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CASE REPORT Open Access

An intriguing journey of encapsulated apocrine papillary carcinoma of the breast

Pratibha Issar, Urshita Shah*, M. Ravindranath and Parag Gupta

Abstract

Background: Encapsulated Apocrine Papillary Carcinoma (EAPC) of the breast are very rare tumors. They usually present as a cystic mass with mural nodule in women aged 44–84 years. Affected patients may be asymptomatic or complain of breast swelling, or nipple discharge. Mammographic features are nonspecific. The tumor appears as a high-density round or oval mass with circumscribed or spiculated margins on mammography. On Ultrasonography (US) a classical lesion appears as predominantly cystic mass with intracystic solid papillary projections and area of vascularity within it. Contrast Enhanced Breast MRI helps to further characterize the lesion by showing intense contrast enhancement in early phase along with washout curve. Histological features of these tumors are similar to those of classical encapsulated papillary neoplasm, in that myoepithelial cells are absent within the papillary structures and at the periphery of the cyst. They show variable degree of cytological atypia and mitotic activity. Such tumors consist of abundant granular eosinophilic cytoplasm and large nuclei with prominent nucleoli and are androgen receptor positive. However, a multidisciplinary approach is crucial for diagnosis and tissue histology is essential to suitably formulate treatment guidelines. Surgical excision is the preferred treating option for these tumors. Little consensus is available about local radiation and adjuvant therapy for the treatment of such tumors, yet they have been reported to have good prognosis.

Case presentation: This rare case report describes the intriguing journey towards the diagnosis of an encapsulated intracystic apocrine papillary carcinoma in a 52-year-old premenopausal female who presented with palpable breast swelling in left breast. The patient underwent mammography, breast ultrasound and breast MRI concluding it to be a BIRADS 4A lesion. Then the patient was subjected to trucut core biopsy and finally surgical excision was performed. On Histopathology this lesion was diagnosed as encapsulated apocrine papillary carcinoma with androgen receptor positivity and triple negative hormonal status. At present patient is on regular follow-up.

Conclusions: Encapsulated intracystic apocrine papillary carcinoma has a favorable prognosis with low recurrence rate and excellent long-term survival regardless of its invasive nature. Therefore, we present this rare entity to highlight the importance of radiological and histopathology findings in its diagnosis.

Keywords: Encapsulated apocrine papillary carcinoma (EAPC), Mammography, Ultrasound, MRI, Immunohistochemistry

Background

Papillary lesions of breast comprise of a heterogenous neoplastic spectrum. Among these, intracystic papillary carcinoma is a rare malignant tumor accounting 1%-2% of all breast carcinomas [1]. Most commonly presenting in postmenopausal women, age of 44–84 years [2], these tumors exist in an encapsulated or invasive form. Clinical symptoms of these tumors range from being

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asymptomatic to presentation in form of nipple discharge or as a breast mass. Radiological imaging helps in characterizing the lesion. Mammography findings are nonspecific. The lesion appears as a high-density round or oval mass with circumscribed or spiculated margins on mammography. On ultrasonography a classical lesion appears as predominantly cystic mass with intralesional solid papillary projections. These projections might demonstrate vascularity on color doppler. Contrast-enhanced Breast MRI helps to further support diagnosis of the lesion. However definite delineation of benign from malignant lesion requires a multidisciplinary approach. The diagnosis of intracystic intraductal papillary carcinoma is based on its immunohistochemical characteristic feature of arborescent fibrovascular core with absent myoepithelial cells. Most commonly used markers for immunohistochemical staining are myoepithelial markers such as p63, smooth muscle actin, calponin and smooth muscle myosin heavy chain [3–5]. Invasive component is present in the wall of the lesion which explains the importance of targeting the wall of the lesion for detecting the presence or absence of myoepithelial cell layer, thus differentiating benign from malignant papillary tumor [6]. These tumors consist of abundant granular eosinophilic cytoplasm and large nuclei with prominent nucleoli. Apocrine Encapsulated Papillary carcinoma is generally estrogen receptor (ER) negative, progesterone receptor (PR) negative and androgen receptor (AR) positive.

In this case report, we want to highlight the imaging and histopathological report of apocrine encapsulated papillary carcinoma of the left breast.

