

## TUBULO-LOBULAR CARCINOMA: AN UNUSUAL MIXED INVASIVE CARCINOMA OF THE BREAST

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### ABSTRACT

Tubulo-lobular carcinoma is a rare variant of mammary carcinoma that displays an admixture of invasive tubules and lobular like cells. It accounts for 1% of breast cancers with dual growth pattern of tubular carcinoma and invasive lobular carcinoma. Tubulo-lobular carcinoma appears to be rare aggressive tumour than tubular carcinoma, but with overall good prognosis. Herein we report a case of 60-year-old female with right breast mass since 4 months. Histopathologically proved as Tubulo-lobular carcinoma; an unusual mixed invasive carcinoma of the breast. We highlight the importance of histopathology for diagnosis of such rare tumours of breast in view of its mixed histopathology and uncertain biological behaviour. Hence better understanding of Tubulo-lobular carcinoma would enable pathological diagnosis to be made regularly and accurately.

**Key Words:** Tubulo-Lobular Carcinoma; Breast Cancer; Mixed Carcinoma

### Introduction

Tubulo-lobular carcinoma is a unique form of invasive breast carcinoma exhibiting both ductal and tubular differentiation.<sup>[1]</sup> The neoplasm exhibits small tubules as well as cords of neoplastic cells in a lobular configuration reminiscent of lobular invasive carcinoma.<sup>[2]</sup> Fisher et al. concluded that this lesion represents a tubular variant of lobular invasive carcinoma in 1977.<sup>[2]</sup> Tubulo-lobular carcinoma is a rare variant of invasive breast cancer and reveals mixed histological features of both tubular and lobular carcinoma with common expression of E-Cadherin, CK-8 and CK34-Beta E12.<sup>[1,3]</sup> A better understanding of Tubulo-lobular would enable pathological diagnosis to be made regularly and accurately.<sup>[1,3]</sup>

We report a case of Tubulo-lobular carcinoma of breast in a 60-year old female. Little is known about Tubulo-lobular carcinoma. The goal of this case report is to advent to this unusual clinical and histopathological diagnosis, to review and discuss diagnostics, differential diagnosis and treatment options.

### Case Report

A 60-year-old female presented to surgical OPD of our hospital with lump in her right breast since 4 months. There was no significant past, personal and family history. The lump was insidious in onset and painless with gradual increase in size. On local examination, the lump measured 4x4 cm in the periareolar and lower

anterior quadrant of right breast. The skin, nipple and areola were normal. Other breast was unremarkable. Right axillary nodes were palpable. Cytology of mass advised by Surgeon which was positive for malignant cells. On admission, her vital were stable and routine investigation such as complete blood count and biochemical and chest X-Ray were within normal limits. She was immunonegative for HIV, HBsAg and HCV. Right sided modified radical mastectomy with axillary dissection was carried and specimen was sent for histopathology. The post-operative period was uneventful.



**Figure-1: Gross appearance Right MRM specimen with elliptical piece of skin**

### Gross Findings

We received right MRM specimen totally measuring

18x10x4 cm. On external examination -skin, nipple and areola was appeared to be normal (Figure 1).

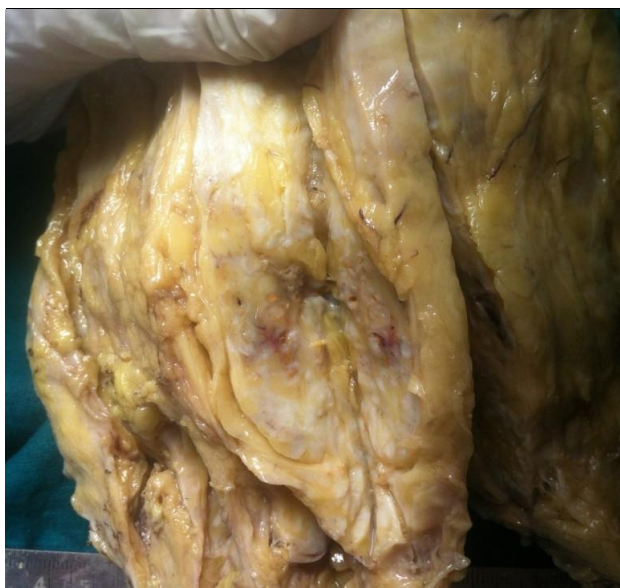


Figure-2: Cut section of MRM specimen showing grey white infiltrative tumour mass

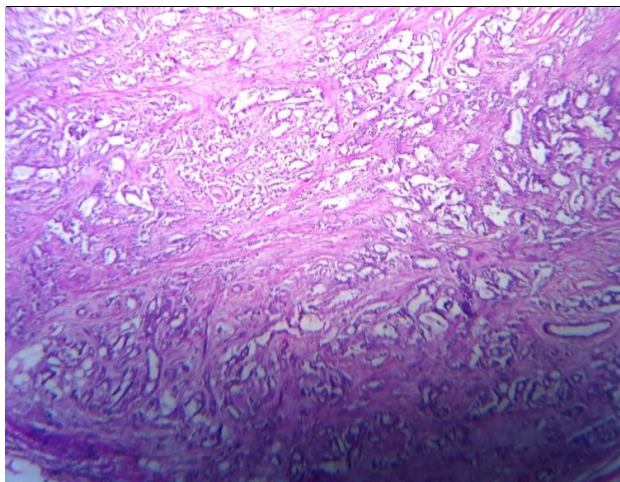


Figure-3: Light microscopy showed tumour composed of neoplastic cells arranged in varied morphological patterns of tubular and lobular carcinoma (H & E stain, x100)

