Spontaneous regression of breast carcinoma: A radio-pathological case report and review of the literature

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Spontaneous regression (SR) is defined as complete or partial disappearance of a proven malignant tumor without adequate medical treatment. Although there have been reports on SR of breast cancers, this phenomenon remains rare. We report a case of SR of breast cancer in a 62-year-old woman who presented to our hospital with a few months history of a painless breast lump. Initial radiological investigations reveal a suspicious mass in the left upper outer quadrant. Histopathology confirms the presence of invasive cancer. The patient initially refused any surgical or medical interventional and defaulted follow-up. The patient presented again after four months with consent for surgical treatment. Repeat ultrasound just before the hook wire localization procedure demonstrated the absence of tumor in the region of interest. The subsequent repeat mammogram and MRI also demonstrated complete regression of breast cancer. MRI however, does reveal a suspicious left axillary lymph node, which was also deemed suspicious on PET-CT. In view of these findings, the patient was counsel for surgery. The exact mechanism of SR of cancer remains unclear in our patient. We are unable to identify the exact mechanism triggering and influencing the SR in our patient. Our hypotheses include substance within the herbal remedies or a carcinoma-directed immune response triggered by the biopsy.

Received on: 07 Aug 2020
Revised on: 18 Sep 2020
Accepted on: 05 Oct 2020

Keywords:
Breast cancer, magnetic resonance imaging (MRI), mammogram (MMG), spontaneous regression, ultrasound (US)

INTRODUCTION

Spontaneous regression (SR) of tumor is rare. SR is defined as complete or partial disappearance of a proven malignant tumor without adequate medical treatment (Cole, 1976b). Although there have been reported cases of SR of malignant tumors, this phenomenon remains rare. Its incidence is less than 1 in 100000 cases (Cole, 1976a, 1981).

SR of breast cancer is even rarer. We report a case of spontaneous regression of invasive breast carci-
A 62-year-old woman, who was previously fit and well, presented with few months’ history of a painless lump in the left breast. She was otherwise asymptomatic. There was no family history of breast carcinoma or other malignancy. She had 3 children and was not on hormone replacement therapy. Physical examination revealed a hard mass of 2 cm in upper outer quadrant of the left breast. The right breast and both axillary regions were normal.

Mammogram (MMG) and breast ultrasound (US) (Figure 1 A & B) were performed at the initial presentation. MMG demonstrated the presence of an irregular high-density mass in the left upper quadrant. Corresponding US demonstrated a suspicious irregular hypoechoic mass with posterior shadowing at the 2 o’clock position, corresponding to the clinically palpable lump. The mass was classified as BIRADS 4c, and US-guided core biopsy was performed for the patients.

Histopathology analysis of the US-guided core biopsy specimens confirmed the diagnosis of hormone receptor-negative invasive ductal carcinoma of no special type (NST) (Figure 2), and the patient was advised for surgery. However, the patient refused any surgical or medical intervention and defaulted follow-up.

Approximately 4 months after the initial diagnosis, the patient presented again to the breast clinic, now with consent for the treatment of her cancer. On repeat, US before hook wire localization procedure, the previously seen suspicious mass in the region of interest at left 2 o’clock position was no longer visualized. (Figure 1D). Patient admitted to consuming some non-specific plant-based herbal remedies during her period of absence.

Repeat MMG (Figure 1C) and breast MRI (Figure 3) also confirm the absence/complete regression of the previously seen carcinoma. MRI, however, revealed a suspicious enlarged left axillary lymph node, which also demonstrated pathological hypermetabolism on PET-CT. In view of these findings, the patient was counsel for mastectomy and axillary dissection, which were performed approximately 6 months after the initial presentation.

The final histopathology analysis of the mastectomy and axillary nodes specimens’ demonstrated fibrocystic change with no residual malignancy (Figure 4). No malignancy was noted in the 13 dissected axillary nodes.

The patient was discharged home 3-days post-surgery and remained well at 6 months follow-up in the surgical clinic.

