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Papillary Carcinoma of Breast – a Rare Entity

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ABSTRACT

Papillary carcinoma is a rare form of breast carcinoma seen mostly in post menopausal women, easily mis-diagnosed as fibroadenoma. These tumors rarely attain a size greater than 3 cm. We present the case of a 65 years old postmenopausal female who presented with a complaint of a lump in left breast which gradually increased to present size in upper outer quadrant since 2 years. FNAC reports suggested it to be fibroadenoma. Lumpectomy was done and specimen was sent for histopathological examination (HPE). HPE report suggested intraductal papilloma with foci of low grade papillary carcinoma. Modified radical mastectomy was done. 2 nodules measuring 0.4 cm in size was seen in axillary region with similar histopathological findings as that in lumpectomy specimen. The patient is on regular follow up.

KEYWORDS : Papillary carcinoma Histopathological examination Imunohistochemistry (IHC) Tumor markers

Case presentation

A 65 yrs old post-menopausal female presented with painless lump in breast in left upper quadrant of 2 years duration,which gradually increased in size.

On examination, a lump measuring 5 × 4 cm, firm, well defined and present in upper-outer quadrant of left breast. Lump was not fixed to skin and underlying pectoralis muscle. Nipple and areola were normal. Axillary lymph nodes were not palpable. Opposite breast, axilla were normal. The patient was k/c/o hypertension on regular medication since 3 years. Fine needle aspiration cytology was done, suggestive of benign fibroadenoma. Lumpectomy was done histopathology examination suggestive of intraductal papilloma with foci of low grade papillary carcinoma. Modified radical mastectomy was done 1 month later. On gross examination lesion was grey white measuring 3×3×2 cm well circumscribed solid cystic mass surrounded with fibrosis. Histopathology reports suggested intraductal papilloma with foci of low grade papillary carcinoma. 2 nodules measuring 0.4 cm in size was seen in axillary region with similar histopathological findings as that in lumpectomy specimen. Tumor was positive for estrogen and progesterone receptors.

Postoperative patient is on tamoxifen with regular follow up.

Introduction

Papillary carcinoma is a rare form of breast carcinoma, accounting 0.5 % of overall breast carcinoma , presenting with bloody nipple discharge, an abnormal mass or radiographic abnormality[2]. Histological characterization suggests proliferations of cells arranged around fibrovascular cores, grossly forming a circumscribedmass[3].Occurs mostly in postmenopausal women in 7th decade of life and occurs in a disproportionate number of non-white women andrare in males. They are easily mis-diagnosed as fibroadenoma. These tumors rarely attain a size greater than 3 cm. They are papillae with fibrovascular stalks and multilayered epithelium.

Papillary carcinoma has low frequency of axillary lymph node metastasis. 5 and 10 years survival rates is similar to mucinious and tubular carcinoma.

Discussion

Papillary carcinoma encompasses a morphologically heterogeneous group of lesions, all of which share a growth pattern characterized by the presence of arborescent fibrovascular stalks lined by epithelial cells. Malignant papillary neoplasms of the breast comprise a number of microscopically distinct lesions including ductal carcinoma *in situ* (DCIS) arising in an intraductal papilloma, papillary DCI, enscapsulated papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma[5-7]. All malignant papillary proliferations of the breast lack an intact myoepithelial cell layer within the papillae, an important feature which allows distinction from benign intraductal papillomas.

Otherwise benign-appearing intraductal papillomas may display proliferative areas which would satisfy criteria for DCIS if observed outside of the context of a papillary lesion. These areas of DCIS are generally composed of uniform appearing cells with low or intermediate grade nuclear aytpia, typically with a solid or cribriform growth pattern. At present, there are no universally accepted guidelines for diagnosing a papilloma with DCIS. Proposed criteria have included the presence of DCIS greater than 3 mm in size[8] and DCIS comprising at least a third but less than 90% of the papillary lesion[7]. Papillary lesions exhibiting atypical features not meeting these thresholds have been classified as atypical papillomas. In contrast, others advocate rendering a diagnosis of DCIS arising in a papilloma regardless of the size or extent of the involved area[6].

