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Synchronous bilateral male breast cancer: A case report and review of literature

Natassia Dunn, Peter D Nguyen,
Sarah W Yuen, Erin Lin

ABSTRACT

Introduction: Male synchronous bilateral breast cancer, defined as contralateral breast cancer diagnosed within 12 months of a previous breast cancer, is extraordinarily rare. This case report aims to provide improved understanding of the nuances in presentation, associated risk factors, and treatment options of synchronous bilateral male breast cancer.

Case Report: A 68-year-old man presented with a one-month history of palpable bilateral retroareolar breast masses. He underwent workup with a bilateral breast ultrasound which showed an irregular hypoechoic mass 8 × 8 × 6 cm in the right breast at 7 o'clock in the retroareolar region and an oval hypoechoic mass 7 × 4 × 7 cm with indistinct margins in the left breast at 8 o'clock in the retroareolar region. Subsequent ultrasound-guided core needle biopsies revealed right breast moderately differentiated invasive ductal carcinoma and left breast high grade ductal carcinoma in situ. He underwent a bilateral simple mastectomy with bilateral axillary sentinel lymph node biopsies and was started on anastrozole at his initial post-operative visit. Four-month surveillance imaging with computed tomography chest, abdomen, pelvis, and dual X-ray absorptiometry showed no evidence of local recurrence or metastases.

Conclusion: Male breast cancer commonly presents as a painless retroareolar mass. Workup should include imaging studies to localize and characterize the lesion and tissue diagnosis via core needle biopsy. Treatment of male breast cancer largely includes simple mastectomy with adjuvant endocrine therapy. Future breast cancer studies should include male cohorts to improve our understanding and treatment options between the two sexes.

Keywords: Adjuvant endocrine therapy, Ductal carcinoma in situ, Invasive ductal carcinoma, Male breast cancer, Simple mastectomy, Synchronous bilateral breast cancer

Natassia Dunn[1], Peter D Nguyen[2], MD, Sarah W Yuen[3], MD, MPH, Erin Lin[4] DO

Affiliations: [1]Medical Student, School of Medicine, University of California Irvine, Irvine, California, United States of America; [2]MD, Resident Physician, Department of Surgery, Division of Surgical Oncology, University of California Irvine, Orange, California, United States of America; [3]MD, MPH, Resident Physician, Department of Surgery, Division of Surgical Oncology, University of California Irvine, Orange, California, United States of America; [4]Associate Clinical Professor, Department of Surgery, Division of Surgical Oncology, University of California Irvine, Orange, California, United States of America.

Corresponding Author: Erin Lin, DO, Associate Clinical Professor of Surgery, Division of Surgical Oncology, Department of Surgery, University of California, Irvine Medical Center, 3800 Chapman Ave, Suite 6200, Orange, CA 92868-3298, United States of America; Email: erinhl@hs.uci.edu

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INTRODUCTION

Male breast cancer is an uncommon diagnosis that accounts for less than 1% of all diagnosed breast cancers worldwide [1–4]. Male synchronous bilateral breast cancer, defined as a contralateral breast cancer diagnosed within 12 months of a previous breast cancer, is extraordinarily rare and the number of these reports are limited [1–9]. Due to the rarity of male breast cancer

and subsequent lack of randomized control trials, the paucity of data lends to extrapolation of many treatment decisions from the management of female breast cancer. While there are similarities in the presentation and management between men and women, there are also notable differences in epidemiology, risk factors, and tumor characteristics. Additional research is necessary to further elucidate the risk factors and optimal treatment modalities for male breast cancer. This case report and review of literature aims to provide improved understanding of the nuances in presentation, associated risk factors, and treatment options of synchronous bilateral male breast cancer.

