# Treatment Options for Rare Cancers: Extramammary Paget's Disease

## *Drug options revealed by genetic analysis of a rare and persistent cancer*

## Quick Summary

- A 78- year old patient was diagnosed with Extramammary Paget's Disease. The cancer started showing signs of growth after remaining benign for three years.
- Established cancer treatment strategies like chemotherapy (2 different drugs), radiotherapy and a targeted drug (Trastuzumab) failed to stop the growth of this rare cancer.
- Genetic analysis of tumor biopsy indicated that a mutation in the *PIK3CA* gene was the causative factor of this disease.
- Everolimus therapy, intended to overcome the effects of the *PIK3CA* mutation, has helped to control the growth of the tumor, providing relief to the patient.
- Genetic analysis should be included in early strategies to treat cancer in order to avoid multiple rounds of therapy with various anti-cancer drugs.

| Treatment Strategy | Time Period | Therapy | Observation |
|---|---|---|---|
| Diagnosis of extramammary Paget's disease | June 2010 | None | |
| Surveillance | June 2010 - March 2013 | None | Diagnosis of Paget's Disease confirmed |
| Chemotherapy | April 2013 - July 2013 | IV Paclitaxol 150mg / week, for 12 rounds | Cancer responded to therapy |
| Surveillance | July 2013 - September 2014 | None | Swelling on the right side of neck observed |
| Radiotherapy | 03/12/2014 - 08/01/2015 | | Radiotherapy provided to control the growth of cancer |
| Surveillance | June 2015 | | Growth of cancer noticed again |
| Advice | January 2016 | Re-biopsy | Cancer started growing aggressively |
| Capecitabine therapy | January 2016 - June 2016 | Capecitabine (500mg, 2-0-2 for 7days on, 7days off) | Thickening of neck skin notes |
| Advice | August 2016 | Genomic profiling of cancer tissue | Cancer biopsy sample was sent to Strand Life Sciences |
| Genomic Profiling | | Strand 152 - gene pan-cancer test | Mutation in PIK3CA gene (PIK3CAH1074R) identified in tumor tissue |
| Everolimus Therapy | August 2016 - Jan 2017 | Everolimus (10mg / day alternating with 5mg / day) | Cancer has stopped growing. Patient has a good quality of life. |

## Introduction

Extramammary Paget's Disease is a rare skin cancer. This kind of cancer is usually evident as bright red patches on the skin. An unusual case of Extramammary Paget's Disease was referred to Strand for genetic diagnosis. The case stretched over a period of 6 years with the cancer progressing from benign to malignant. Despite several rounds of therapies, the tumor showed signs of relentless growth. Genetic analysis of the tumor was then advised and a mutation in the *PIK3CA* gene was identified. The genetic characterization of the tumor turned out to be a key breakthrough. The patient has been prescribed Everolimus therapy to overcome the defective *PIK3CA* mutation and the tumor has stopped growing.

CASE STUDY

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## Patient Profile

A 78- year old man, Mr. G Padmanabhan*, was advised to meet a senior oncologist at Apollo Hospital, Chennai when he spotted a red rash growing on his chest and neck. The doctor diagnosed the rash as Extramammary Paget's Disease. A PET-CT scan showed that nodules of growth were scattered in the area near the collarbone. Since the red skin patches did not show signs of spreading and were not affecting the quality of life of the patient, the doctor adopted a wait and watch approach.

## Surveillance

Padmanabhan underwent regular checkups for the next three years from June 2010 to March 2013. In 2013, the tumor showed signs of growth, confirmed by examining a biopsy of tumor tissue, microscopically.

