

Preoperative Diagnosis of Tubular Adenoma of Breast – 10 years of experience

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Abstract

Background: Tubular adenomas are rare benign neoplasms of female breast affecting women, predominantly of child-bearing age group. Definitive diagnosis of this tumor is usually achieved after histopathological study. Clinical, radiological, and even cytological features are often insufficient for accurate diagnosis. **Aim:** The aim of the present study was planned to analyze clinical and radiological features of histologically confirmed cases of tubular adenoma of breast to find out a clue for accurate preoperative cytological diagnosis. **Materials and Methods:** In our 10-year research program, all histologically confirmed tubular adenoma cases of breast were studied. Clinico-radio-cytological features, if available, were analyzed and tabulated. **Results:** Thirty-three cases of tubular adenoma of breast were studied. Radiological and cytological assessments are available for 12 and 26 cases, respectively. Tubular adenoma could be diagnosed in only two cases (7.7%) by cytological assessment, but in none by radiological assessment. **Conclusions:** Clinico-cyto-radiological assessment could identify the benign nature of the tumors in most cases, but final confirmation was possible only after histopathological study.

Keywords: Breast, large series, pre-operative diagnosis, tubular adenoma

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Introduction

Tubular adenoma is an uncommon benign neoplasm of female breast. Clinically, this is almost indistinguishable from fibroadenoma, one of the common benign breast tumors of young females. Both these neoplasms are similar, in terms of their age-related incidence, because they both involve predominantly young females of reproductive age group. Overall incidence of tubular adenoma among benign breast lesions, as reported by various studies, ranges between 0.13% and 1.7%.^[1,2]

Persaud *et al.* could identify the distinctive histological appearance of this neoplasm as early as 1968.^[3] Reports

on electron microscopical and cytological studies were published almost 15 years later (1983) by Morosset *al.*^[4] But, till now, only a few research articles have been published on this rare tumor, and most of them are case reports.^[1,5,6]

Tubular adenomas of breast are circumscribed, but unencapsulated, lesions. Microscopically, the tumors are composed of densely packed, regular, round tubules. Similar breast lesions are reported in association with pregnancy or the use of oral contraceptives (OCs). The lactating adenomas can be differentiated from tubular adenomas only by historical data (absence of pregnancy, lactation or OC pill use); otherwise, both neoplasms have similar clinical, radiological, and microscopical appearances. Lactating adenomas should be considered tubular adenomas under special physiological conditions. Biological courses of the two neoplasms are benign with no reported incidence of recurrence or increased chance of malignant conversion.^[7-9]

Final diagnosis of tubular adenoma of breast depends upon histopathology. Clinico-radio-cytological studies

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can identify the benign nature of the lesion, but a definitive preoperative diagnosis is still an exception, rather than a rule.^[1,5,6] In the present study, we had the opportunity to study a good number of cases (33 cases) of this rare benign neoplasm. The study was taken up with two main objectives: (i) To analyze the clinico-radiological features of tubular adenoma of breast, particularly to find out if any distinctive pattern exists for preoperative definitive diagnosis; (ii) to study the cytological smears of histology-confirmed tubular adenoma cases and therefore ascertain if the sensitivity of fine needle aspiration cytology (FNAC) can be improved to the extent of enabling pinpointed identification of this neoplasm.

Materials and Methods

Present study was conducted for over 10 years (April 1, 2004–March 31, 2013) at Pathology Department, B.S. Medical College, Bankura, West Bengal, India. All histopathologically confirmed tubular adenoma cases of female breast, encountered by us during the study period, were included in the study population. Written consent was obtained, after proper counseling from each patient to participate in this research project voluntarily.

Detailed clinical and radiological data about the excised neoplasm was collected from the patient's personal records, as well as from the record section of the hospital. In each case, we tried to make a final preoperative assessment of the excised breast tumor, based on clinico-radiological features. Cytological evaluations of these benign lesions were also studied in all possible cases. Slides of aspiration cytology, if available, were reviewed to ascertain if any distinctive pattern exists for definitive preoperative diagnosis. Finally, all the preoperative findings were analyzed, tabulated, and compared with histopathological features.

Results

Of the 1167 female breast biopsies examined in the Histopathology Department of B S Medical College during the study period, only 33 lesions were diagnosed as tubular adenoma (2.83%). Final diagnosis was established in each case after exclusion of such factors as pregnancy, lactation, or OC pill use. Majority of the cases (30 out of 33; 90.9%) were reported from the less than 40-year age group, with maximum cases (14 out of 33; 42.4%) belonging to the 20–30-year age group.

The duration of most neoplasms was at least 6 months or more, with only three cases (9.1%) having shorter than 6-month duration, implying that the growth rate of the tumors was slow. Upper and outer quadrants were the

most common sites of involvement (12 out of 33; 36.4%), the central quadrant being the least common site (2 out of 33; 6%).

The diameter of the lesion was more than 5 cm in only six cases (18.2%) the largest one being 8.5 cm. Majority of the tumors were soft to firm in consistency, and only four (12.1%) were relatively hard. Almost all the neoplasms were freely mobile and well defined, with only two (6%) cases showing restricted mobility and three cases (9.1%) ill-defined margins. Skin ulceration was noted in only one case. Not a single case was associated with axillary lymphadenopathy [Table 1].