CASE REPORT

A 68-year-old man presented with a one-month history of palpable bilateral retroareolar breast masses. Both masses enlarged in size with worsening tenderness; however, he did not experience nipple discharge, breast skin changes, significant weight changes, shortness of breath, or bone pain. He had no known history of trauma to either breast or any new medications. His medical and surgical history was significant for a 30-year history of human immunodeficiency virus (HIV) well controlled with antiretroviral therapy, remote history of left forehead squamous cell carcinoma metastatic to the left parotid gland that underwent Mohs surgery and left superficial parotidectomy with modified radical neck dissection and adjuvant radiation therapy. Patient's pertinent family history included a sister with a diagnosis of breast cancer, but no known family genetic history of BRCA 1 or 2. The patient had a 40-pack-year history but had quit tobacco use 10 years prior and denied a history of alcohol or substance use.

He underwent workup with a bilateral breast ultrasound which showed an irregular hypoechoic mass 8 × 8 × 6 cm in the right breast at 7 o'clock in the retroareolar region and an oval hypoechoic mass 7 × 4 × 7 cm with indistinct margins in the left breast at 8 o'clock in the retroareolar region (both American College of Radiology (ACR) BI-RADS Category 4) (Figure 1). Subsequent ultrasound-guided core needle biopsies revealed right breast moderately differentiated invasive ductal carcinoma (IDC) and left breast high grade ductal carcinoma in situ (DCIS). Immunohistochemistry on both masses was estrogen receptor positive (90%) and progesterone receptor positive (80%). The right breast IDC was E-cadherin positive, HER-2 negative, and had a Ki-67 of 40%. The left breast DCIS had positive CK5/6 and P63. Bilateral breast magnetic resonance imaging (MRI) showed both masses abutting the nipples; however, there was no evidence of suspicious lymphadenopathy (ACR BI-RADS Category 6) (Figure 2). Computed tomography (CT) chest was negative for metastatic spread to the lungs (Figure 3). Genetic testing via Myriad myRisk Hereditary Cancer revealed a deletion mutation of BRCA2 c.5146_5149del (p.Tyr1716Lysfs*8), causing premature truncation of the BRCA2 protein with associated increased cancer risk.

He underwent a bilateral simple mastectomy with bilateral axillary sentinel lymph node biopsies and soft tissue flap reconstruction approximately one month from initial presentation. We opted to excise his nipple areolar complex due to retroareolar location of bilateral breast masses (Figure 4). Frozen section microscopy for bilateral axillary sentinel nodes were negative for carcinoma. Local soft tissue flaps were raised and used to fill the mastectomy defect. The patient tolerated the procedure well without complication and was discharged on the same day in stable condition. Right breast final pathology showed grade 2 invasive ductal carcinoma measuring 9 mm as the greatest dimension and high-grade ductal carcinoma in situ without lymphovascular invasion and negative resection margins (pT1bN0). Left breast final pathology showed intermediate to high grade DCIS measuring 1.5 cm with negative resection margins (pTisN0).

He progressed in the usual post-operative course and was started on anastrozole at his initial post-operative visit. His four-month surveillance imaging with CT chest, abdomen, pelvis, and dual X-ray absorptiometry (DEXA) had no evidence of local recurrence or metastases. The patient ultimately opted to discontinue any further endocrine therapy at this time. The patient was recommended to undergo breast cancer surveillance screening with annual bilateral breast ultrasounds. Given his BRCA2 mutation, he underwent additional screenings for pancreatic cancer and prostate cancer which were without evidence of malignancy. He was doing well at his ten-month clinic visit without any evidence of local or nodal recurrence.

