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CASE BASED REVIEW

Systemic vasculitis involving the breast: a case report and literature review

Jiaqi Ren[1] · Jianying Liu[2] · Jing Su[2] · Jingfeng Zhang[1] · Jinxia Zhao[1]

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Abstract

Systemic vasculitis involving the breast is a rare clinical condition and may mimic breast cancer or mastitis clinically or radiographically. Here, we report a case of polyarteritis nodosa (PAN) with breast involvement and perform a literature review of published cases of systemic vasculitis affecting the breast to better understand this disorder. We report a case of PAN affecting the right breast in a young woman. A retrospective review was performed by searching Medline, Embase, Web of Science, the Cochrane Library, and Scopus for cases of systemic vasculitis involving the breast written in English up to June 1st, 2018. A 27-year-old woman presented with a painful mass in the right breast was diagnosed as PAN by the biopsy. She was treated with prednisone and methotrexate for 6 months, at which time her condition had stabilized and inflammatory markers had normalized. A total of 66 cases were identified, with granulomatosis with polyangiitis (GPA), giant cell arteritis (GCA), and PAN as the main types. The typical manifestation was mass (79.2%, 53/67) in the breast, and all diagnoses were made by the pathology of the breast biopsy. Glucocorticoid and immunosuppressant were the main therapies, and 74.6% (50/67) patients achieved remission during follow-up. Our case and a literature review of 66 cases of systemic vasculitis involving the breast reveal the importance of tissue biopsy to obtain a definitive diagnosis, because the vasculitis subtype strongly influences prognosis.

Keywords Systemic vasculitis · Breast

Introduction

Systemic vasculitis is a group of heterogeneous diseases which mainly manifests as inflammation of the blood vessels. Nearly all organs can be affected, but the skin, kidney, and upper and lower respiratory tract are most commonly involved [1]. However, the breast has rarely been reported as the involved site of systemic vasculitis [2, 3]. Here, we report such a case and perform a review on the published cases of systemic vasculitis involving the breast. The results will help to further delineate the clinical presentation, course, and treatment of this disease.

Case report

A 27-year-old woman came to our hospital with a 40-day history of swollen and painful right breast, with a palpable mass in the outer portion of the breast. She also reported polyarthralgia of 10-day duration. On presentation, she had a low-grade fever but no other discomforts, such as fatigue, cough, rash, myalgia, or oral ulcers. As acute mastitis was considered as a possible diagnosis, she was treated with intravenous antibiotics for 5 days. However, the mass became purulent and fluctuant. Breast ultrasound showed multiple hypoechoic areas near the outer portion of the right

✉ Jinxia Zhao
zhao-jinxia@163.com

Jiaqi Ren
ren_jiaqi@qq.com

Jianying Liu
liujianying@bjmu.edu.cn

Jing Su
sujing@bjmu.edu.cn

Jingfeng Zhang
zhangjingfeng@bjmu.edu.cn

[1] Department of Rheumatology and Immunology, Peking University Third Hospital, No. 49, North Garden Road, Beijing 100191, China

[2] Department of Pathology, School of Basic Medical Sciences, Peking University, Beijing 100191, China

breast and the nipple. Incision and drainage of the right breast were performed, and cefazolin and ornidazole were prescribed for 10 days. Although the symptom of her breast did not become any better, the body temperature returned to normal. Ten days later, multiple joints became persistent painful, including bilateral knee, ankle, wrist, hip, and metacarpophalangeal joints. Her left ankle joint became swollen, and erythema appeared on the left ankle joint and both sides of the anterior tibiae near the knee joints. The ankle lesion was initially about 3 cm in diameter but expanded to 8 cm and was accompanied by an increase in skin temperature. The patient's body temperature rose to 38.5 °C, and she experienced chills. She was prescribed ibuprofen and metamizole sodium without effect, and she experienced a 5-kg loss of body weight in 1 month.

At first admission to our hospital, the patient's temperature was at 38.7 °C, but other vital signs were normal. Physical examination revealed an unhealed wound in the right breast, with rupture and little blood and fluid oozing on the surface. A small amount of necrotic tissue could be seen on the surface, as shown in Fig. 1a. Erythema nodosum was present on the left ankle joint and both knee joints, which were tender upon gentle palpation, without itching and peeling. There was also tenderness on both sides of the gastrocnemius muscle. Laboratory findings disclosed the following: white blood cell count: 10.2×10^9/L (normal: $3.5–9.5 \times 10^9$/L); neutrophil proportion: 84.3% (normal: 40–75%); hemoglobin: 108 g/L (normal: 130–175 g/L); calcitonin: 0.131 ng/mL (normal: < 0.1 ng/mL); erythrocyte sedimentation rate (ESR): 52 mm/h (normal: 0–20 mm/h); C-reactive protein (CRP): 148 mg/L (normal: ≤ 8 mg/L). Abnormal liver function was evident: alanine aminotransferase (ALT): 124 U/L (normal: 9–50 U/L), aspartate aminotransferase (AST): 54 U/L (normal: 15–40 U/L); γ-glutamyl transferase (γ-GT): 676 U/L (normal: 9–50 U/L); alkaline phosphatase (ALP): 381 U/L (normal: 45–125 U/L). Serum immunoglobulin E level was elevated at 700 IU/mL (normal: < 100 IU/mL), as was complement factor C4 (0.421 g/L, normal: 0.12–0.40 g/L). Other routine biochemical tests, including renal function tests, were normal. Pituitary prolactin was normal, and an autoantibody screen was negative (rheumatoid factor, and antinuclear and anti-neutrophil cytoplasmic antibodies). Chest computed tomography reveled a soft-tissue mass on the right breast and swollen axillary lymph nodes on the same side. Ultrasound showed obvious swelling of subcutaneous soft tissue around the left ankle joint and the dorsum of the foot, and effusion of the talofibular joint. Ultrasound of her left knee joint also showed swelling of the subcutaneous soft tissue, but no joint effusion or synovitis. No arterial or venous thromboses of the bilateral legs were noticed on the ultrasound.

