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

Y Gürbüz, S K Özkara

Glycogen-rich clear cell carcinoma of the breast (CCC) 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 of the breast is a rare neoplasm”

DISCUSSION
Glycogen-rich CCC is a rare tumour but it is the most frequent cause of clear cell morphology in breast malignancies. 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. 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. This neoplasm has a tendency to form solid and papillary patterns. To the best of our knowledge, only two clear cell breast carcinomas with a solid papillary pattern have been reported to date. 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. 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.

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.
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. Transitional cell carcinoma of the breast may show a solid papillary pattern, but there are distinct histopathological diagnostic criteria for this neoplasm, such as the presence of umbrella cell layer, specific organisation of transitional cells, and oval elongated nuclei. 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. 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.

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. 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. “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. HMWCK 34β12E is a pan-epithelial CK including CK1, CK3, CK10, and CK14, which is expressed by all epithelial layers of the mammary ducts. In addition, HMWCK 34β12E expression has been reported in invasive breast carcinomas. In RCC, HMWCK 34β12E immunoreactivity has been reported to be negative or rarely positive, as in series investigated by Renshow and Corless that detected positivity in one of 55 cases. 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. 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.

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

<table>
<thead>
<tr>
<th>Diffuse positive immunoreactivity</th>
<th>Sparse weak immunoreactivity</th>
<th>Negative immunoreactivity</th>
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<tbody>
<tr>
<td>HMWCK AE3</td>
<td>HMWCK 34β12E</td>
<td>CK5/6/18 (P34) ER (1DS+6F11)</td>
</tr>
<tr>
<td>CK8/18 (S03)</td>
<td>CK18 (DC10)</td>
<td>CK10 (HP1) PR (kPRα2+kPRα)</td>
</tr>
<tr>
<td>CK7 (K72.7)</td>
<td>CK19 (K19.2)</td>
<td>CK14 (L002) CR (K2H10+PHES)</td>
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<td></td>
<td>Vimentin (V9)</td>
<td>CK17 (E3) SMA (1A4)</td>
</tr>
<tr>
<td></td>
<td>S-100 (4C4.9)</td>
<td>CK20 (K20.8)</td>
</tr>
</tbody>
</table>

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.

REFERENCES

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.

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Accepted for publication 28 January 2003

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.