

This is an Open Access article licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License (www.karger.com/OA-license), applicable to the online version of the article only. Distribution for non-commercial purposes only.

An Unusual Case of Locally Advanced Glycogen-Rich Clear Cell Carcinoma of the Breast

Beatriz Martín-Martín^a Juan D. Berná-Serna^a
Pilar Sánchez-Henarejos^b María J. López-Poveda^c
Juan D. Berná-Mestre^a José R. Rodríguez-García^d

Departments of ^aRadiology, ^bOncology, ^cPathology and ^dObstetrics and Gynecology, Virgen de la Arrixaca University Hospital, Murcia, Spain

Key Words

Glycogen-rich clear cell carcinoma · Locally advanced breast cancer · Mammography · Ultrasonography

Abstract

Glycogen-rich clear cell (GRCC) is a rare subtype of breast carcinoma characterized by carcinoma cells containing an optically clear cytoplasm and intracytoplasmic glycogen. We present the case of a 55-year-old woman with a palpable mass in the right breast and clinical signs of locally advanced breast cancer (LABC). The diagnosis of GRCC carcinoma was based on certain histopathological characteristics of the tumor and immunohistochemical analysis. To our knowledge, this is the first case of GRCC LABC with intratumoral calcifications. There is no evidence of recurrence or metastatic disease after 14 months' follow-up.

Introduction

Glycogen-rich clear cell (GRCC) breast carcinoma is a rare neoplasm of the breast, first described by Hull et al. [1] in 1981, and characterized by carcinoma cells containing an optically clear cytoplasm and intracytoplasmic glycogen [2–10].

We present a case of GRCC locally advanced breast cancer (LABC) with intratumoral calcifications. To our knowledge, such a presentation of GRCC breast carcinoma has not been reported previously.

Case Report

A 55-year-old female patient presented with a 4-month history of a mass in the right breast. Physical examination revealed erythema, hyperemia and tenderness to the touch of the right breast. A palpable mass, hard in consistency and measuring about 15 cm, was present in the right superior and inferior lateral quadrants. Mammography showed a round, high-density mass with almost regular but partially irregular margins, measuring approximately 10 cm with calcifications suspicious of malignancy, and skin thickening (fig. 1). Ultrasound examination of the right breast showed a solid, heterogeneous mass.

Ultrasound-guided core needle biopsy (CNB) of the mass was performed. Microscopic examination of the CNB showed extensive infiltration by a malignant epithelial-type neoplasm, consisting of solid nidi of atypical cells with ample clear cytoplasm, which had distinct and well-defined borders, was optically empty and 'vegetaloid' in appearance (fig. 2), interspersed with small areas of respected mammary parenchyma and extensive areas of necrosis. The nuclei were small and round with hyperchromasia and moderate pleomorphism, and showed a moderate mitotic index. No areas of carcinoma in situ were observed.

On histochemical examination, the neoplastic cells were intensely positive for periodic acid-Schiff (PAS) staining (fig. 3), cytokeratin AE1/AE3, cytokeratin 7 and E-cadherin, and negative for PAS diastase, HER2, and estrogen and progesterone receptors. A total absence of basal cells was shown by staining with P-63. The histopathological diagnosis was GRCC-infiltrating ductal carcinoma.

The patient received neoadjuvant therapy consisting of epirubicin 75 mg/m² and docetaxel 75 mg/m² every 3 weeks for 3 cycles. The clinical response to the chemotherapy treatment was partial. Moreover, the patient presented with a skin ulcer in the area corresponding to the tumor. A modified radical mastectomy with axillary lymph node dissection was performed.

Macroscopic examination of the modified radical mastectomy specimen showed a skin ulcer, below which was a necrotic-looking tumor measuring 7 × 7 × 4 cm. Microscopic examination showed a neoplasm made up of solid nidi of atypical cells with clear cytoplasm and the same histopathological characteristics as described for the CNB. Inside the neoplasm we observed extensive areas of necrosis, as well as fibrosis, acute and chronic inflammatory reactions with the presence of spumous histiocytes, multinucleate giant cells and multiple foci of calcifications located in the midst of the necrotic areas (fig. 4). The pathological diagnosis of GRCC carcinoma, established by CNB, was confirmed. The pathological tumor response after treatment (Miller and Payne system) [11] was stage G2 with a discrete reduction in infiltrating tumor cellularity of less than 30% of the tumor mass. Twelve of the axillary lymph nodes removed were histologically tumor-free. Pathology revealed a T4N0M0 GRCC carcinoma.

The patient was later submitted for chemotherapy (3 cycles of 75 mg/m² epirubicin and docetaxel) followed by radiotherapy of the chest wall and lymph nodes within the axillary and supraclavicular regions (50 Gy). Diagnostic work-up (bone scintigraphy, thoracic, abdominal and pelvic CT scans) revealed no local or distant metastases. Fourteen months after surgery, the patient remains asymptomatic and disease-free.