In the current reported case, the patient complained of polyarthralgia, which prompted us to consider arthritic disease, such as reactive arthritis, rheumatoid arthritis, or some other diseases at first, and the symptoms on her right breast might be caused by infection, tuberculosis, or malignancy. However, the negative autoantibody screen, elevated ESR and CRP level, and the failure of the breast to heal after full course of antibiotics were puzzling.

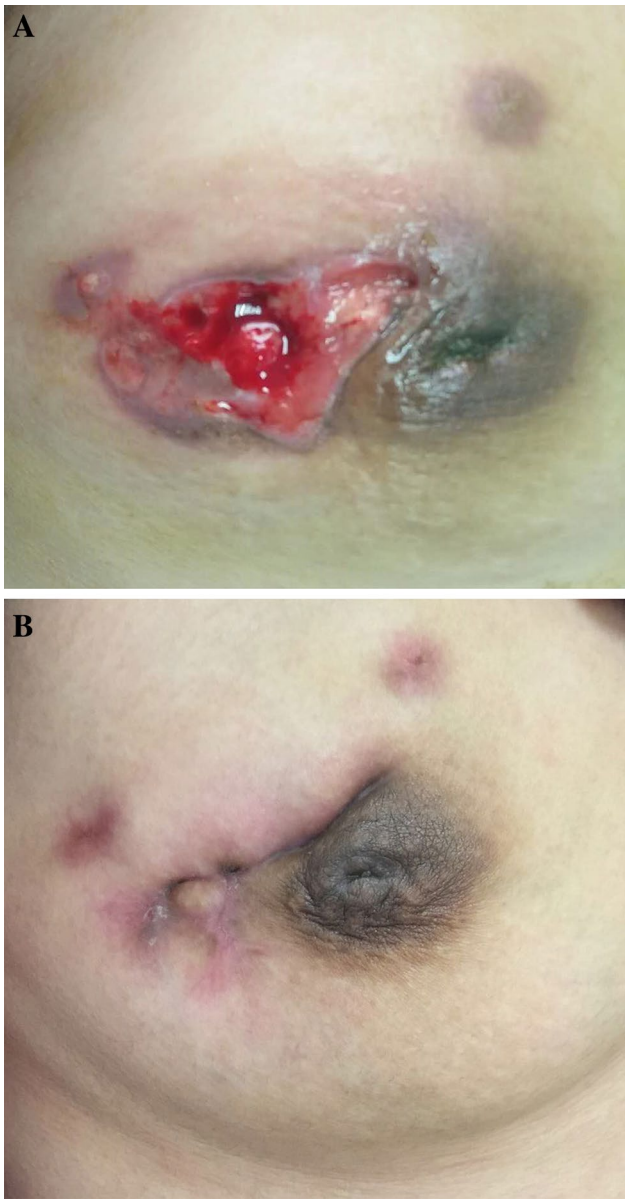

Fig. 1 The clinical manifestation of the patient's right breast. **a** Before treatment: a painful mass on the outer portion of right breast, with rupture and blood and fluid oozing on the surface. **b** After treatment: the wound had got well healed

To make a diagnosis, biopsy of the lesion on the right breast was performed. Histological analysis indicated inflammatory necrosis and multiple arterioles [positive for α-smooth muscle actin (SMA), CD31, elastic fiber staining] were presented as proliferative obliterate endarteritis in

granulation tissue, which was highly suggestive of nodular arteritis or another type of vasculitis (Figs. 2, 3). Biopsy of the nodular erythema on the knee showed infiltration of the vascular wall by inflammatory cells, mainly lymphoid mononuclear cells and a few neutrophils. The inflammation involved small vessels and the periphery of the fat lobule, which is in agreement with changes observed in skin vasculitis, especially PAN. Therefore, the diagnosis of PAN was considered. Full-dose prednisone (1 mg/kg/day) and methotrexate (15 mg/week) were prescribed, and the breast lesion healed after 2 weeks of treatment. Six months later, her condition kept stable (Fig. 1b) and inflammatory markers remained normal. Timeline of clinical features and interventions were summarzied in Fig. 4).

Search strategy

Data sources and searches

We searched PubMed, Embase, the Cochrane Library, Web of Science, and Scopus for cases of systemic vasculitis involving the breast published in English up to June 1st, 2018. The search terms were arteritis, vasculitis, and breast. We reviewed the abstracts of relevant studies and retrieved appropriate articles. We also scrutinized the reference lists of the included studies to identify additional references.

