Original Article

Behçet's disease and breast cancer: A case series study

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ABSTRACT

Introduction: The relation between Behçet's disease (BD) and breast cancer (BC) is unclear. Our purpose is to investigate whether BD has an important effect on BC or vice versa.

Patients and Methods: A total of 12 female BC patients with a diagnosis of BD were identified from a cohort including 5050 BC patients. The demographic data of the selected patients including previous chemotherapy (CT), radiotherapy (RT), hormonal therapy (HT), drugs used for BD, history of thrombotic events, and overall survival were examined.

Results: The rate of BD in the entire cohort was found to be 0.25% (12/4800), and all had early BC at the time of BC diagnosis, with a median age of 47 years (range: 38–51). All patients underwent curative surgery for BC. In the adjuvant setting, CT, RT, and HT were administered in 11 (91%), 10 (83.4%), and 9 (75%) patients, respectively. All patients received acetylsalicylic acid and colchicine for BD. No serious adverse event associated with BC and/or BD was observed. Clinical symptoms in 11 patients with BD were observed to be improved following the BC treatment. Only one patient developed disease progression and then expired.

Conclusion: Unlike the natural behavior of BD, which is well-defined to have an increased risk of thrombosis, BC patients with BD in this study did not have any adverse event. However, due to small sample size, it is difficult to drive any definite conclusion regarding the relation between these two pathologies.

KEY WORDS: Behçet's disease, breast cancer, prognosis, relation, tamoxifen, thrombosis

INTRODUCTION

It has been reported that autoimmune diseases (AiD) may increase the cancer incidence.[1] For instance, the risk of cancer presenting with connective tissue diseases and vasculitis such as rheumatoid arthritis, progressive systemic sclerosis, Sjogren's syndrome, and systemic lupus erythematosus has been shown to be at high rates, however, such relation for Behçet's disease (BD) has remained undefined with limited number of case series.[2,3] AiD accompanying breast cancer (BC) may present with end-organ involvement or may worsen the BC prognosis by increasing the complication rates of radiotherapy (RT), chemotherapy (CT), and surgery; hence may lead to unfavorable outcomes in BC patients.[4,5]

BD is a multisystem, autoinflammatory vasculitis which is mainly characterized by increased predisposition to thromboembolic events, eye involvement, and recurrent orogenital ulcers with neutrophilic inflammation. As compared with the European and American populations, its incidence is significantly more common in Asian countries, with the highest incidence reported in Turkey. Although the main pathogenesis is not well clarified, the genetic locus consisting HLA-B51 allele is considered to have an important key role in the pathophysiology.[6] The incidence of arterial versus venous involvement in BD is reported to be 5% versus 15–30%, respectively, whereas microvascular involvement has been shown to be present in nearly all patients. The vascular involvement of brain is the major cause of mortality and morbidity in BD.[7] Disease- or treatment-related complications in patients with either BC or BD such as thrombosis and bleeding are more frequently documented as compared to healthy people.

So far, the number of studies investigating the relation between BD and BC are limited in literature. In one study, 105 patients with BD

Cite this article as: Karatas F, Sahin S, Aytekin A, Erdem GU, Ates O, Ozisik Y, *et al*. Behçet's disease and breast cancer: A case series study. J Can Res Ther 2018;14:1184-90.

Access this article online

Website: www.cancerjournal.net

DOI: 10.4103/0973-1482.189249

Quick Response Code:

were retrospectively examined in terms of overall cancer incidence, and BC in one patient was the only diagnosis in the entire cohort.[8] Similarly, in another study, only one patient was found to have a diagnosis of BC among a population including 651 patients with BD.[9] Roach *et al*. reported that four patients were found to have a diagnosis of BD among a BC population, suggesting a possible relation between BD and BC.[10] Likewise, Kaklamani *et al*. investigated the overall cancer incidence among 128 patients with BD and reported two cases of kidney and lung cancer.[11] One retrospective analysis in Taiwan population revealed an increased incidence of BC, Hodgkin disease, and hematological solid malignancies among patients with BD.[12] Overall, all the analysis regarding the association between BD and BC have not yet shown a definite relation, thus have remained insufficient to show a likelihood impact of BD on BC, or vice versa, since the studies have been limited by small sample size. In literature, there are available data suggesting that CT and RT in BC may lead to thrombosis through multifactorial pathways.[13] For instance, taxanes and doxorubicin have been shown to cause thrombosis, particularly in cases of increased inflammations.[14-16] Tamoxifen and rarely letrozole were accepted agents leading to thrombotic complications in patients with BC.[17-20]

