

## An Interesting Case of Chimera: Inconclusive BRCA Analysis due to Two Distinct Genetic Profiles in a Single Patient

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### Abstract

**Background:** Our case study proposes an explanation for the inconclusive BRCA testing we received on one of our patients. The BRCA analysis was inconclusive due to the specimen being chimeric, or having two distinct genetic profiles. We propose the Vanishing Twin theory as the most probable explanation. We have found no other reported cases of chimera linked to Vanishing Twin Syndrome in the literature.

**Methods:** In this case report, we have described the presentation and operative course of a single patient of our Breast Center in 2017 to help define the setting of our unique BRCA analysis result.

**Findings:** We have also done an extensive literature search in an attempt to understand the implications of the BRCA analysis result in a chimeric patient. However, our search was not satisfied by any direct evidence. We can only conclude that the Vanishing Twin theory is the most likely explanation of chimera in this single patient.

**Conclusions:** We were unable to find any direct explanation for our results but we do propose this as an interesting case, as chimera is rare. In the future, it would be interesting to research whether chimera is, in fact, linked to Vanishing Twin syndrome, and whether these patients have any distinct protection from or predilection for certain disease processes.

**Keywords:** BRCA analysis; Chimeric; Vanishing twin theory; Pathology; Bilateral mastectomy

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### Introduction

Chimeras are defined as beings formed by combining the whole cells of genetically different organisms into a single organism. The finding of chimera in a human being may be explained by Vanishing Twin Syndrome, history of stem cell treatment, or history of transplant. Because our patient was incidentally found to be chimeric during BRCA analysis and denies history of transplant, her chimera is most probably explained by the Vanishing Twin Syndrome.

### Case Report and Findings

This is a 68 year old female with medical history significant

for diabetes type two and hyperlipidemia who presented to the breast clinic after feeling a right breast mass on self-exam. Identifiable risk factors included early menarche (age 9), family history of breast cancer in her paternal aunt (diagnosed age 60) and maternal cousin (diagnosed age 27). Patient also has a significant family history of a mother with colon cancer (deceased 88 years old) and a father with bladder cancer (deceased 78 years old). On physical exam, there was an obvious four-centimeter mobile mass in the upper outer quadrant of the right breast, 11:00, 6 centimeters from the nipple. A sub centimeter mass like lesion at 12:00, 6 centimeters from the nipple, was noted as well. No palpable masses were noted in the left breast. The ultrasound guided biopsy of the right axillary tail and the 12:00 mass showed

low to intermediate grade ductal carcinoma in situ (DCIS) with extensive necrosis, ER/PR positive. The ultrasound guided biopsy of the left breast revealed well-differentiated infiltrating ductal carcinoma (IDC); ER/PR positive, Ki-67 2%, HER 2 negative. Her MRI showed bilateral breast masses with the one on the right being in close proximity to the pectoralis muscle. A "Know Error" test using a buccal swab specimen from the patient at the time of the breast biopsies was confirmed to be a match with the breast specimens. The patient's BRCA1 and BRCA2 analysis was deemed inconclusive due to evidence of mixed genotypes. The BRCA2 sequencing results consistently showed several benign polymorphic variants at levels that diverged from the 50:50 representations expected for heterozygous germline variants. Additional genotype testing using short tandem repeat markers was performed showing an additional minor allele at several sites. Therefore, it was concluded the patient had two distinct genetic profiles, known as chimera, making her BRCA analysis inconclusive. Her genetic profiles were similar enough to indicate they were first degree relatives. She underwent a bilateral mastectomy and bilateral sentinel node biopsy (SNB). The left breast pathology showed a 1.4 cm well-differentiated IDC, as well as DCIS, with negative sentinel nodes, stage IA. The right breast pathology showed intermediate to high grade 4.5 cm DCIS with necrosis as well as well differentiated 5 mm mucinous type IDC, ER+PR+/ Ki-67 12 percent/Her-2 negative, with negative sentinel nodes, stage IA. She had a low Oncotype Dx score and was started on Aromasin.

## Discussion

We have researched the literature extensively for a clear answer to explain the findings of our patient's two distinct genetic profiles, but have not found a direct answer. We considered

three theories: Vanishing Twin Syndrome, history of transplant, or history of stem cell treatment. The patient's history is negative for the latter two considerations. Therefore, we have concluded that the absorbing twin in utero theory is the most likely explanation for our findings. The Vanishing Twin syndrome is the demonstration of resorption of one or more gestational sacs in multi-pregnancy. This is confirmed via transvaginal ultrasound, most commonly during the first trimester [1,2]. The frequency of vanishing twins is especially high in assisted technology assisted treatment, and has been reported to range from 12-30% [3]. The surviving fetus is at risk for preterm delivery before 34 weeks and low mean birth weight, but otherwise has no adverse outcomes [4]. None of the articles we found during our research focused on the possibility of distinct genetic profiles in their patients nor was it mentioned as a consideration. We were also unsuccessful in identifying any literature describing long term effects on singletons born in the setting of Vanishing Twin [5]. Given the limited amount of information documented in the literature, we are only able to infer that our patient is chimeric, likely due to the absorbing twin in utero theory [6].

## Conclusion

We are unable to find an answer to the reason for our patient's BRCA results demonstrating two distinct genetic profiles. We merely suggest a link to the Vanishing Twin Theory as an explanation. Perhaps in the future, it would be valuable to study the long-term implications of singleton birth following demonstration of multi-pregnancy in a patient as well as to assess the incidence of chimera in those patients. It may also be valuable to outline alternative etiologies of chimera, and the effect that may have on a patient in the long term.

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