Rare disease

Intracystic papillary carcinoma of breast: report of three cases and review of the literature

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Summary

Intracystic papillary carcinoma (IPC) of the breast is a rare malignant tumour, found mainly but not exclusively in elderly women. IPC may be asymptomatic or presents with a palpable mass or blood-stained nipple discharge. The tumour is encysted within a dilated duct with arborisation of the fibrovascular stroma and contains nodules of papillary carcinoma surrounded by a thick fibrous capsule. Frequently excisional biopsy is required for diagnosis. The mainstay of treatment is breast-conserving surgery or mastectomy. Sentinel node biopsy could be considered in invasive cases. Adjuvant radiotherapy (XRT) and/or endocrine therapy is considered in appropriate cases. Prognosis is excellent. We report three such cases of IPC, in elderly women, which were successfully treated.

BACKGROUND

Intracystic papillary carcinoma (IPC) of the breast is a rare malignant tumour, constituting 1–2% of all breast carcinomas in women.¹ There is a lack of guidelines for this unusual but distinct histological subtype of papillary carcinoma (PC). Most studies reported in the past were case reports and small case series but recently there has been a largest review of 917 cases California Cancer Registry (CCR)² and a large case series from Nottingham.³ Histologically, the tumour is encysted within a dilated duct with arborisation of the fibrovascular stroma and contains nodules of PC surrounded by a thick fibrous capsule,^{4–8} hence some favour the term encapsulated PC.⁹ Recent information within the pathology literature has demonstrated that, although IPC was once thought to be a variant of ductal carcinoma in situ (DCIS), some lesions are actually low-risk invasive tumours.^{8–10} These cases are often clinically thought to be breast cysts, for which they can be easily mistaken.

CASE PRESENTATION

Case 1

A 75-year-old lady presented with a 2-week history of left breast lump and no pain or nipple discharge. In the past she had lobular cancer of the right breast treated with wide local excision (WLE), radiotherapy (XRT) and adjuvant endocrine therapy. Clinically, a 4 cm lump was palpable in the left breast with no palpable axillary lymph nodes (LNs).

Case 2

A 78-year-old woman presented with a lump of 2 weeks duration with no pain or nipple discharge in the left breast. On examination, a 4 cm mass was palpable in the upper outer quadrant of left breast with no palpable axillary nodes.

Case 3

A 72-year-old woman who had an excision biopsy from the right breast, followed by WLE and axillary node

sampling 7 years ago for axillary node negative invasive IPC, which was 10–20% estrogen receptor (ER) positive. She was given adjuvant XRT and tamoxifen. She then presented 3 years later with metastatic axillary nodes for which she had axillary clearance. She was then switched to arimidex. She now presented with a lump in the right breast of 3 months duration.

INVESTIGATIONS

Case 1

Mammogram showed mass in the upper outer quadrant of the breast in the periareolar region, graded as M4 and ultrasound (US) showed a cystic mass 3.8×3 cm with multiple septations and intracystic mass with vascularity on Doppler. US of axilla showed no suspicious lymphadenopathy. On US-guided fine needle aspiration (FNA), haemorrhagic cyst fluid is aspirated. FNA of intracystic mass showed cohesive strips and groups of ductal epithelial cells but no evidence of significant atypia or mitotic figures, graded as C3. Excision biopsy was reported as a cystic mass 3×3×3 cm with a central cystic area predominantly composed of blood with occasional papillary structures. Some of the papillary structures contain thin fibrovascular cores with areas of marked epithelial proliferation with nuclear pleomorphism, punched out lumina and mitotic activity. These areas lacked basal cell markers, representing IPC, 1 mm from the nearest margin. There were surrounding several foci of low-to-high-grade ductal carcinoma in situ (DCIS) with a maximum dimension of 30 mm. Some of these areas showed irregular glands, raising the possibility of invasive component, basal cell markers were positive in these areas.

Case 2

The mammogram showed lobulated mass, graded R4. US showed half of the mass being a cyst with intracystic mass, with some vascularity, measuring 4×2.7 cm. Another half showed mixed echogenicity with fat echogenic areas

measuring 3.5×1.6 cm, graded U4. US of the left axilla was normal. US-guided FNA, withdrew blood-stained fluid which on cytology, showed dyscohesive cells which appear to be epithelial in origin with mild nuclear pleomorphism, highly suggestive of malignancy, graded C4.

Case 3

Mammogram showed well-defined mass in lower inner quadrant, graded M3 and US reported large collection with some septations and possible solid areas, graded U3. On US-guided aspiration blood stained fluid was withdrawn, the cytology reported as blood clot containing inflammatory cells but no epithelial cells, graded as C1. Repeat US showed a large collection which had refilled, graded U3.