Case presentation

A 52-year-old premenopausal female presented to the surgery department with left breast lump since 3 months. No history of nipple discharge or nipple retraction was present. There was no history of skin changes associated with the lesion. Family history for breast cancer was absent and past history was non-contributory.

On physical examination, a mass lesion was felt in upper outer quadrant of left breast measuring approximately 3×3 cm. The lesion was not adherent to skin or muscle. No changes were seen in overlying skin. Left nipple appeared unremarkable. No left axillary lymph nodes were palpated. Right breast appeared normal.

The patient was referred to radiology department for mammography and ultrasound of both breasts. A diagnostic mammogram was performed on Alpha—RT (GE). Mammography revealed a heterogeneously dense breast composition. There was a single oval circumscribed hyperdense lesion measuring 3×3.2 cm seen in upper outer quadrant of left breast (Fig. 1a, b). Hypodensity was noticed in the posterior aspect of the lesion. The lesion

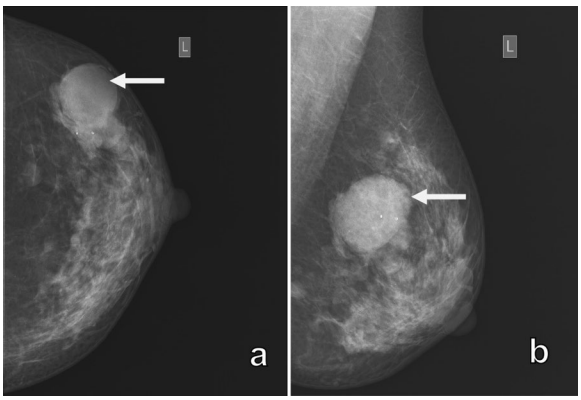

Fig. 1 Mediolateral oblique (**a**) and craniocaudal (**b**) mammography of the breast showing high-density oval circumscribed mass on upper outer quadrant of left breast with few small rounded calcifications associated within it

was seen occupying anterior and middle depth along with few round calcifications were seen within and around the lesion. Few smaller high-density circumscribed oval mass lesions were noted surrounding the lesion. No associated skin or nipple retraction was seen. No skin or trabecular thickening was present. Right breast was unremarkable. Axillary adenopathy was absent. On the basis of mammography findings, BIRADS 4A lesion was made in left breast along with few BIRADS 2 lesions.

Ultrasound of bilateral breasts was performed on Samsung RS 80 A, using linear probe of 4–18 MHz which revealed a circumscribed oval anechoic cystic lesion in left breast in zone 2B. The lesion measured 3.5×2.4 cm. There was echogenic solid mural component with thin internal septations present within the cystic lesion (Fig. 2a). On color doppler study, mild vascularity was present within the solid component (Fig. 2b). The lesion demonstrated a mixed posterior acoustic pattern. Based on these imaging characteristics a diagnosis of BIRADS 4A lesion—complex left breast cyst Type 2 Berg et al. classification was put forth [7]. Surrounding the above lesion few circumscribed oval anechoic cystic lesions were also noticed with no intralesional solid component or internal septations within them. The lesions demonstrated posterior acoustic enhancement. These lesions were considered to be simple breast cysts (BIRADS 2). In order to rule out multiple solid lesions and for preoperative planning, plain and contrast Magnetic Resonance Imaging (MRI) of the breast was performed. MRI of the breast was done on a 1.5 Tesla MR system (GE Signa Excite) using a dedicated 8 channel breast coil. On MRI examination bilateral breast tissue was heterogeneous fibro glandular in nature with minimal background parenchyma enhancement.

