Breast Cancer with Behçet’s Disease: A Short Review

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Abstract

Various immune-mediated disorders are associated with an increased risk of malignancy. Behçet’s disease (BD) is chronic, relapsing, systemic vasculitis of unknown etiology. It is characterized by recurrent urogenital aphthae and systemic manifestations, including ocular disease, skin lesions, gastrointestinal involvement, mammary manifestations, vascular disease, and arthritis. BD has been associated with malignancy in a few case series and case reports. However, the relationship between Behçet’s disease (BD) and breast cancer remains unclear. Here, we consider the relationship between BD and breast cancer through analysis of the medical literature and a review of our own experience.

Keywords: Behçet’s disease; Breast cancer; Immune-mediated disorder

Introduction

Behçet’s disease (BD) is a systemic vasculitis of unknown origin, characterized by oral and genital ulcers and uveitis; however, cutaneous, articular, neurologic, vascular, intestinal, pulmonary and/or mammary manifestations may also be observed [1,2]. Autoimmunity and chronic inflammation are associated with malignancy. Immune-mediated disorders, which result from a dysregulated immune response, often cause chronic inflammation. Chronic and unregulated inflammation can cause malignant cell transformation and carcinogenesis through inflammation-related mechanisms. Chronic exposure to inflammatory mediators, including arachidonic acid metabolites, cytokines, chemokines and free radicals, leads to increased cell proliferation, mutagenesis, oncogene activation and angiogenesis [3,4].

Several epidemiological studies have evaluated the relationship between systemic autoimmune rheumatic disease and cancer [3,4]. BD has also been reported to be sporadically associated with malignancy [4,5]. In particular, BD has been reported to be associated with hematological cancers and bone marrow failure, including myelodysplastic syndrome (MDS) and aplastic anemia (AA) [4,5].

We recently reported the case of a breast cancer patient with a history of prolonged colchicine and Prednisolone use for BD [2]. We herein review the relationship between BD and breast cancer through analysis of the medical literature and a review of our own experience.

Our Experience

The patient was a 72-year-old woman who had developed recurrent painful erosive lesions of the oral mucosa and tongue accompanied by less frequent genital ulcers at 28 years of age. The patient presented with iridocyclitis and thrombophlebitis on the skin of her foot. BD was first described in 1937 by Hulusi Behçet. BD is most frequently seen in the Middle East, Japan and Mediterranean countries [2,8]. It is a multisystem disorder characterized by vascular, neurologic, ocular, gastrointestinal, mucocutaneous and articular abnormalities [2,8]. Yi et al. [6] reported that, among 651 patients with BD in China, 41 patients developed malignancies. The numbers of patients who developed the various types of malignancies were as follows: i) 29 patients developed hematologic malignancies which included MSD in 20 cases, leukemia in seven cases, AA in two cases and lymphoma in one case; ii) 13 patients developed malignant solid neoplasms which

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included gastrointestinal cancer in five cases, bladder cancer in two cases, gynecologic cancer in two cases, pancreatic cancer, thyroid cancer, breast cancer, renal cell carcinoma and metastatic unknown primary cancer in one case each. Older age and longer disease duration were more commonly seen in BD patients with solid neoplasms than in those with hematologic malignancies. In a Korean population-based study, the risks of overall cancer and solid tumor cancer were greater in patients with BD than in the general population. Women with BD had a significantly increased risk for these solid cancers: the lips/oral cavity/pharynx, liver, lungs, breast and eyes [4]. Patients with BD had a greater risk of myelodysplastic syndrome (MDS), but not hematological cancers, than the general population [4]. A Taiwan population-based study also revealed that women with BD had a greater risk of breast cancer than the general population [4,7]. BD treated with colchicine has been associated with infiltrative breast carcinoma [2,8] and we previously reported a sporadic case of breast carcinoma concurrent with BD [4].

The autoimmune nature of BD or the immunosuppressive medicines that are used for its management may cause malignant changes. It remains unclear whether this association is due to compromised tumor-associated immunity or impaired DNA repair. In our case, immunosuppressive medicines might have contributed to the development of breast cancer. On the other hand, mastitis is associated with BD [9]. In this case, mammography enabled us to differentiate tumor from mastitis. The pathological findings confirmed the presence of small-vessel vasculitis. Therefore, in this case it is very difficult to conclude whether BD is related to mastitis or to breast cancer.

In our case, histopathological specimens of the breast showed lymphocytic lobulitis and small vessel vasculitis consistent with BD [2]. These findings are very similar to those seen on the breasts of patients with DM and/or RA. However, our patient had neither DM nor RA. These results suggest that the breast changes in our patient were caused by BD.

Twelve years ago, there were few reports on the association between BD and malignant disease. With our knowledge, BD has thus far been associated with 208 malignancies and 10 breast cancer in the scientific literature [2,6]. Taiwanese and Korean population-based studies revealed that women with BD have an increased risk of breast cancer [4,6]. These results suggest that the autoimmune nature of BD or the immunosuppressive medicines that are used for its management are probable causes of malignant changes in the breast. It is important for breast cancer specialists know that the risk of overall cancer and of breast cancer in particular, are greater in patients with BD than in the general population.

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