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Normalization of Elevated Tumor Marker CA27-29 After Bilateral Lung Transplantation in a Patient With Breast Cancer and Idiopathic Pulmonary Fibrosis

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Solid tumors involving glandular organs express mucin glycoprotein that is eventually shed into the circulation. As a result, these proteins can easily be measured in the serum and be used as potential tumor markers. The most commonly used tumor markers for breast cancer are CA27-29 and CA15-3, which both measure the glycoprotein product of the mucin-1 (MUC1) gene. CA27-29 has been approved by the US Food and Drug Administration for monitoring disease activity in breast cancer patients. Most oncology clinical practice guidelines do not recommend the use of tumor markers for routine surveillance of early stage disease but recognize their utility in the metastatic setting. We present a patient with stage IIIA breast cancer and preexisting hypersensitivity pneumonitis who was found to have an elevated serum tumor marker CA27-29. After successful curative intent treatment of her early stage breast cancer, she developed gradual and progressive worsening of her lung disease with eventual development of severe pulmonary fibrosis requiring bilateral lung transplantation. As part of the pretransplant evaluation, she was found to have an elevation of serum tumor marker CA27-29. While the diagnostic evaluation, including imaging studies, was negative for the presence of recurrent disease, the serial serum tumor marker CA27-29 levels remained persistently elevated. The decision was made for her to undergo bilateral lung transplantation. Shortly after surgery, her CA27-29 tumor marker level returned to normal range, and it has continued to remain in the normal range with no evidence of breast cancer recurrence.

Key words: CA27-29; Tumor markers; Breast cancer; Pulmonary fibrosis

INTRODUCTION

Breast cancer is the most common malignancy affecting women in the US and is second to lung cancer as a cause of cancer-related mortality[1]. Idiopathic pulmonary fibrosis (IPF) is a rare chronic, progressive, interstitial lung disease with an unpredictable clinical course, and this pulmonary disorder is associated with high mortality[2]. In recent years, bilateral lung transplantation has emerged as a viable and life-saving treatment option for this deadly disease. As a result of an increased risk of posttransplant malignancies, most lung transplant programs have implemented vigorous screening strategies, including monitoring of various serum tumor markers, to detect occult or previously treated malignancies in their transplant candidate population[3,4]. Although serial measurements of tumor markers after primary treatment of breast cancer have been shown to discover preclinical recurrence with lead times of 2 to 9 months, the clinical significance of this finding remains unknown. CA27-29, CA15-3, carcinoembryonic antigen (CEA), and HER2 extracellular domain are the most frequently used serologic tumor markers for monitoring disease activity in breast cancer patients[5–7]. The current clinical practice guidelines recognize the clinical utility of tumor markers in the management of metastatic breast cancer but do not recommend them for screening, diagnosis, or surveillance after initial treatment of early stage disease[8–10].

CA27-29 is an epitope on the protein core of the mucin-1 (MUC1) gene product mucin glycoprotein. Elevated CA27-29 levels are primarily associated with metastatic breast cancer but may also be elevated in primary breast or nonbreast malignancies or even nonmalignant conditions (Table 1)[11–15].

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Table 1. Malignant and Benign Conditions Associated With Elevated CA27-29 Levels

Malignant Conditions	Nonmalignant Conditions
Metastatic breast cancer	Acute hepatitis
Primary breast cancer	Liver cirrhosis
Ovarian cancer	Benign breast disorders
Lung cancer	Benign liver disorders
Pancreatic cancer	Ovarian cysts
Colon cancer	
Liver cancer	

Herein we report a case of a breast cancer patient with IPF who had persistently elevated pretransplant CA27-29 levels, which resolved completely to normal range after successful bilateral lung transplantation.

CASE PRESENTATION

A 53-year-old Caucasian woman, with a 4-year history of hypersensitivity pneumonitis, had an abnormal routine mammogram that eventually led to a diagnosis of T1 N2a M0, estrogen receptor (ER)- and progesterone receptor (PR)-positive and HER-2/neu receptor-negative, stage IIIA left-sided breast cancer, and a right-sided ductal carcinoma in situ. Following bilateral mastectomy and left-sided axillary node dissection, she received four cycles of doxorubicin, cyclophosphamide, and four cycles of paclitaxel adjuvant chemotherapy followed by left-sided postmastectomy radiation and adjuvant hormonal treatment with letrozole for a planned 10-year period. During the follow-up for her breast cancer, her lung function progressively declined, resulting in refractory end-stage lung failure due to IPF. She underwent evaluation for bilateral lung transplantation as her only possible life-saving treatment option. The serum tumor marker CA27-29, which was checked as part of the pretransplant workup, was found to be elevated at 67 U/ml (normal: 0–38 U/ml). Extensive workup, including several imaging studies, failed to detect the presence of recurrent disease. Serial follow-up serum CA27-29 levels, measured at multiple time points prior to transplant, remained persistently elevated, with the highest value being 105 U/ml. After a long battle of getting all the pretransplant workup completed, managing to stay on the transplant waiting list, and securing insurance coverage for the lung transplant, she was fortunate enough to undergo a successful bilateral lung transplantation procedure at 11 years from her initial diagnosis of hypersensitivity pneumonitis and 7 years from her breast cancer diagnosis. Shortly after her transplantation, her serum tumor marker CA27-29 level returned to normal range (13 U/ml) and has continued to be in the normal range (Fig. 1). The patient is now at 2.5 years posttransplant with normal lung function and no evidence of breast cancer recurrence.