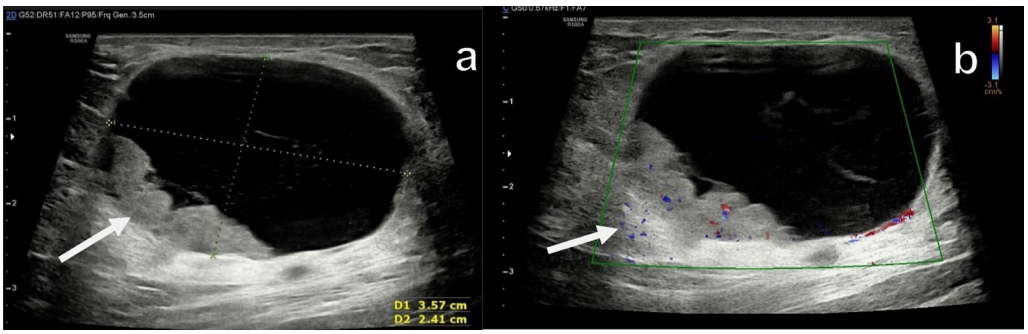

Fig. 2 Ultrasonography demonstrates an oval, circumscribed cystic lesion with an echogenic solid mural component within it (**a**) and color doppler showing vascularity in solid component (**b**)

Left Breast showed a single oval circumscribed mass measuring $3.0 \times 3.7 \times 3.1$ at 2–3o'clock position in upper outer quadrant. The mass demonstrated predominantly T1W hypointense signal intensity, T2W/T2W FS hyperintense fluid signal intensity with mean wall thickness of 2.2 mm. There was internal solid mural nodule component projecting within the lumen from the medial aspect of the lesion. The solid component measured 1.4×1.1 cm. Few thin (1 mm) internal septations were seen within the lesion. The solid component demonstrated intermediate signal intensity on T2W and T2W FS. The solid component demonstrated diffusion restriction, appearing hyperintense on DWI with corresponding hypointense signal on ADC (ADC Value was 1.4^{e-09}). The wall of the lesion and the internal solid component demonstrated Type II kinetic curve showing rapid uptake of contrast in initial phase and washout pattern in later phase, consistent with complex breast cyst BIRADS 4A (Fig. 3a–d). Few oval circumscribed non enhancing lesions showing fluid signal intensity were seen adjacent to the above mentioned lesion in left breast in outer quadrant appearing T1W hypointense, T2W/T2W FS hyperintense, suggestive of simple breast cysts BIRADS 2.

No associated skin or nipple retraction was seen. No skin or trabecular thickening was present. Right breast was unremarkable. Axillary adenopathy was absent.

Based on cumulative mammographic, sonographic and MRI findings a diagnosis of BIRADS 4A complex left breast cyst requiring histopathological correlation was concluded and the patient was scheduled for a US-guided Trucut biopsy. However due to unforeseen second COVID wave in India and since the patient also tested COVID positive, biopsy could not be performed. The patient turned up for biopsy directly after 6 months, without any treatment done in between. An US was done to assess the change in lesion characteristics which revealed an increase in the size of the intralesional solid mural component as compared to previous scan (Fig. 4a). MRI breast was performed for academic purpose which showed increase in the size of intralesional solid mural component measuring 1.9×1.7 cm (Fig. 5a, b). The patient was subjected to Trucut breast biopsy (Fig. 4b) which revealed that the epithelial cells are arranged in papillary architecture with hyalinized vascular cores and mild anisonucleosis, favoring papillary lesion of the breast. For further evaluation lumpectomy was advised. On gross examination, the lumpectomy appeared as gray-white to gray-yellow soft tissue, measuring $5 \times 3 \times 2$ cm approximately. Cut section revealed evidence of solid and cystic areas, largest cyst measuring 1.2 cm diameter, filled with brownish fluid associated with two adjoining nodular lesions measuring 2 cm and 0.8 cm diameter. The larger nodular lesion was filled with friable, papillary gray-white tissue. On microscopy the sections studied showed breast tissue with ectatic ducts, one of the ducts showed intraductal tumor having tubulo-papillae pattern. The epithelial cells lining the tumor showed mild to moderate atypical nuclei with abundant eosinophilic cytoplasm and loss of polarity. On immunohistochemistry, Androgen Receptor (AR) was positive in epithelial cells. Myoepithelial cells expressed calponin, p63 (focal weak) and CK5/6 (focal weak). Ki-67 was 15% in maximum proliferating areas. Hormone receptor studies revealed ER- negative, PR-negative, Her2neu- negative status. Final diagnosis of encapsulated papillary carcinoma with extensive apocrine metaplasia was made along with fibrocystic changes in adjacent areas. The patient opted for mastectomy with axillary dissection (level I and II) which revealed no residual invasive tumor and no lymph node involvement (Fig. 6).