Discussion

GRCC breast carcinoma is a rare neoplasm of the breast, with an incidence of between 1.4 and 3% of all breast cancers [2, 4, 7]. This tumor has particular morphological characteristics that distinguish it from other breast tumors, although it does share other characteristics with clear cell carcinoma of the lung, endometrium, cervix, ovary, kidneys and salivary glands [5]. The cells of GRCC carcinoma contain clear polygonal cytoplasm, round or oval hyperchromatic nuclei and prominent nucleoli. The cytoplasm contains abundant granules of hydrosoluble glycogen, which can be extracted during processing of the samples, giving it an ample, vacuolated

appearance. Furthermore, it contains PAS-positive material with a weak reaction to diastase [2, 3].

Fewer than 100 instances of GRCC carcinoma of the breast have been described since the first case was reported in 1981 [1–10]. Patient age varies from 35 to 78 years, and tumor size ranges from 2 to 5 cm, with the largest lesion found to be 10 cm on clinical examination [5, 9]. In our case, the size of the tumor on physical examination was 15 cm. Furthermore, clinical signs of LABC have been observed previously [12]. Therefore, the case presented here is the most voluminous GRCC carcinoma reported in the literature. Intratumoral calcifications seen on mammography were also observed in the present case, which is extremely rare.

The differential diagnosis includes breast carcinomas with ample cytoplasm such as lipid-rich clear cell carcinoma, signet ring cell carcinoma, other secretory subtypes of ductal or lobular carcinoma and metastatic clear cell renal carcinoma [5, 6, 10]. There are various histological patterns of GRCC carcinoma (well-differentiated tubular, papillary and solid), which may or may not be associated with an intraductal carcinoma component [6–9]. Hormone-receptor analysis showed that approximately 50% of tumors were estrogen receptor-positive, but all the lesions studied were negative for progesterone receptors [1, 5]. In our patient, both estrogen and progesterone receptors were negative.

As far as treatment is concerned, mastectomy and axillary dissection are usually performed, and more than 50% of patients studied had a metastatic tumor in the axillary lymph nodes [1, 4, 5, 9]. However, our patient received a combined treatment of chemotherapy, surgery and radiation therapy, due to the characteristics of the tumor (LABC). The prognosis of this type of breast cancer is still a subject of controversy, although GRCC breast carcinoma generally tends to follow an aggressive clinical course [2, 3, 5, 7].

In conclusion, to our knowledge, this is the first case of GRCC LABC with intratumoral calcifications and should be added to the differential diagnosis of breast carcinomas. Our T4N0M0-staged patient is disease-free 14 months after surgery.

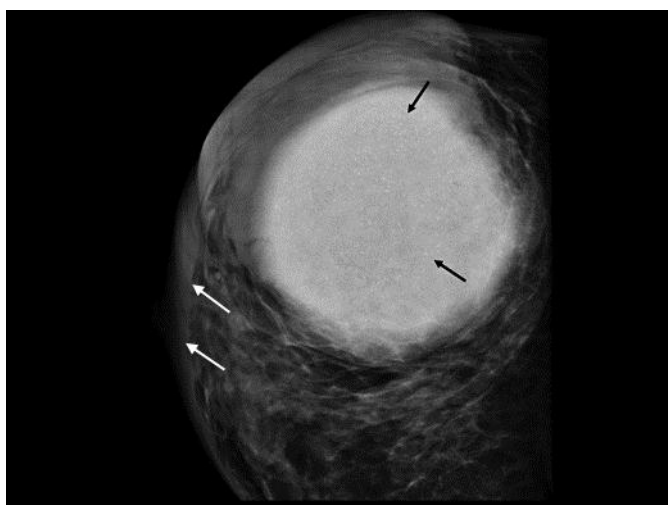


Fig. 1. Craniocaudal mammogram showing a mass with calcifications (black arrows) and skin thickening (white arrows).

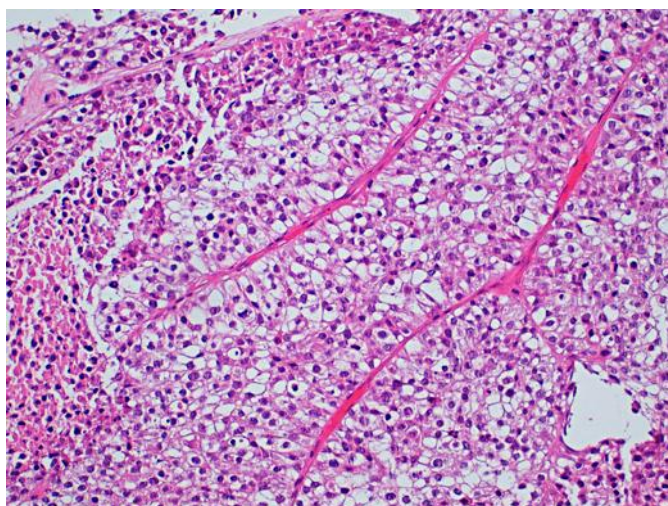


Fig. 2. Photomicrograph of the tumor (H&E; ×200). The tumor cells show ample clear cytoplasm with well-defined limits and a ‘vegetaloid’ appearance.

