



DIAGNOSTIC CHALLENGES OF INVASIVE TUBULAR CARCINOMA OF THE BREAST: A CASE REPORT

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ABSTRACT

Background: Invasive tubular carcinoma is an uncommon, well-differentiated special histologic type of breast carcinoma characterized by bland cytological features and predominantly tubular architecture. Although it generally has a favorable biological behaviour, its bland morphology can create substantial diagnostic difficulty, particularly in fine-needle aspiration cytology and limited core biopsy specimens. The distinction from benign proliferative and sclerosing lesions may be challenging because malignant cytologic atypia can be inconspicuous and the diagnosis of invasion depends heavily on architectural assessment. **Case Presentation:** A 42-year-old woman presented with a palpable lump in the upper outer quadrant of the right breast for 4 months. Ultrasonography demonstrated an ill-defined hypoechoic lesion measuring 3.0 x 2.9 x 2.0 cm at the 10 o'clock position, with mild internal vascularity and focal calcific specks, categorized as BI-RADS IVB. Fine-needle aspiration cytology showed monolayered sheets and papillary fragments of ductal epithelial cells with mild anisonucleosis and occasional myoepithelial cells and was interpreted as a proliferative breast lesion. Subsequent biopsy and trucut biopsy demonstrated atypical/ proliferative epithelial lesions without definite invasion. Lumpectomy eventually demonstrated a 3.1 cm invasive tubular carcinoma, Nottingham grade 1, associated with intermediate-grade ductal carcinoma in situ and an extensive intraductal component. Lymphovascular and perineural invasion were identified, and one resection margin was involved. Immunohistochemistry demonstrated estrogen receptor and progesterone receptor positivity with a low Ki-67 proliferation index of 8-10 %. HER2 testing was not performed because of financial constraints. Completion modified radical mastectomy showed no invasive carcinoma in the breast, but metastatic carcinoma was identified in 6 of 22 axillary lymph nodes with perinodal extension. **Conclusion:** This case illustrates the diagnostic limitations of cytology and limited biopsy sampling in invasive tubular carcinoma. Bland cytological features and preservation of apparently ductal architecture may result in underrecognition of malignancy, whereas the definitive diagnosis requires adequate tissue demonstrating the characteristic invasive architecture and absence of myoepithelial cells around malignant tubules. Clinico-radiological correlation and escalation to adequate tissue sampling are essential when a radiologically suspicious breast mass persists despite equivocal cytological or core-biopsy findings. The unexpected presence of multiple axillary nodal metastasis in this otherwise low-grade tumor also emphasizes that favourable histological appearance does not exclude clinically important regional disease.

KEYWORDS : Tubular Carcinoma; Breast Carcinoma; Diagnostic Challenge; Fine-Needle Aspiration Cytology ; Core Needle Biopsy ; Axillary Lymph Node Metastasis ; Case Report

INTRODUCTION

Tubular carcinoma is a distinct special histologic type of invasive breast carcinoma characterized by well-formed, usually single-layered tubules lined by relatively uniform neoplastic epithelial cells within a desmoplastic or fibroelastic stroma. It is uncommon, accounting for approximately 1-2 % of invasive breast carcinomas in many series, and is generally associated with low histologic grade, hormone receptor positivity and a favorable prognosis [1,2].

The characteristic bland morphology of tubular carcinoma is also responsible for an important diagnostic pitfall. On fine-needle aspiration cytology, the tumor may show cohesive epithelial groups with relatively uniform cells, scant atypia and variable numbers of myoepithelial cells. Consequently, cytological specimens may be interpreted as benign or proliferative breast lesions, particularly when the characteristic tubular architecture is not adequately represented [3-5]. In one radiologic-pathologic series, the reported sensitivity of fine-needle aspiration for tubular carcinoma was substantially lower than that of large-core biopsy, emphasizing the limitations of cytology for establishing this diagnosis [5].

The diagnostic problem may persist in limited core biopsies because assessment of invasion requires adequate architectural context. Tubular carcinoma may enter the differential diagnosis of sclerosing adenosis, radial scar and other benign proliferative lesions. Contemporary reviews emphasize that limited breast biopsy material can result in both the underdiagnosis of malignancy and overdiagnosis of benign lesions, making correlation with imaging and clinical findings particularly important [6].

