



TUBULAR ADENOMA OF THE BREAST: CASE SERIES AND REVIEW OF LITERATURE.

General Surgery

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ABSTRACT

Introduction: Tubular adenomata are benign, epithelial tumours of the breast. They are rare, with the few cases in literature reported in women of the early reproductive age-group.

Case Series: We herein describe a small series of four cases of tubular adenoma, encountered in women of different age-groups with conflicting clinical and cyto-radiological findings, precluding definitive preoperative diagnosis. Excision biopsies of the lumps were undertaken after confirming their benign nature. The final diagnoses were revealed following histopathological examination.

Discussion: Although uncommon, tubular adenomata should be differentiated from other benign and malignant breast lesions. The final diagnosis often comes as a histological surprise emphasizing the importance of histopathological assessment. Nonetheless, these tumours are neither known to recur post-excision nor do they undergo malignant transformation. An understanding of their benign nature and the excellent prognosis associated is essential in planning management and reassuring patients regarding favourable long-term outcomes.

KEYWORDS

Tubular adenoma; Breast; Benign.

INTRODUCTION

Tubular adenomas are benign, epithelial neoplasms of the breast. Also termed pure adenomas, these tumours are very rare, comprising 0.13-1.7% of all benign breast lesions.¹

First described in 1968 by Persaud et al as a "fibroadenoma with a predominantly glandular component", few cases of this entity have been reported in literature, most of them presenting in young females of the early reproductive age-group; more than 90% of patients are under the age of 40.^{2,3,4} In this setting, they tend to be clinically indistinguishable from the fibroadenoma, the most common benign breast tumour in women.⁵

Clinically, both fibroadenomata and tubular adenomas appear as well-circumscribed swellings, with a firm consistency and unrestricted mobility. These common features as well as the equivocal findings on radiological imaging and cytology make preoperative differentiation almost impossible. It is only following histopathological examination (HPE) of the resected specimen, which reveals the characteristic homogenous lobular proliferation and closely packed small ducts with minimal supporting stroma, that the definitive diagnosis is reached.^{6,7} The prognosis, nevertheless, remains excellent: these benign neoplasms, are

not known to recur, they do not undergo malignant transformation and have no metastatic potential.^{8,9}

We herein describe a series of four cases of tubular adenoma of the breast in women of different age-groups, presenting as painless, progressive breast lumps, some with conflicting clinical, cytological and radiological findings. The final diagnosis in all four cases came as a histological surprise reiterating the importance of HPE in the confirmation of these neoplasms.

CASE SERIES

This is a small case series of four patients who presented to the General Surgery department of Bangalore Medical College and Research Institute, Bangalore between January 2015 and January 2017 with progressive breast lumps of long-standing duration. All four patients were asymptomatic apart from the swelling. They were neither pregnant nor lactating at the time of presentation and did not give any history of oral contraceptive pill (OCP) usage. The details of the patients with regard to age, duration of swelling, physical examination findings and preoperative investigations have been summarized in **Table 1**. As part of the standard work-up for breast diseases, all patients underwent triple assessment before surgical excision.

Table 1: Case summaries of the patients with regard to age, duration of symptoms, physical examination findings and radiological investigations.

	Age (years)	Duration of Swelling (months)	Side	Size (cm)	Location (Quadrant)	Consistency	Mobility	Margin	Imaging	BIRADS
1	16	6	Right	7x6	Inner	Firm	Restricted	Well-defined	USG	2
2	19	4	Left	3x3	Upper-outer	Firm	Mobile	Well-defined	USG	2
3	34	8	Left	4x5	Upper-outer	Firm	Mobile	Well-defined	USG	2
4	45	4	Left	6x4	Central	Firm-hard	Restricted	Well-defined	Mammogram	3

CASE 1

A 16 year-old adolescent girl presented with a gradually enlarging lump in her right breast of 6 months' duration. There was no history of pain or associated menstrual irregularities. The opposite breast was clinically normal. Her family history was insignificant. Menarche had been attained at 14 years.

On examination, a solitary, well-circumscribed lump measuring 7cm by 6cm was noted involving the inner quadrants of the right breast, which was non-tender, firm in consistency with slightly restricted mobility. There were no skin alterations or nipple discharge. The axilla and supraclavicular fossa were clinically normal.

Ultrasound of the right breast revealed a large well-circumscribed hypoechoic lesion with features suggestive of a giant fibroadenoma

chiefly involving the medial quadrants and extending into the adjacent quadrants. This was in conformity with the FNAC findings (**Figure 1A-B**).

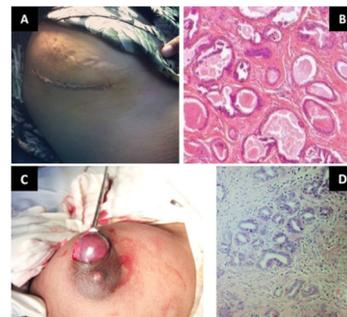


Figure 1A-B: Case 1. Inframammary incision employed in tumour excision (**Figure 1A**). H&E Section. Uniform, densely-packed, prominent tubular structures surrounded by a scanty intervening stroma. Cytological atypia is absent (**Figure 1B**).