Today, the clinical importance of BD in the etiology of BC is still uncertain. However, it is known that there is a high tendency to thrombosis in patients with BC due to the increased rate of coagulation disorders associated with CT, RT, paraneoplastic events, and tamoxifen. Colchicine is effective and standard of care in the long-term treatment in patients with BD, whereas acetylsalicylic acid (ASA) or warfarin is more widely used in the treatment of thrombosis.[21-24] The most efficient immunosuppressive (IS) agents used in BD are steroids, cyclosporine, and azathioprine. Long-term use of these agents with an IS dose, but not higher dose, has not yet been shown to have a carcinogenic effect.[25,26] However, it is accepted that IS agents and steroids used in BD may also have a role in disease progression or disease recurrence in BC.[27]

Herein, we intended to perform a demographic study of BC and BD in light of the literature reviews, with the goal of investigating the likelihood impacts of BD on BC or vice versa.

PATIENTS AND METHODS

Medical records of 5050 patients with BC followed between 1997 and 2016 were retrospectively analyzed. Of the patients, 12 female BC patients who had either subsequent or previous diagnosis of BD were enrolled into this study. Demographic data and clinicopathologic features of BC patients with a diagnosis of BD were evaluated. Six of the patients, who were diagnosed with BD prior to BC diagnosis, were known to receive IS agents for systemic involvement; however, data regarding the treatment of these patients could not be used in this study since the information was not properly recorded.

Statistical analysis

The computer program of "Statistical Package for the Social Sciences" version 18.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for all statistical analysis. The interval between the diagnosis of BD and BC was defined as "the time until BC." Recurrence-free survival was defined as the time from BC diagnosis to any event of recurrence or to the date of the last visit in patients who have no recurrence. The time from the date of BC diagnosis until the date of death or to the date of the last visit was defined as "overall survival."

RESULTS

The median age of 12 patients was 47 (range: 38–56) years, and the time until BC was 14 (range: 1–36) years. All patients underwent surgery of either modified radical mastectomy or breast-conserving surgery plus axillary lymph node dissection with a curative intent. Except a mild degree and clinically insignificant lymphedema which developed only in three patients, none of the patients experienced any other treatment-related complication. Nine (75%) patients had a hormone-positive tumor, hence received adjuvant aromatase inhibitor (18%) or tamoxifen (63%). Of the 12 patients, 11 (91%) were treated with CT in the adjuvant setting and 1 was treated in the neoadjuvant setting. Detailed demographic data and histopathological characteristics of patients are shown in Table 1a and b Ten (83.3%) patients were given adjuvant RT without occurring any adverse event. The treatments during and after the diagnosis BC shown in Table 2. There was no case of secondary primary malignancy at the baseline or at follow-up. No thromboembolic event due to BC or BD developed in the 12 patients. Only one patient had BC recurrence and expired due to disease progression. The clinical outcomes of both disease shown in Table 3.

There was no new case of uveitis, neurological attack, and end-organ involvement due to BD during or following BC treatment. Moreover, the oral-genital ulcers and erythema nodosum were completely regressed in nearly all patients following CT, except in one patient in whom complaints continued at a moderate level. In addition, the need for IS drugs and colchicine therapy were reduced in a majority of the patients following CT [Table 4].

DISCUSSION

Our findings regarding the incidence rate of BD among BC patients were similar to general incidence reported for Turkey and other East Asian populations.[28-30] However, among a retrospective series of BC patients, of patients who also had a previous diagnosis of BD disease ($n = 12$), it would be difficult to speculate on "incidence of BD in BC patients." Thus, it is apparently difficult to drive any definite conclusion regarding the etiological relation between BD and BC. On the other hand, it would also be possible to hypothesize in