We present a case of invasive tubular carcinoma in a 42-year-old woman in whom cytology and successive limited biopsies did not demonstrate definite invasion, whereas lumpectomy established the diagnosis. The case is additionally notable for the presence of an extensive intraductal component, lymphovascular and perineural invasion, involved surgical margin and metastatic disease in 6 of 22 axillary lymph nodes. The case highlights the importance of maintaining diagnostic suspicion when a radiologically suspicious lesion persists despite bland or equivocal pathology.

Case Presentation

Patient Information

A 42-year-old woman presented with a palpable lump in the upper outer quadrant of the right breast that had been present for approximately 4 months.

There was no family history of breast or ovarian carcinoma. Also the patient was perimenopausal surviving with two kids both healthy and normal. Left breast was normal.

The patient had no documented history of previous treatment for breast malignancy before the present episode.

Clinical Findings

The clinically palpable lump measured approximately 3.1 x 2.9 cm and was located in the upper outer quadrant of the right breast. Overlying skin was unremarkable. Also there was no nipple discharge. Axillary lymph nodes were non-palpable.

Diagnostic Assessment

Ultrasonography
Son mammography demonstrated an ill-defined hypoechoic lesion measuring approximately 3.0 x 2.9 x 2.0 cm at the 10 o'clock position of the right breast. The lesion demonstrated mild internal vascularity and a few calcific specks.

No cyst, nodule or ductal dilatation was identified in the left breast. Bilateral axillary lymph nodes were categorized as BI-RADS IVB, indicating a suspicious abnormality requiring tissue diagnosis.

The imaging appearance was important in the subsequent diagnostic pathway because tubular carcinoma frequently presents as an irregular or spiculated lesion, sometimes with calcifications. However imaging findings are not sufficiently specific to establish tubular carcinoma, and histopathological assessment remains necessary [5,7].

Fine-needle Aspiration Cytology

Fine-needle aspiration of the right breast lump yielded cellular smears

against a hemorrhagic background. The smears demonstrated monolayered sheets and papillaroid fragments of ductal epithelial cells. Occasional myoepithelial cells were attached to epithelial fragments. The cells were predominantly monotonous, with mild anisonucleosis in occasional cells. Bare nuclei and occasional stromal fragments were present.

The cytological impression was:
Proliferative breast lesion, right breast.

Although no significant cytological atypia was identified in the material examined, the combination of the patient's age, lesion size and suspicious sonographic appearance prompted recommendation for core needle biopsy for definitive histopathological evaluation.

The initial interpretation illustrates an important diagnostic problem in tubular carcinoma. Published cytological series have documented bland and orderly epithelial cells, variable myoepithelial representation and relatively subtle atypia. Consequently, tubular carcinoma may be interpreted as benign or proliferative lesion on cytology [3,4].

Initial Breast Biopsy

A right breast biopsy was subsequently performed.

Gross examination demonstrated three linear tissue cores measuring 1.5, 1.4 and 0.5 cm, all of which were submitted for histological examination.

Microscopically, the biopsy consisted of ducts lined by epithelial proliferation. The individual cells were relatively monotonous and possessed mildly enlarged, rounded, vesicular nuclei. The stroma was fibrotic and contained a moderate mixed inflammatory infiltrate.

The impression was:
Atypical epithelial proliferation.
Further evaluation by frozen section was advised.

Trucut Biopsy

A subsequent trucut biopsy of the right breast lesion yielded multiple gray-white tissue cores, the largest measuring 1.5 cm and the smallest measuring 0.3 cm. The tissue was submitted entirely.

Microscopic examination demonstrated ducts lined by proliferative epithelium, with focal atypical ductal epithelial cells. The surrounding stroma was fibrocollagenous. No definite invasive malignancy was identified in the tissue examined.

The impression was:
Proliferative breast lesion.
Frozen section was advised.

Thus, two separate limited tissue samples failed to demonstrate unequivocal invasion despite persistent clinicroadiological suspicion.

Lumpectomy

Because of the persistent suspicious breast lesion and inconclusive tissue diagnosis, right breast lumpectomy was performed.