The results of clinical assessment [Table 2] show that, of the 33 neoplasms, 28 (84.8%) were recognized as benign, 4 clinically suspected (12.1%), and 1 malignant (3%). Twelve lesions, including the five clinically suspected or the malignant ones, were examined by ultrasonography (USG) and/or mammography [Table 2]. Radiologically, 11 lesions appeared benign and 1 clinically malignant, the malignancy being doubtful. But, specific diagnosis of tumor was not possible in any of the cases.

Cytological evaluation of the lesions (available in 26 out of 31 cases; 83.9%) shows that definitive diagnosis of tubular adenoma was possible in only 2 cases (7.7%). Majority of the lesions (65.4%) were interpreted as fibroadenoma, with only one case (3.85%) demonstrating atypical features [Table 3].

Discussion

In the present study, the reported incidence of tubular adenoma among female breast biopsies was 2.83%, which is slightly higher than the maximum incidence of 1.7% reported by previous studies.^[1,7-9] We could not find any explanation for this higher incidence in our series.

Majority of the cases in our study group are younger than 40 years, which is comparable with the findings of other studies.^[1,10] According to previous researchers, the size (in terms of diameter) of the neoplasms varied between 1 and 7.5 cm, and their duration between 2 and 12 months; these findings are similar to those of our studies.^[1,11-13] Clinical features, suggestive of possible malignancy, such as hard consistency, restricted mobility, ill-defined margins, and skin ulcerations, were found in four, two, three, and one cases, respectively [Table 1]. On clinical assessment, four cases were suspected to be possible malignant owing to the presence of one or more of the above-mentioned features. In one case, its clinical assessment was malignant neoplasm, based on higher age (48 years), shorter duration (2 months), larger tumor size (8.5 cm in diameter), relatively hard consistency, ill-

Table 1: Clinical presentation of cases of tubular adenoma of breast

Total number	Age distribution (years)		Size distribution (cm)			Consistency		Mobility		Margin		Skin changes				
	≤20	21-30	31-40	41-50	>50	<2	2-5	>5	Soft to firm	Hard	Mobile	Fixed	Well defined	Ill defined	Present	Absent
33	7	14	9	3	0	12	15	6	29	4	31	2	30	3	1	32

Table 2: Clinico-radiological evaluation of the breast lesions

Total number	Clinical assessment		Radiological assessment			
	Category	No. of cases	No. of cases from different clinical groups undergoing assessment		Radiological diagnosis	
			Benign	Suspicious	Benign	Malignant
33	Benign	28	7	-	7	-
	Suspicious of malignancy	4	4	-	4	-
	Malignant	1	1	-	1	-
	total	33	12	11	11	1

defined margins and less mobile swelling with stretching and small ulceration of the overlying skin. Similar findings were also reported earlier.^[6]

USG of breast was done on 12 cases, including the 4 clinically suspected cases and the malignant lesion. Of these, in 11 cases sound transmission revealed well circumscribed, hypoechoic masses, which are consistent with what benign breast lesions manifest. In one case, which was the largest lesion in our series, the echo pattern was inhomogeneous with focal loss of circumscription, implying that it can be suspected to be clinically malignant. Different studies also reported benign nature of tubular adenoma, based on USG data.^[1,5,6] For example, Soo *et al.*^[5] could identify, based on USG, all the 16 cases of tubular adenoma in their series as benign. However, they failed to identify the specific pattern of sound transmission that can be helpful in definitive diagnosis.

Mammography of the five clinically suspected or malignant lesions in our series reveals well defined masses or shadows without any calcification, confirming the benign nature of four cases. But in the case of the fifth one, which happens to be the largest lesion in our series, no clear cut verdict about its benign nature was possible owing to the presence of micro-calcifications. Previous studies also reported benign nature of tubular adenoma, based on mammography.^[1,5,6] For example, Soo *et al.*^[5] found calcification in 3 out of 16 cases of tubular adenoma of breast in their series. They contend that the clustered pattern of micro-calcification, encountered in all the three cases, with distinctly linear, branching or cast like calcifications, is typical of *in situ* or invasive malignancy. A few radiologists hypothesize that tubular adenoma of breast can be diagnosed on mammography, based on dense punctuate or irregular micro-calcifications without cast-like or branching forms that are tightly grouped within a mass. But, till now, radiological assessment is far from achieving a solution to definitive diagnosis.^[5,14]

Twenty-six out of 33 cases in our series were subjected to cyto-evaluation. Examination of the smears reveals that 65.4% of them can be interpreted as fibroadenoma, based on the presence of tight clusters of benign breast duct cells often with focal papillary configurations, plenty of bare nuclei and variable amounts of stromal fragments. In five cases (19.2%), the presence of abundant relatively loose cell clusters suggests fibroadenoma with epithelial hyperplasia. Similar finding were reported by other studies.^[1,7-9,12] In two cases (7.7%), we could identify the lesions as tubular adenoma, based on the presence of small three dimensional cell balls or clusters and tubular structures, with or without acini [Figure 1] and the recommendations by Shet *et al.*^[12] Kumar *et al.*^[15] also could identify one out of six cases of tubular adenoma

during cytological study of breast lesions. In a single case of our series, we reported epithelial atypia and recommended urgent mastectomy. This refers again to the largest neoplasm in our series, with suspected clinical malignancy and micro-calcification on mammography. Clinico-radiological features, coupled with enhanced cellularity of the smears containing tubular fragments with focal presence of dysplasia (probably as a consequence of degeneration), were the causes behind

