Glycogen Rich Clear Cell Carcinoma (GRCC) of the breast may not have a poor prognosis

Muna M. Baslaim a,⁎, Enaam M. Junainah b, Hadeel H. Ahmad a, Anmar F. Semilan a, Ahmed O. Al-Ghamdi a, Noora O. Rahimuddin a, Budoor A. Salman c

a Department of Surgery, Breast Unit, King Fahd General Hospital, Jeddah, Saudi Arabia
b Breast Pathology, Breast Unit, King Fahd General Hospital, Jeddah, Saudi Arabia
c Surgical Research Unit, Breast Unit, King Fahd General Hospital, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received 9 December 2016
Received in revised form 21 February 2017
Accepted 21 February 2017
Available online 27 February 2017

Keywords:
Case report
Glycogen rich clear cell carcinoma
Rare breast carcinoma sub-types

ABSTRACT

INTRODUCTION: Glycogen Rich Clear Cell Carcinoma (GRCC) is a rare variant of breast carcinomas and believed to be linked with a poor prognosis.

CASE SUMMARY: We are presenting a 60-year-old Saudi lady with a 2 cm GRCC carcinoma associated with clear cell ductal carcinoma in situ (DCIS) and no axillary lymph node involvement. The tumor was Estrogen and Progesterone receptors (ER & PR) positive and HER 2-neu negative. She underwent mastectomy with sentinel lymph node biopsy followed by hormonal therapy. She is alive and free of disease for 35 months.

CONCLUSION: The prognosis of GRCC may not be different from other types of invasive breast cancer.

© 2017 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Glycogen Rich Clear Cell Carcinoma (GRCC) is a rare variant of breast carcinoma [1]. It is considered a member of a heterogeneous group of neoplasms, including signet-ring, secretory and lipid-rich carcinomas of the breast [2]. Contradicting reports were published discussing the aggressive nature of this entity and its poor prognosis; others concluded that the behavior of GRCC carcinoma carries a comparable prognosis to the conventional ductal carcinomas [3–10,12,13].

We report a case of GRCC carcinoma with no axillary lymph node involvement. A literature review is included.

This work has been reported in line with the SCARE criteria [14].

2. Case summary

A 60-year-old Saudi lady presented with a right breast mass noticed few weeks back. She is a known case of hypothyroidism on Thyroxin tablets. She is a mother of 9 children whom she breast-fed for an average period of 18 months. No family history of malignancy was documented. Examination showed a healthy lady with a right breast 10 o’clock firm oval slightly nodular mass measuring 2 × 1.5 cm with no palpable axillary lymph nodes. Mammogram showed a fatty breast with an asymmetric density in the right upper outer quadrant with no calcifications (Fig. 1A); spot magnification compression view revealed an ill-defined elongated mass with faint calcifications (Fig. 1B). Right breast ultrasound showed a hypo-dense lobulated horizontally oriented lesion (Fig. 2A) measuring 1.3 × 0.8 cm with mild increased peripheral vascularity (Fig. 2B). Magnetic Resonant Imaging (MRI) of the breast showed an irregularly enhancing lesion with distortion and benign looking axillary lymph nodes (Fig. 3). Ultrasound guided trucut needle biopsy showed invasive ductal carcinoma; grade II with polygonal cells that contain clear cytoplasm consistent with the diagnosis of Glycogen Rich Clear Cell Carcinoma (GRCC).

She underwent simple mastectomy with sentinel lymph node biopsy. Final pathology confirmed the diagnosis of GRCC carcinoma with extensive solid type clear cell ductal carcinoma in-situ (Fig. 4A). The malignant cells were round to polygonal, forming cords and nests, containing clear cytoplasm and constitute more than 90% of the tumor (Fig. 4B). The glycogen granules in the clear cytoplasm are positive (Fig. 4C) for Periodic Acid-Schiff staining (PAS) and negative for diastase-periodic acid stain (d-PAS). Immunohistochemistry assessment of the tumor showed positive estrogen (ER) and progesterone receptors (PR). Allred score for ER was 7 (proportion score of 4 and intensity score of 3) which reflects a 75% chance of benefit from hormonal treatment. The tumor cells showed negative HER 2-neu receptors and >15% Ki 67 positivity. The sentinel lymph node showed no metastatic malignant cells. The patient was treated with hormonal therapy in the form of Aromatase inhibitors; Letrozole 2.5 mg daily. She is alive and free of disease for 35 months.

http://dx.doi.org/10.1016/j.jjscr.2017.02.044
2210-2612/© 2017 The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
3. Discussion

Glycogen Rich Clear Cell Carcinoma (GRCC) is a rare variant of breast carcinoma with an incidence of 1.4–3% [1]. It is the commonest cause of clear cell morphology in breast malignancies [3].

