



RESEARCH ARTICLE

GLYCOGEN RICH CLEAR CELL CARCINOMA (GRCC): A RARE VARIANT OF BREAST CANCER

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Abstract

Glycogen rich clear cell carcinoma (GRCC) is a rare subtype of breast cancer. 150 cases have been reported in the literature, thus, making its prognosis unclear and vary from one literature to another. We reported a 56-year-old woman with a right breast nodule classified ACR 4. The micro biopsy made twice was negative. Benignity was therefore highly suspected. However, the tumorectomy confirmed to be a 3.2 cm glycogen-rich clear cell carcinoma without lymph node involvement. The patient was treated with chemotherapy followed by targeted-therapy (Trastuzumab /Herceptin). She is alive and free of disease for 29 months. The purpose of reporting this case is to increase the knowledge about this rare subtype of breast malignant neoplasm and chance of better survival.

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Introduction:-

Glycogen rich clear cell carcinoma (GRCC) is a rare breast cancer, make up 1.4–3% of all breast malignancies [1, 2]. This subtype is defined by the presence of more than 90% of the neoplastic cells with abundant clear cytoplasm containing glycogen [1]. The median age is 57 years (41-78 years). The first case was reported in 1981 by Hull et al [3].

This variant of breast cancer is one of an heterogeneous group of neoplasms, including signet-ring, secretory and lipid-rich carcinomas of the breast [3]. A great discussion arises regarding his prognosis. Usually, he tends to follow an aggressive clinical presentation [4]. However, our case is about a 56-year-old woman with a right breast nodule classified ACR 4. The micro biopsy made twice was negative. Tumorectomy showed a 3.2 cm glycogen-rich clear cell carcinoma without lymph node involvement.

Case Report:

A 56-year-old female patient presented with a right breast mass noticed 3 months back. She is a single and menopausal women. No family history of malignancy was documented. Physical examination revealed a 3.2 cm solitary hard mass located at the right breast, with no palpable axillary lymph nodes. There was no skin changes or nipple discharg. Mammogram and ultrasound showed a fibro-nodular mastosis of both breasts with a suspicious nodule between the 2 upper quadrants of the right breast. The Tru-cut needle biopsy made twice was negative for malignancy. So, the patient underwent simple tumorectomy. The pathological examination of the specimen showed a 3.2 cm cmfirmly well circumscribed lesion with unremarkable surrounding fibrofatty tissue. The histological examination showed a Grade 3 invasive clear cell (glycogen rich) carcinoma composed of clear cells with pleomorphic nuclei (Fig. 1) with extensive solid type clear cell ductal carcinoma in-situ (Fig. 2). Vascular

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invasion was noted. The tumor cells showed intense positivity for Periodic Acid Schiff (PAS), diastase sensitive (Fig.3) and Alcian Blue coloring negativity, confirming glycogen content in tumor cells. The immunohistochemistry profile showed many cells were positive for Her2 score 3 (Fig. 4), but negative for ER and PR.

Mastectomy with excision of axillary lymph nodes was performed, showing absence of tumor residue and no lymph nodes metastasis. The possibility of metastasis was excluded by clinical and radiological investigations. The final pathological stage was pT2 N0 M0.

The patient was treated with chemotherapy followed by targeted-therapy (Trastuzumab /Herceptin). She is alive and free of disease for 29 months.

Discussion:-

Glycogen rich clear cell carcinoma is defined by the World Health Organization (WHO) by the presence of more than 90% of neoplastic cells with abundant clear cytoplasm containing glycogen [5]. Most of patients have above 50 years of age. Breast mass is the commonest reported symptom [6]. Usually, the tumor size is between 1 to 6.5 cm; in some cases, the tumor size can reach 15 cm [7]. The tumor growth period ranges from 2 months to 2 years; in our case, this period is 3 months [8]. Radiologically, a calcified mass was the commonest finding that is well defined on breast ultrasound [6].

Histologically, the growth pattern is similar to an infiltrating ductal carcinoma. The tumor cells have optically clear cytoplasm containing glycogen but no mucin or lipids [9]. The Periodic Acid Schiff stain (PAS) is always positive confirming the glycogenic nature of the cytoplasm granules. These are not stained by diastase-periodic acid stain (d-PAS). The nuclear and cytoplasmic ratio is usually low. Nuclear membranes is irregularly thick [10]. As our case, intra-ductal clear cell component is usually present. Hayes et al. reported 21 GRCC cases; 8 of them were intraductal GRCC [4].