DISCUSSION

Despite the high detection rate of breast cancer, complete SR of breast cancer is extremely rare. Everson & Cole (Cole, 1976b) defined SR as partial or complete, temporary or permanent disappearance of tumor in the absence of specific therapy. There have been only a handful of reported cases of SR of breast cancer available in the literature. Everson & Cole (Cole, 1976b) reported the largest series of SR of tumors, 22 of which are breast in origin. However, in this large series, no distinction between benign or malignant breast tumors was made. Other reported cases and series of SR of breast cancers are as summarized in Table 1. Some of these reported cases also attempted to determine the cause for the SR.

The various mechanisms that have been postulated include immunological, endocrine, metabolic, surgical, postoperative events, elimination of a carcinogen or an antigen, inhibition of angiogenesis, tumor necrosis, oncogene, growth factor, or cytokine changes, genetic and epigenetic factors, induction of benign differentiation and apoptosis. Other unconventional causes include psychological factors (Challis and Stam, 1990; Bramhall et al., 2014). 71 out of 176 cases of SR of cancer reported by Cole (Cole, 1976a, 1981) were associated with peri-operative events. The biopsy or surgical procedure performed on the primary tumor could have induced an anti-tumor immunological response involving infiltration of lymphocytes into the tumor and recognition of specific tumor antigens (Cole, 1976a, 1981). In our patient, the US-guided biopsy that she had may have triggered an anti-tumor immune response, thus causing the SR.

Many cancer patients also use complimentary or alternative medicine along with conventional treatment (Burstein et al., 1999; Cassileth and Deng, 2004). Complementary medicine includes a variety of behavioral techniques and clinical approaches, including the use of herbal remedies (Burstein et al., 1999). There are numerous plant/herbal species that are utilized as anticancer agents by various traditions around the world (Jaradat et al., 2016). Our patient admitted to consuming some herbal remedies for her cancer. It is reported that the anti-cancer properties of these herbs are likely due to the presence of phenols and polyphenols. Other compounds within the plants with possible anti-cancer properties include flavonoids, tannins, stilbenes, diarylheptanoids, coumarins, phenolic acids, quinones and lignans (Shah et al., 2013; Khazir et al., 2014).
Figure 1: MLO MMG views (A&C) and US (B&C) of the left breast demonstrated presence of a suspicious lesion (white arrow) which was no longer seen 4 months later.

Figure 2: (A&B) HPE showing malignant cells with mitosis (yellow arrow). (C) ER- in tumor (yellow arrow) but (+) in normal ducts (red arrow) (D) CerbB-2 over-expression 3+

Figure 3: Breast MRI demonstrated absence of any suspicious lesion in both breasts. An enlarged left axillary lymph node (white arrow) with loss of fatty hilum was seen.
Table 1: Review of reported series and cases of SR of breast cancer and their possible mechanisms

| Author          | No of cases | Diagnosis                  | Possible Mechanism                                         |
|-----------------|-------------|----------------------------|-----------------------------------------------------------|
| Dussan et al.   | 1           | Invasive Ductal Carcinoma   | T-cell mediated immune response                            |
| Maillet et al.  | 2           | Invasive Ductal Carcinoma   | Carcinoma-directed immune response triggered by the biopsy |
| Iihara et al.   | 1           | Diffuse large B-cell Lymphoma |                                                           |
| Asano et al.    | 1           | Invasive Ductal Carcinoma   |                                                           |
| Oya et al.      | 1           | Diffuse large B-cell Lymphoma |                                                           |
| Tanaka et al.   | 1           | Angiosarcoma                |                                                           |
| Tokunaga        | 1           | Invasive Ductal Carcinoma   | T-cell mediated immune response                            |

Figure 4: (A-D) H&E x 40 showing fibrocystic changes surrounded by a mild condensed lymphocytic infiltrate and patchy haemorrhage. No residual malignancy.

2014). Unfortunately, the safety and efficacy of many of these remedies have not been supported by scientific evidence. This may be relevant to our case as our patient also admitted to consuming plant-based herbal remedies to cure her cancer during her default period.