On cut section-grayish white tumour with infiltrating border measuring 4x3x2 cm was seen (Figure 2). Nearest peripheral surgical margin is deep and 0.2cm away from tumour and formed by fascia. The skin, nipple, areola and all peripheral margins are free from tumour. Axillary dissection reveals 8 lymph nodes.

**Light Microscopy**

Multiple section studied shows tumour composed of neoplastic cells arranged in sheets, cords, tubules, cribriform, lobules and solid patterns (Figure 3). The tumour cells exhibit intermixed pattern of small, rounded tubules with lobular like single cells infiltrating

around the ducts in fibrous stroma (Figure 4).

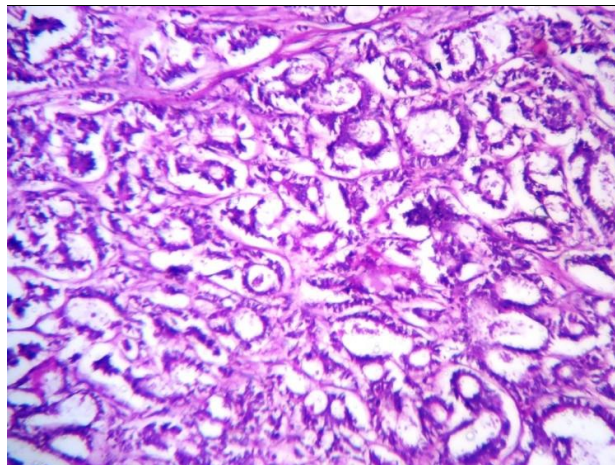


Figure-4: The tumour cells exhibit intermixed pattern of small, rounded tubules with lobular like single cells infiltrating around the ducts in fibrous stroma (H & E stain, x100)

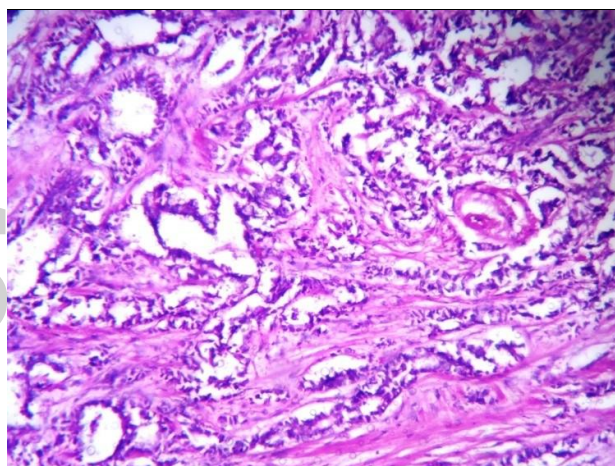


Figure-5: Focal areas shows cords of small cells arranged in diffuse and targetoid patterns along with less angulated and round tubules (H & E stain, x400)

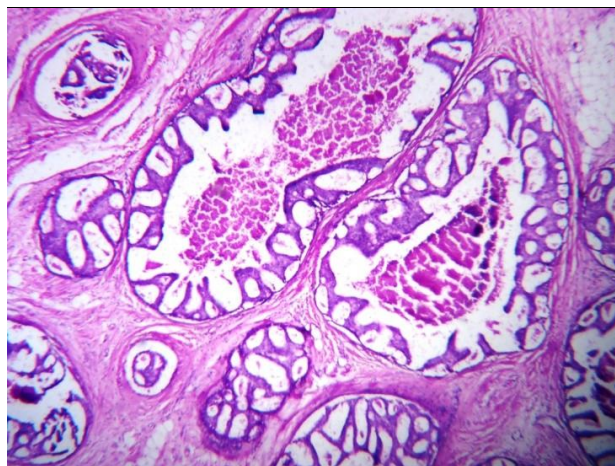


Figure-6: Foci of DCIS- cribriform and comedo patterns were noted in between the tubular and lobular patterns (H & E stain, x400)

The individual tumour cells are small round to oval with

minimal hyperchromatic nuclei with inconspicuous nucleoli. The tubules typically lack apical snouts and are smaller with fewer angulations. Focal areas shows cords of small cells arranged in diffuse and targetoid patterns (Figure 5). The intervening fibrocollagenous stroma shows mild to moderate desmoplasia. Many foci of DCIS-solid, cribriform and comedo patterns were noted in between the tubular and lobular pattern (Figure 6). Skin, areola and all peripheral margins are free from tumour. Out of 8 lymph nodes, 2 nodes were involved by tumour. Tumour showed ER and PR positivity.

