CASE REPORT

Clear cell carcinoma of the breast with solid papillary pattern: a case report with immunohistochemical profile

Y Gürbüz, S K Özkara

J Clin Pathol 2003;**56**:552–554

Glycogen rich clear cell carcinoma of the breast is a rare neoplasm with different morphological characteristics to ordinary breast carcinomas. However, it has some common features with clear cell carcinomas of other organs. This report describes a case of clear cell carcinoma of the breast with a solid papillary pattern centrally localised in the left breast of a 45 year old woman. Antibodies directed against cytokeratin 7 (CK7), CK10, CK14, CK17, CK18, CK19, CK20, CK5/6/18, CK8/18, high molecular weight cytokeratin AE3, high molecular weight cytokeratin 34βE12, the oestrogen receptor, the progesterone receptor, chromogranin, S-100 protein, smooth muscle actin, vimentin, and carcinoembryogenic antigen were applied to analyse the immunophenotypical profile of this rare neoplasm.

Glycogen-rich clear cell carcinoma (CCC) of the breast is a rare neoplasm. It has an incidence of between 1.4% and 3% of all breast carcinomas.¹ The criteria used for the diagnosis of this tumour are that it consists predominantly of cells with clear and occasionally finely granular cytoplasm containing periodic acid Schiff (PAS) positive, diastase labile material in at least 90% of the tumour area.² This tumour is a distinct entity that has different morphological characteristics to ordinary breast carcinomas and shares some characteristics of clear cell carcinomas of other organs.² In this case report, we present a glycogen rich CCC of the breast with a solid papillary pattern. A panel of antibodies directed against cytokeratin 7 (CK7), CK10, CK14, CK17, CK18, CK19, CK20, CK5/6/18, CK8/18, high molecular weight cytokeratin AE3 (HMWCK AE3), high molecular weight cytokeratin 34βE12 (HMWCK 34βE12), the oestrogen receptor (ER), the progesterone receptor (PR), chromogranin (CR), S-100 protein, smooth muscle actin (SMA), vimentin, and carcinoembryogenic antigen (CEA) were applied to analyse the immunophenotypical profile of this neoplasm.

"Glycogen-rich clear cell carcinoma of the breast is a rare neoplasm"

CASE REPORT

A 45 year old woman with a centrally localised mass in her left breast had undergone excisional biopsy. On macroscopical examination, the tumour was localised in a cystically dilated duct, it measured 3 × 3 × 2.5 cm, and had papillary projections and solid areas on cross section (fig 1A). Microscopical examination revealed that the tumour was composed of a combination of solid areas and papillary projections with fibrovascular cores and areas of invasion. More than 90% of the tumour cells had wide polygonal clear cytoplasm, distinct cell borders, round and central nuclei, and prominent nucleoli. Atypia and pleomorphism were conspicuous in some areas (fig 1B). There

were foci of necrosis and abscess in the tumour and the whole tumour was embedded. Squamous or transitional differentiation and gland formation were not detected. The wall of the duct that the tumour originated from had granulation tissue and the epithelium was not evident. There was stromal invasion in the form of solid nests (fig 1C). There were no proliferative epithelial changes except for apocrine metaplasia in the adjacent breast tissue, which was confirmed by examination of the radical mastectomy material four months later. Neither residual tumour nor lymph node metastasis were observed in the radical mastectomy specimen. A detailed radiological and clinical survey did not reveal metastatic foci or other primary tumours. The patient has been followed for 27 months with no evidence of recurrence or metastasis.

On histochemical examination, the cytoplasm of some cells showed diffuse PAS positive staining or had PAS positive and diastase labile granules of 2–3 µm in diameter. There was no evidence of intracytoplasmic mucin on PAS/Alcian blue staining. Antibodies against CK7, CK10, CK14, CK17, CK18, CK19, CK20, CK5/6/18, CK8/18, HMWCK AE3, HMWCK 34βE12 (Dako, Carpinteria, California, USA), ER, PR, CR, S-100, SMA, vimentin, and CEA (Neomarkers Corp, Fremont, California, USA) were used for immunohistochemical analysis. Table 1 summarises the histochemical and immunohistochemical results. The tumour was ER and PR negative and HMWCK AE3, CK7, and CK8/18 were strongly positive (fig 2).