Study selection

Two authors independently scanned the titles and abstracts for the following inclusion criteria: (1) cases of systemic vasculitis involving the breast, (2) published in English language, and (3) published in a peer-reviewed journal. Reviews and other study types lacking clinical data from individual patients were excluded. There was no disagreement between the two reviewers at any point in the selection process.

Data extraction and study quality assessment

Two investigators extracted the following data independently using a standard form: author, publication year, clinical history, laboratory values, histopathologic features, treatment, and outcomes [4].

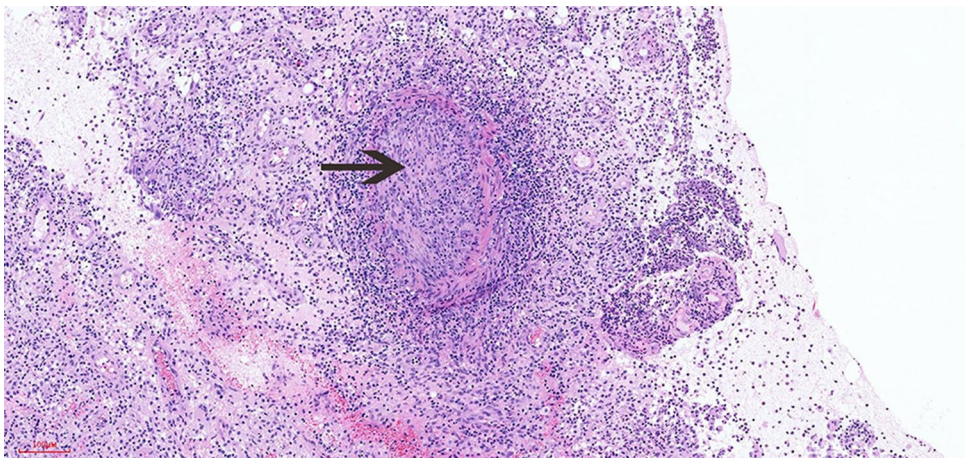

Fig. 2 Photomicrographs of the patient's right breast biopsied specimen. Occlusion of the vessel, destruction of the vascular wall infiltrated with inflammatory cells, mainly lymphocytes, and a small amount of neutrophils (hematoxylin and eosin stains; original magnification ×100)

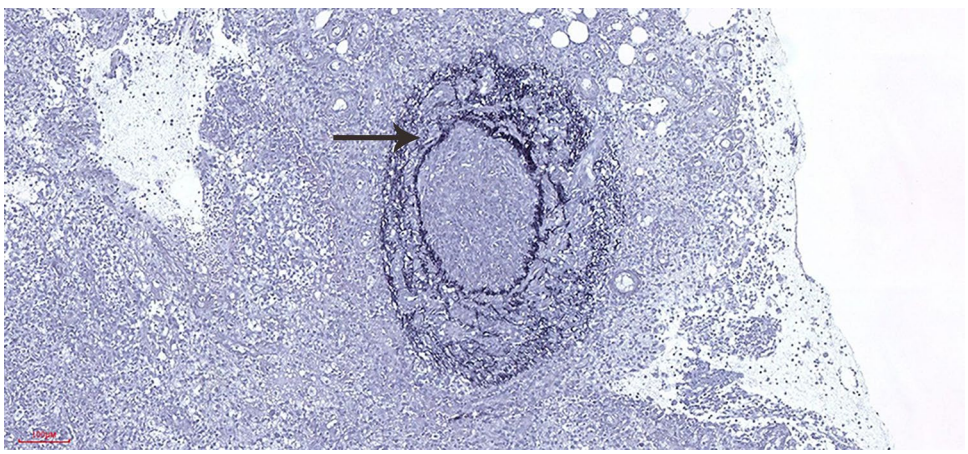

Fig. 3 Photomicrographs of the patient's right breast biopsied specimen. This confirmed that the involved vessels were arteries (elastic fibers staining; original magnification ×100)