Glycogen rich carcinomas arise in many other organs, for example: endometrium, lung and kidney. The tumor is characterized by a clear appearance of the cytoplasm, indicates the presence of either glycogen or mucin [11]. Because of the clear appearance, many other tumors should be differentiated from this variant of breast cancer. Firstly, primary cancers of the breast like signet ring cell carcinoma and lipid rich carcinoma. Secondly, from benign neoplasms such as benign myoepithelioma and clear cell hidradenoma. Finally, metastatic clear cell carcinoma from other organs such as lung, ovary, kidney and adrenal gland. Clinical examination, radiological investigations and immunohistochemistry markers are often sufficient to confirm the diagnosis and exclude these possibilities. [12]

Mastectomy and axillary dissection is the surgical treatment performed in the majority of patients, more than half had metastatic tumor in the axillary lymph nodes [13]. However, our patient has negative axillary lymph nodes despite the large size of tumor.

There is a big discussion about the prognosis of this entity. Toikkanen and al, concluded that this variant is more aggressive than other common breast malignant neoplasm [14]. However, Baslaim MM and al, suggest that the prognosis of GRCC is similar to other breast carcinomas [15]. In our case, the prognosis looks good with 29 months of survival.

Conclusion:-

GRCC is a rare subtype of breast carcinomas, whose prognosis remains unclear due to its rarity and limited research. However, more studies are needed to understand its prognosis and effective management.

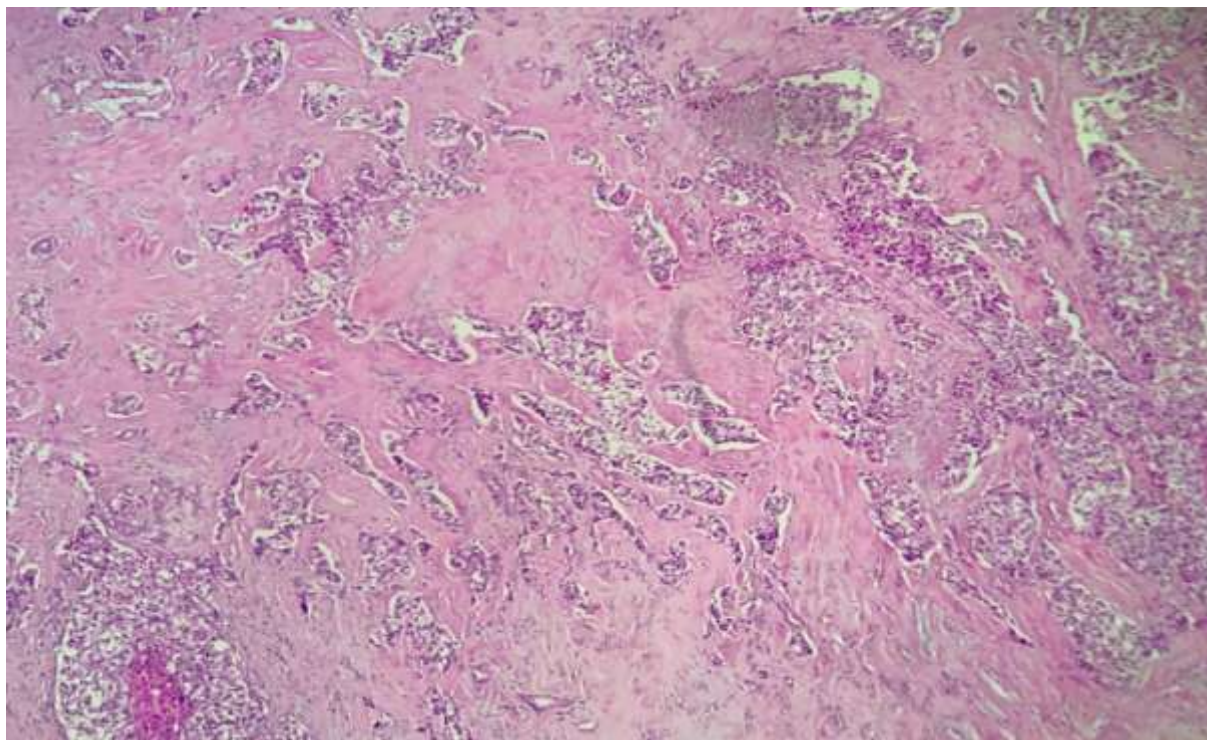


Figure 1:- Shows microscopic appearance of the tumor composed of large polygonal cells with pleomorphic nuclei and well defines nuclear membrane (H&E stain, X10).