DISCUSSION

Glycogen rich CCC is a rare tumour but it is the most frequent cause of clear cell morphology in breast malignancies.³ The tumour is composed of cells with polygonal clear cytoplasm, centrally localised hyperchromatic, round/oval nuclei, and prominent nucleoli. The cytoplasm of the neoplastic cells typically contains PAS positive, diastase labile granules and intracytoplasmic mucin production is also seen.⁴ The histopathological pattern of glycogen rich CCC of the breast may be well differentiated tubular, papillary, and/or solid, which may or may not be associated with an intraductal component.¹ This neoplasm has a tendency to form solid and papillary patterns.^{3,4} To the best of our knowledge, only two clear cell breast carcinomas with a solid papillary pattern have been reported to date.^{3,4} The case reported by Hull *et al* had separate areas of papillary and solid patterns and consisted of single layered cuboidal and columnar clear cells.⁴ The second case was an intraductal tumorous growth of 4 mm in diameter, sharing similar histopathological features with our case—namely, fibrovascular cores and multilayered solid tumour cells.³

Abbreviations: CCC, clear cell carcinoma; CEA, carcinoembryogenic antigen; CK, cytokeratin; CR, chromogranin; ER, oestrogen receptor; HMWCK, high molecular weight cytokeratin; PAS, periodic acid Schiff; PR, progesterone receptor; RCC, renal cell carcinoma; SMA, smooth muscle actin

Figure 1 (A) Tumour with a solid papillary pattern located within a cystically dilated duct. (B) Cells with centrally localised, round, hyperchromatic, atypical nuclei, prominent nucleoli, polygonal clear cytoplasm, and distinct cell borders (haematoxylin and eosin stain; original magnification, $\times 310$). (C) The tumour invaded the stroma forming solid nests (haematoxylin and eosin stain; original magnification, $\times 125$).

Solid papillary growth in breast malignancies is rare. Papillary carcinomas may have solid areas but a diffuse solid pattern without gland formation or a cribriform pattern is uncommon in these tumours.¹ Transitional cell carcinoma of the breast may show a solid papillary pattern, but there are distinct histopathological diagnostic criteria for this neo-

Figure 2 Diffuse and strong cyokeratin 8/18 immunoreactivity in the tumour cells (original magnification, $\times 310$).

plasm, such as the presence of umbrella cell layer, specific organisation of transitional cells, and oval elongated nuclei.⁵ Solid papillary carcinoma is a recently described entity with a mixed solid and papillary pattern. This tumour consists of uniform spindle cells that contain intracellular and extracellular mucin and show neuroendocrine differentiation.⁶ Ecrin acrospiroma, a benign appendageal tumour, may have both a solid papillary and clear cell appearance in the epidermis and may be among the differential diagnoses.⁵

Clear cell carcinomas occur in many organs. These tumours are characterised by a solid, papillary, or tubulocystic pattern. Glycogen rich CCC is the counterpart of this tumour in breast tissue.¹ This rare neoplasm shares some morphological and histochemical properties with other clear cell carcinomas, particularly renal cell carcinoma (RCC). The clear cell appearance in both of these neoplasms arises from the glycogen content.⁷

“Defining the exact immunophenotypical characteristics and the mechanisms of glycogen accumulation in this rare tumour requires more detailed, multicentric studies comprising large series”

To our knowledge, the immunophenotypical profile of this rare neoplasm has not been reported previously. The expression of CK7, CK8/18, CK18, and CK19 can be detected in both breast carcinoma and RCC.⁷⁻⁸ HMWCK 34 β 12E is a pan-epithelial CK including CK1, CK5, CK10, and CK14, which is expressed by all epithelial layers of the mammary ducts. In addition, HMWCK 34 β 12E expression has been reported in invasive breast carcinomas.⁹⁻¹¹ In RCC, HMWCK 34 β 12E immunoreactivity has been reported to be negative¹² or rarely positive, as in series investigated by Renshaw and Corless that detected positivity in one of 55 cases.¹³ We found diffuse and strong CK8/18 expression in the cytoplasm of the tumour cells (fig 2). Coexpression of vimentin and CK is a classic feature of RCC but it can also be identified in high grade invasive ductal carcinomas.⁷⁻¹⁴ The absence of ER and PR expression may be interpreted as a feature of a non-breast carcinoma phenotype, but can also be seen in high grade carcinomas. Focal S-100 protein expression of a clear cell breast tumour could suggest a diagnosis of myoepithelioma, but the stromal invasion and negative immunoreactivity with SMA and CK14 are helpful immunohistochemical features in the differential diagnosis from myoepithelioma. S-100 immunoreactivity can be seen in 48% of breast malignancies, but it is also a common feature of RCC.¹⁵⁻¹⁶

In conclusion, we consider glycogen rich CCC to be a tumour with similar morphological characteristics to clear cell

Table 1 Immunophenotypical profile of our case

Diffuse positive immunoreactivity	Sparse weak immunoreactivity	Negative immunoreactivity	
HMWCK AE3	HMWCK 34β12E	CK5/6/18 (LP34)	ER (1D5+6F11)
CK8/18 (5D3)	CK18 (DC10)	CK10 (LHP1)	PR (hPRa2+hPRa)
CK7 (K72.7)	CK19 (K19.2)	CK14 (LL002)	CR (LK2H10+PHE5)
	Vimentin (V9)	CK17 (E3)	SMA (1A4)
	S-100 (4C4.9)	CK20 (Ks20.8)	

The antibodies used are given in parenthesis.