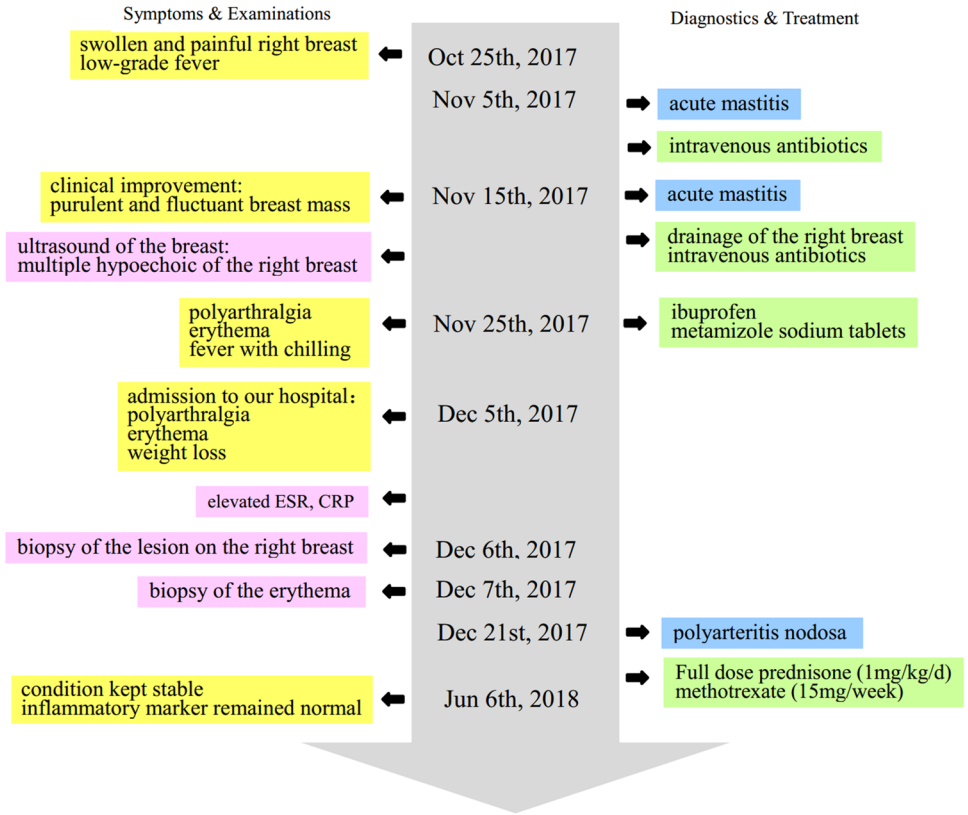

Fig. 4 Timeline of clinical features and interventions

Results

In addition to our case, 66 cases were identified by the literature review (Table 1). Detailed patient characteristics are shown in Table 1. The main types of vasculitis affecting the breast were granulomatosis with polyangiitis (GPA, $n=23$), giant cell arteritis (GCA, $n=17$), and PAN ($n=17$). Three cases of eosinophilic granulomatosis with polyangiitis (EGPA) [5–7], three of Behcet's disease [8–10] and two of microscopic polyangiitis (MPA) [11, 12], and two of unclassified vasculitis made up the remainder of the 67 cases.

The patients with breast-involved vasculitis were 54.2 ± 14.7 years of age (mean $\pm$ SD) with a range of 21 [13] to 78 [14] years. However, the mean ages of patients with different types of vasculitis varied. Among the 67 cases, the disease duration ranged from a few weeks to several months. Breast involvement was the first symptom in some patients and appeared after diagnosis or treatment in others. The typical formation was a mass. Primary ulceration of the breast occurred in only two patients [9, 15], but could have been secondary to the breast mass. Bilateral involvement of the breast was about twice as common as unilateral involvement. Breast involvement alone was observed in only 22.4% (15/67) patients, mainly PAN and GCA patients, whereas the majority (77.6%) presented with extramammary manifestations such as myalgia, arthralgia, headache, rash, cough, and hematuria.

As for the laboratory test, anemia was found in some cases. Inflammatory parameters of ESR and CRP were commonly elevated in all kinds of systemic vasculitis. Diagnosis of all cases was made after breast biopsy and pathological examination, because mammography and ultrasound of the breast were not specific for the diagnosis. As shown in Table 2, 25/67 patients underwent mammography, with the results ranging from normal to increased dense mammary parenchyma, heterogeneous breast tissue, vascular calcification, skin or trabecular thickening, and nodular masses. Ultrasound was performed in 18 patients, which revealed 11.1% (2/18) with skin thickening, 55.56% (10/18) with lesions with or without necrosis or calcifications, 22.2% (4/18) with hypoechoic mammary parenchyma or infiltration of the breast, and 11.1% (2/18) with penetration of the blood vessels. Notably, 35.0% (7/20) and 30.0% (6/20) patients with mass detected on breast examination could be detected on mammography and ultrasound, respectively.

The main therapies for systemic vasculitis involving the breast were glucocorticoid and immunosuppressant. Of the 67 patients, 44 (65.7%) received oral or intravenous glucocorticoid. Of these, 16 patients were treated with glucocorticoids alone and remitted, and 28 patients were given combined therapy with glucocorticoid and immunosuppressant, mainly cyclophosphamide and azathioprine. Besides, some patients became well after rituximab [2], mastectomy [14, 16], loxoprofen sodium [17], or even no treatment [18].