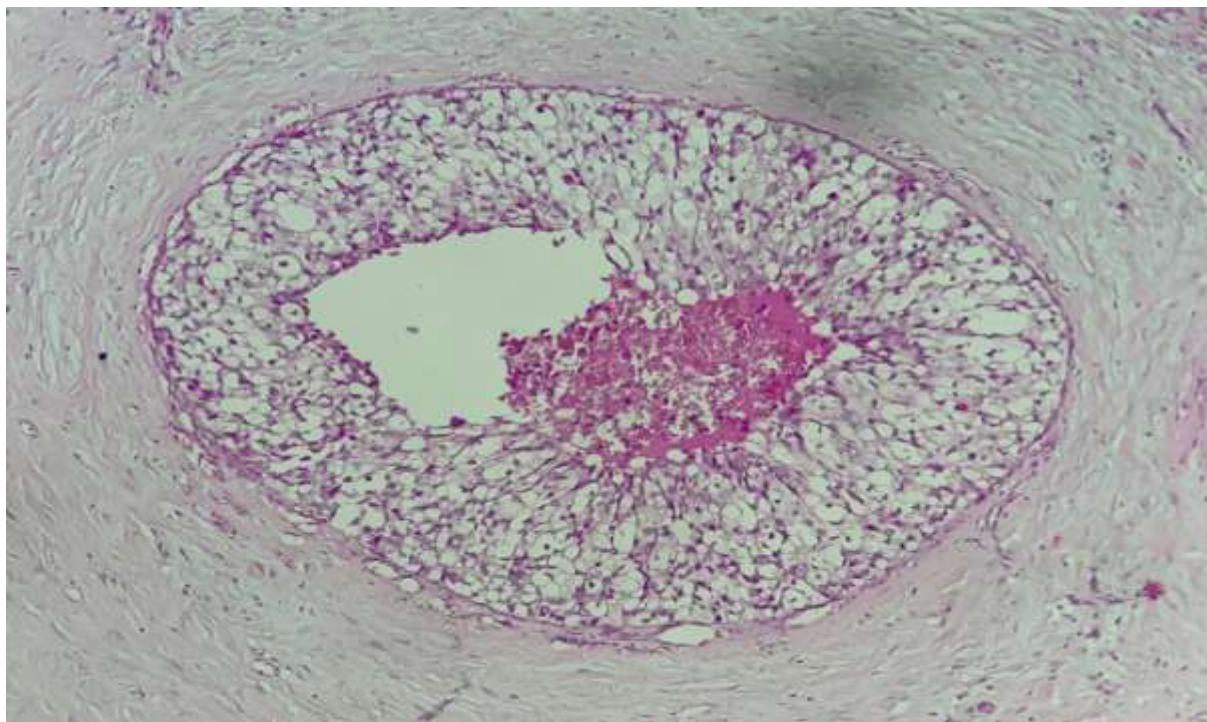


Figure 2:- DCIS of solid type, intermediate grade. Note the clear cytoplasm in the populated cells of the DCIS (H&E × 20).

