The Gulf Journal of Oncology

Indexed By PubMed and Medline Database

Issue 52, Sep 2026
ISSN No. 2078-2101







Under the Patronage and Honoring of HRH Prince Saud bin Nayef bin Abdulaziz, Governor of the Eastern Province: Saudi Cancer Foundation Successfully Launches "AlSharqia Wardiyah 18"

The Official Journal of the Gulf Federation For Cancer Control

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Case Report

Tubulolobular Carcinoma of the Breast: First Case Report from Saudi Arabia

Mehad Ahmed[1], Wafaey Badawy[2], Samah O. Mohager[1]

[1] Prince Sattam Bin Abdulaziz University, Department of Basic Medical Sciences, College of Medicine. AlKharj, Riyadh, Saudi Arabia.

[2] Department of Histopathology, Armed Forces Hospital, Alkarj, Riyadh, Saudi Arabia

Abstract

Tubulolobular carcinoma (TLC) of the breast is a singular invasive carcinoma with dual histologic features of both tubular and lobular elements within the same lesion. We report a right breast lump for 2 month in a 68–year–old lady. A simple mastectomy of the right breast was done for her and the surgical pathology report confirmed the diagnosis of tubulolobular carcinoma. This is the first documentation of the clinicopathologic features of this tumor in Saudi Arabia. Examination of the literature shows that to date, agreement on the classification of this tumor has not been reached, and although immunohistochemistry has a role, the histomorphologic features are still the mainstay for diagnosis.

Keywords: breast tumor, case report, Tubulolobular carcinoma, histopathology

Introduction

Tubulolobular carcinoma (TLC) is a low–to–intermediate grade invasive neoplasm of the breast with mixed histologic features. It represents a morphological mixture of properties from both invasive carcinoma of no special type and invasive lobular carcinoma.

We report a case of TLC in a 68–year old Saudi women, this type of neoplasm is rare and there is no reported case of before in the Middle East. Although it was first described in 1977[1], little breakthrough has been achieved in categorizing and classifying it. This report aims to contribute to the understanding of the clinical presentation, radiologic features, histopathologic morphology, and immunohistochemical profile of this lesion in Saudi Arabia, as a representative of the region. Furthermore, a literature review of the newest updates is included.

Case Presentation

A 68–year–old Saudi woman presented to the outpatient clinic with a right breast lump for 2 months. There was no family history of breast cancer. On examination, there was a right breast swelling measuring 2X2 cm located in the outer lower quadrant. The right nipple was found to be slightly deviated but not retracted; there was a focal area of skin thickening and tethering related to the mass. The left breast and both axillae were unremarkable.

Mammogram disclosed bilateral heterogeneously dense breasts, as well as two high–density spiculated masses in the right breast lower outer quadrant, 8 cm from the nipple and along the 12:00 axis about 2.5 cm from the nipple, measuring approximately 1.5 x 1 cm and associated with architectural distortion and amorphous microcalcifications. On the left side, there is asymmetry in the outer aspect of the left breast without suspicious mass or distortion on Tomosynthesis. No suspicious microcalcifications are noted.

Ultrasonography findings of the right breast included 2 irregular, deeply hypoechoic masses with spiculated margins, associated with strong posterior acoustic shadowing. No associated signs of skin invasion.

Computed tomography (CT) with contrast of the chest showed a 4 mm solid nodule in the right lower lobe, suspicious for malignancy. No definite abdominopelvic metastasis.

Positron emission tomography (PET) of the whole body showed 2 hypermetabolic right breast nodules compatible with breast cancer. No Fluorodeoxyglucose (FDG)–avid

Corresponding author: Mehad Ahmed, Assitant Professor, Department of Basic Medical Sciences, College of Medicine. Al Kharj, Riyadh, Saudi Arabia, P.O. 16278,
Email: ma.ahmed@psau.edu.sa, mehadalfatih@gmail.com

axillary lymphadenopathy was noted. The rest of the scan was metabolically unremarkable.

Based on the previous findings, the patient underwent a simple mastectomy of the right breast with sentinel lymph node dissection and the specimen was sent for histopatholgy.

Gross Description

We received a right breast simple mastectomy specimen weighing 593 grams, measuring 20 x 20 x 4cm in total, overlined by an unremarkable ellipse of skin measuring 16 x 10cm, with a nipple areolar complex measuring 4 x 4 cm.

