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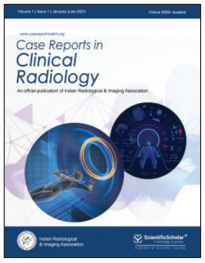

Case Report

Spontaneous regression of biologically aggressive breast carcinoma: A case report

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ABSTRACT

The spontaneous regression of cancer is the partial or complete remission of a tumor without treatment, and this has been linked to trauma and infection. The present case details the rare spontaneous regression of a triple negative Grade III ductal carcinoma in the breast. The findings suggest that in our case, this may have been triggered by biopsy and marker clip deployment, and it highlights the importance of being aware of this unusual occurrence so timely diagnosis can be made without causing undue anxiety in patients.

Keywords: Breast cancer, Spontaneous regression, Immunogenic cell death, Case report

INTRODUCTION

The spontaneous regression of cancer is the partial or complete remission of a tumour without treatment, and this has been linked to trauma and infection. The present case details the rare spontaneous regression of a triple negative grade III ductal carcinoma in the breast.

CASE REPORT

A 69-year-old female presented with a 9-day history of a hard lump in the right breast. Physical examination revealed an indeterminate 1.5 cm irregular mass in the right upper inner quadrant of the breast with no axillary lymphadenopathy. She had bilateral salpingo-oopherectomy for a strong family history of ovarian cancer in her mother and maternal grand-mother. No food allergies or intolerances.

A mammogram was performed and compared with a mammogram performed 12 months back, which revealed a new dense mass in the 12 o'clock sector of the right breast (measuring 14 × 12 mm) [Figure 1a and b]. The mass appeared rounded with a slightly irregular margin. The mammographic breast density was BIRADS-B. There were no other significant findings.
Ultrasound revealed a rounded and spiculated hypoechoic mass at the 12 o'clock position (measuring 12 × 10 mm) [Figure 1c and d]. The overall appearances were suspicious for malignancy. No abnormal axillary nodes were identified on the ipsilateral side.

A needle core biopsy was taken using a 14G Trucut device and a T3 hydromark clip was deployed into good position. Histology revealed a triple negative (estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor receptor 2 negative) invasive ductal

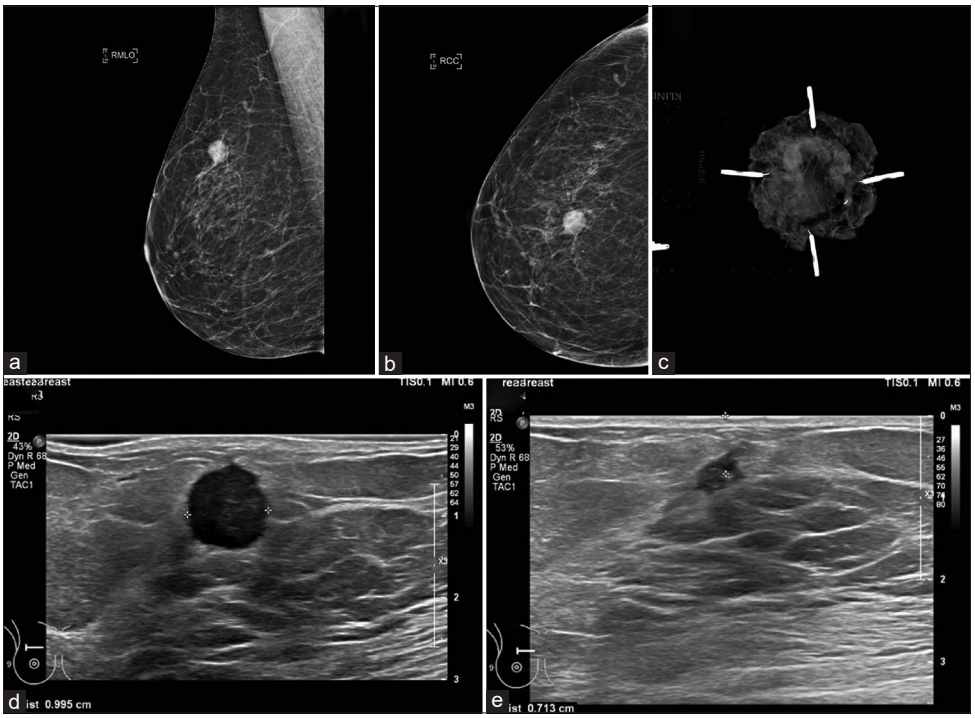

Figure 1: Preoperative imaging. (a) Right mediolateral oblique mammogram with a dense, ill-defined mass at 12'o clock. (b) Right craniocaudal mammogram with a dense, ill-defined mass at 12 o'clock. (c) Specimen radiograph demonstrating the marker clip which was situated within the lesion at the time of biopsy. (d) Ultrasound of the right breast with an irregular hypoechoic mass measuring 10 mm on the day of diagnosis. (e) Ultrasound of the right breast demonstrating the same lesion a month later, on the day of surgery, measuring 5 mm without preoperative chemotherapy or endocrine treatment.

carcinoma Grade III. A granulomatous reaction to the tumor was noted in the core biopsy specimen. No lymphovascular space invasion was noted.