Grossly, the unoriented lumpectomy specimen measured 7.2 x 4.5 x 4.1 cm and included an overlying skin flap measuring 5.3 x 3.9 cm. Serial sectioning revealed a small gray-white, firm-to-hard, irregularly shaped mass with ill-defined, spiculated margins measuring 3.1 x 2.7 x 2.0 cm.

The closest surgical cut margin was 0.2 cm from the tumor. The tumor was 1.7 cm from the base and 2.1 cm from the overlying skin.

Microscopic examination established the diagnosis of:
Invasive tubular carcinoma, grade 1, of the right breast.

The modified Scarff-Bloom-Richardson/ Nottingham score was 4 (tubule formation 1+, nuclear pleomorphism 2+, mitotic activity 1), corresponding to histologic grade 1.

The maximum invasive tumor dimension was 3.1 cm.

Associated ductal carcinoma in situ (DCIS) of nuclear grade 2 was present, showing cribriform, comedo and solid patterns. An extensive intraductal component was identified.

Lymphovascular emboli and perineural invasion were present.

One resection margin was involved by tumor. The base was free of tumor, and the overlying skin flap was uninvolved. The adjacent breast parenchyma was otherwise unremarkable apart from foci of calcification.

The final lumpectomy diagnosis was:

Invasive tubular carcinoma, grade 1, right breast, 3.1 cm, associated with intermediate-grade DCIS and extensive intraductal component, with lymphovascular and perineural invasion and involvement of one resection margin.

Immunohistochemistry

- The tumor was positive for estrogen receptor (ER) and progesterone receptor (PR). The Ki-67 proliferation index was approximately 8-10%.
- HER2/neu testing was not performed because of financial constraints.
- The hormone-receptor-positive, low-proliferative phenotype is consistent with the characteristic biological profile reported for tubular carcinoma [1,2]
- Tubular carcinomas are usually ER and PR positive and generally demonstrate low proliferative activity; HER2 positivity is uncommon [2].

Therapeutic intervention

Following lumpectomy, the involved surgical margin and subsequent pathological findings prompted completion right modified radical mastectomy with axillary lymph-node dissection.

Modified radical mastectomy

The specimen measured 20.6 x 14.0 x 4.4 cm and was oriented with a short superior and long lateral suture. The overlying skin flap measured 16.8 x 9.1 cm. A scar measuring 8.5 cm was present on the skin flap. The nipple and areola were grossly unremarkable.

Serial sectioning demonstrated a lumpectomy cavity in the upper outer quadrant measuring 6.0 x 5.5 cm. The cavity wall showed whitish fibrotic areas. The cavity wall was 1.0 cm from the base and 1.3 cm from the overlying skin. No grossly identifiable residual tumor was present.

Microscopic examination demonstrated no residual invasive carcinoma in the multiple sections examined. The lumpectomy cavity wall showed diffuse fibrosis, cystic change, foamy macrophages and foreign-body giant-cell reaction, compatible with post-procedural changes. The nipple and areola were unremarkable, and Paget disease was not identified. The overlying skin and base were free of tumour. The remaining breast parenchyma was predominantly fibrotic.

Axillary Lymph Nodes

Twenty-two right axillary lymph nodes were dissected from the axillary fat. The largest measured 2.4 x 1.5 x 0.9 cm.

Metastatic carcinoma was identified in 6 of 22 lymph nodes, with perinodal extension.

The mastectomy specimen therefore showed:

- No residual invasive carcinoma in the breast at the site of previous lumpectomy.
- Metastatic carcinoma in 6/22 axillary lymph nodes.
- Perinodal extension.
- No paget disease.
- No involvement of the skin or base.

Pathological Staging

pT2 pN2a (AJCC 8th edition), based on the 3.1 cm primary tumor and metastasis in 6 of 22 axillary lymph nodes.

The completion mastectomy showed no residual invasive carcinoma in the breast after prior lumpectomy.

