

CASE REPORT

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Bilateral chest wall sarcomas associated with silicone implant capsules in a patient with Li-Fraumeni syndrome

Meenakshi Bansal, Stephenn Vega, Gabrielle A. Yeane, Xi Wang

ABSTRACT

Introduction: The carcinogenicity of silicone implants has been confirmed in rodents but is not evident in human breast. **Case Report:** We report a patient with Li-Fraumeni syndrome who developed bilateral chest wall unclassified sarcomas tightly associated with the capsule of silicone implants placed during treatment for her right breast cancer. **Conclusion:** Our case may suggest that genetic instability could increase the probability of carcinogenesis of silicone implants. Caution should be exercised when making management plans for these patients.

Keywords: Breast cancer, Li-Fraumeni syndrome, Sarcoma, Silicone implant

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INTRODUCTION

The long-term safety of silicone implants has been a particular concern since introduced in the first augmentation mammoplasty in 1962 [1]. Experimental studies have shown its carcinogenicity in rodents [1, 2]. However, studies and comprehensive reviews have not supported an association between silicone implants and malignant solid tumors in human breasts. Nevertheless, studies have shown that silicone implants are associated with lymphomas [3, 4]. Case reports on silicone implant-related sarcomas are very rare.

CASE REPORT

A 35-year-old female was diagnosed with a clinical stage III (T2 N2 M0) grade 2 invasive ductal carcinoma in her right breast in September 2008 (Figure 1). The carcinoma cells exhibited immunopositivity for ER, PR and Her2. She underwent neoadjuvant chemotherapy, bilateral mastectomy with tissue expander, adjuvant chemotherapy and right chest wall radiation, which were completed in January 2010. Bilateral silicone implants were placed in June 2010. In August 2011, the patient noticed a palpable mass adjacent to her left breast implant. An excisional biopsy showed a 2.0 cm tumor mass associated with the fibrous capsule of the silicone implant. Microscopically, the tumor consisted of pleomorphic spindle cells with pink cytoplasm in a collagen background, without a specific growth pattern. The mitotic rate was very high, including atypical mitosis. Scattered multinucleated giant cells were also present. The tumor cells were intimately mingled with the fibrous

capsule of the implant, with focal silicone granulomas, infiltrating through the fibrous capsule into surrounding soft tissue (Figure 2). Immunohistochemical staining showed that the tumor cells were negative for keratin markers (cytokeratin cocktail, CK5/6, p63, CK14 and 34BE12) and vascular markers (CD34 and CD31). A diagnosis of unclassified pleomorphic sarcoma was made after an expert consultation. Ten months thereafter, a follow-up chest CT scan identified a round lesion deep to the right breast implant with interval progression. Local wide excision identified a 3.0 cm spindle cell neoplasm associated with the capsule of the silicone implant. It was morphologically mildly different from the previously diagnosed sarcoma on the left side, being more cellular and pleomorphic. The tumor cells were very focally positive for p63 but negative for cytokeratin cocktail, CK5/6, 34BE12, CD34 and CD31. A diagnosis of high-grade sarcoma was made. The patient underwent a genetic consultation and was negative for BRST gene mutations but positive for a nonsense mutation in the p53 gene (X54156.1:g.12083G-A).

The patient's other personal history included multiple moles removed in the earlier years prior to the breast cancer diagnosis; a total hysterectomy with bilateral salpingo-oophorectomy in August 2010 with unremarkable findings; and a pituitary adenoma removed in May 2013. Her family history of cancer was as follows: father with prostate cancer at age 62, paternal grandfather with gastric cancer at age 81, maternal grandfather with leukemia at approximately ~30 years of age, maternal grandmother with melanoma at age 55, and maternal uncle with sarcoma (type not clear) at age 67.

DISCUSSION

Li-Fraumeni syndrome [5] is a rare autosomal-dominant disease characterized by predisposition to a wide range of cancers among family members. In the US, approximately 400 individuals from 64 families have this disorder, according to a US registry of Li-Fraumeni syndrome patients. The malignancies commonly arising in Li-Fraumeni families include breast cancers (25%), soft tissue sarcomas (20%), bone sarcomas (15%), brain tumors (13%), and adrenal gland carcinoma. Leukemia and melanoma are also frequently associated with Li-Fraumeni syndrome. Other carcinomas, such as prostate carcinoma, have also been reported. The history of malignancies for our index patient and her family members clearly fulfill the criteria for Li-Fraumeni syndrome. The germline TP53 mutation further confirmed this diagnosis.