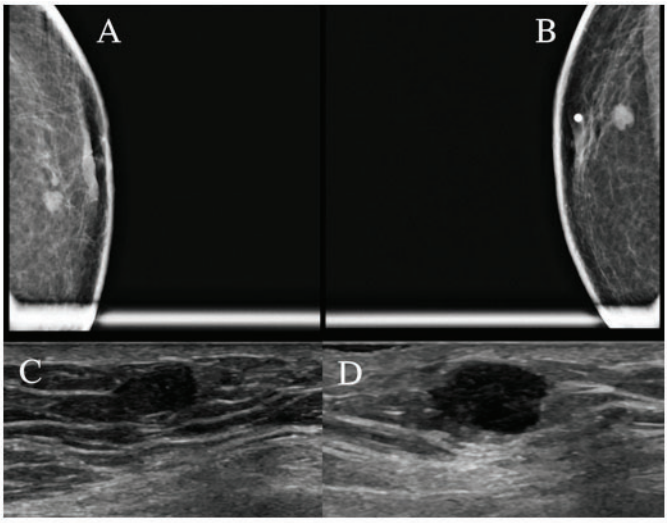

Figure 1: Bilateral breast diagnostic mammogram and ultrasound. (A) Left breast cranial caudal view. (B) Right breast cranial caudal view. (C) Left breast ultrasound with a 0.7 × 0.4 × 0.7 cm hypoechoic mass at the 8 o'clock retroareolar region. (D) Right breast ultrasound with a 0.8 × 0.5 × 0.9 cm hypoechoic mass at the 7 o'clock retroareolar region.

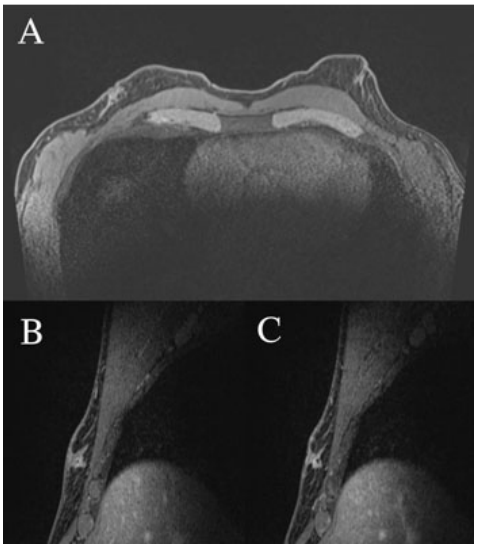

Figure 2: Bilateral breast diagnostic magnetic resonance imaging. (A) Axial view. (B) Right breast sagittal view. (C) Left breast sagittal view.

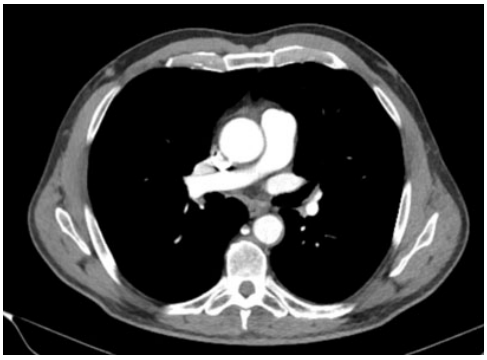

Figure 3: Computed tomography chest, right breast 8 mm nodule consistent with known biopsy-proven breast cancer. No evidence of metastatic spread to the lungs or lymph nodes.

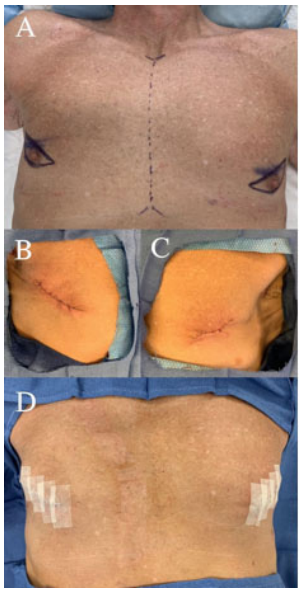

Figure 4: Intraoperative planning and surgical outcome. (A) Preoperative incision. (B) Right breast skin closure. (C) Left breast skin closure. (D) Bilateral breast with final dressings in place.