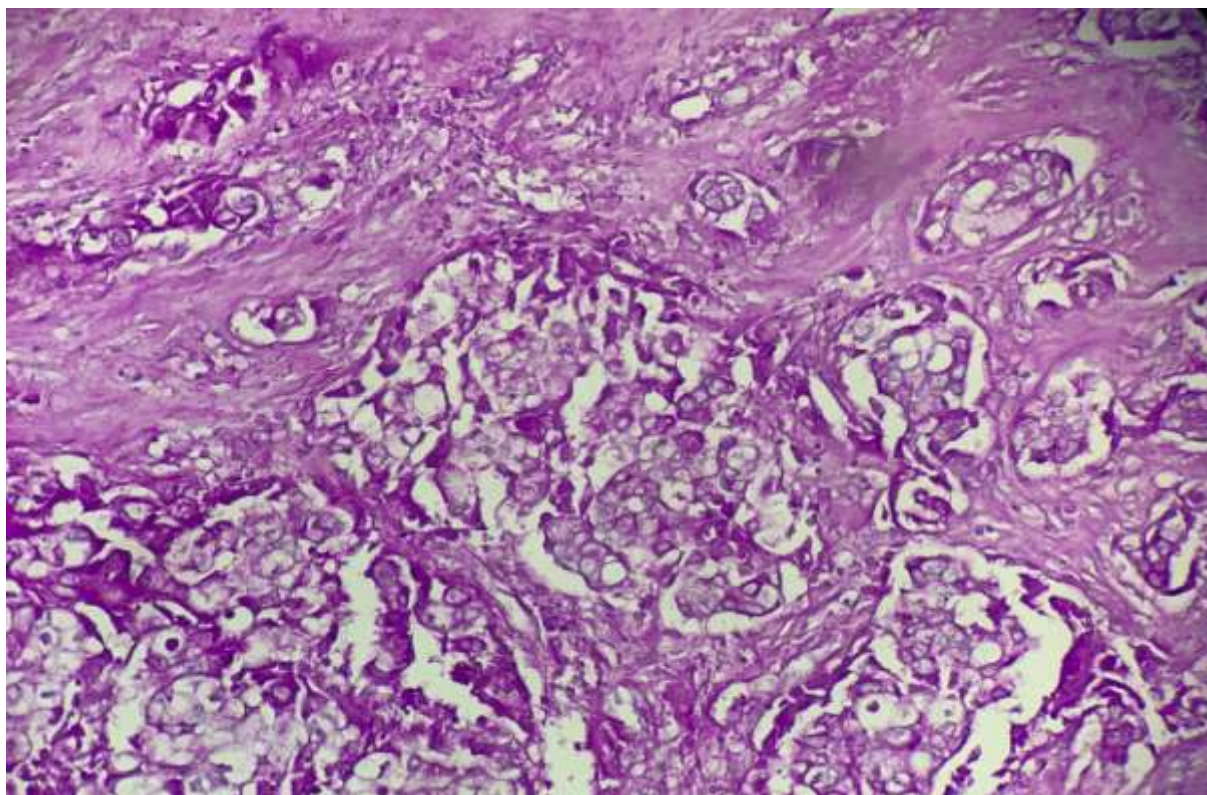


Figure 3:- Shows microscopic appearance of the tumor cells in GRCC of breast strongly positive for PAS stain (PAS stain, X40).