CK, cytokeratin; CR, chromogranin; ER, oestrogen receptor; HMWCK, high molecular weight cytokeratin; PR, progesterone receptor; SMA, smooth muscle actin.

Take home messages

- This is only the third case of glycogen rich clear cell carcinoma of the breast with a solid papillary pattern to be reported to date
- To our knowledge, the immunophenotypical profile of this rare neoplasm has not been reported previously
- This rare neoplasm has different morphological characteristics to ordinary breast carcinomas, but has some common features with clear cell carcinomas, particularly renal cell carcinoma
- We regard this neoplasm as a high grade ductal carcinoma with diffuse intracytoplasmic glycogen accumulation

tumours of other organs, but that still retains the basic immunophenotypic characteristics of common breast malignancies. Therefore, we regard this neoplasm as a high grade ductal carcinoma with diffuse intracytoplasmic glycogen accumulation. Defining the exact immunophenotypical characteristics and the mechanisms of glycogen accumulation in this rare tumour requires more detailed, multicentric studies comprising large series.

Authors' affiliations

Y Gürbüz, S K Özkara, Department of Pathology, Kocaeli University, Medical School, 41900, Derince, Kocaeli, Turkey

Correspondence to: Dr S K Özkara, Mustafa Pasa Mahallesi, Bagdat Caddesi, 0712. Sokak, No: 19/6, 41400, Gebze, Kocaeli, Turkey; Erkacar@sisecam.com.tr

Accepted for publication 28 January 2003

REFERENCES

- 1 **Tavassoli FA**. Infiltrating carcinoma: special types. In: *Pathology of the breast*, 2nd ed. Stanford Connecticut: Appleton & Lange, 1999:481–570.
- 2 **Toikkanen S**, Juensuu H. Glycogen rich clear cell carcinoma of the breast: a clinicopathologic and flow cytometric study. *Hum Pathol* 1991;**22**:81–3.
- 3 **Hayes MMM**, Seidman JD, Ashton MA. Glycogen-rich clear cell carcinoma of the breast. A clinicopathologic study of 21 cases. *Am J Surg Pathol* 1995;**19**:904–11.
- 4 **Hull MT**, Warfel KA. Glycogen-rich clear cell carcinomas of the breast. A clinicopathologic and ultrastructural study. *Am J Surg Pathol* 1986;**10**:553–9.
- 5 **Mooney EE**, Tavassoli FA. Papillary transitional cell carcinoma of the breast: a report of 5 cases with distinction from eccrine acrospiroma. *Mod Pathol* 1999;**12**:287–94.
- 6 **Maluf HM**, Koerner FC. Solid papillary carcinoma of the breast. A form of intraductal carcinoma with endocrine differentiation frequently associated with mucinous carcinoma. *Am J Surg Pathol* 1995;**19**:1237–44.
- 7 **Ordóñez NG**, Rosai J. Urinary tract, kidney, renal pelvis and ureter, bladder and male urethra. In: Rosai J, ed. *Ackerman's surgical pathology*, 8th ed. St Louis: Mosby, 1996:1059–220.
- 8 **Rosai J**. Breast. *Ackerman's surgical pathology*, 8th ed. St Louis: 1996:1565–660.
- 9 **Monifar F**, Man YG, Lining RA, et al. Use of cytokeratin 34 beta E12 as an adjunct in the diagnosis of mammary intraepithelial neoplasia-ductal type benign and malignant intraductal proliferations. *Am J Surg Pathol* 1999;**23**:1048–58.
- 10 **Dairkee SH**, Puett L, Hackett AJ. Expression of basal and luminal epithelium specific keratins in normal, benign and malignant breast tissue. *Natl Cancer Inst* 1988;**80**:691–5.
- 11 **Gown AM**, Vogel AM. Monoclonal antibodies to human intermediate filamentous proteins. III. Analysis of tumours. *Am J Clin Pathol* 1985;**84**:413–24.
- 12 **Renshaw AA**, Zhang H, Corless CL, et al. Solid variant of papillary clear cell carcinoma: clinicopathologic and genetic features. *Am J Surg Pathol* 1997;**21**:1203–9.
- 13 **Renshaw AA**, Corless CL. Papillary renal carcinoma. Histopathology and immunohistochemistry. *Am J Surg Pathol* 1995;**19**:842–9.
- 14 **Domagala W**, Wozniak L, Lasota J, et al. Vimentin is preferentially expressed in high grade ductal and medullary, but not in lobular breast carcinomas. *Am J Pathol* 1990;**137**:1059–64.
- 15 **Dwarakanath S**, Lee AK, Dellellis RA, et al. S-100 protein positivity in breast carcinomas: a potential pitfall in diagnostic immunohistochemistry. *Hum Pathol* 1987;**18**:1144–8.
- 16 **Kusama K**, Asano M, Moro I, et al. Tumor markers in human renal cell carcinoma. *Tumour Biol* 1991;**12**:189–97.