TREATMENT

Case 1

She then had WLE and sentinel node biopsy, which was reported as remnant of IPC, present within 1 mm from inferior margin and node negative. She then had inferior cavity margin excision which showed margins were clear. She was referred to oncologist for XRT and hormonal treatment as the tumour cells were 100% oestrogen and progesterone receptor (ER/PR) positive.

Case 2

She went on to have WLE and axillary node sampling which was reported as a cystic mass 3×2×2 cm. Within the cyst were papillary and solid areas, microscopically composed of papillae of monotonous cells (figure 1) with mitotic activity. The myoepithelial cells are absent in this cystic mass (figure 2). The appearances were of IPC with areas of low- and intermediate-grade DCIS adjacent to cystic mass. The whole tumour measured 3 cm in maximum dimension, completely excised, node negative and 100% ER and 90% PR positive. She was referred to an oncologist for XRT and endocrine therapy.

Case 3

She had the lump excised which showed features of recurrent invasive IPC. The excision was incomplete and the tumour was weakly ER/PR positive and Her2 negative. She later had right mastectomy and axillary dissection

Figure 1 Encysted papillary carcinoma. HE. Magn ×2.

Figure 2 Absence of 34BE12 (myoepithelial marker) in the centre as well as in the periphery of the lesion. IHC. Magn ×2.

and was put on letrozole. Mastectomy did not show any residual malignancy and no nodes were found.

OUTCOME AND FOLLOW-UP

All the three cases were successfully treated.

DISCUSSION

IPC generally occurs in older postmenopausal women aged more than 60 years.^{4 11 12} In our three cases, the age was more than 70 years. IPC is not an entity unique to women, occasionally being found in men.^{6 13–15} In CCR 3.5% were men² and in a series of 302 cases by Rakha *et al*,³ 2% were men.

The histological classification of IPC has been confusing, within the surgical and pathology literature regarding its categorisation and nomenclature.^{8–10} In 1980, a classification system was developed, which divided PCs into the invasive and non-invasive forms.⁷ The non-invasive form was then further subdivided into the diffuse form, the papillary variant of DCIS (involving multiple small and medium sized ducts), and the localised form, termed 'intracystic' or 'encysted' PC (IPC)^{7 13} and solid variant of PC (SPC).³ Recently, the term encapsulated PC has been introduced to include IPC and SPC, which are typically circumscribed and often encapsulated.³ IPC describes a solitary tumour in an encysted or dilated duct.⁷ The presence of a layer of myoepithelial cells (MECs) at the periphery of areas of PC have historically been used to define a lesion as in situ rather than invasive.⁹ Recent studies have shown that, in contrast to papillary DCIS, IPC does not appear to have an MEC layer surrounding the tumour nodules.^{8–10} PC can be present as an isolated lesion or associated with conventional nonpapillary in situ or invasive carcinoma.³ IPC may be part of a spectrum of progression intermediate between in situ and invasive disease.^{8–10} Rakha *et al*,³ in their case series of PC, grouped the patients as pure EPC (pure IPC and pure SPC), papillary DCIS and PC associated with DCIS and/or microinvasion or pseudoinvasion.³ Staining of myoepithelial/basal cell markers is absent.

Gross appearance of IPC may show a cyst surrounded by a fibrous wall containing dark-brown blood clots.¹⁶ All three of our cases had haemorrhagic fluid in the cystic lump. Microscopic features include arborisation of fibrovascular stroma covered by a single or multiple layers of

cells and as mentioned above, a lack of myoepithelial cells.^{4 5 17} The tumour may be unifocal or multifocal. IPC occurs often as only a small focus of stromal invasion and is almost always detected at the periphery of the lesion.^{4 11}

IPC may present with a palpable mass or blood-stained nipple discharge. It may also be asymptomatic and identified at screening mammography.^{1 4 5 11–13 18 19} Axillary nodal metastases are infrequent. On mammography, IPC is seen as a round, oval or lobulated mass, most frequently in the retroareolar region.^{20 21} The margins of the mass are usually circumscribed but may be obscured or indistinct. US usually reveals a cystic mass, with or without septations, with solid papillary masses projecting into the cyst lumen.^{20 21} Haemorrhage within the cyst is frequently present due to ruptured capillaries within the cyst wall or haemorrhagic infarction of the tumour cells. Colour doppler US is helpful to demonstrate the intramural blood flow. Differentiation between in situ and invasive PC is difficult by FNA or core biopsy because the centre of the lesion is often targeted, and invasion is often found at the periphery of the tumour. Therefore, excisional biopsy is often performed when PC is suggested.^{5 12 13 19} Two of our cases needed excision biopsy before definitive surgical treatment.

