tumor tissue, using the Strand Advantage 48-gene test, was advised in addition to surgery and radiotherapy.
- A cancer-causing mutation was identified in the PIK3CA gene in the tumor tissue.
- Based on the identification of the mutation, Namita received Everolimus therapy, resulting in improved quality of life for one year, despite living with an aggressive cancer.

Introduction

Angiosarcomas are cancers that develop from the cells that line our blood vessels. These kinds of cancers can form in the liver, spleen, breast and skin tissues.

Angiosarcomas have a very poor outcome. The 5-year disease-free survival rate for angiosarcomas is as low as 15% if the cancer is aggressive. Even in low-grade angiosarcoma cases, the 5-year disease- free survival rate is 76%. Statistics from the Mayo Clinic show that the average survival time for angiosarcoma patients is 48 months (Bordoni et al. 2016) .

As far as therapy options go, surgery to remove solid tumors, followed by chemotherapy and radiation are the known best practices for this cancer. Targeted therapy options are very few and depend upon the identification of mutations in tumor tissue. One such rare case of angiosarcoma was referred to Strand Life Sciences for identification of genetic mutations that caused the cancer.

Patient Profile

- 24-yr-old female patient with non-malignant but large mass angiosarcoma involving both breasts and right ovary
- Rare case of breast angiosarcoma with no established treatment options and poor prognosis

Treatment Strategy:

- Cytoreductive surgery to remove ovarian mass and lesions from both breasts performed
- Genetic analysis of tumor tissue was advised. An FFPE block of the tumor was provided for genetic analysis.

* Name changed to protect patient privacy

CASE STUDY

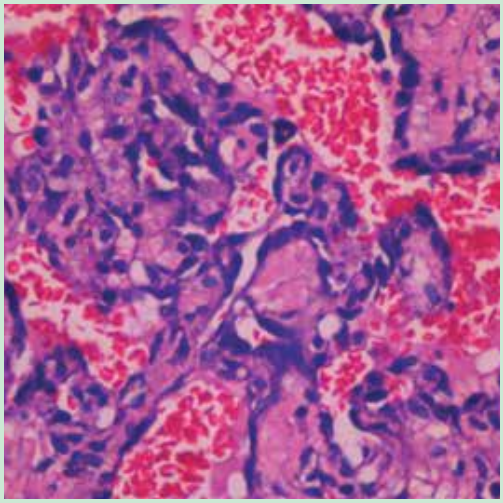
Tackling Rare Cancers: Angiosarcoma of the Breast
Leveraging Genetic Knowledge to Provide Therapeutic Relief

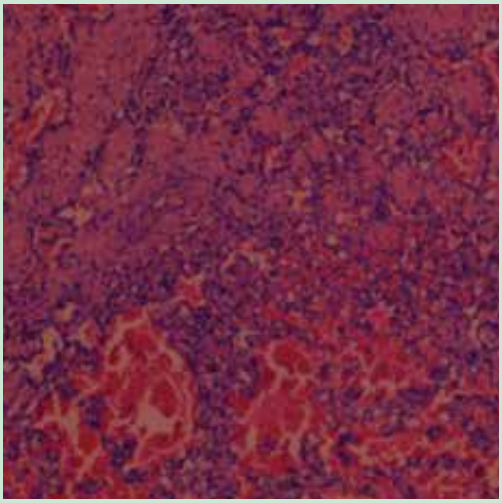
Patient Profile

Namita (name changed to protect patient privacy), a 24- year-old woman was referred to Dr. Dinesh Pendharkar at the Asian Institute of Oncology, Mumbai. Her main complaints were the presence of lumps in both breasts and as well as pain in the abdominal region. Ultrasound imaging revealed that both breasts had complex lumps of cancer and a tumor mass was present on Namita's right ovary. Additionally, cancer cells were present in the ascitic fluid (fluid present in the abdomen) asell. The cancer had started as an angiosarcoma in breast tissue and had begun spreading all over the body.

Histopathological Characterization of Tumor Tissue

The diagnosis of angiosarcoma was confirmed by examining tumor tissue under the microscope as well.





Treatment Strategy:

Surgery to remove the primary tumors followed by chemotherapy is one of the options for treatment of angiosarcomas. Radiotherapy is also an option. Paradoxically, radiotherapy of the breast can also cause secondary angiosarcomas (Plichta & Hughes 2017). In this particular case, the tumors seen in the breast and the ovary were also large in size (6*5*4 cm in the right breast and 9.8*7*5 cm in the left breast). The chances of survival of patients with angiosarcomas larger than 5 cm in size are extremely low.

Considering these facts, Dr. Pendharkar sought to understand the genetic basis of this cancer and accordingly had a sample of tumor tissue (FFPE block) sent to Strand Life Sciences.