Table 1a: Patient's characteristics

Characteristic	*n* (%)
Patients with BD, *n* (%)	12 (100)
Median age (year)	47 (37-56)
The time until BC (year)	14 (1-36)
Histopathological subtype, *n* (%)	
IDC	10 (83.4)
ILC	1 (8.3)
Signet cell	1 (8.3)
T-stage, *n* (%)	
1	3 (25.0)
2	8 (66.7)*
3	1 (8.3)
4	0 (0)
Pathological nodal involvement, *n* (%)	
Yes	7 (58.4)
No	5 (41.6)
Distant metastasis, *n* (%)	
Yes	0 (0)
No	12 (100)
Disease stage, *n* (%)	
I	2 (16.6)
II	2 (16.6)
III	8 (66.7)
CT, *n* (%)	
AC - T	5 (41.7)
AC	3 (25)
CMF	2 (16.6)
No	2 (16.6)
Surgery, *n* (%)	
MRM	7 (58.4)
BCS + LND$	5 (41.6)
No	0 (0)
Adjuvant hormonal therapy, *n* (%)	
Yes	9 (75.0)
No	3 (25.0)
RT, *n* (%)	
Yes	10 (83.4)
No	2 (16.6)
Colchicine#, *n* (%)	
Yes	11 (91.7)
No	1 (8.3)
Acetylsalicylic acid#, *n* (%)	
Yes	12 (100)
No	0 (0)
Corticosteroid#, *n* (%)	
Yes	2 (16.6)
No	10 (83.4)

*One patient received neoadjuvant CT due to clinical N2 disease, #During BC treatment, $Two patients underwent surgery of sentinel lymph node dissection. BD=Behçet's disease, AC – T=Subsequently taxane following doxorubicin + cyclophosphamide, AC=Doxorubicin+cyclophosphamide only, CMF=Cyclophosphamide + methotrexate +5-fluorouracil, MRM=Modified radical mastectomy, BCS + LND=Breast-conserving surgery + lymph node dissection, IDC=Invasive ductal carcinoma, ILC=Invasive lobular carcinoma, BC=Breast cancer, CT=Chemotherapy, RT=Radiotherapy

our patients that there was no increased risk of recurrence or increased rate of locoregional/metastatic disease due to BD; however, the study was limited by a small number of patients, hence required a large sample size to make such a certain conclusion.[31]

In our study, while some patients with BD had used IS therapy prior to the BC diagnosis, none of them required further IS therapy during BC treatment, and only one patient needed IS therapy after the BC treatment. Besides, patients with BD did not have any relapsing episode or end-organ involvement following the BC diagnosis. This might be partly due to the IS effects of CT, particularly cyclophosphamide. In literature, data regarding the incidence of BD among cancer patients are available for the last two decades. Therefore, recently discovered–IS agents used in BD may play a role in the development of cancer disease.[11]

Few studies have reported that incidence of autoimmunity may increase in patients with cancer or may lead to the development of some specific cancer types.[32,33] By contrast, there are also available data suggesting that autoimmunity may have an effect in decreasing the incidence of some cancer types.[34] For instance, the low incidence rate of malignant melanoma in patients with vitiligo is a typical and considerable example for this risk reduction.[34] Besides, it has been shown that the recurrence rate in BC is not increased in patients with AiD.[35] However, these studies regarding the relation between cancer and autoimmunity have not included the patients with BD and have not investigated the association of BD with malignancies. In a retrospective analysis by Hemminki *et al*. totaling approximately 200,000 patients diagnosed with any of 33 different types of autoimmune disorders, a low-frequency rate of BC was reported among patients with AiD, however, any effect of BD on BC patients could not be shown in terms of recurrence, complication, and survival.[36] A surveillance, epidemiology, and end results analysis by Gadalla *et al*. including 84,778 women patients aged between 67 and 79 reported that systemic AiD did not lead to an increase in BC incidence. In addition, same authors reported that AiD decreased the incidence of hormone negative-BC which has a poorer prognosis than hormone positive-BC.[37] Accordingly that the incidence rate of BD prior to the BC diagnosis in our study was similar to those reported for the general population. Moreover, none of our patients experienced a secondary primary cancer before or after BC diagnosis, reflecting an insignificant relation between BD and BC.