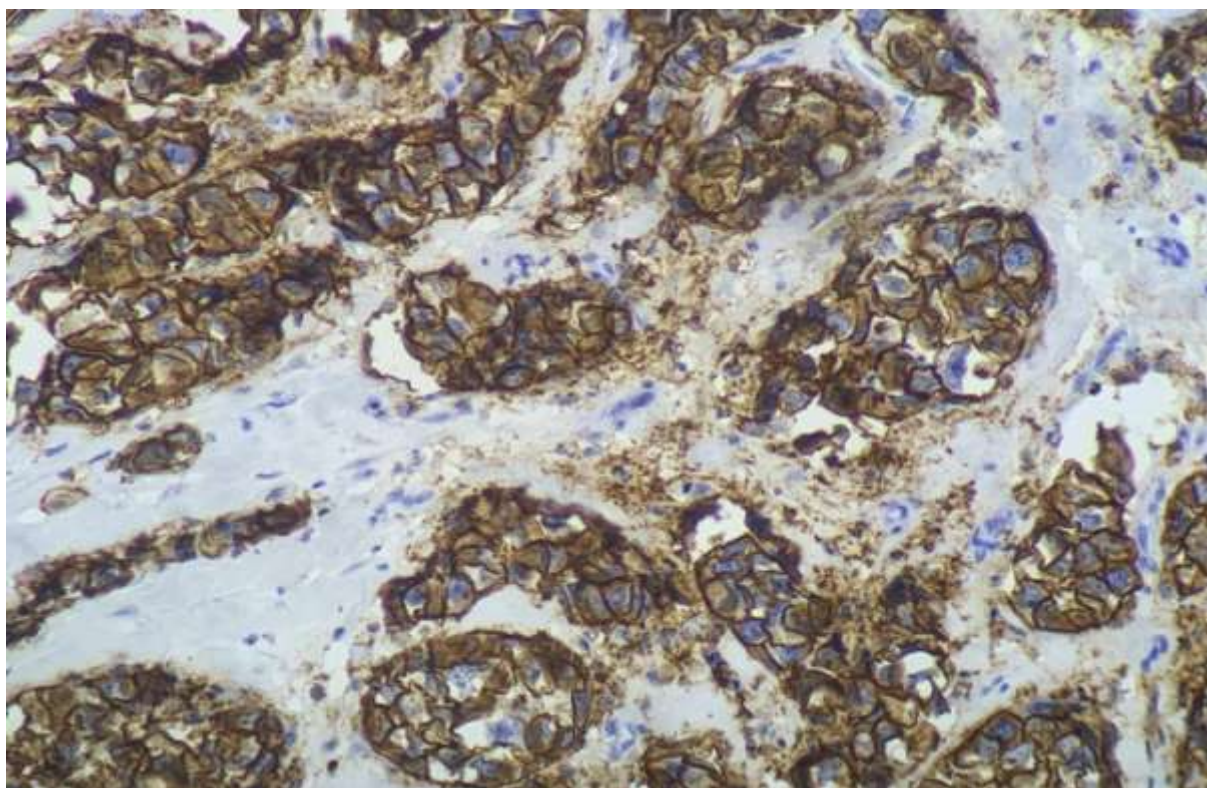


Figure 4:- Tumor cells show strong positivity for Her2/neu immunohistochemistry marker.

Reference:-

1. Yerushalmi R, Hayes MM, Gelmon KA. Breast carcinoma rare types: review of the literature. *Ann Oncol* 2009;20: 1763–70. <https://doi.org/10.1093/annonc/mdp245>.
2. Tavassoli FA. *Pathology of the Breast*. 2nd ed. Stamford: Appleton and Lange, 1999;527.
3. Hull MT, Priest JB, Broadie TA, Ransburg RC, McCarthy LJ. Glycogen-rich clear cell carcinoma of the breast: a light and electron microscopic study. *Cancer* 1981;48:2003–09. [Cross].
4. Hayes MMM, Seidman JD, Asthon MA: Glycogen rich clear cell carcinoma of the breast. A clinicopathologic study of 21 cases. *Am J Surg Pathol* 1995, 19:904-911.
5. F.A. Tavassoli, P. Devillee, *World Health Organization Classification of Tumors. Tumors of the Breast and Female Genital Organs*, 2nd ed., IARC Press, Lyon, France, 2003.
6. 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.
7. Martín-Martín B, Berná-Serna, et al: An unusual case of locally advanced glycogen-rich clear cell carcinoma of the breast. *Case Rep Oncol* 2011;4:452–457.
8. Salemis NS: Intraductal glycogen-rich clear cell carcinoma of the breast: a rare presentation and review of the literature. *Breast Care* 2012;7:319–321.
9. F.A. Tavassoli, *Infiltrating carcinoma: special types*, in: *Pathology of the Breast*, 2nd ed., Appleton & Lange, Norwalk Connecticut, 1992, pp. 390–393
10. S.E. Kim, J.S. Koo, W.H. Jung, Immunophenotypes of glycogen rich clear cell carcinoma, *Yonesi Med. J.* 53 (6) (2012) 1142–1146.
11. Markopoulos C, Mantas D, Philipidis T, Kouskos E, Antonopoulou Z, Hatzinikolaou M, et al. Glycogen-rich clear cell carcinoma of the breast. *World J Surg Oncol* 2008;6:44.
12. Alvarez MAD. Glycogen-rich clear cell carcinoma of breast: a case with an unusual macroscopic presentation and a good clinical outcome. *J Med Surg Pathol* 2016;2:139.
13. Rosen PP: Glycogen-rich carcinoma. *Rosen's Breast Pathology*. Lip-pincot-Raven 2001:557-559.
14. Toikkanen S, Juensuu H. Glycogen rich clear cell carcinoma of the breast: a clinicopathologic and flow cytometric study. *Hum Pathol* 1991;22:81–3.
15. Baslaim M, Junainah E, Ahmed HH, Semilan AF, Al-Ghamdi AO, Rahimuddin NO, et al. Glycogen Rich Clear Cell Carcinoma (GRCC) of the breast may not have a poor prognosis. *Int J Surg Case Rep* 2017;33:92–6.