Table 1 The summary of the characteristics of the patients

	PAN	GPA	GCA	MPA	EGPA	Behcet's disease	Others	Total
Case number % (no./total no.)	25.4 (17/67)	34.3 (23/67)	25.4 (17/67)	3 (2/67)	4.5 (3/67)	4.5 (3/67)	3 (2/67)	100 (65/67)
Mean age ± SD (years)	52.4 ± 18.2	49.8 ± 12.4	63.6 ± 7.4	45.5 ± 20.5	64.0 ± 14.2	36.6 ± 12.5	61.0 ± 7.1	54.2 ± 14.7
Gender % (no./total no.)								
Male	0 (0/17)	4.3 (1/23)	0 (0/17)	0 (0/2)	33.3 (1/3)	0 (0/3)	0 (0/2)	3 (2/67)
Female	100 (17/17)	95.7 (22/23)	100 (17/17)	100 (2/2)	66.7 (2/3)	100 (3/3)	100 (2/2)	97 (65/67)
Duration % (no./total no.)								
≤ 1 month	35.3 (6/17)	34.8 (8/23)	64.7 (11/17)	0 (0/2)	0 (0/3)	33.3 (1/3)	0 (0/2)	38.8 (26/67)
> 1 month	35.3 (6/17)	30.4 (7/23)	11.8 (2/17)	100 (2/2)	100 (3/3)	33.3 (1/3)	100 (2/2)	34.3 (23/67)
NA	29.4 (5/17)	34.8 (8/23)	23.5 (4/17)	0 (0/2)	0 (0/3)	33.3 (1/3)	0 (0/2)	26.9 (18/67)
Formation % (no./total no.)								
Mass	88.2 (15/17)	91.3 (21/23)	88.2 (15/17)	0 (0/2)	0 (0/3)	66.7 (2/3)	0 (0/2)	79.1 (53/67)
Ulcer	5.9 (1/17)	0 (0/23)	0 (0/17)	0 (0/2)	0 (0/3)	33.3 (1/3)	0 (0/2)	3 (2/67)
Others	5.9 (1/17)	8.7 (2/23)	11.8 (2/17)	100 (2/2)	100 (3/3)	0 (0/3)	100 (2/2)	17.9 (12/67)
Bilateral % (no./total no.)								
Yes	35.3 (6/17)	17.4 (4/23)	41.2 (7/17)	50 (1/2)	67.7 (2/3)	33.3 (1/3)	50 (1/2)	32.8 (22/67)
No	64.7 (11/17)	82.6 (19/23)	58.8 (10/17)	50 (1/2)	33.3 (1/3)	67.7 (2/3)	50 (1/2)	32.8 (22/68)
Extramammary % (no./total no.)								
Yes	64.7 (11/17)	87 (20//23)	64.7 (11/17)	100 (2/2)	100 (3/3)	100 (3/3)	100 (2/2)	77.6 (52/67)
No	35.3 (6/17)	13.0 (3/23)	35.3 (6/17)	0 (0/2)	0 (0/3)	0 (0/3)	0 (0/2)	22.4 (15/67)
ESR % (no./total no.)								
Normal	11.8 (2/17)	8.7 (2/23)	0 (0/17)	0 (0/2)	0 (0/3)	0 (0/3)	100 (2/2)	9 (6/67)
High	70.6 (12/17)	43.5 (10/23)	82.4 (14/17)	100 (2/2)	33.3 (1/3)	33.3 (1/3)	0 (0/2)	59.7 (40/67)
NA	17.6 (3/17)	47.8 (11/23)	17.6 (3/17)	0 (0/2)	67.7 (2/3)	66.7 (2/3)	0 (0/2)	31.1 (21/67)
CRP % (no./total no.)								
Normal	17.6 (3/17)	4.3 (1/23)	0 (0/17)	0 (0/2)	0 (0/3)	0 (0/3)	50 (1/2)	7.5 (5/67)
High	47.1 (8/17)	26.1 (6/23)	23.5 (4/17)	100 (2/2)	33.3 (1/3)	0 (0/3)	50 (1/2)	32.8 (22/67)
NA	35.3 (6/17)	69.6 (16/23)	76.5 (13/17)	0 (0/2)	67.7 (2/3)	100 (3/3)	0 (0/2)	59.7 (40/67)
ANCA % (no./total no.)								
Negative	47.1 (8/17)	8.7 (2/23)	11.8 (2/17)	0 (0/2)	33.3 (1/3)	0 (0/3)	0 (0/2)	19.4 (13/67)
Positive	23.5 (4/17)	43.5 (10/23)	5.9 (1/17)	100 (2/2)	33.3 (1/3)	0 (0/3)	50 (1/2)	28.4 (18/67)
NA	29.4 (5/17)	47.8 (11/23)	82.4 (14/17)	0 (0/2)	33.3 (1/3)	100 (3/3)	50 (1/2)	52.2 (35/67)
Glucocorticoid % (no./total no.)								
Yes	58.5 (10/17)	73.9 (17/23)	58.8 (10/17)	100 (2/2)	100 (3/3)	33.3 (1/3)	50 (1/2)	65.7 (44/67)
No	29.4 (5/17)	21.7 (5/23)	35.3 (6/17)	0 (0/2)	0 (0/3)	66.7 (2/3)	50 (1/2)	28.4 (19/67)
NA	11.8 (2/17)	4.3 (1/23)	5.9 (1/17)	0 (0/2)	0 (0/3)	0 (0/3)	0 (0/2)	4 (4/67)
Immunosuppressant % (no./total no.)								
Yes	23.5 (4/17)	69.6 (16/23)	0 (0/17)	100 (2/2)	33.3 (1/3)	0 (0/3)	100 (2/2)	37.3 (25/67)
No	64.7 (11/17)	26.1 (6/23)	94.1 (16/17)	0 (0/2)	0 (0/3)	0 (0/3)	0 (0/2)	49.3 (33/67)
NA	11.8 (2/17)	4.3 (1/23)	5.9 (1/17)	0 (0/2)	67.7 (2/3)	100 (3/3)	0 (0/2)	13.4 (9/67)
Outcomes % (no./total no.)								
Remission	76.5 (13/17)	82.6 (19/23)	82.4 (14/17)	0 (0/2)	33.3 (1/3)	67.7 (2/3)	50 (1/2)	74.6 (50/67)
No remission	5.9 (1/17)	0 (0/23)	11.8 (2/17)	50 (1/2)	0 (0/3)	33.3 (1/3)	50 (1/2)	9 (6/67)
Died	6.3 (1/17)	13 (3/23)	0 (0/17)	50 (1/2)	33.3 (1/3)	0 (0/3)	0 (0/2)	9 (6/67)
NA	11.8 (2/17)	4.3 (1/23)	5.9 (1/17)	0 (0/2)	33.3 (1/3)	0 (0/3)	0 (0/2)	7.5 (5/67)