CONCLUSION

Like the majority of the reported cases, the exact mechanism of SR of cancer remains unclear in our patient. We are unable to provide a definitive cause of the mechanisms triggering and causing the SR. Our hypotheses include anti-tumor immune response triggered by the biopsy procedure or anti-cancer properties of the consumed herbs. Further researches are needed to determine causes for SR of cancer and ultimately towards finding a cure for cancer.

Funding Support

The authors declare no competing financial interests.

Conflict of Interest

The authors of this manuscript declare no conflict of interest.

REFERENCES

Asano, Y., Kashiwagi, S., Goto, Wk 2015. A Case of Spontaneous Regression of Breast Cancer with Multiple Lung Metastases. Gan To Kagaku Ryoho, 42(12):1800–1802.

Bramhall, R. J., Mahady, K., Peach, A. H. S. 2014. Spontaneous regression of metastatic melanoma – Clinical evidence of the abscopal effect. European Journal of Surgical Oncology (EJSO), 40(1):34–41.

Burstein, H. J., Gelber, S., Guadagnoli, E., Weeks, J. C. 1999. Use of Alternative Medicine by Women with Early-Stage Breast Cancer. New England Journal of Medicine, 340(22):1733–1739.

Cassileth, B. R., Deng, G. 2004. Complementary and Alternative Therapies for Cancer. The Oncologist, 9(1):80–89.

Challis, G. B., Stam, H. J. 1990. The Spontaneous Regression of Cancer: A review of cases from 1900 to 1987. Acta Oncologica, 29(5):545–550.

Cole, W. H. 1976a. Relationship of causative factors in spontaneous regression of cancer to immunologic factors possibly effective in cancer. Journal of Surgical Oncology, 8(5):391–411.

Cole, W. H. 1976b. Spontaneous regression of cancer and the importance of finding its cause. Natl...
Cole, W. H. 1981. Efforts to explain spontaneous regression of cancer. *Journal of Surgical Oncology*, 17(3):201–209.

Dussan, C., Zubor, P., Fernandez, M., Yabar, A., Szunyogh, N., Visnovsky, J. 2008. Spontaneous Regression of a Breast Carcinoma: A Case Report. *Gynecologic and Obstetric Investigation*, 65(3):206–211.

Iihara, K., Yamaguchi, K., Nishimura, Y., Iwasaki, T., Suzuki, K., Hirabayashi, Y. 2004. Spontaneous regression of malignant lymphoma of the breast. *Pathology International*, 54(7):537–542.

Jaradat, N. A., Shawahna, R., Eid, A. M., Al-Ramahi, R., Asma, M. K., Zaid, A. N. 2016. Herbal remedies use by breast cancer patients in the West Bank of Palestine. *Journal of Ethnopharmacology*, 178:1–8.

Khazir, J., Mir, B. A., Pilcher, L., Riley, D. L. 2014. Role of plants in anticancer drug discovery. *Phytochemistry Letters*, 7(1):173–181.

Maillet, L., *et al.* 2014. Spontaneous regression of breast cancer after biopsy: About two cases. *Obstetrics and Fertility Gynecology*, 42(4):269–272.

Oya, M., Hirahashi, M., Ochi, M., Hashimoto, M., Ohshima, K., Kikuchi, M., Tsuneyoshi, M. 2009. Spontaneous regression of primary breast lymphoma. *Pathology International*, 59(9):664–669.

Shah, U., Shah, R., Acharya, S., Acharya, N. 2013. Novel anticancer agents from plant sources. *Chinese Journal of Natural Medicines*, 11(1):16–23.

Tanaka, Y., Uchida, A., Umemoto, T., Morishima, I., Kikuchi, K., Tohno, E., Ueno, E. 2015. Spontaneous regression of breast angiosarcoma after conservative treatment with radiotherapy: a case report and review of the literature. *Journal of Medical Ultrasonics*, 42(3):427–432.

Tokunaga, E. 2014. Case Report Spontaneous regression of breast cancer with axillary lymph node metastasis: a case report and review of literature. *International Journal of Clinical and Experimental Pathology*, 7(7):4371–4380.