DISCUSSION

Bilateral synchronous male breast cancer is an extremely uncommon diagnosis and accounts for less than 0.5–0.6% of all diagnosed breast cancers [6]. However, the incidence of male breast cancer has slowly been increasing from 0.96 to 1.08 per 100,000 population [6, 9]. Due to its rare incidence, the various genetic and environmental risk factors for male breast cancer are not well understood. These include family history of breast cancer and genetic factors such as Klinefelter's syndrome (47, XXY), androgen receptor mutations, or BRCA mutations, with BRCA-2 carrying an 80-fold increased risk of breast cancer compared to the general population. Additionally, hormonal imbalance between estrogen and testosterone has been hypothesized to contribute to the development of male breast cancer including obesity, testicular disease (mumps, orchitis, orchiectomy, undescended testis, and cryptorchidism), liver disease contributing to hyperestrogenic states, and radiation exposure [1–3, 5, 9].

Male breast cancer differs from female breast cancer in prevalence, signs and symptoms, imaging validity, and treatment plans. The mean age at diagnosis for males is 67, which is five years later than women [10]. Additionally, the mean tumor size is often larger, with more frequent nodal involvement, higher frequency of androgen and estrogen receptor positivity, and higher stage [3, 10]. Like females, the most common type of male breast cancer is invasive carcinoma with the most common histologic type being invasive ductal carcinoma [3]. Common presentations of male breast cancer include a painless palpable retroareolar mass, nipple retraction, skin ulceration, bloody nipple discharge, and palpable axillary lymphadenopathy, many of which are similar to the signs and symptoms of female breast cancer and should warrant further workup in such patients [3, 9, 11]. However, since male breast tissue is often undersized, it has been shown that the nipple is most commonly involved at earlier stages and the mass is often localized to the subareolar region, with less frequency in the upper outer quadrant compared to women [11, 12]. Like female breast cancer, the first line method for diagnosis is mammography, which is highly sensitive (~92%) and specific (~90%), usually appearing as a unilateral, distinct density with irregular margins [3, 11, 13]. Use of magnetic resonance imaging (MRI) has been shown to be variable in its clinical use, with some sources stating its use to be limited in male cases, while others reporting that it is recommended in cases when initial imaging is indeterminate and can be successful in assessment of the male breast [1]. Unlike in women, ultrasound has been shown to not be as useful for the primary diagnosis but can be used to supplement the aforementioned cross-sectional imaging, especially when patients are younger than 25 years. An ultrasound suggestive of breast cancer shows a unifocal solid, hypoechoic mass with irregular margins, often with axillary nodes enlarged

[13]. According to the ACR Appropriateness Criteria, if there is an indeterminate breast mass found, the initial recommended imaging study is ultrasound if the male patient is younger than age 25 and mammography if the patient is older than age 25 [14]. Similarly to women, core needle biopsy is the standard of care to establish a histologic diagnosis [9].

Due to the rarity of male breast cancer and subsequent lack of randomized prospective studies in this population, the treatment of early-stage male breast cancer is typically extrapolated from that of early-stage female breast cancer with upfront oncologic resection followed by adjuvant endocrine treatment, chemotherapy, or radiotherapy, depending on varying prognostic factors [11]. Historically, radical mastectomy began as the main surgical intervention for breast cancer, but was gradually replaced by less invasive surgical interventions, with a shift toward modified radical mastectomy with axillary lymph node dissection in the 1970s. Since that time, as axillary dissections have become less common, simple mastectomy with sentinel lymph node biopsy is largely the treatment of choice. Per the American Society of Clinical Oncology (ASCO) guidelines, this treatment algorithm is also appropriate for men. Breast conserving surgery is a common approach for women with early-stage breast cancer; however, this is rarely performed in males. Following surgery, like women, ASCO recommends that men with hormone receptor positive breast cancer should be offered adjuvant endocrine therapy, such as tamoxifen, for an initial duration of five years. If contraindicated, patients may also be offered a gonadotropin-releasing hormone (GnRH) agonist with an aromatase inhibitor [15–17]. Those who still have a high risk of recurrence can continue hormone therapy for an additional five years. Unfortunately, while a survival benefit has been demonstrated with adjuvant hormone therapy, many men choose to discontinue therapy due to frequent side effects, including weight gain and decreased libido [16].

