Clinicopathological Features and Outcomes of Apocrine Triple-Negative Breast Cancer: A Distinct Subtype with Favorable Prognosis

Thamilyn Yoshizaki Saruwatari,[1] Debora Guilherme de Rodrigues de Souza,[1] Viviane Primo Basilio de Souza,[1] Lurick Rodrigues Soares,[1] Vladmir Cordeiro,[1] Marina De Brot,[1] Solange Sanches,[1] Fabiana Makdissi,[1] Elizabeth Santana dos Santos,[1]

[1]A.C. Camargo Cancer Center, São Paulo, Brazil

ABSTRACT

Triple-negative breast cancer (TNBC) is traditionally associated with aggressive clinical behavior and limited therapeutic options, representing a major clinical challenge. However, emerging evidence suggests that TNBC is a heterogeneous group comprising biologically distinct subtypes with variable prognoses. Among these, apocrine TNBC represents a rare histological variant characterized by distinct morphological features and molecular profile that may confer a more indolent clinical course. Despite its triple-negative immunophenotype, apocrine TNBC appears to behave differently from the basal-like subtype, raising important questions regarding its prognosis and management. This study presents a series of apocrine TNBC cases, aiming to describe their clinicopathological characteristics and clinical outcomes, and to contribute to the growing recognition of this unique subtype within the TNBC spectrum.

INTRODUCTION

Triple-negative breast cancer (TNBC) accounts for 15–20% of all breast cancers and is characterized by its biological aggressiveness and less favorable clinical outcomes Among TNBC, apocrine tumor represents a rare histological variant characterized by distinct morphological features and molecular profile that may confer a more indolent clinical course, with survival significantly better when compared to metaplastic and NST TNBC. As defined by the 2019 World Health Organization (WHO) classification, apocrine tumor is a special subtype characterized by the absence of estrogen receptor (ER) and progesterone receptor (PR) expression and positivity for androgen receptor. Retrospective cohort studies indicate that patients with apocrine TNBC, often older than 50 years, present with smaller, well- to moderately differentiated tumors compared to other TNBC subtypes However, data on the response to neoadjuvant or adjuvant chemotherapy in apocrine TNBC remain limited, and clinical decision-making often relies on guidelines developed for NST TNBC

METHODS

Patients: We selected patients with non-metastatic apocrine TNBC, clinical stages I, II, and III, treated surgically between June 2008 and February 2010 in a Cancer Center. All patients received neoadjuvant or adjuvant chemotherapy.

Study Design: This is a retrospective, single-center case series. Data were collected from electronic medical records. Tumor histological types were classified according to the International Classification of Diseases for Oncology (ICD-O), 3rd edition, and tumor staging was categorized per the American Joint Committee on Cancer (AJCC), 8th edition.

Statistical Analysis: Descriptive statistics were calculated using frequencies and percentages for categorical variables and means with ranges for continuous variables.

Table 1A. Clinicopathological and molecular features

Characteristic	Apocrine Carcinoma (N=13)
Age, years	61 (35–71)
Clinical T stage	
T1	7 (54%)
T2	4 (31%)
T4b	1 (8%)
Unknown	1 (8%)
Clinical N stage	
N0	11 (85%)
N2	1 (8%)
Unknown	1 (8%)
BRCA1 mutation	
No	11 (85%)
Yes	2 (15%)
Ki67	
≤20%	6 (46%)
>20%	7 (54%)
Histological grade	
Grade 2	8 (62%)
Grade 3	5 (38%)
Androgen receptor (AR)	
Negative	4 (31%)
Moderate (2+)	3 (23%)
Strong (3+)	6 (46%)
Mitotic index	
Low (≤10/10 HPF)	3 (23%)
Intermediate (11–20)	6 (46%)
High (≥21)	4 (31%)
Lymphovascular invasion (LVI)	
No	12 (92%)
Yes	1 (8%)
Perineural invasion (PNI)	
No	12 (92%)
Yes	1 (8%)

Table 1B. Treatment characteristics

Treatment	Apocrine Carcinoma (N=13)
Neoadjuvant chemotherapy	
No	10 (77%)
Yes	3 (23%)
Adjuvant chemotherapy	
No	4 (31%)
Yes	9 (69%)
Chemotherapy duration (months)	4.5 (3–6)
Surgery	
Breast-conserving surgery	7 (54%)
Mastectomy	6 (46%)
Radiotherapy	
No	3 (23%)
Yes	10 (77%)
Total dose (Gy)	42.5 (40–52.5)
Number of fractions	16 (15–28)
Pathological complete response (pCR)*	
No	2 (67%)
Yes	1 (33%)

*pCR evaluated only in patients who received neoadjuvant chemotherapy (n=3)

RESULTS

Median age at diagnosis was 61 years (range 35–71 years). Follow-up ranged from 19.9 to 187 months (1.7–15.6 years).

Most tumors were clinically early-stage, T1 tumors accounted for 54% of cases and T2 tumors were present in 31% of patients. 85% of patients were clinically node-negative (N0) (Table 1A).

69% of tumors was Androgen receptor (AR) positive (Table 1A).

Neoadjuvant chemotherapy was administered in 3 patients, with pathological complete response (pCR) achieved in only one case (Table 1B).

Disease recurrence occurred in 2 patients (15%): one with distant metastasis (contralateral breast) and one with locoregional recurrence (breast skin/chest wall).

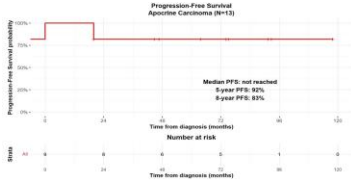
Median progression-free survival was not reached (Figure 1).

The both cases (local recurrence and contralateral breast) were treated with mastectomy.

In the final analysis, 12 patients (92.3%) were free of metastases, with 1 patient lost to follow-up.

No one patient received immunotherapy

Figure 1. PFS Kaplan-Meier Curve



DISCUSSION

The mean age of 59.5 years and predominance of T1c and N0 tumors align with prior findings suggesting that apocrine TNBC occurs in older patients with smaller, well-differentiated tumors. The low rates of local recurrence and distant metastasis and high rate of patients alive without disease (92.3%) support the hypothesis of a more favorable prognosis compared to NST TNBC.

The response to neoadjuvant chemotherapy was limited, with only one patient achieving pCR, suggesting that apocrine TNBC may have variable sensitivity to standard regimens like ACddT and TC.

The AR positivity in 69% of patients suggests potential for AR-targeted therapies, an area warranting further investigation. Radiotherapy was widely used (92.3%), with doses consistent with breast cancer guidelines.

Limitations include the small sample size and retrospective design, which preclude robust inferential analyses. Missing data for some variables, such as clinical staging and Ki67, may also limit conclusions. Future studies with larger cohorts and detailed molecular analyses are needed to confirm these findings and explore treatment response predictors.

CONCLUSION

- Pure apocrine carcinoma in this cohort was predominantly early-stage, AR-positive, and showed low rates of aggressive features (LVI/PNI).
- With multimodality treatment, patients experienced favorable long-term clinical outcomes (median follow-up >6 years).