The lower likelihood of recurrence risk or disease progression in our BC patients with BD might be explained with the increased T-cell response due to autoimmunity which is inherent in BD. One another hypothesis for the decreased recurrence risk in patients with BD might be due to the use of colchicine treatment which is widely used in the treatment of BD. Colchicine acts as a microtubule inhibitor, with a similar activity as taxanes which are commonly used in the treatment of BC. In addition, data regarding the use of colchicine as a chemotherapeutic agent in cancer treatment are currently available.[38] For instance, there are few studies indicating that colchicine might be effective in the treatment of metastatic hepatocellular and cholangiocellular carcinoma.[39,40] Furthermore, Kuo Ming-Chun *et al*. found that long-term use of colchicine in patients with gout reduced the incidence rates of cancer development (hazard ratios = 0.85, 95% confidence interval = 0.77–0.94; P = 0.001).[41] Nowadays, multiple

Table 1b: Demographic features of all patients

Patient	Age years (BC)	Stage of BC	Laterality of BC	Location of BC (quadrant)	BC histology	Grade[$]	Immunohistochemical features	Menopausal status in time of the diagnosis	Time of BD to BC (years)
1	51	T2N1M0	Right	Upper out	ILC	II	ER+, PR+, HER-2−	Post	Unknown
2	40	T2N0M0	Right	Upper out	IDC + ILC	II	ER+, PR+, HER-2−	Pre	1
3	40	T2N2M0	Left	Upper out	SRC-C	II	ER+, PR+, HER-2+	Pre	4
4	39	T1N0M0	Right	Upper out	IDC	II	ER+, PR+, HER-2−	Pre	8
5	50	T2N0M0	Left	Lower inner	IDC	III	ER−, PR+, HER-2−	Pre	25
6	38	T1N0M0	Left	Upper out	IDC	III	ER+, PR+, HER-2−	Pre	14
7	56	T2N1M0	Right	Upper out	IDC + ILC	III	ER−, PR−, HER-2−	Post	4
8	48	T2N0M0	Left	Upper out	IDC	II	ER+, PR+, HER-2−	Pre	25
9	55	T1N1M0	Left	Lower inner	IDC	II	ER+, PR+, HER-2−	Post	36
10	41	T3N1M0	Left	Upper out	IDC	I	ER+, PR+, HER-2−	Pre	20
11	52	T2N1M0	Left	Upper out	IDC	II	ER−, PR−, HER-2−	Post	7
12	46	T2N1M0	Right	Lower out	IDC	III	ER−, PR−, HER-2+	Post	36

[$]Histopathological grade, BC=Breast cancer, SRC-C=Signet ring, IDC=Invasive ductal carcinoma, ILC=Invasive lobular carcinoma, PR=Progesterone receptor, ER=Estrogen receptor, HER-2=Human epidermal growth factor receptor 2, BD=Behçet's disease

Table 2: The treatments during and after the diagnosis of breast cancer

Patient	Colchicine	ASA (mg)	CT	CT setting	HT, (years)	Surgery	Adjuvant RT
1	Yes	100	AC×4 + weight×12	Neoadjuvant	Letrozole, (5)	MRM	Yes
2	Yes	100	AC×4	Adjuvant	Tamoxifen, (5)	MRM	No
3	Yes	100	AC×4+ weight×12+Tx	Adjuvant	Tamoxifen, (5)	MRM	Yes
4	Yes	100	No	None	Tamoxifen, (6)	BCS+SLND	Yes
5	Yes	100	AC×4	Adjuvant	Tamoxifen, (5)	MRM	No
6	Yes	100	No	None	Tamoxifen, (5)	BCS+SLND	Yes
7	Yes	100	CMF×6	Adjuvant	None	BCS+ALND	Yes
8	Yes	100	AC×4	Adjuvant	Tamoxifen, (5)	MRM	Yes
9	Yes	100	CMF×6	Adjuvant	Anastrozole, (5)	BCS+ALND	Yes
10	Yes	100	AC×4+ weight×12	Adjuvant	Tamoxifen, (5)	MRM	Yes
11	Yes	100	AC×4+ weight×12	Adjuvant	None	BCS+ALND	Yes
12	Yes	100	AC×4+ weight×12+Tx	Adjuvant	None	MRM	Yes

ASA=Acetylsalicylic acid, CT=Chemotherapy, HT=Horonotherapy, RT=Radiotherapy, AC×4=Four cycles of adriamycin+cyclophosphamide/21 day, AC×4+ weight×12=Four cycles of adriamycin + cyclophosphamide/21 day, followed by 12 cycles weekly paclitaxel, Tx=Trastuzumab up to 1 year starting with paclitaxel. CMF×6=Six cycles of cyclophosphamide + methotrexate+5-fluorouracil, MRM=Modified radical mastectomy, BCS=Breast-conserving surgery, ALND=Axillary lymph node dissection, SLND=Sentinel lymph node dissection