On the cut section, an ill–defined white solid mass at 12 o'clock measuring 3 x 2 x 1 cm away from the deep margin by 1.5 cm was seen. Another ill–defined white solid mass was identified in the upper outer quadrant at 9 o'clock measuring 3x1.8 x 1.5, abutting the deep margin. The distance between the two masses was 4cm. The remaining breast parenchyma shows a yellow fatty cut surface.

Light microscopy

The tumor showed dual components: a tubular component composed of small ovoid elongated bent teardrop–shaped infiltrating glands with open lumens (figure 1), a single layer of cuboidal to columnar epithelial cells with uniform, small to intermediate–sized nuclei(figure 2), mild pleomorphism and low nuclear grade, sparse mitosis, lack of myoepithelial layer, and variable apical snouts. As well as Lobular component showing: discohesive tumor cells permeating the fibroelastotic desmoplastic stroma in linear arrays, cords and single cells with targetoid growth pattern around benign ducts (Figure 3).

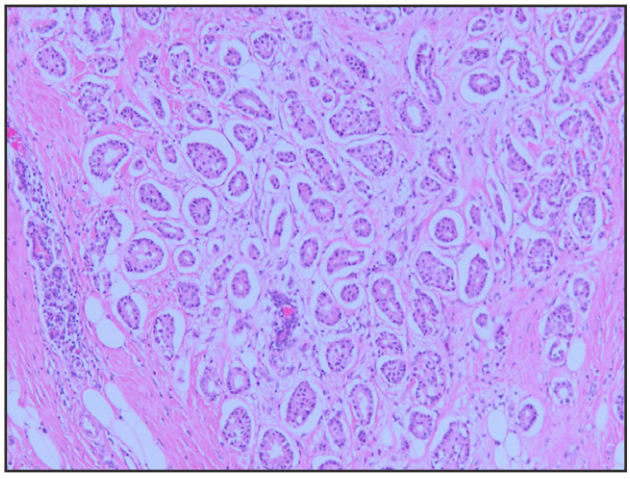


Figure 1: tubular components, some are tear drop shaped infiltrating breast tissue surrounded by desmoplastic reaction with a nearby normal breast lobule. (hematoxylin and eosin (H&E), original magnification X20)

These small monomorphic tumor cells have relatively uniform vesicular nuclei and small punctate nucleoli, with scant cytoplasm, infrequent mitoses and a nuclear grade score of 1 to 2. Fibroelastotic desmoplastic reaction in the stroma was noted.

There is lymphovascular Invasion (Figure 4), extensive ductal carcinoma in situ with comedo (figure 5)and solid patterns.

Stromal tumor infiltrating lymphocytes were less than 5%. The two sentinel lymph nodes examined showed that metastatic were not detected for on H & E slides. Skin and all peripheral margins were free from tumour.

Immunohistochemical staining results showed diffuse strong intense nuclear positivity for estrogen(ER) (figure 6)progesterone(PR) and cytokeratin 5/6 (CK 5/6)(figure 7), strong positive E–cadherin staining (Figure 8), GATA binding protein 3 (GATA3) positivity (Figure 9), 10–20% positivity for KI–67, and diffusely negative HER–2/neu.

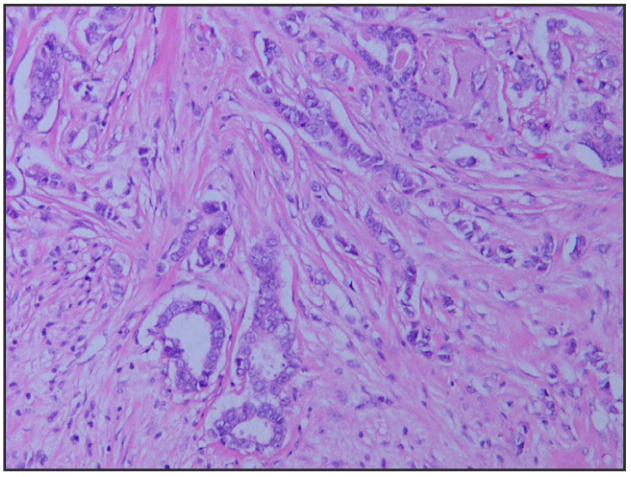


Figure 2: shows both tubular component, some teardrop–shaped, and lobular component, it also shows the monotonous nuclear features of this tumor(H&E, original magnification X40)