There are no clear guidelines for the management of IPC.² Several studies have shown that prognosis is excellent and recurrence rates low, regardless of the intervention.^{6 15 22} The mainstay of treatment is surgical excision either breast-conserving surgery or mastectomy.² The surgical management of IPC seems to parallel that of invasive ductal carcinoma, with a lower rate of breast conservation in older studies.¹³ More recent studies show a tendency towards breast conservation with no significant increase in tumour recurrence or cancer-related deaths.^{6 15 22 23} In series by Rakha *et al*,³ 22% had mastectomy. The extent of the local resection margin and the role of mastectomy are not yet defined.^{5 23} Two of our cases had WLE. The third case needed mastectomy as it was a recurrence 7 years after WLE and XRT.

There is no consensus as to the role of axillary staging procedures for IPC. Within the CCR, less than 8% of IPC cases were reported to have LN positivity. It was not reported what percentage of patients underwent axillary sampling and hence the rate may not be accurate. Most studies show a low rate of LN involvement, though axillary dissections were not consistently performed and therefore there are no concrete indications for axillary dissection.^{6 13 14 22} In the series by Rakha *et al*,³ 1% were LN positive. All our cases were node negative but the third case, which initially was node negative, went on to have axillary node metastasis 3 years later. Some believe that approach to LN sampling should be same as conventional DCIS,³ though sentinel LN biopsy has been advocated particularly where coexisting conventional carcinoma is likely.^{5 12 13 19 24–26} or reported on the excisional biopsy of the breast lump and when US axilla shows suspicious looking nodes.³

In addition to surgical excision, several studies have reported on the use of adjuvant radiation, chemotherapy and/or endocrine therapy in the management of IPC, though the need remains unclear.^{6 15 17 22 23} In their review of the treatment and outcome of 40 patients with IPC,

Solorzano *et al* reported that 30% of the patients had received adjuvant radiotherapy. The use of radiation did not change the incidence of local recurrence or likelihood of death compared with those who did not receive radiation.⁶ Within this study, no criteria for how patients were chosen to receive radiation were mentioned. In addition, there has been no clear indication for adjuvant endocrine therapy, even among patients with ER-positive tumours. The addition of hormonal treatment did not seem to have impacted on outcome.^{15 22} Given the overall good prognosis and that no adjuvant treatment has been shown to increase cancer-free survival, there could be a concern for a potential overtreatment in these cases,^{8 22} particularly in older patients treated with mastectomies or lumpectomies with radiation. Endocrine treatment should definitely be considered for those not fit for surgery, those with recurrent disease,³ those with unusual morphological high-risk features, such as signet-ring cell morphology²⁷ and those treated with lumpectomy without radiation. All three of our cases were ER positive and were given endocrine therapy. All three received XRT after WLE, though the recurrent case went on to have mastectomy.

The CCR illustrates an observed cumulative survival rate of more than 60% at 10 years and relative survival rate of more than 90% of that of general population at both 5 and 10 years.² In CCR, a total of 917 cases of IPC were identified. Forty-seven per cent of cases were CIS while 53% of cases had invasion. Most of the invasive cases were localised at the time of diagnosis (89.6%). At 10 years, patients with CIS and invasive disease had a similar relative cumulative survival (96.8% and 94.4%, $p=0.18$). They concluded that there was apparently no significant difference in the long-term survival of patients in the two histologically derived subgroups of IPC. There is an excellent prognosis for patients diagnosed with IPC regardless of whether the tumour is diagnosed as in situ or invasive. The survival rate of patients with all other types of invasive breast cancer excluding IPC was lower.² Eight per cent of IPC cases, in series by Rakha *et al*,³ had recurrences. All our patients are alive, first case is alive for 8 months, second for 4 months and third for 7 years from diagnosis.

In conclusion, IPC is a rare tumour with an excellent prognosis. The tumour affects predominantly older women, but can also be diagnosed in younger women and men. Surgery is the mainstay of treatment followed by adjuvant XRT and endocrine therapy. The role of chemotherapy may be limited. Whether the tumour is classified as invasive or in situ, the long-term outcome in patients with IPC is good.

Learning points

- ▶ Intracystic papillary carcinoma should be considered as a possible diagnosis particularly in the elderly with a cystic breast lump.
- ▶ Ultrasound and fine needle aspiration will be helpful to make the diagnosis, and should be considered in someone who has blood-stained fluid on aspiration of cyst, which keeps recurring.
- ▶ The prognosis is excellent with treatment.

Competing interests None.

Patient consent Obtained.

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Dhebri AR, Ahmad A, Shah N, Arora PK. Intracystic papillary carcinoma of breast: report of three cases and review of the literature. *BMJ Case Reports* 2012;10.1136/bcr-2012-007237, Published XXX

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