Glycogen-Rich Clear Cell Carcinoma of the Breast: Two-Case Report

Cuizhi Geng
Xiaoling Wang
Zhonglin Fan
Zhi Chen
Li Ma
Shijie Wang

Department of Surgery, the Fourth Hospital of Hebei Medical University, Shijiazhuang, Hebei Province 050011, China.

Correspondence to: Cuizhi Geng
E-mail:gengcuizhi@hotmail.com

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Primary clear cell carcinoma of the breast is a rare tumor with different morphological characteristics compared to ordinary breast carcinomas. The clear cell morphology of the neoplastic population in these tumors has been ascribed to the presence of intracellular lipid, mucin or glycogen, or to myoepithelaial, apocrine, or neuroendocrine differentiation. We describe 2 cases of glycogen-rich clear cell carcinoma of the breast as follows.

Case Reports

Case 1

A 51-year-old woman presented with a history of a palpable lump in her right breast for 3 months. The lump had been slowly increasing in size but was not painful, and there was no associated skin involvement or nipple discharge. Physical examination revealed a firm, palpable mass in the superior inner quadrant of the right breast. The mass was not fixed to the skin or to deep structures, but many of the axillary lymph nodes were detected. Mammography demonstrated an irregular, speculated mass with no calcification. Needle biopsy was performed, indicating malignant cells. So a modified radical mastectomy was performed immediately. On microscopical examination, sectioning revealed a circumscribed 3× 3 × 2.5 cm yellow-tan mass with a vaguely nodular cut surface and gelatinous foci. Microscopically, the cells were seen to contain abundant fine cytoplasmic granules with periodic acid-Schiff (PAS) staining (Fig.1), most of which was digested with diastase. All of the axillary lymph nodes situating in levels I, II and III metastases were observed on pathological examination. The tumor was ER (++), PR(-), HER-2(+), cathe-D(+) and VEGF(-). After operation the patient received chemotherapy with CAF for 6 cycles. Until now the patient has been followed for 27 months with no evidence of recurrence or metastases of the lung, bone or liver.

Case 2

A 32 year-old woman presented after noticing a firm mass in her right breast. On examination, a 3 × 2.5 × 2 cm, hard, nontender lump was identified in the upper outer quadrant of the right breast. After an excisional biopsy was performed, the patient received a modified radical mastectomy. Microscopical examination revealed that more than 90% of the tumor cells had a wide polygonal clear cytoplasm, distinct cell

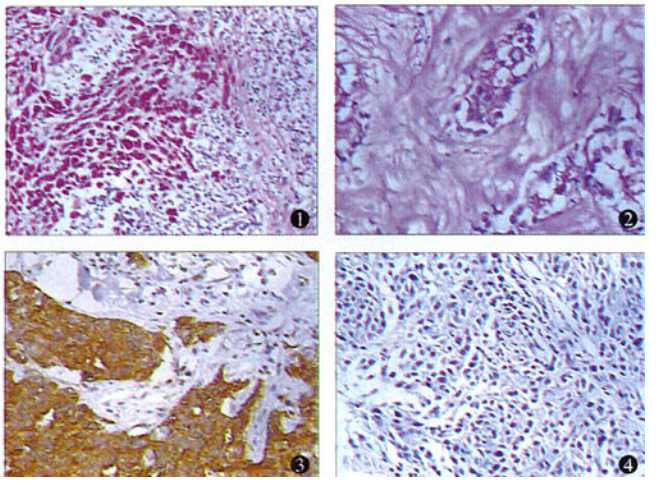

Fig.1. Glycogen-rich clear cell of carcinoma of the breast(GRCC) (PAS × 150).
Fig.2. Glycogen-rich clear cell of carcinoma of the breast (GRCC) (PAS× 350).
Fig.3. Glycogen-rich clear cell of carcinoma of the breast (CK+) (× 350).
Fig.4. Glycogen-rich clear cell of carcinoma of the breast (NSE-) (× 150).

borders, round and central nuclei, and prominent nucleoli. The features of ductal differentiation were noted in this case. On histochemical examination, the cytoplasm of some cells showed diffuse PAS positive staining (Fig.2). Immunohistochemical stains of the tumor cells were ER(+), PR(++), HER-2(+), ER-β(+), VEGF(++), CK(+)(Fig.3) and NSE(-)(Fig.4). No axillary lymph node metastases were detected. No recurrence or metastasis were found by 17 months of follow-up.

Discussion

Clear cells can be seen in normal breast ducts and lobules as a result of cytoplasmic clearing in myoepithelial cells, in foci of apocrine and clear cell metaplasia, or as a component of pregnancy-induced or pregnancy-like changes.[1] However, primary clear cell neoplasms of the breast are rare with an incidence of between 1.4% and 3% of all breast carcinomas.[2,3] The first case of glycogen-rich clear cell carcinoma (GRCCC) of the breast was reported by Hull et al. in 1981.[4] The tumor is composed of cells with a polygonal clear cytoplasm, centrally localized hyperchromatic, round/oval nuclei, and prominent nucleoli. The criteria of GRCCC used for the diagnosis 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 tumor area.[5] Two cases which we described above had these features. Immunohistochemical markers that have been used in an effort to classify clear cell carcinomas include cytokeratin, S-100 protein, SMA, GCDFP-15, NSE, and chromogranin. Either needle biopsy or ice-pathology detection during operation is likely to result in a mistake of pathological diagnosis due to a lack of specific features. Paraffin sections and/or immunohistochemical markers are the gold standard of pathologic diagnosis of GRCCC.

Some investigators have reported that clear cell breast cancers exhibit more aggressive clinical behavior than the usual types of carcinoma,[6] while others have suggested that the presence of a clear cell morphology, notably the presence of glycogen, does not appear to influence the clinical outcome once stage and grade are taken into account.[7] In our patients, both stage and grade were similar, but with a different status of axillary lymph node metastasis. Despite the presence of histologic markers of aggressive behavior in our patients, they remain well without having had further treatment. Therefore, we consider GRCCC to be a tumor with similar morphological characteristics to clear cell tumors of other organs, but that still retains the basic immunophenotypic characteristics of common breast malignancies. Defining the exact immunophenotypic characteristics and mechanisms of glycogen accumulation in this rare tumor requires more detailed, multicentric studies comprised of a large series.[8,9]

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