Noticeably, the intensity of treatment differed for breast vasculitis. For GCA patients, no patients received immunosuppressant, but achieved high proportion of remission (10/17, 82.7%) and no one died due to this disease. The proportion of using glucocorticoid was higher in GPA patients (17/23, 73.9%) than PAN patients (10/17, 58.5%), as well as use of the immunosuppressant (16/23, 69.6% vs 4/17, 23.5%), and remission rate (19/23, 82.6% vs 13/17, 76.5%). In general,

Table 2 The mammography and ultrasound features of the patients

Authors	Year	Diagnosis	Formation	Mammography	Breast ultrasound
Lee [20]	2017	PAN	Mass	Heterogeneously dense, mild skin thickening, increased parenchymal densities, trabecular thickening in both breasts	Skin thickening, increased echogenicity in the subcutaneous fat layer of both breasts, tubular and reticular anechoic fluids within the fat layer, no definite mass, but hypoechoic circumferential wall thickenings of the artery with perivascular fat infiltration along the vessel
Griffiths [21]	2017	PAN	Mass	No architectural distortions and calcifications	
Shimamura [22]	2015	PAN	Mass	No architectural distortions and calcifications	No architectural distortions and calcifications
Khalil [9]	2009	PAN	Mass	No fibro-glandular parenchyma	A 2.0 cm complex cyst with internal echoes of low signal intensity and a rather irregular thickened capsule
		PAN	Tenderness	Vascular calcifications throughout both breasts, no focal masses	Inflamed fibro-glandular tissue in the retroareolar region
Hong [23]	2007	PAN	Mass	A 1.8 cm, heterogeneous and irregular shaped mass-like lesion	Multifocal microcalcifications
Orbo [14]	1989	PAN	Mass	A dense area in the right mammary gland above the nipple, calcification of arteries in both breasts	
Lluch [13]	2018	GPA	Mass	Several solid nodules with ill-defined margins in the right breast	Various hyperechoic solid lesions, some of them with anechoic areas of necrosis
Ryba [24]	2017	GPA	Thickening		Knobby changes in the right breast
Mengoli [25]	2017	GPA	Mass		A retro areolar, hypoechoic, irregularly shaped and partially necrotic lesion (3.7 cm across), no lymphadenopathy
Georgescu [26]	2015	GPA	Mass		A poorly defined mass in the left breast with multiple pleomorphic calcifications inside the mass and in its proximity
Neralic-Meniga [18]	2006	GPA	Mass	Multiple, delineated masses within the heterogeneous parenchyma, without associated micro calcifications	Multiple solid hypoechoic lesions with a homogeneous internal echo pattern and smooth margins, anechoic areas of necrosis in some of the lesions
Erysami [27]	2006	GPA	Mass	A 1.9 cm × 1.7 cm lesion	A 1.9 cm × 1.7 cm lesion
Stappaerts [19]	1999	GPA	Mass		Compatible with the presence of a malignant tumor
Gobel [28]	1995	GPA	Mass	A large opacification with a indistinct border in right breast	
Deininger [29]	1985	GPA	Mass	A poorly outlined mass with diameter of 2.5–3.0 cm with an heterogeneous structure and radian sours	
		GPA	Induration	Heterogeneous structure and poorly bounded mass with cordlike indurations to the nipple and thickening of the skin	
Hinze [30]	2011	GCA	Mass	Heterogeneous density breast tissue	
Kadotani [15]	2010	GCA	Mass	Bilateral vascular calcification with dense mammary parenchyma but no evidence of malignancy	Slightly hypoechoic mammary parenchyma, no mass lesions in the breasts
Kafantari [31]	2008	GCA	Mass	A mass measuring 2 cm × 1.5 cm, causing a significant disruption in the architecture of the surrounding breast tissue	
Marie [32]	2008	GCA	Mass	Normal	
Anim [33]	2004	GCA	Tenderness	No definite masses or changes to suggest malignancy, but infiltration in the upper outer quadrants of both breasts	Infiltration of both breasts, no definite masses or changes to suggest malignancy

Table 2 (continued)

Authors	Year	Diagnosis	Formation	Mammography	Breast ultrasound
Kim [30]	1990	GCA	Mass	No mass lesions, but several enlarged heterogeneous echogenicity without any definite fluid collection	
Lee [34]	2017	EGPA	None	A 2.3 × 1.1 × 0.4 cm area of altered echotexture in the left breast	A 2.3 × 1.1 × 0.4 cm area of altered echotexture in the left breast
Visentin [2]	2012	EGPA	Edema	Bilateral gynecomastia with skin thickening and mammary fat reticulation, lymphatic stasis involving the left breast	A bilateral gynecomastia with signs of lymphatic stasis involving the left breast
Devinck [7]	2011	MPA	Redness	A retro areolar lesion of 2.5 cm in diameter with penetration of the blood vessels	A retro areolar lesion of 2.5 cm in diameter with penetration of the blood vessels
Villalba-Nuno [3]	2002	EGPA	Redness	Bilateral diffuse increase in parenchymal density with skin thickening	Bilateral diffuse increase in parenchymal density with skin thickening
Soleto [4]	2002	Behcet's disease	Mass	Increased focal density in the retroareolar mammary parenchyma	A hypoechoic nodule with poorly defined margins located at radial
Zardawi [35]	2004	Others	Redness	A slight increase in the density of the right breast tissue	