Table 3: Clinical outcomes and complications in breast cancer with Behçet's disease

Patient	Complication of CT	Complication of RT	Recurrence	Exitus	Thrombosis[#]	Lymphedema*	Secondary Malignancy	Hospitalization	RFS (BC) months	OS (BC) months
1	No	No	No	No	No	No	No	No	42.1	50.1
2	No	No	No	No	No	Mild	No	No	109.6	124.2
3	No	No	No	No	No	Mild	No	No	51.8	55.8
4	No	No	No	No	No	No	No	No	70.9	79.5
5	No	No	Yes	Yes	No	No	No	No	12.8	18.0
6	No	No	No	No	No	No	No	No	3.68	40.0
7	No	No	No	No	No	No	No	No	23.7	25.3
8	No	No	No	No	No	No	No	No	97.2	111.4
9	No	No	No	No	No	No	No	No	10.6	14
10	No	No	No	No	No	Mild	No	No	32.1	37.7
11	No	No	No	No	No	No	No	No	15.7	49.3
12	No	No	No	No	No	No	No	No	2	2

[#]After BC, *After breast surgery. CT=Chemotherapy, RT=Radiotherapy, BC=Breast cancer, RFS=Recurrence-free survival, OS=Overall survival

colchicine derivatives have been synthesized for the cancer treatment.[8]

One another noteworthy finding of this research was that BC patients with BD were likely to be at earlier ages at BC presentation. This might be explained with close follow-up intervals in these selected patients. However, it is important to note that our sample size is inconclusive to make a judgment regarding on this issue. The incidence of lymphedema following BC surgery was likely to be in mild degree with an expected frequency in BC patients.

It is also important to note that BC patients with BD using an intense CT or hormonal therapy (HT) (such as tamoxifen and letrozole) in the adjuvant or metastatic setting are under a high risk of developing thrombosis; however, none

Table 4: Clinical manifestations of Behçet's disease and their change during and after breast cancer treatment

Patient#	Period	Pain[a]	Oral after	Genital ulcer	Vascular event	GIS	Arthritis*	Neurological	EN	Uveitis	IS	Patient's complaints
1	Before BC	Yes	Yes	Yes	No	No	Yes	No	No	No	No	Patient has no
	During CT	No	No	No	No	No	No	No	No	No	No	complaint of BD
	During RT	No	No	No	No	No	No	No	No	No	No	
	Current	Yes	No	No	No	No	No	No	No	No	No	
2	Before BC	Yes	Yes	Yes	No	No	No	No	No	No	No	Patient has no
	During CT	Yes	Yes	No	No	No	No	No	No	No	No	complaint of BD
	Current	No	No	No	No	No	No	No	No	No	No	
3	Before BC	Yes	Yes	Yes	No	No	No	No	No	No	No	Arthralgia has
	During CT	No	No	No	No	No	No	No	No	No	No	completely
	During RT	No	No	No	No	No	No	No	No	No	No	disappeared
	Current	Yes	No	No	No	No	No	No	No	No	No	
4	Before BC	Yes	Yes	Yes	No	No	No	No	No	No	No	Arthralgia has
	During RT	No	No	No	No	No	No	No	No	No	No	completely
	Current	Yes	No	No	No	No	No	No	No	No	No	disappeared
5	Before BC	Yes	Yes	Yes	No	No	No	No	No	No	No	Patient has no
	During CT	Yes	Yes	No	No	No	No	No	No	No	No	complaint of BD and
	Current	Ex+	No	No	No	No	No	No	No	No	No	does not need to use colchicine
6	Before BC	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	Patient has no
	During RT	No	No	No	No	No	No	No	No	Same	No	complaint of BD and
	Current	No	No	No	No	No	No	No	No	Same	No	does not need to use colchicine
7	Before BC	Yes	Yes	Yes	No	No	Yes	No	No	Twice	Cyclophosphamide, Prd	Patient has no complaint of BD within
	During CT	No	No	No	No	No	No	No	No	No	No	the 6 months after CT.
	During RT	No	No	No	No	No	No	No	No	No	No	After the 6 months,
	Current	Yes	No	No	No	No	Yes	No	No		MMF, Prd	she complaints with a mild severity of joint pain
8	Before BC	Yes	Yes	Yes	No	No	Yes	No	Yes	No	No	Patient has no
	During CT	No	No	No	No	No	No	No	No	No	No	complaint of BD and
	During RT	No	No	No	No	No	No	No	No	No	No	does not need to use
	Current	No	No	No	No	No	No	No	No	No	No	colchicine
9	Before BC	Yes	Yes	Yes	No	No	Yes	No	No	No	No	Patient has no
	During CT	No	No	No	No	No	No	No	No	No	No	complaint of BD and
	During RT	No	No	No	No	No	No	No	No	No	No	does not need to use
	Current	No	No	No	No	No	No	No	No	No	No	colchicine
10	Before BC	Yes	Yes	Yes	No	No	No	No	No	No	No	Patient has no
	During CT	No	No	No	No	No	No	No	No	No	No	complaint of BD and
	During RT	No	No	No	No	No	No	No	No	No	No	does not need to use
	Current	No	No	No	No	No	No	No	No	No	No	colchicine
11	Before BC	Yes	Yes	Yes	No	No	No	No	Yes	No	No	Patient has no
	Before CT	No	No	No	No	No	No	No	No	No	No	complaint of BD and
	During RT	No	No	No	No	No	No	No	No	No	No	does not need to use
	Current	No	No	No	No	No	No	No	No	No	No	colchicine
12	Before BC	Yes	Yes	No	No	Yes	No	No	No	Once	Prd, cyclophosphamide	Patient has a reduced complaint of BD, and
	During CT	No	No	No	No	No	No	No	No	No	No	her visual defect is
	During RT	No	No	No	No	No	No	No	No	No	No	stable
	Current	Yes	No	No	No	Yes	No	No	No	No	No	