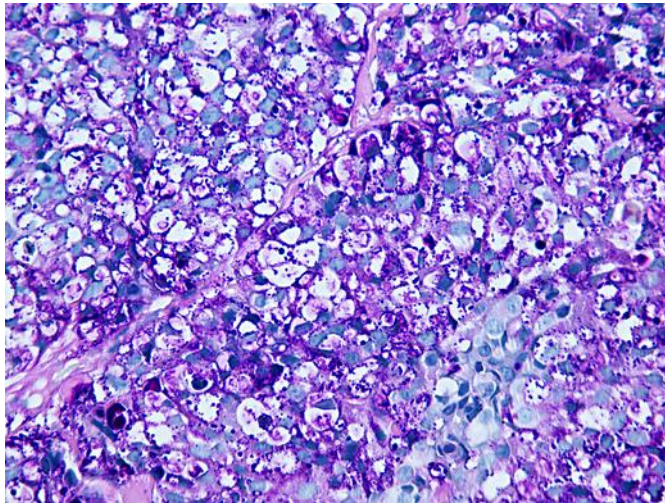


Fig. 3. Positive (PAS; $\times 400$). PAS reactivity is strong.

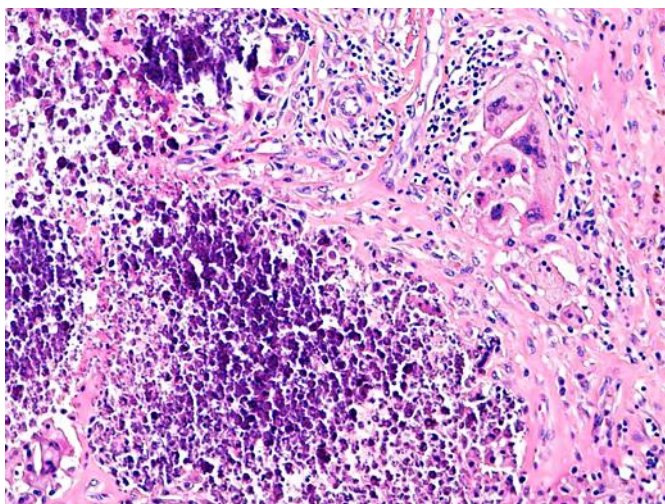


Fig. 4. Photomicrograph of the tumor (H&E; $\times 100$). Abundant calcifications and inflammatory infiltrate with multinucleate giant cells in the midst of the tumor necrosis.

References

- 1 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;48:2003–2009.
- 2 Fisher ER, Tavares J, Bulatao IS, Sass R, Fisher B: Glycogen-rich, clear cell breast cancer: with comments concerning other clear cell variants. *Hum Pathol* 1985;16:1085–1090.
- 3 Hull MT, Warfel KA: Glycogen-rich clear cell carcinomas of the breast. A clinicopathologic and ultrastructural study. *Am J Surg Pathol* 1986;10:553–559.
- 4 Toikkanen S, Juensuu H: Glycogen rich clear cell carcinoma of the breast: a clinicopathologic and flow cytometric study. *Hum Pathol* 1991;22:81–83.

- 5 Hayes MM, Seidman JD, Ashton MA: Glycogen-rich clear cell carcinoma of the breast: a clinicopathologic study of 21 cases. *Am J Surg Pathol* 1995;19:904–911.
- 6 Gürbüz Y, Özkara SK: Clear cell carcinoma of the breast with solid papillary pattern: a case report with immunohistochemical profile. *J Clin Pathol* 2003;56:552–554.
- 7 Kuroda H, Sakamoto G, Ohnisi K, Itoyama S: Clinical and pathological features of glycogen-rich clear cell carcinoma of the breast. *Breast Cancer* 2005;12:189–195.
- 8 Markopoulos C, Mantas D, Philipidis T, Kouskos E, Antonopoulou Z, Hatzinikolaou M, Gogas H: Glycogen-rich clear cell carcinoma of the breast. *World J Surg Oncol* 2008;6:44.
- 9 Rosen PP: Glycogen-rich carcinoma; in Rosen PP (ed): *Rosen's Breast Pathology*, ed 3. Philadelphia, Lippincott Williams and Wilkins, 2008, pp 613–615.
- 10 Thondavadi SR, Krishnamurthy J, Gubbanna VM: A case report of glycogen-rich clear cell carcinoma of breast. *Indian J Pathol Microbiol* 2010;53:374–375.
- 11 Ogston KN, Miller ID, Payne S, Hutcheon AW, Sarkar TK, Smith I, Schofield A, Heys SD: A new histological grading system to assess response of breast cancers to primary chemotherapy: prognostic significance and survival. *Breast* 2003;12:320–327.
- 12 Shenkier T, Weir L, Levine M, Olivetto I, Whelan T, Reyno L: Clinical practice guidelines for the care and treatment of breast cancer: 15. Treatment for women with stage III or locally advanced breast cancer. *CMAJ* 2004;170:983–994.