the prognosis for patients with systemic vasculitis involving the breast was relatively good, with 74.6% (50/67) achieving remission during follow-up, but there were still five patients [5, 12, 13, 19–21] dead due to the involvement and failure of vital organs. Although only two patients were diagnosed with MPA, neither achieved remission.

Discussion

The breast is a rare organ that can be affected by systemic vasculitis. The first case of systemic vasculitis with breast involvement was GCA, reported in 1950 by Waugh [22]. By now, GPA, PAN, EGPA, MPA, and Behcet's disease of the breast have been reported.

Our literature review identified 66 additional cases of vasculitis involving the breast. In some cases, the precipitating factor for breast involvement could be found; for example, mammoplasty [23], silicone breast implants [12, 24], radiotherapy of the breast [25], and invasive ductal carcinoma of the breast [26].

Symptoms of breast involvement can occur at the time of diagnosis or later on. There are two basic manifestations of the breast: masses and ulcerations. Compared to the limited manifestation of the breast, the external manifestations of mammary are more common. Systemic symptoms, including fever, fatigue, weight loss, arthralgia, and rash, can be signs for systemic vasculitis, but are not specific for the disease subtype. Several characteristic features are helpful for classifying vasculitis. For example, polymyalgia rheumatica (PMR)-like symptoms and involvement of the carotid arteries and their branches, especially temporal arteries, are commonly associated with GCA [27]. A history of asthma, allergic rhinitis, and paranasal sinusitis can be helpful in diagnosing EGPA.

Radiological manifestations of the breast are various, as mentioned above, but none is specific for vasculitis, let alone the category. Imaging findings included calcifications and vessel penetration [11, 13, 16, 17, 28], but were detected at low rates (5/47) by mammography and breast ultrasound. Nodular lesions were easily detected; however, they can be mistaken for malignant lesions, leading to mastectomy or wide excision that was unnecessary for the treatment of breast vasculitis. Some images revealed homogeneous or increased dense mammary parenchyma [16, 17, 27–30], suggesting the presence of both multiple small nodules and diffuse edema. Taken together, these findings suggest that mammography and breast ultrasound are not reliable for the diagnosis of breast vasculitis.

The diagnosis made by the biopsy and pathology of the breast should be the gold diagnostic criteria, which have been illustrated very clearly in many papers [3, 5, 28, 31]. Histologically, it is easy to distinguish vasculitis from

malignancy, but not from non-puerperal mastitis, which encompasses all causes of inflammatory changes in the female breast and mammilla not related to lactation. The etiology of non-puerperal mastitis is still unknown, with mammary duct ectasia (MDE), periductal mastitis (PDM), and granulomatous lobular mastitis (GLM) being the most frequent subtype classifications. No vessels should be involved, which is the main difference from vasculitis. Thus, vessel-specific stains, like SMA, CD31, and elastic fibers stains, can be helpful for the diagnosis of vasculitis.

Other differential diagnoses include malignancy of the breast [32, 33], sarcoidosis, fungal infections, tuberculosis, and Mondor's disease [3, 31, 33], all of which have been clearly described in previous articles. In our case, unclassified systemic vasculitis cannot be completely excluded based on the histopathology. However, as the main vessels involved were muscular arterioles, and the clinical manifestation of the patient including fever, weight loss, polyarthralgia, erythema, and the tenderness on both sides of the gastrocnemius muscle, all point to PAN as the most likely diagnosis.

Once the diagnosis was made, the treatment of this disease was straightforward, mainly, consisting mainly of glucocorticoid and immunosuppressant therapy. In general, prognosis was good and most patients achieved remission within a few months of treatment. However, the treatment regimen and outcomes differed for each disease subtype. Most GCA patients entered remission by the single drug of glucocorticoid, but, for GPA patients and PAN patients, most of whom need immunosuppressant on the basic treatment of glucocorticoid could get good prognosis, as well. Unlike them, the prognosis of MPA patients was the worst. Collectively, the analysis of our patient and the literature indicate that distinction between localized and systemic involvement is critical for treatment, because systemic involvement, particularly the kidneys, heart, and liver, carries a poor prognosis.

Conclusion

In total, we reviewed the clinical features and outcome of 67 cases of systemic vasculitis involving the breast, which included GPA, GCA, PAN, MPA, EGPA, and Behcet's disease. Tissue biopsy is essential for making diagnosis, and the prognosis of diseases is relatively good, but upon to the types.

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Compliance with ethical standards

Conflict of interest Jiaqi Ren, Jianying Liu, Jing Su, Jingfeng Zhang, and Jinxia Zhao declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All authors fulfilled the ICMJE authorship criteria.

Informed consent Written informed consent was obtained from the patient prior to submission of this article for consideration as a case-based review.