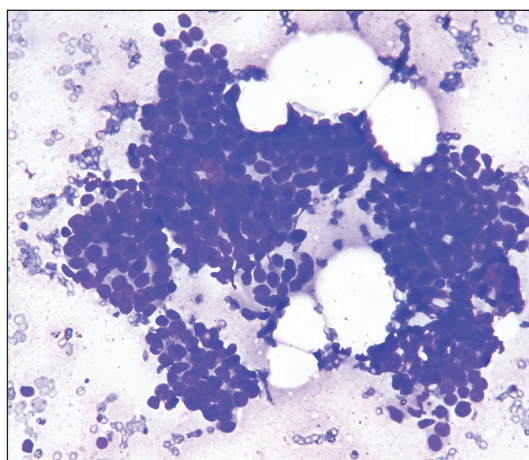


Figure 1: Cytomorphology of tubular adenoma showing formation of acinar structures by benign duct epithelial cells with scanty fibrous stroma (Leishman-Giemsa stain, 40× view)

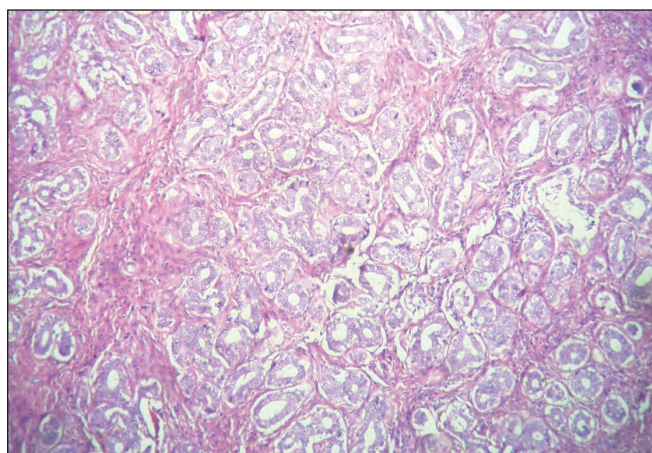


Figure 2: Histopathology of tubular adenoma showing densely packed tubules lined by double layer of cells with scanty intervening stroma (H & E stain, 10× view)

our misdiagnosis. Several cytopathologists consider that excess tubular fragments might cause an erroneous diagnosis of tubular adenosis or tubular carcinoma. Associated features like degeneration, necrosis, or mucin secretion could further enhance the confusion associated with diagnosing of malignancy.^[12,16,17]

Histopathological study of all our cases shows sharply demarcated unencapsulated lesions comprising densely packed tubules lined by a double layer of cells, with a little intervening stroma [Figure 2], which conclusively suggest that the lesions are of tubular adenoma. Neither dysplastic feature was noted in the lining epithelium, nor any evidence of tubular compression. Many researchers strongly believe that confirmation of tubular adenoma by histopathological study is possible without any ambiguity and hence should be considered as the gold standard for diagnosis.^[1,7-9] Other benign breast lesions (such as fibroadenoma, ductal adenoma, nipple adenoma, tubular adenosis) can be differentiated by typical circumscription, scanty stroma, and uniformly and densely packed tubules, as noted during histopathological study. Lactating adenoma, as already mentioned, can only be differentiated by historical data. These neoplasms also show prominent lactational changes in the lining epithelium of glands.^[3,7] Histologically, the only malignant lesion that can be confused for tubular adenoma is tubular carcinoma. Stellate infiltrative growth pattern, lack of circumscription and absence of double layering of tubules help in clinching the diagnosis of malignancy.^[3,6,7,9]

Conclusion

Based on the study of one of the largest series of tubular adenoma of breast, as reported in English literature, we conclude that this rare benign neoplasm can be identified with certainty only after HP examination. Clinico-radiocytological evaluation can help identify the benign nature of a breast lesion, but early preoperative definitive diagnosis is still beyond our reach. We also came across cases where radiology, or even cytology, failed to exclude possible malignant nature of the lesion. We sincerely hope that the result of our study would encourage further research activities in the field of diagnostic pathology

Table 3: Cytological evaluation of cases of tubular adenoma

Total no. of cases undergoing cytology	Cytological diagnosis	Number	Percentage
26	Fibroadenoma	17	65.4
	Fibroadenoma with epithelial hyperplasia	5	19.2
	Fibroadenoma with atypical epithelial hyperplasia	1	3.85
	Tubular adenoma	2	7.7
	Malignancy	0	0
	Inadequate aspiration	1	3.85

to find out possible ways of definitive preoperative identification of tubular adenoma of breast.

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