Timeline

Time point	Clinical event	Diagnostic/pathological finding
Month 0	Presentation	42-year-old-woman with right breast lump of 4 months' duration

Initial assessment	Clinical examination	Lump approximately 3.1 x 2.9 cm, upper outer quadrant
Initial imaging	Sonomammography	3.0 x 2.9 x 2.0 cm ill-defined hypoechoic lesion at 10 o'clock; mild vascularity and calcific specks; BI-RADS IVB
First tissue evaluation	FNAC	Proliferative breast lesion; no significant cytological atypia
Subsequent biopsy	Core biopsy	Atypical epithelial proliferation; no definite invasion
Subsequent trucut biopsy	Core tissue	Proliferative breast lesion with focal atypical ductal cells;no definite invasion
Definitive breast surgery	Lumpectomy	3.1 cm invasive tubular carcinoma,grade1, with DCIS,extensive intraductal component,lymphovascular and perineural invasion; involved margin
Biomarker assessment	IHC	ER positive, PR positive, Ki-67 8-10%; HER2 not performed because of financial constraint
Completion surgery	Modified radical mastectomy	No residual invasive carcinoma in breast
Axillary dissection	22 lymph nodes	6/22 positive with perinodal extension
Final pathological assessment	Integrated diagnosis	Invasive tubular carcinoma, pT2 pN2a based on original primary tumor and nodal disease

DISCUSSION

Diagnostic Challenge in Tubular Carcinoma

The central diagnostic challenge in this case was the discrepancy between the clinically and radiologically suspicious lesion and the relatively bland findings in sequential cytological and core-biopsy specimens.

Tubular carcinoma is a low-grade special histologic type of breast carcinoma. Its characteristic morphology consists of haphazardly arranged, rounded, oval or angulated tubules lined by a single layer of relatively uniform epithelial cells within a cellular or desmoplastic stroma. The cells generally show limited nuclear pleomorphism and low mitotic activity[1,2].

The paradox is that the same bland morphology that contributes to its favorable biological behavior may make the lesion difficult to recognize in limited samples. On FNAC, tubular carcinoma can consist predominantly of cohesive, monotonous epithelial groups with little overt atypia. Myoepithelial cells may also be present in aspirated fragments, further complicating interpretation [3-5].

The cytological findings in the present case-monolayered sheets, papillaroid fragments, monotonous cells, mild anisonucleosis and occasional myoepithelial cells-therefore provide an understandable explanation for the initial interpretation as a proliferative breast lesion.

Published data support this diagnostic limitation. In a series of 78 tubular carcinomas, fine-needle aspiration had a sensitivity of approximately 50%, whereas large-core biopsy demonstrated substantially higher sensitivity[5].The authors emphasized that tubular carcinoma may coexist with DCIS or other invasive carcinoma components, further complicating sampling and interpretation.

Difficulty in Limited Core Biopsies

The first biopsy and subsequent trucut biopsy in the present case demonstrated epithelial proliferation and focal atypia but did not show definite stromal invasion.

The diagnosis of invasive tubular carcinoma depends not simply on cytological atypia but on architecture and demonstration of an invasive pattern. In particular, malignant tubules lack the continuous myoepithelial layer expected around benign ducts. When only a limited portion of a lesion is sampled, this relationship may not be adequately represented.

Sclerosing adenosis and other sclerosing breast lesions are important mimics. The literature has long recognized the difficulty in distinguishing tubular carcinoma from sclerosing adenosis particularly when the lesion is composed of small tubules within a fibrotic stroma[6,9].

Modern reviews of breast pathology similarly emphasize that core needle biopsy has become central to preoperative diagnosis, but limited sampling can create both false-negative and false-positive interpretations. When clinicoradiological findings remain suspicious and pathology is discordant or indeterminate, additional tissue sampling is warranted [6].

In the present case, the persistence of a BI-RADS IVB lesion of approximately 3 cm provided an important reason not to regard the bland cytological and core-biopsy findings as definitive exclusion of malignancy.

Radiological-pathological Correlation

The imaging findings in this case were compatible with spectrum described for tubular carcinoma. Published studies have reported tubular carcinoma as an irregular or spiculated lesion on a mammography and as an irregular or ill-defined hypoechoic mass on ultrasonography. Microcalcifications may also occur[7].

The present lesion was hypoechoic and ill-defined, demonstrated mild vascularity and contained calcific specks. Although these findings are not diagnostic of tubular carcinoma, the radiological suspicion appropriately prompted tissue diagnosis.