[a]Musculoskeletal pain, +Exitus due to metastatic BC, A telephone questionnaire for the complaints of BD was performed in all patients. *The aching muscle-joint regions before BC diagnosis, #1, 3, 5, 6, 7, 10, and 11 had positive pathergy test. GIS=Gastrointestinal system. EN=Erythema nodosum. IS=Immunosuppressive drugs, Prd=Prednisolone or methyl prednisolone, MMF=Mycophenolate mofetil, CT=Chemotherapy, BC=Breast cancer, BD=Behçet's disease, RT=Radiotherapy

of our patients experienced any thrombotic event during or following BC treatment.[13] This finding may partly be attributed to the chronic use of ASA treatment in these group of patients.[42]

In some retrospective studies, RT during AiD has been shown to lead to an increased incidence of lung pathologies, scarring, and tissue necrosis.[5,43] Unfortunately, the data concerning the relation between RT side effects and BD are limited in the literature. Only one BC patient with BD was reported to have a severe skin necrosis related to RT.[44] By contrast, none of our patients had such a side effect during or after RT.

Cyclophosphamide is effectively used in AiDs at a much lower dose as compared to those used in the treatment of

other cancer types such as BC. Furthermore, novel targeted therapies or conventional chemotherapeutic agents have been shown to provide some clinical improvements through IS effects in AiD. For instance; interferon, natalizumab, rituximab or high-dose cyclophosphamide in multiple sclerosis; high-dose cyclophosphamide in autoimmune aplastic anemia; etanercept and infliximab in BD; rituximab in systemic lupus erythematosus; and methotrexate in rheumatoid arthritis.[45] In our study, the treatments used in BC did not have any objective or subjective negative impact on the prognosis of BD. On the contrary, we observed that CT was likely to be associated with a durable complete recovery in the clinical findings of BD.

Aside from its retrospective nature, the most important limitation of our study was that the numbers of cases were too small to drive a definite conclusion or to make a comparative statistical analysis. One another important limitation was the lack of data regarding the quality of life for both diseases. We were therefore unable to demonstrate whether BD has any negative or positive impact on the quality of life in BC or vice versa.

CONCLUSION

We did not observe any negative effect of Behçet's disease on BC or vice versa. CT regimens (such as cyclophosphamide, adriamycin, and taxane) or HT (such as tamoxifen) may safely be given in BC patients with BD using colchicine treatment. Despite the multiple etiological factors predisposing to increased risk of thrombosis in these patients, ASA alone seems to be safe and also has enough therapeutic efficacy in preventing the vascular events. Finally, colchicine treatment might have a potential role as an anticancer drug in BC. However, more prospective studies including a large number of patients are warranted with the goal of identifying possible effects of BD on BC prognosis or vice versa.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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