Conclusions

Papillary lesions of breast comprise of a heterogenous neoplastic spectrum. The various lesions included under this group are intraductal papilloma, papilloma

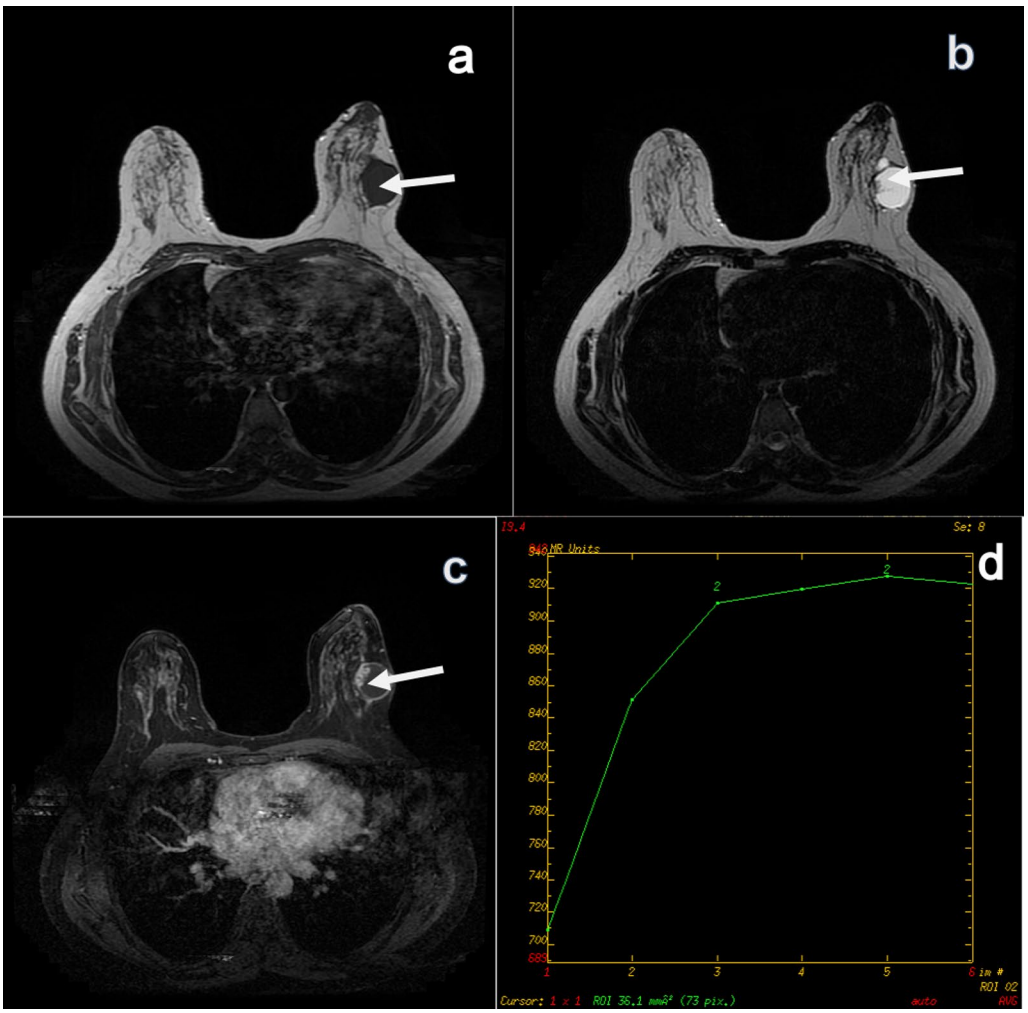

Fig. 3 MRI showing solid component appearing T1 isointense (**a**), T2 hypointense (**b**), post contrast enhancing lesion (**c**), type II kinetic curve (**d**)