An important lesson is therefore that a bland pathological interpretation should be interrupted in the context of the imaging findings.

Radiological-pathological discordance should prompt review, repeat sampling or excision rather than simple reassurance.

Histopathological Diagnosis

The lumpectomy specimen finally provided sufficient architectural information to establish invasive tubular carcinoma.

The tumour was 3.1 cm in maximum dimension and was histologically grade 1, with a Nottingham score of 4. The low grade was consistent with the expected morphology of tubular carcinoma.

Tubular carcinoma is generally considered a low- grade carcinoma, and strict morphological criteria are important because tumors with substantial non-tubular invasive components may behave differently. The WHO- based approach generally requires the great majority of the invasive tumor to show tubular morphology for classification as pure tubular carcinoma [2].

Associated DCIS and Extensive Intraductal Component

The lumpectomy also demonstrated intermediate-grade DCIS with cribriform, comedo and solid architectural patterns and an extensive intraductal component.

The presence of an extensive intraductal component is relevant to margin assessment and may contribute to local disease extent. Previous pathological observations have described an association between tubular carcinoma and intraductal malignant epithelial proliferations and have emphasized the importance of careful assessment of the surrounding tissue and margins [10].

In this case, one resection margin was involved by tumor, providing a direct pathological rationale for additional surgical management.

Lymphovascular and Perineural Invasion

An additional notable feature was the presence of lymphovascular emboli and perineural invasion in an otherwise grade 1 tumor.

Tubular carcinoma is generally associated with favorable biological behaviour and relatively low rates of nodal and distant dissemination. However, nodal metastasis is documented and should not be excluded solely because the primary tumor demonstrates low-grade tubular morphology [1,2,11].

The present case reinforces this point because 6 of 22 lymph nodes contained metastatic carcinoma, accompanied by perinodal extension.

This represents substantial regional disease despite the low histological grade of primary tumor.

Axillary Lymph-node Metastasis

Historical series have reported that lymph-node metastasis is uncommon in pure tubular carcinoma, although they can occur [1].

The relatively extensive nodal involvement in the current patient is therefore a particularly important feature of the case. It demonstrates that the favorable histological appearance of tubular carcinoma should not be interpreted as equivalent to absence of metastatic potential.

Several factors may be relevant to this observation. First, the lesion was relatively large at 3.1 cm. Second, lymphovascular invasion was documented in the primary tumor. Third, the tumor had an extensive intraductal component. Finally, the diagnosis was established only after excision because the preceding limited samples failed to demonstrate definite invasion.

Immunophenotype

The tumor was ER and PR positive and demonstrated a low Ki-67 proliferation index of 8-10%. This phenotype is consistent with the usual immunophenotypic profile of tubular carcinoma, which is commonly hormone receptor positive and associated with low proliferative activity[2].

HER2 Testing was not performed because of financial constraints.

Staging Considerations

The original lumpectomy demonstrated a 3.1 cm invasive carcinoma, corresponding to pT2 based on tumor size. Six of 22 axillary lymph nodes contained metastatic carcinoma, which corresponds to pN2a in the absence of other information that would alter nodal categorization.

The later completion mastectomy showed no residual invasive carcinoma in the breast. This should not be interpreted as pT0 in this clinical sequence because the primary carcinoma had already been excised by lumpectomy and there is no documented neoadjuvant treatment. CAP/AJCC guidance specifically distinguishes post-neoadjuvant ypT0 from staging after sequential surgical removal of the primary lesion [8].

Accordingly, the most appropriate integrated anatomic staging description from the information supplied is:

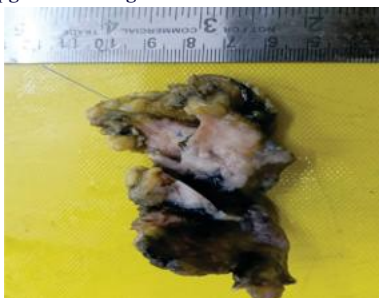
Invasive tubular carcinoma of the right breast, 3.1 cm, grade 1, pT2 pN2a (AJCC 8th edition), with 6/22 axillary lymph nodes positive and perinodal extension.

The managing multidisciplinary team should determine the final clinical, pathological and biomarker information.