Surgical Removal of Tumors and Post-Surgical Chemotherapy

Tumors in Namita's breasts and the one on the ovary were removed surgically. The right ovary was also removed in order to ensure complete removal of cancer tissue.

She was also given four rounds of post-surgical chemotherapy with iphosphamide / doxorubicin.

Genetic Analysis of Angiosarcoma Tissue

- The Strand Advantage 48-gene panel test was advised in this case. This test includes a set of genes that are known to be mutated in most cancers, effectively making it a pan-cancer genetic test.
- A mutation in the PIK3CA gene - Chr3: 178916929G>C c.316G>C p.Gly106Arg – was identified in the angiosarcoma tissue
- The identified mutation has been previously reported in endometrial cancer (Cancer Genome Atlas Network et al. 2012), clear-cell renal cell carcinoma (Sato et al., 2013) and colorectal adenocarcinomas (Cancer Genome Atlas Network et al. 2012).
- This is known to be an activating mutation thereby resulting in excessive activity of this enzyme, causing uncontrolled cell division (Rudd et al. 2011).

Targeted Therapy

Namita's cancer was caused by the excessive activity of the protein product of the PIK3CA gene. In such cases, drugs like Everolimus can be prescribed to counteract this overactive protein, to stop the growth of cancer cells. Everolimus has been tested for restricting the growth of cancers like colorectal cancer (Liu et al. 2015; Yuge et al. 2015), by a similar mechanism of action.

Namita was prescribed Everolimus at 10 mg/day. The therapy worked well to improve the quality of her life for the subsequent year, despite the aggressive nature of the angiosarcoma.

Conclusions

- Rare cancers have limited treatment options. Angiosarcomas, which are cancers that develop from the cells of blood vessels, are highly aggressive cancers.
- Genetic analysis of Namita's angiosarcoma tissue helped to identify the causative mutation.
- The identification of the mutation helped to identify a specific drug, Everolimus, to treat her cancer post-surgery.
- Targeted therapy with Everolimus helped to improve Namita's quality of life for one year, despite living with an aggressive cancer.

Case Summary:

- 24-year-old female patient with angiosarcoma of the breast.
- Disease with bleak prognosis
- No available treatment
- Exhausted chemotherapy options
- Genetic testing for mutations allowed for selection of everolimus- a drug that can inhibit the physiological action of the mTOR (mammalian target of rapamycin) protein. mTOR is a downstream effector of PI3K, the product of the *PIK3CA* gene. Inhibition of mTOR therefore results in inhibition of cell proliferation and angiogenesis. Everolimus therapy was therefore effective in delaying the progression of her angiosarcoma.

References:

1. *Bordoni, D. et al., 2016. Primary angiosarcoma of the breast. International journal of surgery case reports, 20S(Suppl), pp.12–5. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26867719 [Accessed May 8, 2017].*

2. *Cancer Genome Atlas Network, D.M. et al., 2012. Comprehensive molecular characterization of human colon and rectal cancer. Nature, 487(7407), pp.330–7. Available at: http://www.nature.com/doifinder/10.1038/nature11252 [Accessed April 21, 2017].*

3. *Liu, Y. et al., 2015. Biomarker Signatures Correlate with Clinical Outcome in Refractory Metastatic Colorectal Cancer Patients Receiving Bevacizumab and Everolimus. Molecular Cancer Therapeutics, 14(4), pp.1048–1056. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25695956 [Accessed May 8, 2017].*

4. *Plichta, J.K. & Hughes, K., 2017. Radiation-Induced Angiosarcoma after Breast-Cancer Treatment. New England Journal of Medicine, 376(4), pp.367–367. Available at: http://www.nejm.org/doi/10.1056/NEJMicm1516482 [Accessed May 8, 2017].*
Rudd, M.L. et al., 2011. A unique spectrum of somatic PIK3CA (p110alpha) mutations within primary endometrial carcinomas. Clinical cancer research : an official journal of the American Association for Cancer Research, 17(6), pp.1331–40. Available at: http://clincancerres.aacrjournals.org/cgi/doi/10.1158/1078-0432.CCR-10-0540 [Accessed April 21, 2017].

5. *Yuge, R. et al., 2015. mTOR and PDGF Pathway Blockade Inhibits Liver Metastasis of Colorectal Cancer by Modulating the Tumor Microenvironment. The American Journal of Pathology, 185(2), pp.399–408. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25478811 [Accessed May 8, 2017].*

Strand Center for Genomics & Personalized Medicine
(A unit of Strand Life Sciences Pvt. Ltd.)
UAS Alumni Association Building, Veterinary College Campus, Bellary Road, Hebbal, Bangalore – 560 024
Phone: 1800-1022-695, support.strandx@strandls.com, www.strandls.com

#StayAheadOfCancer

Strand Center for Genomics & Personalized Medicine is accredited by

CAP ACCREDITED # 8750941

Certificate No. M-0849