Papillary DCIS is characterized by the presence of fibrovascular fronds lined by neoplastic epithelium. The lining epithelium is typically comprised of monomorphic, stratified columnar cells; however, solid, cribriform, or micropapillary proliferations may also be observed. Nuclei are usually of low or intermediate grade. The papillae are devoid of myoepithelial cells, though as with other morphologic types of DCIS, a myoepithelial layer is retained at the periphery of the involved duct. Lesions are frequently multifocal and peripheral in distribution.

Encapsulated papillary carcinoma is the term used to describe a solitary, centrally located malignant papillary proliferation involving a cystically dilated duct. Histologically, the lesion is well circumscribed, with the involved duct surrounded by a thick fibrous capsule . The

duct is filled by slender fibrovascular stalks lacking myoepithelial cells. Various patterns include stratified spindle cell, cribriform and solid arrangements. Low or intermediate nuclear grade is typical of these lesions, with high grade nuclear atypical rarely observed. Although morphologically well delineated and traditionally considered to represent a variant of DCIS, immunohistochemical studies have failed to consistently demonstrate the presence of a myoepithelial cell layer at the periphery of encapsulated papillary carcinomas[9,10]. Other authors, however, feel encapsulated papillary carcinomas are best considered in situ carcinomas despite the absence of surrounding myoepithelial cells based on the finding of an intact basement membrane, as shown by collagen type IV expression, at the periphery of the majority of encapsulated papillary carcinomas, as well as the demonstrated clinically indolent behavior of these lesions[7,11].

A minority of encapsulated papillary carcinomas may be associated with a component of invasive carcinoma (invasive carcinoma arising in an encapsulated papillary carcinoma). In cases of encapsulated papillary carcinomas with associated invasion, it is currently recommended that staging be determined based on the sizedof the invasive component only, without consideration of the encapsulated component of the tumor, in order to prevent overtreatment[5,6].

Solid papillary carcinoma appears microscopically as well circumscribed, densely cellular, expansile nodules of epithelial cells[12-13]. The neoplastic cells are oval or spindle shaped, exhibit low to intermediate grade nuclear atypia, and have a monotonous appearance. Many cases exhibit neuroendocrine features characterized by argyrophilia and immunoreactivity for chromogranin A. Associated intracellular and extracellular mucin is also a common finding. Interestingly, while the nodular appearance of solid papillary carcinoma was initially thought to result from proliferating neoplastic cells involving large or dilated ducts, immunohistochemical studies have demonstrated an absence of myoepithelial cells at the periphery of the nodules in some cases[13-15]. As with encapsulated papillary carcinoma, the apparent absence of myoepithelial cells in a subset of solid papillary carcinomas has prompted the suggestion that solid papillary carcinomas may represent invasive tumors with pushing borders, rather than purely in situ intraductal lesions. Solid papillary carcinomas are often accompanied by associated areas of invasive carcinoma. The invasive component most frequently manifests as a mucinous or neuroendocrine like carcinoma, though other histologic types of invasive carcinoma may also be observed [12-13].

Encapsulated and solid papillary carcinomas are not currently classified as invasive papillary carcinomas, though as previously discussed, a subset of these tumors may represent low grade carcinomas exhibiting an expansile type of invasion. Invasive papillary carcinoma should not be confused with invasive micropapillary carcinoma, which is a clinically and pathologically separate entity. In contrast with invasive papillary carcinoma, invasive micropapillary carcinoma morphologically lacks true fibrovascular cores, and is characterized by neoplastic cells arranged in solid nests or tubules surrounded by clear spaces . The distinction of invasive papillary from micropapillary carcinoma has relevant clinical implications as the latter is considered an aggressive form of mammary carcinoma frequently associated with lymph-vascular invasion and axillary lymph node metastasis[17-19].