While radiotherapy is mandatory with breast conserving surgery in women, there is differing data regarding the benefit of radiation therapy following mastectomy in males, who more often undergo simple or modified radical mastectomies [18–21]. Because male breast cancer is often more aggressive and found in advanced stages, adjuvant loco-regional radiotherapy is more frequently performed than with female breast cancer [11]. While some studies have shown radiotherapy to improve local recurrence or overall survival rates, especially those with positive lymph nodes, these arguments for other subgroups of patients are not yet widely supported [18]. Recommendations for radiotherapy are otherwise similar between males and females and indications for radiation in male breast cancer include tumor size larger than 5 cm, positive lymph nodes, or positive resection margins [11]. Additionally, chemotherapy indications and prognostic factors frequently used in women can also be applied to men, including positive nodal disease tumors larger than 1 cm or those negative for hormone receptors [11, 22]. Table 1 summarizes published case reports since 2000 to include pathology, treatment, and outcome.

Table 1: Review of synchronous male breast cancer case reports since 2000

Publication	Age	Left breast pathology	Right breast pathology	Surgical intervention	Neoadjuvant chemotherapy	Adjuvant chemotherapy	Radiation	Endocrine therapy	Reported outcome
Forloni et al. (2001) [2]	45	Infiltrating ductal carcinoma	Ductal carcinoma in situ	Bilateral radical mastectomy	No	No	No	No	Disease free 24 months
Okada et al. (2003) [3]	45	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral total mastectomy	No	No	No	No	NA
Lambley et al. (2005) [4]	84	Infiltrating ductal carcinoma	Ductal carcinoma in situ	Bilateral modified radical mastectomy	No	No	No	Yes	Disease free 12 months
Melenhorst et al. (2005) [5]	63	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	No	Yes	Yes	Disease free 12 months
Franceschini et al. (2006) [6]	50	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral modified radical mastectomy	No	No	Yes	Yes	NA
Staerkle et al. (2006) [7]	30	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral modified radical mastectomy	No	No	No	No	NA
Sosnovskikh et al. (2007) [8]	50	Invasive papillary carcinoma	Ductal carcinoma in situ	Left modified radical mastectomy and right subcutaneous mastectomy	No	No	No	Yes	Disease free 6 months

Table 1: *(Continued)*

Publication	Age	Left breast pathology	Right breast pathology	Surgical intervention	Neoadjuvant chemotherapy	Adjuvant chemotherapy	Radiation	Endocrine therapy	Reported outcome
Hirose et al. (2007) [9]	47	Noninvasive ductal carcinoma	Invasive ductal carcinoma	Bilateral simple mastectomy	No	No	No	Yes	NA
Qureshi et al. (2007) [10]	26	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral total mastectomy	No	No	No	No	NA
Ucar et al. (2008) [11]	74	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	Right modified radical mastectomy and left simple mastectomy	No	Yes	Yes	No	NA
Spencer and Shutter (2009) [12]	58	Invasive lobular carcinoma	Invasive lobular carcinoma	None (hospice)	No	No	No	No	Hospice care for metastatic disease
Maksimovic (2010) [13]	54	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	Bilateral modified radical mastectomy	No	No	Yes	Yes	NA
Yaman et al. (2010) [14]	66	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	Yes	Disease free 24 months
Hoque et al. (2010) [15]	61	Invasive ductal carcinoma	Ductal carcinoma in situ	Left modified radical mastectomy and right simple mastectomy	No	No	No	Yes	Disease free 60 months
Noor et al. (2011) [16]	54	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral subcutaneous mastectomy	No	No	No	No	Disease free 18 months
Lemoine et al. (2011) [17]	15	Ductal carcinoma in situ	Ductal carcinoma in situ	bilateral total mastectomy	No	No	No	No	Disease free 36 months
Al-Saleh et al. (2011) [18]	68	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral total mastectomy	No	No	No	No	NA
Sun et al. (2012) [19]	54	Ductal carcinoma in situ	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	Yes	NA
Chern et al. (2012) [20]	61	Ductal carcinoma in situ	Invasive ductal carcinoma	Left simple mastectomy and right modified radical mastectomy	No	No	No	No	NA
Hernandez et al. (2013) [21]	70	Invasive ductal carcinoma and invasive papillary carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	No	No	Yes	NA
Garcia-Mejido et al. (2013) [22]	75	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral total mastectomy	No	No	Yes	Yes	NA
Takalkar et al. (2014) [23]	75	Infiltrating ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	Yes	No	Yes	Yes	Disease free 18 months
Jagtap et al. (2014) [24]	70	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	No	NA