Following the results of imaging and biopsy, the patient was recommended a wide local excision and sentinel lymph node biopsy by the breast multidisciplinary team. A month after initial diagnosis, on the morning of surgery, ultrasound scans to localize the tumor before surgery showed that the size of the tumor had reduced to 5 × 5 mm [Figure 1e]. The patient also reported being unable to feel the lump a few days after the core biopsy. A granulomatous reaction to the tumour was noted in the core biopsy specimen [Figure 2a-d]. No lymphovascular space invasion was noted.

Under ultrasound guidance, a skin mark was placed over the site of residual cancer. At surgery, an incision was placed over this skin mark. Wide local excision was achieved, taking tissue down to the fascia. Specimen x-ray obtained in theater revealed the marker clip within an apparent opacity which was thought to represent the residual carcinoma.

Initial post-operative histology revealed marker clip associated with a brisk inflammatory response [Figure 3a-c]but no residual neoplasia. Further sections of the marker clip site were examined, which revealed a single duct containing atypical epithelial proliferation, likely to be inflammatory. Immunohistochemistry (IHC) of the marker clip site was then undertaken. Cytokeratin staining highlighted a population of atypical epithelial cells within the dense inflammatory cell infiltrate [Figure 3d], interpreted to represent degenerate neoplastic cells measuring 3.8 mm.

Whilst thorough histological analysis was being carried out, the patient underwent a targeted ultrasound of the right breast to ensure there was no residual lesion visible. Based on the final histology work up including IHC, the residual lesion seen on ultrasound on the day of surgery was believed to have been removed.

The patient was recommended adjuvant radiotherapy to the right breast and discussion for adjuvant chemotherapy. However, she decided to get a second opinion, genetic testing, and genotype analysis of the core biopsy and excision samples to ensure that both samples belonged to her. The analysis confirmed that this was the case.

Ultimately, the patient decided to undergo bilateral mastectomy due to her strong family history and her BRCA gene mutation.

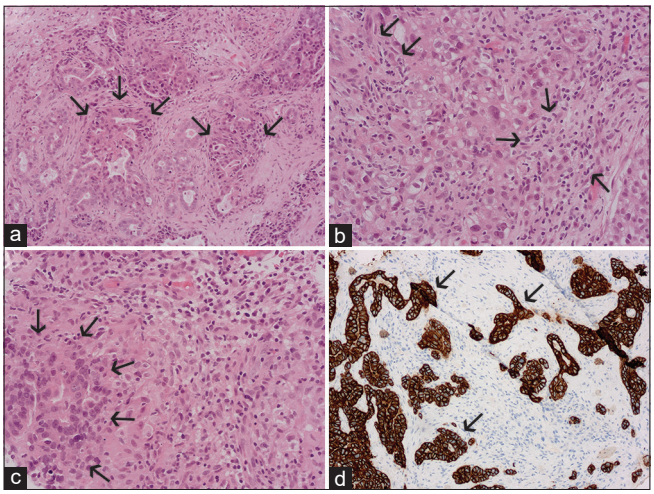

Figure 2: Preoperative core biopsy histology. (a) Core biopsy of grade III carcinoma in situ. (b) Inflammatory cell infiltrate associated with the cancer. (c) Cancer with granulomatous inflammatory cell infiltrate. (d) Cytokeratin immunostain demonstrating the brown malignant epithelial cells.

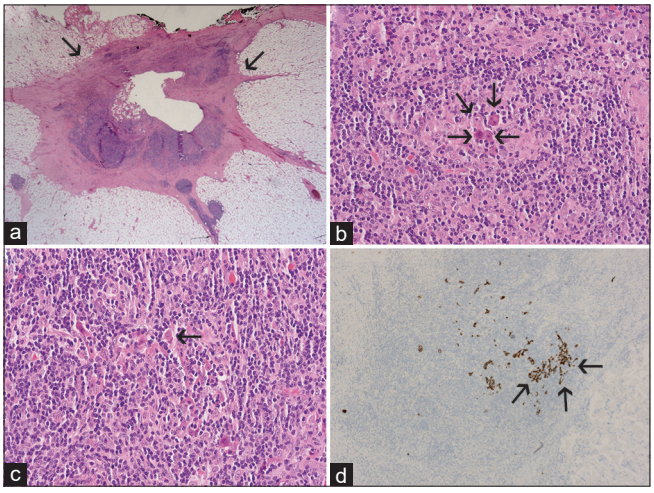

Figure 3: Postoperative histology. (a) Site of radiological abnormality containing marker clip and inflammatory cell infiltrate. (b) High power of inflammatory cell infiltrate with four neoplastic cells with denser pink cytoplasm centrally. (c) Different field of B. (d) Cytokeratin immunostain demonstrating dispersed brown malignant epithelial cells in the inflammatory cell infiltrate.

DISCUSSION

Spontaneous regression of cancer is possible, but it remains a rare occurrence. There have been case reports of its occurrence in breast cancer, but most have been linked to choriocarcinoma, melanoma, neuroblastoma, and renal cell carcinoma.[1] Our case adds to the existing small literature on this subject.