Although soft tissue sarcoma is within the spectrum of the malignancies in Li-Fraumeni syndrome, the presentation of the bilateral chest wall sarcomas in our index patient remains interesting. According to literature, most reported sarcomas in Li-Fraumeni syndrome are childhood sarcomas, such as rhabdomyosarcoma [6].

Further, Hisada et al. quantified the frequency of multiple primary cancers in 200 individuals from 24 Li-Fraumeni kindreds originally diagnosed with cancers during 1968 to 1986 and found that only 15% developed second cancer, 4% developed third cancer and 2% eventually developed fourth cancer [7]. In contrast, our index patient developed two non-childhood sarcomas tightly associated with the silicone implant capsule and silicone granulomas after her primary breast carcinoma, whereas no sarcoma was identified at any other anatomic locations in her body.

Whether silicone implantation predisposes recipients to an increased risk for cancer has been long debated. After certain latent period, solid silicone compound implanted subcutaneously can elicit mesenchymal sarcoma at the implantation site in susceptible rodents through so-called solid-state carcinogenesis [8, 9], with an incidence of approximately 29–40% following the placement of a single implant [10]. In human breast, there has been only one convincing case report of a 55-year-old female who developed “malignant fibrous histiocytoma” after receiving silicone injection augmentation mammoplasty 19 years previously [11]. However, well-designed epidemiologic and experimental studies have not found convincing evidence implicating silicone implantation as a human risk for post-implant sarcoma [12, 13]. The difference in propensity towards sarcomas with silicone implantation between human and rodents might be explained by their contrasting genetic stabilities [14]. Therefore, cancer risk may be increased in the patients with genetic instability syndromes, such as in our index patient. Similar presentation has been reported in a Li-Fraumeni patient who received conservative surgery and radiation for a primary breast carcinoma [15].

Post-radiation breast sarcoma is a well-known complication for women treated with adjuvant radiation for breast cancer. Taghian et al. reported nine cases of radiation-induced sarcomas in 6919 patients treated for breast cancer, with a cumulative incidence 0.2%

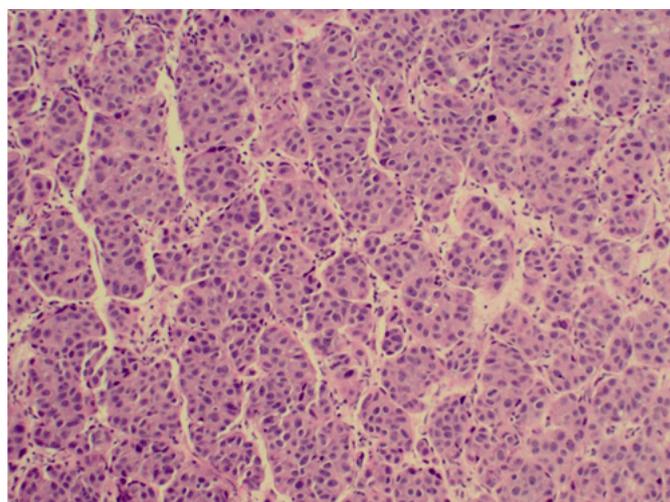


Figure 1: The primary invasive ductal carcinoma, Modified Bloom-Richardson grade II (H&E stain, x100).

(0.09–0.47) at 10 years [16]. However, we do not consider radiation as the primary insult for the bilateral sarcomas in our case. First, the left chest wall was not within the irradiated field but developed sarcoma prior to the irradiated side. Second, the short latent time and high incidence rate are very unusual for post-radiation sarcoma. Nevertheless, we believe that the relative higher cellularity and pleomorphism in the right chest wall sarcoma could be related to the radiation effect.