Pathologic characterization of papillary lesions of the breast is based primarily on morphologic considerations. In particular, loss of myoepithelial cells within the fibrovascular papillae is the most important feature for the identification of malignant papillary proliferations and their separation from benign intraductal papillomas. Myoepithelial cells are, however, frequently difficult to discern on routine hematoxylin and eosin stained preparations. As such, immunohistochemistry is often utilized as an adjunct for evaluating the presence and distribution of myoepithelial cells in papillary neoplasms of the breast. Papillomas exhibit distinct, uniform staining of myoepithelial cells within the constituent papillae of the lesion as well as surrounding the periphery of the involved duct in a contiguous fashion. In contrast, malignant papillary proliferations generally lack immunohistochemical expression of myoepithelial cell associated antigens within the papillary processes, though focal or patchy areas of immunoreactivity may be present in cases of DCIS arising within a preexisting benign intraductal papilloma. Myoepithelial cells are not consistently detected at the peripheral aspects of papillary DCIS, encapsulated papillary carcinoma, and solid papillary carcinoma, and partial, discontinuous, or absent staining may be observed in these particular lesions. The individual markers exhibit variable sensitivity and also show different degrees of cross reactivity with cell types other than myoepithelial cells such as stromal myofibroblasts, pericytes and vascular smooth muscle cells, which can potentially complicate interpretation of positive staining. Most laboratories thus employ a panel of several myoepithelial cell markers very useful in assessment of invasion which are These are S-100 , α-smooth muscle actin, smooth muscle myosin heavy chain, calpolin, mapsin, CD10, P63 and high molecular weight cytokeratin. The examination of myoepithelial cells and basement membrane is an important step in diagnosis of invasion. Of these smooth muscle myosin heavy chain and P63 are specific for myoepithelial cells [13-15, 20-23]. P63 is a special myoepithelial marker which stains the cell nucleus only.

Treatment

Treatment modalities include Local or Systemic. Local includes surgery and radiation therapy. Surgery includes lumpectomy, mastectomy (partial , complete, radical) depending on extent of lesions. Radiation therapy after surgery. Systemic therapy include chemotherapy, hormonal therapy and targeted therapies. Most of cases of papillary carcinoma is estrogen receptor and progesterone receptor positive.

Fig 1 - Gross specimen showing cystic and greyish white solid papillary area.

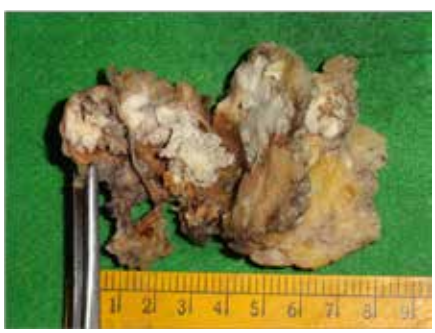


Fig 2 – Histopathologic picture showing papillae lined by neoplastic cells with fibrovascular core

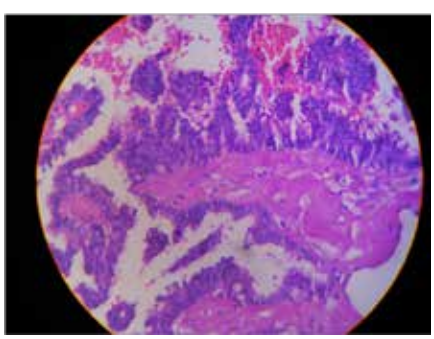
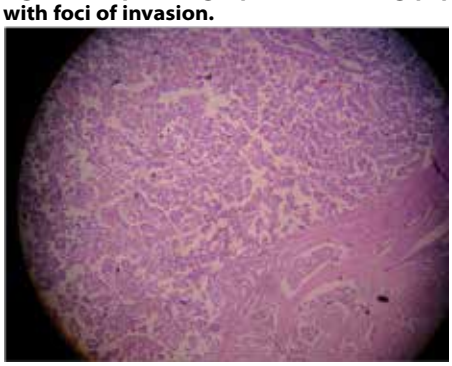


Fig 3 .Histopathologic picture showing papillary tumor with foci of invasion.



Conclusion

Papillary carcinoma is a rare form of breast carcinoma, accounting 0.5 % of overall breast carcinoma.75 % of papillary carcinoma spread via lymph nodes , but overall papillary carcinoma has better prognosis than other tumors of breast,mostly seen in postmenopausal women in 7th decade of life and occurs in a disproportionate number of non-white women and rare in males. They are easily mis-diagnosed as fibroadenoma. These tumors rarely attain a size greater than 3 cm.

Most cases papillary carcinoma are low grade, slow growing cancer with good prognosis . Many papillary carcinoma do not have distant metastasis.

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