with atypical ductal hyperplasia (ADH), papilloma with ductal carcinoma in situ (DCIS), encapsulated papillary carcinoma, solid papillary carcinoma and invasive papillary carcinoma [6]. Papillary carcinoma is characterized by malignant proliferation of epithelial cells supported by arborescent fibrovascular core [3]. Intracystic papillary carcinoma is a rare malignant tumor accounting 1–2% of all breast carcinomas [1]. Most commonly it presents in postmenopausal women, aged 44–84 years [2]. The patient presents with a slow enlarging palpable breast mass [8] or nipple discharge (bloody discharge or serosanguinous discharge) [6]. Alternatively, the patient might be asymptomatic and the lesion may be detected on routine screening. Mammographic studies reveal EPC to be an equal or high-density round or oval mass with circumscribed margins, or may show indistinct margins in areas of invasion. EPC is located in the central portion (in retro areolar region) of the breast in nearly 50% of patients [4]. Spiculated margins are infrequent and need not be a sign of invasion, but can be related to sclerosis and inflammation of the surrounding tissue, with resultant disruption of the regular rounded contour of the lesion [9]. Multiple masses may be present, often within one quadrant [10]. Calcifications may be associated but are relatively uncommon, reported in 4/31 (13%) cases of EPC in one series [11]. When present, both pleomorphic and coarse heterogeneous calcification morphologies have been described [11]. On ultrasonography, the lesion appears as single or multiple predominantly cystic masses, with or without septa, and with solid papillary masses projecting into the cystic lumen from the inner wall [8]. The cystic component of the lesion leads to posterior acoustic enhancement. The presence

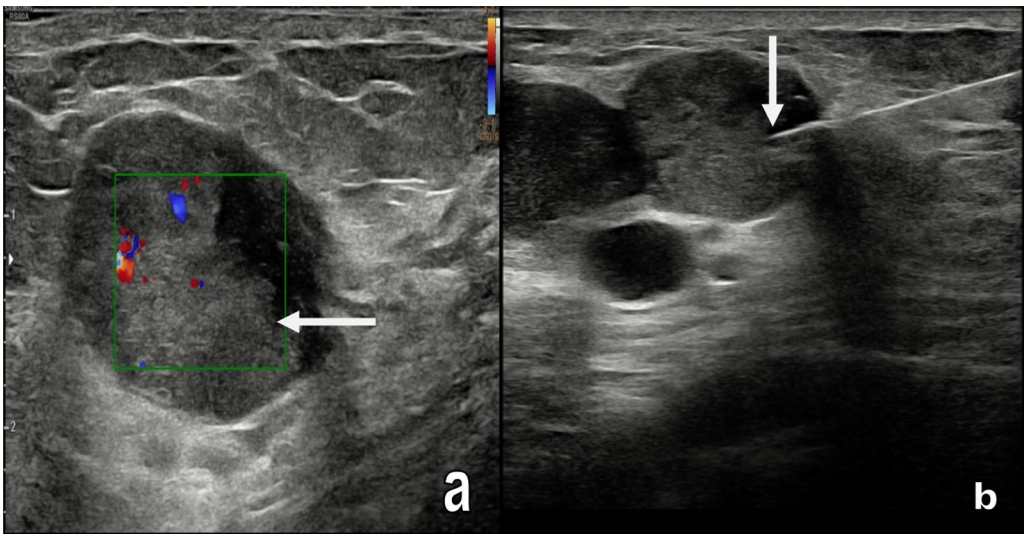

Fig. 4 Ultrasound images showing type 4 complex cyst with vascularity on color Doppler (**a**) and biopsy needle seen inside the lesion (**b**)