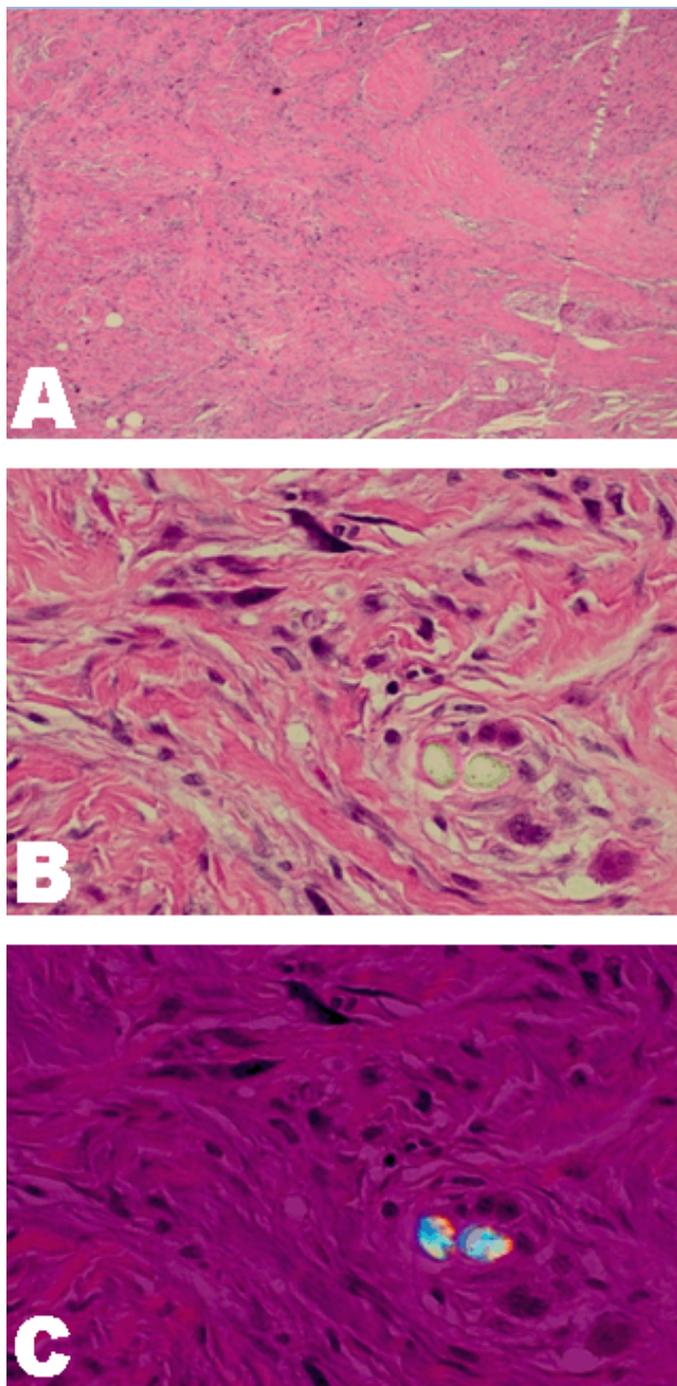


Figure 2: Unclassified pleomorphic sarcoma of the left chest wall. (A): Tumor infiltrating through the fibrous capsule and mixed with silicone granulomas (right lower corner, H&E stain, x40), (B): Tumor mixed with silicone granulomas (x100), (C): silicone granuloma (polarized, x100).

Nervous system neoplasms associated with Li-Fraumeni syndrome are predominantly astrocytomas but also include choroid plexus tumor, medulloblastoma, and others [17]. However, pituitary adenoma has not been reported in this syndrome. The pituitary adenoma in our index patient was a 1.6-cm ACTH-cell-type tumor with some neuronal differentiation by immunohistochemistry. The patient's endocrinologists determined the tumor to be nonfunctional because she had normal cortisol levels and MR imaging and ultrasound indicated no adrenal gland abnormalities. Endocrine system tumors have also been found to have p53 mutations in Li-Fraumeni syndrome [18]. However, pituitary adenoma was not included among these tumors. Currently, whether the pituitary adenoma in our index patient was related to Li-Fraumeni syndrome is unclear.

CONCLUSION

We report a case with bilateral chest wall sarcomas associated with silicone implant capsules in a Li-Fraumeni patient. Our observations suggest that caution should be exercised when making management plans for individuals with genetic instability syndromes, such as Li-Fraumeni, particularly when considering prophylactic bilateral mastectomies with silicone implants.

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Dr. Christopher Fletcher in Brigham and Women's Hospital was consulted and agreed with the diagnosis.

Author Contributions

Meenakshi Bansal – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Stephenn Vega – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Gabrielle A. Yeane – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Xi Wang – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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