The mechanisms of spontaneous regression are not well understood, but it has been linked to trauma and infection. Possible causes include tumor microenvironment disruption, apoptotic or non-apoptotic cell death, and withdrawal of a carcinogenic agent.[2]

Infections stimulate the immune response to recruit immune cells and cytokines, which may play a role in the spontaneous regression of cancer.[2] However, not all cases have been preceded by a viral or bacterial infection.

The case above details the spontaneous regression of a Grade III ductal carcinoma in-situ following a biopsy and marker clip placement. As tumor cells require rich blood supply to proliferate, the disruption of tumor by the needle core biopsy may have impaired its blood supply and induced spontaneous regression.[2] Pre- and post-operative histology for the present case reported a granulomatous reaction and an inflammatory response, which suggests the primary mechanism to be an immune-mediated response, resulting in size discrepancy between pre-operative imaging and post-surgical excision size. Interleukin-4, a cytokine produced by mast cells and T lymphocytes, may induce apoptosis and inhibit the growth of breast cancer cells.[3]

In 2020, there was a case report on the recurrence of an estrogen receptor positive breast cancer in a male patient following temporary spontaneous regression.[4] Hormones and endocrine factors have been cited in the literature as a possible cause of spontaneous regression, and with the well-known influence of hormones in breast cancer, it is possible that the estrogen receptor status of the breast cancer may have an influence on the frequency of spontaneous regression. The American Journal of Clinical Oncology published a review in 1998, which demonstrated a higher prevalence of relapse in estrogen receptor positive breast cancer cases 8 years after mastectomy, as compared to estrogen receptor negative cases.[5,6] It was postulated to be the result of antineoplastic processes – the spontaneous regression of subclinical microscopic recurrences in estrogen receptor positive cases led to an 8 year interval before the first recurrence.[5] The expression of hormone receptors in patients with estrogen receptor positive breast cancer increases the frequency of apoptosis.[5]

The literature has shown that the exposure to radiation, such as high-intensity focused ultrasound, may also activate the immune cells and induce tumor remission, possibly due to an unusual sensitivity of the tumor.[7] For the present case, it is possible that the exposure to radiation may have induced a spontaneous regression.

CONCLUSION

The findings suggest that in our case, spontaneous regression may have been triggered by biopsy and marker clip deployment, and it highlights the importance of being aware of this unusual occurrence so timely diagnosis can be made without causing undue anxiety in patients.

TEACHING POINTS

1. Being aware of this rare phenomenon will lead to a more informed conversation with the patient, reducing anxiety, preventing delays in management, and protection of resources
2. The reduction in the size of the tumor reported by the patient and on pre-operative localization ultrasound and the significance of the granulomatous reaction reported on the original core biopsy should lead to more intense histological analysis including use of immunohistochemistry.

MCQS

1. What percentage of breast cancer detected by screening in the UK is a ductal carcinoma *in situ*?
   a. 45%
   b. 5%
   c. 20%
   d. 60%

Answer Key: c

2. Which of the following is true regarding triple-receptor negative breast cancers (TNBC)?
   a. TNBCs have the highest rate of recurrence within the first 5 years after diagnosis
   b. The incidence of late recurrence after 5 years in TNBC is less when compared to hormone receptor positive cancers
   c. The commonest site of distant recurrence is the lungs/pleura
   d. All of the above

Answer Key: d

3. Which of the following statements is false regarding the spontaneous regression of cancer?
   a. Spontaneous regression of renal cell carcinoma is rare
   b. Exposure to radiation may induce the remission of cancer
   c. Non-apoptotic cell death is a possible mechanism of spontaneous regression
   d. Spontaneous regression is a common phenomenon in estrogen receptor positive breast cancer

Answer Key: d

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Takayama S, Satomi K, Yoshida M, Watase C, Murata T, Shiino S, *et al*. Spontaneous regression of occult breast cancer with axillary lymph node metastasis: A case report. Int J Surg Case Rep 2019;63:75-9.
2. Radha G, Lopus M. The spontaneous remission of cancer: Current insights and therapeutic significance. Transl Oncol 2021;14:101166.
3. Gooch JL, Lee AV, Yea DY. Interleukin 4 inhibits growth and induces apoptosis in human breast cancer cells. Cancer Res 1998;58:4199-205.
4. Katano K, Yoshimitsu Y, Kyuno T, Haba Y, Maeda T, Kitamura S. Temporary spontaneous regression of male breast cancer: A case report. Surg Case Rep 2020;6:311.
5. Ricci SB, Cerchiari U. Spontaneous regression of malignant tumors: Importance of the immune system and other factors (review). Oncol Lett 2010;1:941-5.
6. Ricci SB, Coradini D, Di Fronzo G, Bartoli C, Villa S. Estrogen-receptor status of patients who underwent mastectomy for breast cancer with a disease-free interval of not less than 8 years. Am J Clin Oncol 1998;21:250-2.
7. Everson TC, Cole WH. Spontaneous regression of cancer: Preliminary report. Ann Surg 1956;144:366-83.

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