DISCUSSION

The cancer-associated antigen CA27-29 is one of several tumor markers used for the early detection of cancer recurrence or for monitoring response to anticancer treatments in the metastatic setting. While current oncology practice guidelines discourage the routine use of tumor markers for the surveillance of early stage breast cancer in asymptomatic patients, their use is supported in the metastatic setting in predicting response to therapy[8–10]. Our patient had her tumor marker checked as part of her pretransplant workup, and she was found

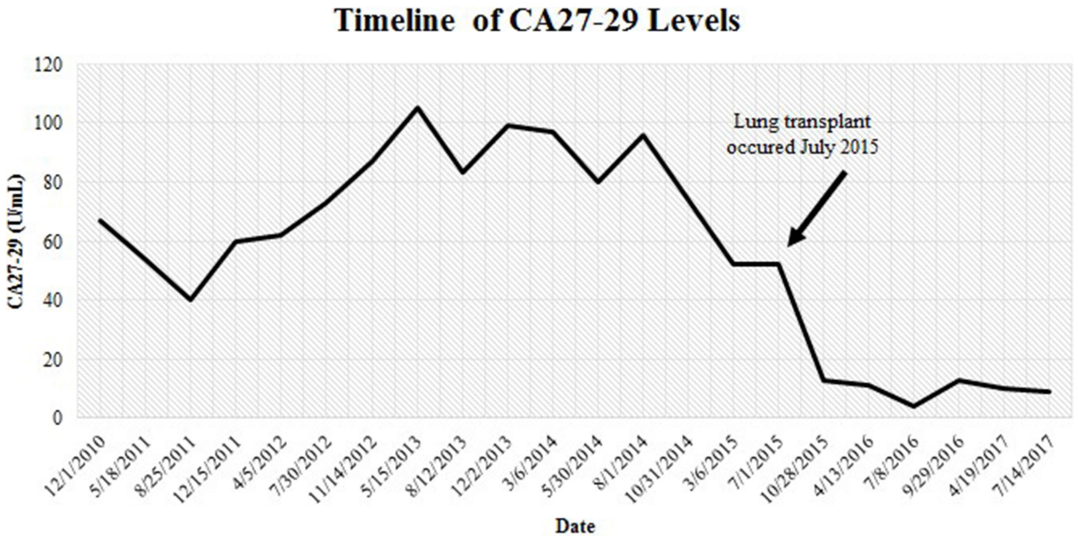

Figure 1. CA27-29 levels prior to and after bilateral lung transplantation.

to have persistently elevated CA27-29 levels despite no evidence of metastatic disease through extensive additional workup. While she was more than 5 years out from the date of her initial breast cancer diagnosis, elevated CA27-29 levels triggered significant anxiety, leading to extensive workup for the possibility of occult or recurrent disease and almost caused her to be removed from the transplant waiting list. In the face of rapid life-threatening deterioration of her lung function and negative exhaustive workup for malignancy, she was finally accepted for bilateral lung transplantation and underwent this life-saving procedure. Following her transplantation, CA27-29 levels returned to the normal range. Now, at 2.5 years posttransplant, her CA27-29 levels remain in the normal range, and she also continues to have good lung function.

IPF is a progressive life-threatening interstitial lung disease of unknown etiology[16]. A variety of serum markers, such as surfactant proteins, KL-6, LDH, and CC chemokine ligand 18, have been investigated for utility to predict disease activity and survival in this disease[17,18]. Furthermore, several tumor markers such as CEA, CA15-3, CA19-9, and CA27-29 have been shown to be elevated in the serum of IPF patients without any evidence of malignancy, suggesting a correlation with the extent of pathologic changes in the lungs[17,19]. It has been suggested that epithelial toxicity due to chronic fibrotic process along with metaplastic changes occurring in the bronchial glandular epithelium of IPF patients may be the reason for elevated cancer-associated serum antigen assays. Furthermore, elevated levels of serum mucinous marker CA19-9 have been shown to be associated with poor prognosis in IPF patients[20]. Following successful lung transplantation, significant reduction in high CA15-3 levels of pretransplant patients with IPF has also been reported[17]. Recently, a small series of four breast cancer patients, two with interstitial lung fibrosis and two with fibrotic lung disease, have been shown to have persistent elevations of serum tumor marker CA27-29 without any evidence of breast cancer recurrence[19]. To our knowledge, this case is now the fifth case reported in the literature with breast cancer and fibrotic lung disease whose elevated CA27-29 levels were not due to breast cancer recurrence but to fibrotic lung disease. In addition, our case is the only one reported demonstrating the reversal of elevated tumor marker CA27-29 after successful lung transplantation.

CONCLUSION

Elevations in MUC1 glycoprotein marker CA27-29 can be observed in breast cancer and other solid tumors, as well as in nonmalignant conditions. Based on this case, IPF should also be included in the list of nonmalignant conditions presented in Table 1. Elevated serum tumor makers in pulmonary fibrosis seem to be associated with the MUC1 gene product glycoprotein antigen being shed into the circulation due to continual epithelial cell damage from fibrotic lung disease. It is logical to hypothesize that reversal of this process may occur after successful lung transplantation, leading to normalization of tumor markers. Increased awareness of this possibility can help avoid extensive, repetitious pretransplant staging workup in patients with a prior history of breast cancer and elevated tumor markers. The elevated serum tumor marker CA27-29 should not exclude cancer survivors from transplantation candidacy as long as they have been cancer free for more than 5 years and a reasonable workup is negative for the presence of cancer recurrence.

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