## Discussion

Infiltrating duct carcinoma (IDC) is the most common type of invasive breast carcinoma accounting for 65% - 85% of invasive breast lesions.<sup>[4,5]</sup> Historically, invasive lobular carcinoma (ILC) represented the second most common subtype of mammary neoplasia, accounting to about 5-10% of the disease.<sup>[6]</sup> The clinical behaviour of invasive lobular carcinoma has been known to be different since its recognition as a distinct clinicopathological entity.<sup>[7]</sup> Lobular carcinomas are more frequently hormone receptor positive display a higher incidence of synchronous, contralateral primary tumours with multicentric disease.<sup>[8]</sup>

Tubulo-lobular carcinoma (TLC) accounts for 1% of breast cancers described by Fisher in 1977. He characterized over 1000 mammary carcinomas and recognized that the histological subtypes could be mixed.<sup>[2]</sup> They characterized approximately 1/3rd of the lesions as IDC with one or more combine features.<sup>[2]</sup> Slightly more than half of the combined tumours were IDC with a tubular component and combinations with lobular carcinoma were detected in 6% of cases.<sup>[2]</sup> It has been also said that prognosis and survival of invasive breast carcinoma depends on the histology of the tumor.<sup>[9,10]</sup>

TLC is a rare and unique variant of invasive breast carcinoma as its name suggest, displays an admixture of minimally pleomorphic invasive tubules, as seen in classic tubular carcinoma and dyscohesive cells with lower nuclear grade, as seen in classic lobular carcinoma.<sup>[11]</sup> The study published in 1977 by fisher et al.<sup>[2]</sup> concluded that these neoplasms, while showing features common to both pure tubular and lobular carcinoma are better categorized as a tubular variant of lobular carcinoma. Hence traditionally, it has been considered a tubular variant of lobular carcinoma.<sup>[12]</sup>

Recent studies have demonstrated intact E-Cadherin expression in the neoplastic cells, suggesting that these are actually representing a variant of ductal carcinoma with lobular growth patterns.<sup>[12]</sup> In a significant number of cases, the in situ carcinoma consists of both DCIS and LCIS.

In our case mixed pattern of tubular and lobular carcinoma was seen with large foci of comedo, cribriform DCIS. Most of the patient with TLC presents with a palpable, firm mass. At mammography, the tumour appear as a speculated or ill-defined irregular mass without micro calcification similar to invasive lobular and tubular carcinoma. It shows a propensity for multifocality with 19-29% of patient having multifocal disease.<sup>[12]</sup> The mean age of the patients was 59 years, with a range of 45-79 years.<sup>[13]</sup>

Grossly TLC appeared as an indurated grey tan mass. Tumours are small in size than IDC but similar to tubular carcinoma ranging from 0.5-2.5 cm.<sup>[12]</sup> Histopathologically TLC demonstrates mixed features of tubular and lobular carcinomas. The tumour displays an ultimate admixture of small, round tubules and cords of small cells arranged in diffuse and targetoid pattern. The tubules typically lack apical snouts and are smaller and less angulated than those seen in tubular carcinoma. The overall infiltrative pattern is highly reminiscent of classical ILC. The neoplastic cells are uniform with small rounded nuclei and inconspicuous nucleoli. The stroma is densely collagenous, often with prominent elastosis. The tumour is histologically grade I by SBR (Modified) Grading System.<sup>[12]</sup> The DCIS or LCIS may be seen in up to 50% of cases.<sup>[12]</sup>

Immunohistochemistry reveals strong positivity for ER and PR but no reactivity for HER2 or p53. Both tubules and single cells file or cords expressed E-Cadherin.<sup>[3]</sup> In our case, clinical, gross and histological features were consistent with the above discussion. In our case ER and PR reactivity was seen. E-Cadherin was not performed due to limited resources.

Regarding treatment, all patients of TLC underwent MRM with axillary dissection.<sup>[3]</sup> Tubular carcinomas, mixed ductal and lobular carcinoma are the main differential diagnosis of TLC.<sup>[12]</sup> Histopathologically they are differentiated from each other. In tubular carcinoma, larger and more angulated tubules are seen. Furthermore, the single cell growth pattern (Indian file) characteristics of lobular component and is not observed

in tubular carcinomas. Mixed ductal and lobular carcinoma exhibits distinctive and separate foci of IDC, ILC and neoplastic cell in each component shows different E-Cadherin reactivity patterns. In contrast, the tubular and lobular components of the TLC share the same E-Cadherin expression.<sup>[12]</sup> However, the treatment of TLC is largely determined by tumour size and nodal status.<sup>[12]</sup>

## Conclusion

Tubulo-lobular carcinoma is a rare variant of mammary carcinoma that displays both tubular and lobular patterns histologically with E-Cadherin reactivity of ductal immunophenotype. Hence it may be better termed as Ductal carcinoma, tubulolobular variant. The overall prognosis of Tubulo-lobular carcinoma was favourable with 10year survival in greater than 90% of cases.

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