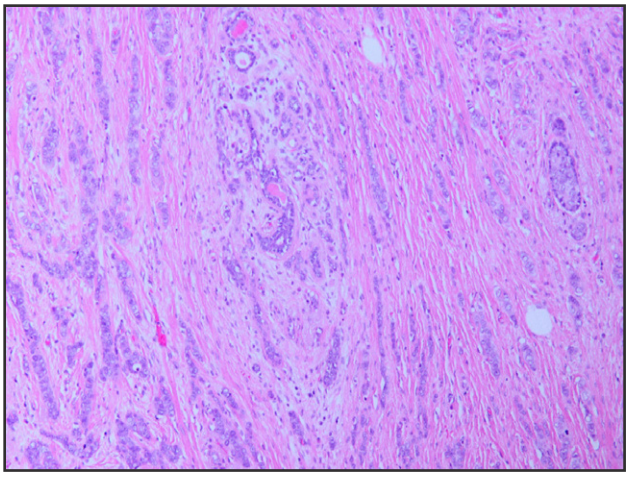


Figure 3: targetoid growth pattern of the tumor around benign glands, (H&E, original magnification X20)

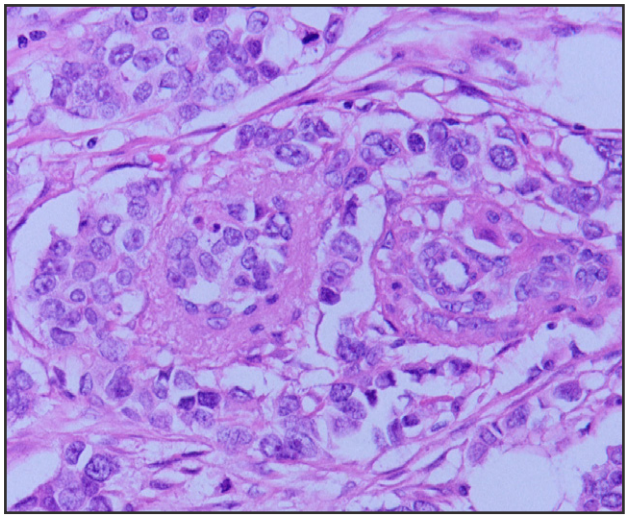


Figure 4: shows lymphovascular invasion of TLC, (H&E, original magnification X40)

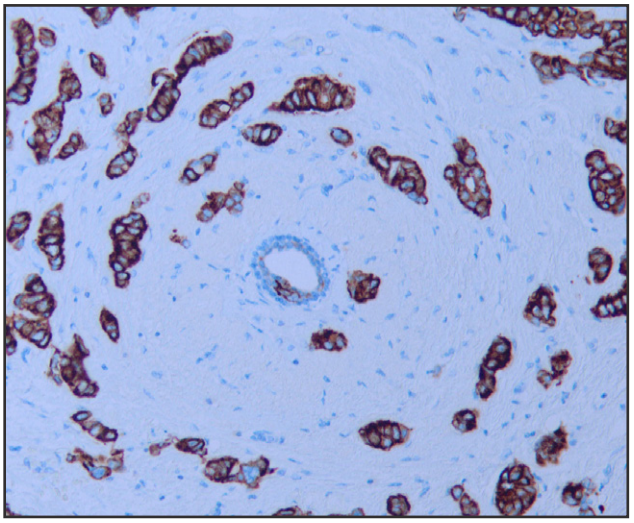


Figure 7: strong cytoplasmic positivity for Cytokeratin 5/6, showing targetoid growth pattern of the tumor (Cytokeratin 5/6, original magnification X20)

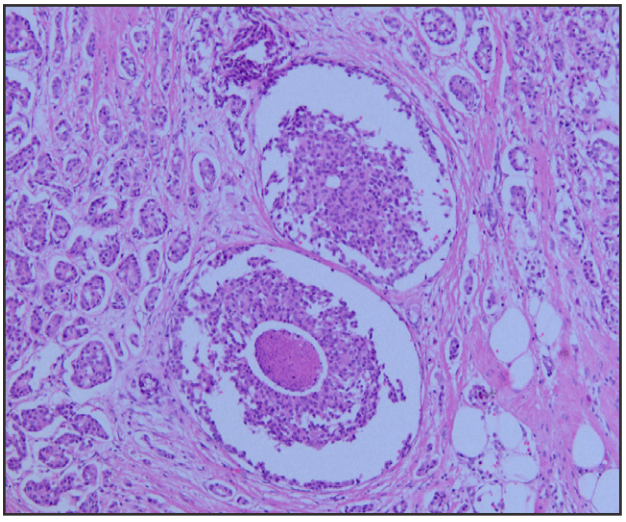


Figure 5: shows tubular component and DCIS with comedo necrosis (H&E, original magnification X40)