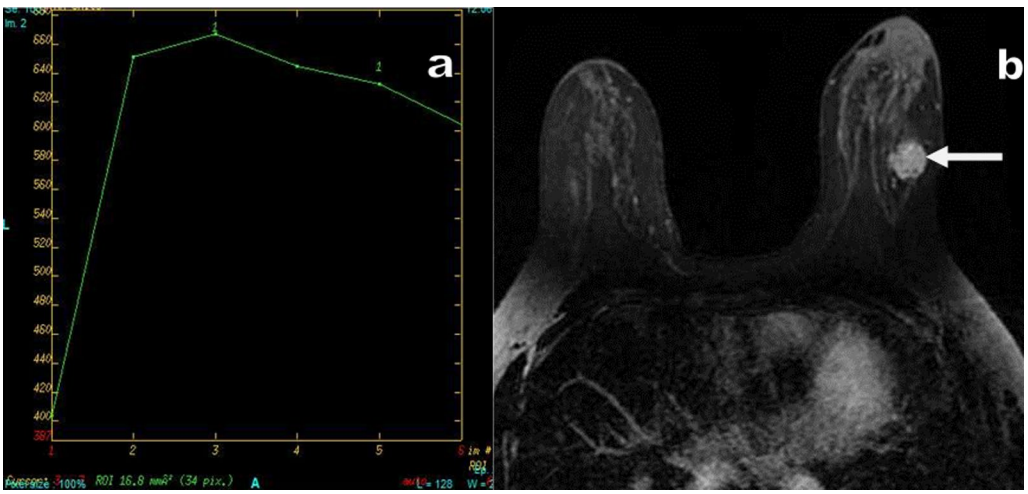

Fig. 5 MRI depicting. **a** Type III kinetic curve. **b** MRI showing increase in size of solid enhancement component

of fluid-debris levels in the cyst is usually related to spontaneous hemorrhage resulting from ruptured capillaries in the cyst wall or hemorrhagic infarction of the tumor cells [12]. Thus, on ultrasonography a classical lesion appears as predominantly cystic mass with intralesional solid papillary projections. These projections might demonstrate vascularity on color doppler. On MRI, the lesion appears as a round or oval mass with circumscribed margins. The internal composition is typically heterogeneous, with multiple nodular masses of intermediate signal intensity projecting from the periphery into the lumen. The signal intensity also depends on the intracystic fluid composition. If the contents of the cyst are serous, it will appear hypointense on T1W and hyperintense on T2W. Presence of haemorrhagic contents leads to hyperintense signal intensity on both T1- and T2W images and fluid–fluid levels may be seen on T2W images [13]. On Dynamic contrast enhancement (DCE) MRI, there is enhancement of the walls of the lesion, the intralesional septations and solid components. Time–signal intensity curves obtained for the mural nodules with dynamic MR imaging can show a great increase in signal intensity in initial 2 min followed by a washout pattern, a finding that indicates the presence of cancer [14]. Fine-needle aspiration and core needle biopsy may