CONCLUSION

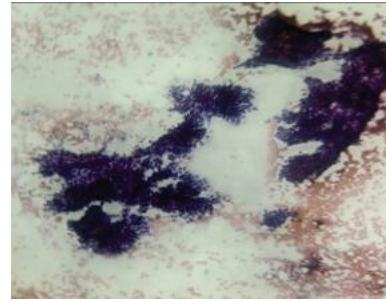
This case demonstrates that invasive tubular carcinoma can be difficult to diagnose when only cytological or limited core-biopsy material is available because the tumor cells may be remarkably bland and architectural evidence of invasion may be absent from the sampled tissue. A suspicious imaging finding should therefore remain clinically significant when pathology is equivocal or discordant. Adequate tissue sampling, careful assessment of invasive architecture and correlation between radiology, cytology and histopathology are essential. Although tubular carcinoma is generally a low-grade, hormone-receptor-positive tumor with favorable biological characteristics, this case demonstrates that clinically significant lymphovascular invasion and axillary nodal metastases can occur and should not be excluded on the basis of low histological grade alone.

“Figure 1.jpg” Gross Image



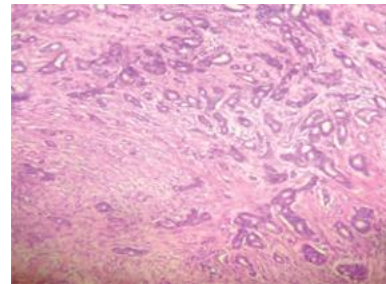
Serially sectioned right breast lumpectomy specimen demonstrating an irregular gray-white firm-to-hard mass with ill-defined spiculated margins measuring 3.1 x 2.7 x 2.0 cm.

“Figure 2.jpg” Fine-needle Aspiration Cytology



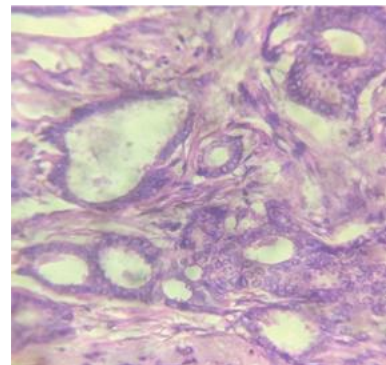
Representative cytological smears demonstrating cohesive monolayered sheets and papillary fragments of relatively monotonous ductal epithelial cells against a hemorrhagic background. Mild anisonucleosis is present in occasional cells, with occasional attached myoepithelial cells and bare nuclei.

“Figure 3.jpg” Invasive Tubular Carcinoma-Low-Power Histology



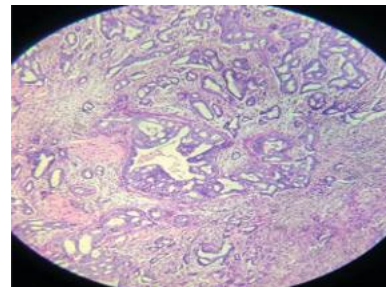
Representative hematoxylin and eosin-stained section showing an invasive proliferation of small, relatively uniform tubules within desmoplastic stroma, characteristic of tubular carcinoma.

“Figure 4.jpg” Invasive Tubular Carcinoma-High-Power Histology



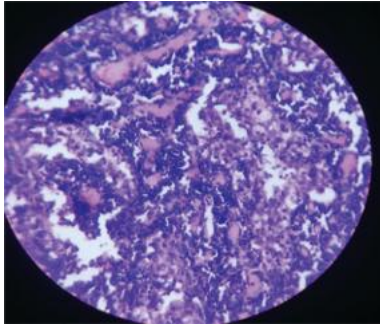
High-power view demonstrating relatively uniform neoplastic epithelial cells arranged around open tubular lumina with low-grade cytological features. The bland cytology highlights the potential diagnostic difficulty in limited biopsy material.

“Figure 5.jpg” Associated Ductal Carcinoma in Situ



Representative section demonstrating associated DCIS with cribriform architectural pattern and intermediate nuclear grade.

“Figure 6.jpg” Axillary Lymph-Node Metastasis



Representative lymph-node section demonstrating metastatic carcinoma within an axillary lymph node.

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