The originally reported case by Hull et al. in 1981 was a slowly growing mass over 20 years and has no axillary lymph node involvement [1]. In 1985, Fisher et al. published their series of 45 cases of GRCC with a disease-free survival that was significantly less (p value = 0.0038) than the commonly encountered breast carcinomas. They considered the case reported initially by Hull a benign breast tumor analogous to dermal eccrine acrospiromas like hidradenoma, spiradenoma or myoepithelioma [6].
According to the world Health Organization (WHO) classification, in GRCC carcinoma, more than 90% of the neoplastic cells have abundant clear cytoplasm-containing glycogen [11]. Table 1 summarizes the published studies from different countries on GRCC with variability in the% of clear cells used to classify the lesion. This might explain the variability in reporting GRCC cases as well as their prognosis. Most of the GRCC cases were above 50 years of age. The duration of symptoms was not clearly stated. The commonest reported presenting symptom was a breast mass [7]. Some reported skin involvement (dimpling, edema, fixation or nipple retraction) in 50% of their cases [4,5]. There were no specific radiologic characteristics associated with GRCC carcinoma, the commonest finding was a calcified mass that is relatively well defined on breast ultrasound [7,10]. Our case had a relatively benign appearance that can mimic a fibro-adenoma. The lobulated appearance combined with the peripheral vascularity in a 60 years old lady warranted biopsy. MRI showed an irregularly enhancing lesion typical of a mammary carcinoma.

Microscopically, the growth pattern is that of the usual infiltrating ductal carcinoma however other patterns may be seen like papillary, lobular or tubular ones. The neoplastic cells are characterized by an optically clear cytoplasm which contains glycogen but no lipids or mucin [1]. Within the cytoplasm, there are fine glycogen granules which are stained by Periodic Acid Schiff stain (PAS) but not stained by diastase-periodic acid stain (d-PAS). They have a relatively low nuclear and cytoplasmic ratio, irregularly thickened nuclear membranes and prominent nuclei [9]. The glycogen in the cell is extracted during tissue processing for histologic assessment leaving the vaculated cytoplasm; hence the differential diagnosis includes lipid rich carcinoma, signet-ring cell carcinoma, histiocytoid carcinoma, adenoxyepithelioma, clear cell hidradenoma and eccrine spiradenoma [1,2,10].

Intra-ductal clear cell component is commonly present as seen in our case. Hayes et al. reported 21 GRCC cases; 8 of them were intraductal GRCC showing different histologic subtypes like solid, papillary, micropapillary and cribriform [3]. Kim et al. reported 3 cases of GRCC seen over 10 years. They Used 12 different antibodies to study the phenotype of these tumors and concluded that the immune-phenotype of GRCC is not uniform and might be similar to that of the conventional carcinoma. In their cases, P53 – which is considered a poor prognostic marker – was variably present with variable percentage (15–60%) of Ki-67 [9].

Varga et al. studied Her 2 overexpression in aggressive histologic subtypes of invasive breast cancer. Among his series, there were 12 cases of GRCC, 3 of them displayed Her 2 overexpression [12]. The reported amplification rate of the Her 2 gene in GRCC was similar to that among breast cancers generally from 0 to 33% [9,12].

The commonest surgical approach reported in the literature for cases of GRCC carcinoma was in the form of mastectomy with sentinel lymph node biopsy or axillary dissection regardless of the tumor size, conservative surgery was less practiced [3–10,12,13]. The role of neo-adjuvant chemotherapy was not discussed in the published literature as well. This might be related to the poor understanding of this rare entity and the conflicting reports about its therapeutic response and prognosis.

Different reports were published discussing the aggressive nature of this entity. In these reports, the tumor grade was II–III, hormone receptors assessment was not always documented,
4. Conclusion

The contradicting reports about the prognosis of GRCC carcinomas of the breast might be related to inconsistency in the classification and the percentage of clear cell changes reported in the tumor; a unified pathologic interpretation is crucial. Based on the tumor grade, axillary lymph node involvement and hormone receptor status, their management will be no different than the commonly seen infiltrating ductal carcinoma.