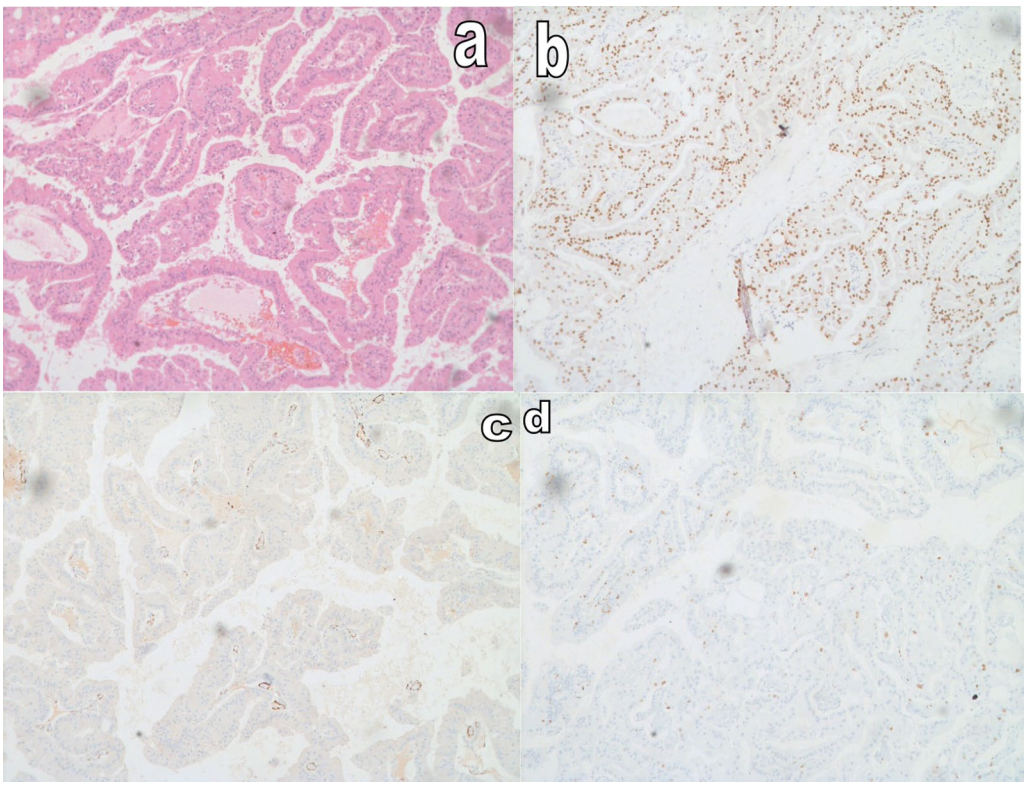

Fig. 6 Ectatic duct showing intra ductal tumor arranged in tubulo-papillary pattern on histopathology (**a**), AR positive in epithelial cells (**b**). Myoepithelial cell express calponin (**c**), KI-67 index of 15% (**d**)

be unable to allow differentiation between in situ and invasive lesions because invasion is often identified at the periphery of the tumor. Therefore, surgical excision is performed for adequate histologic diagnosis and treatment [15]. Histopathologically, EPC is characterized by delicate papillae lined with a monotonous population of neoplastic epithelial cells supported by thin fibrovascular stalks forming a circumscribed expansile mass surrounded by a thick external fibrotic capsule [3, 4]. Encapsulated papillary carcinomas typically demonstrate low- or intermediate-grade nuclei and a low mitotic index [5, 16]. The absence of a complete myoepithelial cell layer at the periphery of EPC is a characteristic finding and can be confirmed by absence of immunohistochemical staining with myoepithelial markers, including p63, smooth muscle actin, calponin, and smooth muscle myosin heavy chain [3–5]. EPC shows strong immunopositivity for estrogen receptor (ER) and progesterone receptor (PR) and is negative for Her2neu [17]. In 2009, Seal et al. [18] reported five cases of otherwise classical EAPC in which the epithelial cell component showed apocrine morphology with cytonuclear atypia. Myoepithelial cells were absent within or at the periphery of the lesions [18]. Immunohistochemical studies, performed in three cases, demonstrated a triple negative profile [18]. All lacked evidence of malignancy in the breast tissue outside the lesion [18]. Sentinel lymph node biopsy performed in three cases were negative [18]. Kovari et al. [18] recently reported the first case of EAPC with invasive carcinoma, showing apocrine morphology. The main differential diagnosis is benign papillary apocrine hyperplasia within a large cyst with diminished or absent myoepithelium [19]. Our case presented as a palpable mass lesion with triple negative and androgen receptor positive status. It has been found that high grade encysted papillary carcinoma, associated with invasion is usually triple negative and behaves like invasive counterpart [17]. Pure ICPC has a slow growth rate with an excellent prognosis and a 10 years survival rate is approaching 100% [1, 15]. The treatment of choice for pure ICPC is surgical excision, which may take the form of mastectomy or, more frequently, segmental resection [1]. There is little consensus on the roles of local radiation therapy or endocrine therapy in the treatment of isolated ICPC; however, patients with an adjacent focus of ductal carcinoma in situ or microinvasive carcinoma are treated according to the standard of care for the

most aggressive component [20]. Thus, encapsulated apocrine papillary carcinomas of the breast are rare breast lesions. Radiological imaging features and histopathological findings help in correct diagnosis of this tumor in order to frame appropriate treatment.

Abbreviations
MRI: Magnetic resonance imaging; T2W: T2 weighted image; DCE: Dynamic contrast enhancement; DWI: Diffusion weighted imaging; BIRADS: Breast Imaging-Reporting and Data System; ACR: American College of Radiology; US: Ultrasound; EAPC: Encapsulated apocrine papillary carcinoma; ICPC: Intra cystic papillary carcinoma.

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Author contributions
PI, US: Conception, design of work, acquisition, analysis & interpretation of data. RM: Analysis (Pathology & Immunohistology) & manuscript revision. PG: Design of work & insights into treatment procedure (performing surgeon). All authors have read and approved the final manuscript.

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Availability of data and materials
Yes, the datasets used and or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Institutional Ethics Committee, JLN Hospital & Research Centre, Steel Authority of India Ltd- Bhilai Steel Plant. Ethics Committee Registration No. NECRBHR. No personal details of the participants are presented.

Consent for publication
Written informed consent to publish this information was obtained from the study participant.

Competing interests
The authors declare that they have no competing interests.

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