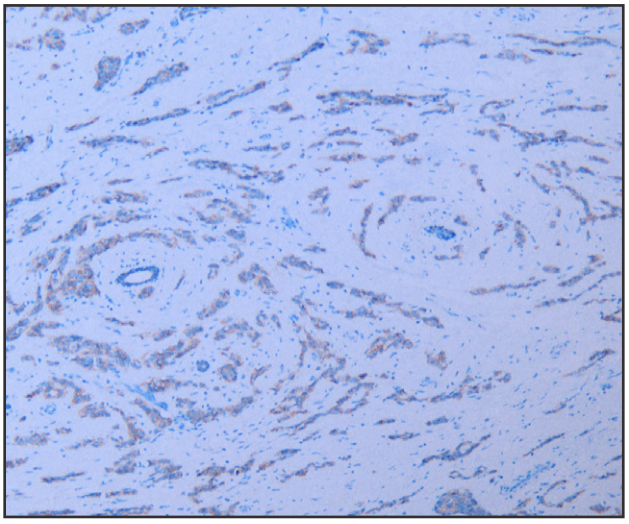


Figure 8: shows membranous positivity for E cadherin that highlight targetoid pattern of tumor (E cadherin, original magnification X10)

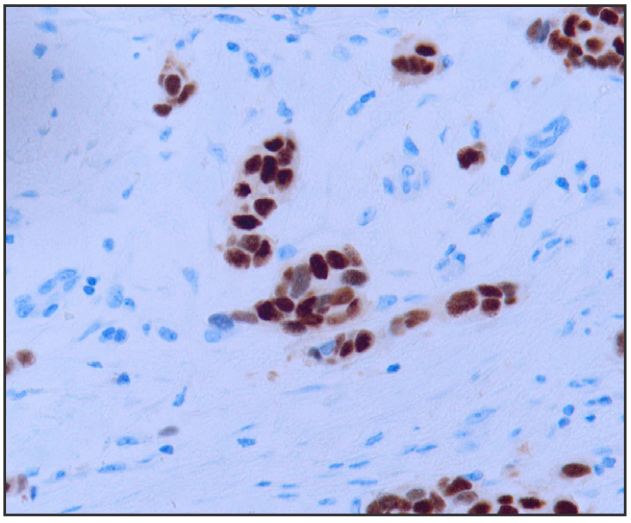


Figure 6: immune staining show positive staining for ER in both lobular and tubular pattern (estrogen, original magnification X40)

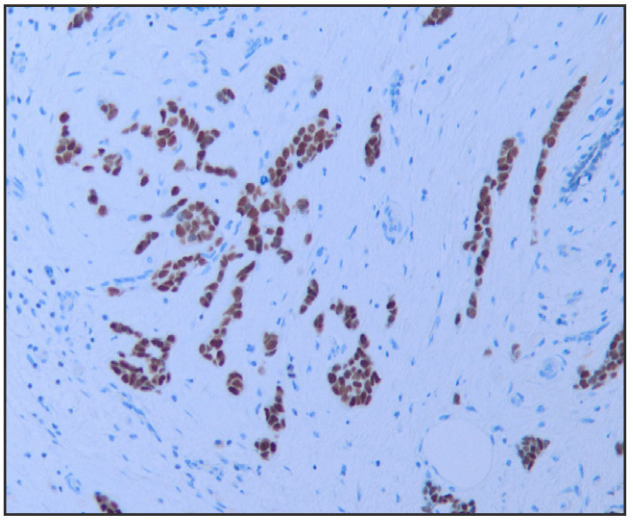


Figure 9: Both histologic patterns of TLC highlighted by GATA3–positive cells (GATA3, magnification x20)

P63 was negative in the tubular component. The sentinel lymph node disclosed isolated tumor cell cluster by cytokeratin stain, less than 2 mm in greatest extent.

The final histological stage using Nottingham Histologic Score was grade 1. The final diagnosis is Tubulolobular carcinoma T2N0MX.