Conflict of interest

All authors declare no conflict of interest.

Funding

No source of funding.

Ethical approval

King Fahd Hospital approved this case report.

Consent

No consent was obtained from the patient in this case report.

Author contributions

Muna M. Baslaim: Study design, data collection, writing the paper.
Enaam M. Junainah: Pathologic assessment, images, literature review.
Hadeel H. Ahmad: Pathologic assessment, images, literature review.
Anmar F. Semilan: Data collection, obtain images, literature review.
Ahmed O. Al-Ghamdi: Writing the manuscript.
Noora O. Rahimuddin: Writing the manuscript.
Budoor A. Salman: Data collection, obtain images, review manuscript.

References

[1] F.A. Tavassoli, Infiltrating carcinoma: special types, in: Pathology of the Breast, 2nd edn, Appleton & Lange, Norwalk Connecticut, 1992, pp. 390–393.
[2] M.T. Hull, J.B. Priest, T.A. Broadie, et al., Glycogen-rich clear cell carcinoma of the breast: a light and electron microscopic study, Cancer 48 (1981) 2003–2009.
[3] M.M. Hayes, J.D. Seidman, M.A. Asthon, Glycogen rich clear cell carcinoma of the breast: a clinicopathologic study of 21 cases, Am. J. Surg. Pathol. 19 (1995) 904–911.
[4] M.T. Hull, K.A. Warfel, Glycogen-rich clear cell carcinomas of the breast: a clinicopathologic and ultrastructural study, Am. J. Surg. Pathol. 10 (1986) 553–559.
[5] S. Toikkana, J. Juensuu, Glycogen rich clear cell carcinoma of the breast: a clinicopathologic and flow cytometric study, Hum. Pathol. 22 (1) (1991) 81–83.
[6] E.R. Fisher, J. Tavares, I.S. Bulatao, et al., Glycogen- rich, clear cell breast cancer: with comments concerning other clear cell variants, Hum. Pathol. 16 (1985) 1085–1090.
[7] X. Ma, Y. Han, Y. Fan, et al., Clinicopathologic characteristics and prognosis of glycogen-rich clear cell carcinoma of the breast, Br. J. 20 (2) (2014) 166–173.
[8] H. Kuroda, G. Sakamoto, K. Ohnisi, et al., Clinical and pathological features of glycogen-rich clear cell carcinoma of the breast, Breast Cancer 12 (2005) 189–195.
[9] S.E. Kim, J.S. Koo, W.H. Jung, Immunophenotypes of glycogen rich clear cell carcinoma, Yonesi Med. J. 53 (6) (2012) 1142–1146.
[10] C. Markopoulos, D. Mantas, T. Philippidis, et al., Glycogen-rich clear cell carcinoma of the breast, World J. Surg. Oncol. 6 (2008) 44.
[11] F.A. Tavassoli, P. Devilee, World Health Organization Classification of Tumors. Tumors of the Breast and Female Genital Organs, 2nd ed, IARC Press, Lyon, France, 2003.

Her2-neu tests were not mentioned and the use of adjuvant chemotherapy details were not available [4–6]. In one of them, adjuvant radiotherapy was provided for 83% of the patients but no mention of chemotherapy [5]. Fisher et al. concluded that the adverse influence of GRCC on survival is more related to their histologic grade and the presence of nodal metastases [6]. This was similar to the conclusions mentioned in other reports with a prognosis that is similar to other breast carcinomas [3,7–10,12,13].
[12] Z. Varga, J. Zhao, C. Ohlschlegel, et al., Preferential HER-2/neu overexpression and/or amplification in aggressive histological subtypes of invasive breast cancer, Histopathology 44 (2004) 332–338.

[13] Y. Gürbüz, S.K. Özkara, Clear cell carcinoma of the breast with solid papillary pattern: a case report with immuno-histochemical profile, J. Clin. Pathol. 56 (2003) 552–554.

[14] R.A. Agha, A.J. Fowler, A. Saetta, I. Barai, S. Rajmohan, D.P. Orgill, the SCARE Group, The SCARE statement: consensus-based surgical case report guidelines, Int. J. Surg. 34 (2016) 180–186.