Figure 1C-D: Case 2. Intraoperative delivery of the adenoma using a periareolar incision (**Figure 1C**). H&E Section showing close packing of uniform small tubules lined by inner cuboidal epithelium and outer myoepithelium. The stroma is sparse. Focal areas show cystically dilated ducts (**Figure 1D**).

CASE 2

A 19 year-old woman presented with a lump in the left breast which she had noticed 4 months prior. There was no history of variation in size of the swelling, cyclical breast pain, fever, nipple retraction or discharge. The opposite breast was unremarkable. Family history was not significant. Menarche had been attained at 14 years and menstrual cycles were regular. She denied the use of OCPs.

On examination, a solitary, well-defined lump measuring 3cm by 3cm was noted in the upper outer quadrant of the left breast. It was non-tender, firm in consistency and mobile. There were no other significant findings apart from the swelling. Regional nodes were impalpable.

A clinical diagnosis of fibroadenoma of the left breast was made, which was supported by cytology and imaging (**Figure 1C-D**).

CASE 3

A 34 year-old, multiparous woman presented with a gradually progressive, painless lump in the left breast which she had noticed 8 months ago. She did not complain of any nipple discharge, fever or cyclical breast pain. The opposite breast was clinically normal. There was no history of breast or ovarian cancer in the family. She had attained menarche at the age of 14 and did not give any history of menstrual irregularities or OCP usage.

On examination, a solitary, well-circumscribed lump measuring 4cm by 5cm was palpable in the upper outer quadrant of the left breast. It was non-tender, firm in consistency and mobile. There were no other clinically significant findings. Axillary and supraclavicular nodes were not palpable.

Sonomammogram showed a well-circumscribed, hypo-echoic lesion with posterior acoustic enhancement and few subcentimetric nodes in the left axilla. Cytological evaluation confirmed the lesion as benign, with features suggesting a fibroadenoma (**Figure 2A-C**).

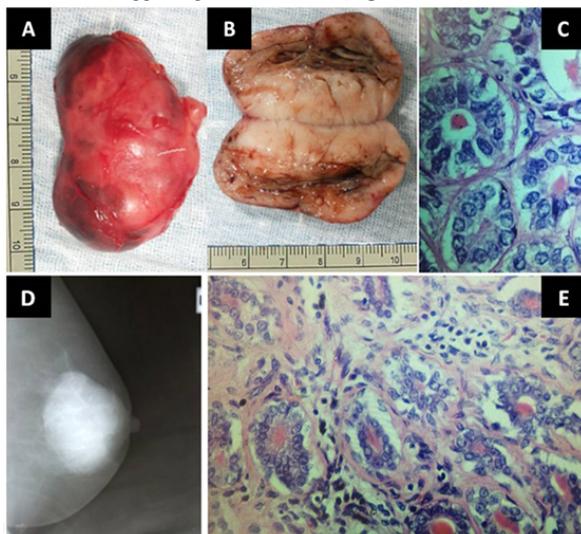


Figure 2A-C: Case 3. Gross: well-circumscribed, rounded, soft tissue mass measuring 5cm (in the largest dimension) by 4cm by 3cm (**Figure 2A**). Cut Section shows a predominantly solid, homogenous, greyish white mass (**Figure 2B**). H&E Section showing prominent, closely approximated, uniform, tubular structures lined by a single layer of epithelial cells and an attenuated layer of myoepithelial cells. Surrounding stroma is scanty and relatively acellular. No atypical cells are seen (**Figure 2C**).

Figure 2D-E: Case 4. Mammogram (left breast, MLO view). Well-defined, oval soft tissue opacity in the retro-areolar region with no calcific foci within (**Figure 2D**). H&E Section. Homogenous, densely-packed, lobular proliferation with small ducts and minimal supporting stroma. Cell nuclei are round to oval with inconspicuous nucleoli (**Figure 2E**).

CASE 4

A 45 year-old, perimenopausal woman presented with a gradually enlarging, painless lump in the left breast which had first come to her notice 4 months ago. There was no history of cyclical breast pain, nipple discharge or fever. Her past medical history was insignificant. There was no family history of breast or ovarian cancer. She had attained menarche at the age of 12 years and denied any history of menstrual irregularities or OCP usage.

On examination, a solitary, circumscribed lump measuring 6cm by 4cm was palpable in the central region of the left breast. It was non-tender, firm-to-hard in consistency and with restricted mobility. There were no skin changes or nipple retraction or discharge. The opposite breast was unremarkable. Axillary and supraclavicular lymph nodes were clinically impalpable.

Considering the patients age and nulliparous status, and the size, rate of growth and variable consistency of the lump, further investigations were undertaken.

On mammography, a well-defined, soft tissue opacity was seen in the retro-areolar region of the left breast with minimal internal vascularity and no calcific foci. FNAC revealed benign ductal epithelial cells in sheets and clusters with bare nuclei in the background suggestive of fibroadenoma (**Figure 2D-E**).