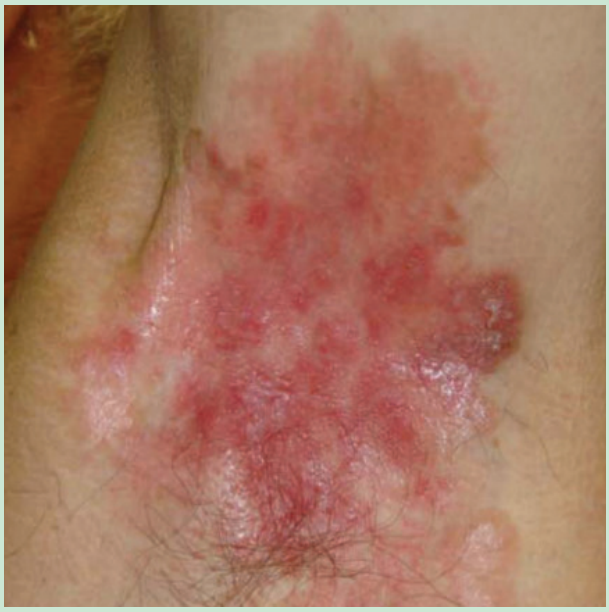

**Figure 1:** Erythematous spread of Paget's disease near the armpit.

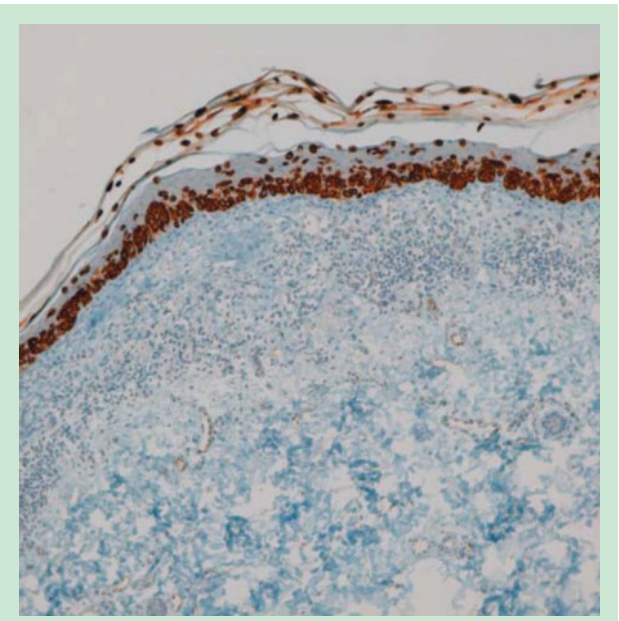

**Figure 2:** Immunohistochemical staining for cytokeratin7 – CK7 reactivity evident in the intradermal tissue, indicating spread of Paget's disease

*(Ref:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0365-05962013000500828)*

*Name changed to protect patient privacy

## Therapeutic Interventions

Conversion of the tumor from a benign growth to the malignant one prompted the prescription of chemotherapy. Padmanabhan underwent 12 cycles of chemotherapy with Paclitaxel (150 mg/ week) between April 2013 and July 2013. The tumor remained quiescent for another year but a PET-CT scan done in September 2013 showed that the cancer cells in the nodes in his neck region had become active again.

Subsequently, Padmanabhan was treated with radiotherapy in January 2015 and subsequently with a targeted drug called Trastuzumab until December 2015.

Padmanabhan was given a second session of chemotherapy with Capecitabine 500 mg, 2-0-2, 7 days on and 7 days off, between January 2016 and June 2016.

However, by this time the tumor had become quite aggressive and was not responding to known anti-cancer therapies.

## Genetic Analysis

In order to understand why the cancer had become so aggressive, the doctor advised Padmanabhan to get his tumor tissue tested for the presence of genetic changes.

Accordingly, a sample of his tumor tissue was sent to Strand Life Sciences, Bangalore.

## Strand 152-gene Test

Identification of genetic mutations from a tumor is like looking for a needle in a haystack. There are some genes known to be mutated in most cancers. Strand's 152-gene test is a pan-cancer test that includes genes that are quite frequently mutated in most cancers.

Padmanabhan's biopsy of Extramammary Paget's Disease was analysed using the 152-gene test. A mutation in the *PIK3CA* gene was present in the tumor tissue. This mutation, *PIK3CA*H1074R, makes this gene remain active all the time, causing uncontrolled cell division.

## Targeted Therapy against *PIK3CA*

The identification of this gene mutation turned out to be a significant development. There are drugs that help to overcome mutations in *PIK3CA* and stop cell division. One such drug, Everolimus (10 mg/day alternating with 5 mg /day), was prescribed to Padmanabhan in August 2016.

## Present Status

As of 2017, the patient is responding to the drug and the patches of extramammary Paget's disease visible on the head and neck are reducing. The patient is surviving and satisfied with therapy options created by genetic analysis.

## Conclusions

- Genetic analysis of Padmanabhan's rare cancer revealed the presence of a mutation in the *PIK3CA* gene, thereby facilitating the prescription of Everolimus therapy.

- Padmanabhan had undergone several rounds of treatment with chemotherapy, radiotherapy and Trastuzumab therapy with only temporary halt in the growth of the tumor.

- Genetic analyses should be included in the early work-up of cancer patients in order to identify targeted therapies that can provide early relief to patients.

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