Post–operation, the patient was on regular follow–up in the oncology clinic for four months; she was on letrozole 2.5 mg daily – an aromatase inhibitor used principally to treat hormone receptor–positive breast cancer in postmenopausal women as adjuvant therapy, and there was no indication for adjuvant radiotherapy.

Discussion and Conclusion

Tubulolobular carcinoma (TLC) is an unusual type of breast cancer that displays admixed traits of lobular and ductal carcinoma simultaneously[2]. It represents only one to two percent of mammary carcinomas [3]. This type has an intermediary prognosis, poorer than pure tubular carcinoma but better invasive lobular carcinoma[1], based on multifocality and positive axillary lymph nodes[4,5]. Histologically it is consist of an amalgamation of well–formed tubular formations and small discohesive tumor cells aligned in a single–file growth pattern[6]. the characteristics of TLC tumor cells show low nuclear grade, low mitotic count, some may exhibit cytoplasmic vesicles, linear pattern of cell growth and tubular structures formation within the same tumor [7]. In addition, ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) is regularly associated with this lesion[8], in fact Lobular carcinoma in situ has been detected in about one third of this neoplasm. In our case, many foci of DCIS were observed showing solid, cribriform and comedonecrosis architectural patterns, but no LCIS was noted.

Fisher et al. were the first to designate this type of mammary carcinoma; it was categorized initially as a special type of lobular invasive carcinoma. Afterwards, three–D modelling of tubular carcinomas (TC) and TLC showed that they both consist of ductal formations that are linked by linear strings of individual cells, but in the instance of TLC, the single–cell files that link the tubular structures were usually more elongated[9].

Clinical presentation at the time of initial diagnosis is usually a firm, immobile mass. The tumor size is usually less than 2.5 cm. Multifocal masses are probable [10]. In mammogram, it appears as a poorly–defined, asymmetrical, uniformly dense mass without microcalcifications[11]. By sonography, it usually presents as a hypoechoic nodule with asymmetrical outline and spiculated borders[12]. It presents generally at early stages[5] which corresponds to our case, which presented at stage I. Ages in the largest cohort of cases diagnosed with TLC spanned women from 43 to 79 years, and it has been detected in both male and female subjects[10]. The patient's age in this case was within this range, a demographic that is comparable to that of those with breast carcinomas of no special type.

The immunohistochemical profile of tumor cells shows strong estrogen, progesterone, membranous E–cadherin and beta–catenin positivity in both tubular and lobular components, cytoplasmic high molecular weight keratin, and they are invariably HER2(Human Epidermal Growth Factor Receptor 2) negative[12].

The differential diagnosis of TLC includes Tubular carcinoma, Mixed Non Special type –Lobular Carcinoma, as well as Invasive Lobular Carcinoma with Tubular Elements[7] Studies show that metastases, when they happen, are composed predominantly of tubules[5] and show ductal differentiation[13].

Although TLC was initially regarded as an unusual type of lobular carcinoma; due to of the mounting evidence gained from immunohistochemical profile, previous ultrastructural evidence, and clinical behaviour, the current view is shifting to regard it as a ductal carcinoma with lobular elements[10]. In the latest edition of WHO series in classification of tumor, no formal change in terminology has been adopted; nevertheless, E–cadherin markers has been proposed as a basis to categorize lesions that exhibit TLC distinguishing histologic features hereafter into, those that are E–cadherin positive as invasive breast carcinoma (IBC) of no special type, whereas those lacking E–cadherin expression are considered as Inavasive Lobular Carcinoma (ILC) with tubular elements, regarding cases that exhibit dual E–cadherin expression, negative in lobular component and positive in tubular structure, classification as mixed ILC and tubular carcinoma is the recommended nomenclature[14].

Although our case presented with typical clinical, radiologic, histopathologic and immunohistochemistry of TLC, the correct diagnosis requires a high index of suspicion, specially in fine needle aspiration cytology and small biopsies; furthermore, proper and thorough grossing is required for it not to be missed.

Conclusion

TLC is an uncommon type of invasive breast carcinoma with a generally favourable prognosis; nevertheless it still defies certain classification, and further studies await to amass sufficient evidence to achieve a complete understanding of this lesion. There is a notable research gap about this lesion in Saudi Arabia, and our case report aims to contribute to filling this gap.

Funding and Conflict of Interest

This study is supported via funding from Prince Sattam bin Abdulaziz University project number (PSAU/2023/1444). There is no conflict of interest.

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