Routine investigations were normal in all four patients. Clinical, cytological and radiological investigations confirmed the benign nature of the swellings although the definitive diagnosis could not be achieved preoperatively. An excision biopsy was performed in all four patients and the specimens analysed. Evaluation of multiple sections showed uniform, densely packed tubular structures lined by a single layer of cuboidal epithelium and an outer attenuated myoepithelial cell layer surrounded by scanty stroma. There was no evidence of cytological atypia in any of the specimens. Based on these findings, a final diagnosis of Tubular Adenoma was made, highlighting the importance of subjecting all excised specimens to histopathological assessment regardless of the preoperative cytology report in order to arrive at the diagnosis. Following excision, all patients were reassured and counselled regarding follow-up. No recurrences have been noted till date.

DISCUSSION

Adenomas are benign, epithelial neoplasms of the breast; they were first classified based on histology by Hertel et al (1976) into true adenomas, nipple adenomas and fibroadenomata.⁸

True adenomas were further subclassified as tubular, lactating, apocrine, ductal, and pleomorphic adenomas.¹⁰ Among these, lactating and tubular adenomas are the most commonly encountered true adenomas in clinical practice, with both occurring during the reproductive age.¹¹ Tubular adenomas that occur during physiological conditions such as pregnancy or lactation, or with OCP use have been termed lactating adenomas.⁵

Tubular adenomas are uncommon, pure epithelial neoplasms of the breast comprising up to 1.7% of all benign breast tumours.¹ They are common in young women, with a mean age at presentation of 10-20 years and are almost unknown in post-menopausal females.¹² They are not associated with pregnancy or OCPs.

With regard to the age-related incidence and mode of presentation (as solitary, well-circumscribed, firm masses), tubular adenomas are clinically indistinguishable from the more common fibroadenoma, making preoperative diagnosis difficult. Sengupta et al (2014) reported that a specific diagnosis was reached in only 2 of the 31 patients (7.7%) who underwent FNAC and in none on imaging.⁵ Radiographically, these neoplasms resemble noncalcified fibroadenomata in appearance.⁶ Although, tubular adenomas may not have concordant clinical, cytological and radiological findings, these studies are primarily useful in identifying the benign nature of disease.

The definitive diagnosis of a tubular adenoma can be made only on histopathology. Thus, an excision biopsy is both diagnostic and therapeutic. Histologically, these tumours are variants of pericanalicular fibroadenoma with a florid adenosis-like epithelial proliferation. They are separated from adjacent breast tissue by a pseudocapsule, and are hence, well-circumscribed, with a predominant epithelial component evident as prominent, closely approximated, uniform, tubular or acinar structures and a relatively scant, sparsely cellular intervening stroma.^{7,13} These criteria serve to differentiate tubular adenomas (and the other "true" breast adenomas) from fibroadenoma and nipple adenomas. Fibroadenoma have an epithelial component comprising large ducts and an abundant stroma.¹¹

Studies have postulated that tubular adenomas and fibroadenoma represent histogenetically related neoplasms; some areas in a tubular adenoma resemble the fibroadenoma with respect to morphological and immunohistochemical features.^{9,14}

Apart from fibroadenoma, the histological differential diagnoses include nipple adenoma, sclerosing adenosis and eccrine spiradenoma.⁸ Tubular adenomas also need to be differentiated from malignant lesions of the breast especially in older women in whom they are very rare. On mammography, in such cases, tubular adenomas may resemble malignant masses with numerous punctate or irregular microcalcifications inside dilated acini. Awareness of these findings is important when considering any discrepancies in the clinical, imaging and cytologic findings.⁵

False-positive cytological results for malignancy, although rare, have been reported in some cases of tubular adenoma as also with other hypercellular benign breast lesions such as papillomas and atypical ductal hyperplasia.¹⁵ Degenerative changes or infarction can be associated with atypia simulating malignancy on FNAC.¹⁶ Although exceptionally rare, cases of in situ and invasive carcinoma have been described in neoplasms of long-standing duration.^{17,18,19,20} Features that suggest malignancy include rapid growth of a lump, presence of hypercellularity or atypia on cytology and microcalcifications on imaging.

However, tubular adenomas are neither associated with increased risk of malignant transformation nor are they known to recur following excision; hence, excision or enucleation is all that is required for definitive treatment. Knowledge about the benign nature of these tumours, the non-specific and often misleading clinical and radiological characteristics and the excellent prognosis, is essential in formulating appropriate management plans and preventing unnecessarily aggressive treatment.

CONCLUSION

Tubular adenomas of the breast are benign, pure epithelial lesions predominantly occurring in young women of reproductive age in whom they are indistinguishable from the common fibroadenoma. In practice, these lesions are exceptionally rare and the diagnosis often comes as a histological surprise. An excision biopsy followed by HPE is necessary to obtain a definite diagnosis; hence, surgery is both diagnostic and therapeutic.

Recurrence and malignant transformation of these neoplasms are rare and the prognosis remains excellent. Thus, an understanding of the epidemiology of this entity, its non-specific, often misleading clinical, cytological and radiological characteristics and overall prognosis is essential in order to prevent unnecessarily aggressive treatment when planning management, and to reassure the patient regarding the benign nature of these tumours.

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