Table 1: *(Continued)*

Publication	Age	Left breast pathology	Right breast pathology	Surgical intervention	Neoadjuvant chemotherapy	Adjuvant chemotherapy	Radiation	Endocrine therapy	Reported outcome
Nwashilli et al. (2015) [25]	75	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral simple mastectomy	No	Yes	No	No	Recurrence at 18 months
Zangouri et al. (2016) [26]	63	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	Yes	Disease free 48 months
Frey et al. (2016) [27]	62	Encapsulated papillary carcinoma and ductal carcinoma in situ	Invasive ductal carcinoma and ductal carcinoma in situ	Bilateral modified radical mastectomy	No	No	No	No	NA
Akinci et al. (2019) [28]	72	Intracystic papillary carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	Yes	NA
Lehrberg et al. (2020) [29]	52	Invasive ductal carcinoma	Ductal carcinoma in situ	Bilateral simple mastectomy	No	Yes	No	Yes	NA
Kadam et al. (2020) [30]	60	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	Yes	Yes	NA
Kanayama et al. (2020) [31]	71	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	Yes	Yes	NA
Horta et al. (2020) [32]	26	Ductal carcinoma in situ	Ductal carcinoma in situ	Bilateral subcutaneous mastectomy	No	No	No	No	Disease free 18 months
Sharbatdaran et al. (2021) [33]	65	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	No	Yes	No	Yes	NA
Ozgur et al. (2022) [1]	64	Invasive ductal carcinoma	Invasive ductal carcinoma	Bilateral modified radical mastectomy	Yes	No	Yes	Yes	Disease free 12 months

Abbreviations: ASCO: American Society of Clinical Oncology, ACR: American College of Radiology, CT: computed tomography, DCIS: ductal carcinoma in situ, GnRH: gonadotropin-releasing hormone, ICD: invasive ductal carcinoma, MRI: magnetic resonance imaging, NCCN: National Comprehensive Cancer Network.

Unfortunately, there are no current widely adopted or screening guidelines for male breast cancer, even for those with known genetic mutations [4]. The National Comprehensive Cancer Network (NCCN) guidelines recommend screening high risk males (strong family history or genetic predisposition) with monthly self-examinations and annual physical exams starting at age 35 [4, 12]. While the incidence of male breast cancer is low, providers should still be cognizant of these associations. Once symptoms or presentation is recognized, increased awareness and further investigation into the proper workup of male breast cancer will prevent delays in both diagnosis and treatment for many patients. In addition to the physical aspects of male breast cancer, the diagnosis carries its own psychological burden, as it is often viewed as a "cancer of a female," due to the increased incidence in women compared to men. It is important that male patients be offered resources to address the additional mental health impacts from their diagnosis.

CONCLUSION

Male breast cancer commonly presents as a painless retroareolar mass. Workup should include imaging studies to localize and characterize the lesion and tissue diagnosis via core needle biopsy. Treatment of male breast cancer largely includes simple mastectomy with adjuvant endocrine therapy. Future breast cancer studies should include male cohorts to improve our understanding and treatment options between the two sexes.

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Author Contributions

Natassia Dunn – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Peter D Nguyen – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Sarah W Yuen – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Erin Lin – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.