References

1. Firestein GS, Kelley WN (2013) Kelley's textbook of rheumatology, 9th edn. Elsevier/Saunders, Philadelphia
2. Lluch J, Montserrat Perez-Tapia L, Taco-Sanchez MDR, Narvaez J (2018) Breast involvement in granulomatosis with polyangiitis. Joint Bone Spine. https://doi.org/10.1016/j.jbspin.2018.05.004
3. Tabbarah A, Voltaggio L (2017) Giant cell arteritis of the breast. Arch Pathol Lab Med 141(9):1283–1287. https://doi.org/10.5858/arpa.2016-0285-RS
4. Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD (2011) Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int 31(11):1409–1417. https://doi.org/10.1007/s00296-011-1999-3
5. Lee MXW, Teng GG, Raju GC, Lim AYN (2015) Catastrophic subarachnoid hemorrhage in eosinophilic granulomatosis with polyangiitis without asthma. Int J Rheum Dis 20(12):2127–2131. https://doi.org/10.1111/1756-185x.12594
6. Visentin MS, Salmaso R, Modesti V, Ometto F, Ruffatti A, Punzi L, Doria A (2012) Parotid, breast, and fascial involvement in a patient who fulfilled the ACR criteria for Churg–Strauss syndrome. Scand J Rheumatol 41(4):319–321. https://doi.org/10.3109/03009742.2012.672593
7. Villalba-Nuno V, Sabate JM, Gomez A, Vidaller A, Catala I, Escobedo A, Torrubia S (2002) Churg–Strauss syndrome involving the breast: a rare cause of eosinophilic mastitis. Eur Radiol 12(3):646–649. https://doi.org/10.1007/s003300100949
8. Soleto MJ, Marcos L (2002) Behcet's disease involving the breast. Eur Radiol 12(Suppl 3):S98–S100. https://doi.org/10.1007/s00330-002-1420-4
9. Bergant AM, Widschwendter M, Sepp N (2000) Bilateral nipple ulcers in a breastfeeding woman: a manifestation of Behcet's disease? BJOG 107(10):1320–1322
10. Dündar SV, Sivri B, Gököz A (1988) Vasculitis of breast in Behçet's disease—a case report. Angiology 39(10):921
11. Devinck M, Vander Cruyssen B, Lambein K, De Keyser F, Praet M, Brusselle G (2011) Microscopic polyangiitis involving the breast. Acta Clin Belg 66(2):139–141. https://doi.org/10.2143/ACB.66.2.2062535

12. Iyoda M, Ito J, Nagai H, Sato K, Kuroki A, Shibata T, Kitazawa K, Sugisaki T (2005) Microscopic polyangiitis after silicone breast implantation. Clin Exp Nephrol 9(3):252–254. https://doi.org/10.1007/s10157-005-0366-7
13. Khalil HH, Marsden J, Akbar N, Gordon P, Roberts J, Schulte KM (2009) Polyarteritis nodosa of the breast: presentation and management. Int J Surg 7(5):446–450. https://doi.org/10.1016/j.ijsu.2009.06.005
14. Ng WF, Chow LT, Lam PW (1993) Localized polyarteritis nodosa of breast—report of two cases and a review of the literature. Histopathology 23(6):535–539
15. Dhaon P, Bansal N, Das SK, Wakhlu A, Tandon V (2013) Cutaneous polyarteritis nodosa presenting with digital gangrene and breast ulcer. Int J Rheum Dis 16(6):774–776. https://doi.org/10.1111/1756-185X.12187
16. Orbo A, Bostad L (1989) Vasculitis of the breast. Case report and literature review. APMIS 97(11):1003–1006
17. Kadotani Y, Enoki Y, Itoi N, Kojima F, Kato G, Lee CJ (2010) Giant cell arteritis of the breast: a case report with a review of literatures. Breast Cancer 17(3):225–232. https://doi.org/10.1007/s12282-009-0120-1
18. Levy A, Weinberger A, Mor C, Pinkhas J (1986) Localized polyarteritis nodosa: cases involving the lower extremities and the breast. Rheumatol Int 6(1):43–44
19. Jordan JM, Rowe WT, Allen NB (1987) Wegener's granulomatosis involving the breast: report of three cases and review of the literature. Am J Med 83(1):159–164. https://doi.org/10.1016/0002-9343(87)90513-4
20. Neralic-Meniga I, Ivanovi-Herceg Z, Mazuranic I, Puljic I, Zekan M, Gorecan M, Kos M (2006) Wegener's granulomatosis of the breast. Wien Klin Wochenschr 118(3–4):120–123. https://doi.org/10.1007/s00508-006-0536-y
21. Stappaerts I, Colpaert C, Verbraecken J, Van Marck E, Vermeire P (1999) Granulomatous mastitis as presenting sign of Wegener's granulomatosis. Acta Clin Belg 54(4):207–210. doi:https://doi.org/10.1080/17843286.1999.11754233
22. Waugh TR (1950) Bilateral mammary arteritis; report of a case. Am J Pathol 26(5):851–861
23. Griffiths A, Patel A, Roth MZ (2017) Polyarteritis nodosum of the breast in a patient with history of bilateral augmentation mammoplasty. Aesthetic Plast Surg 41(3):560–562. https://doi.org/10.1007/s00266-017-0825-z
24. Yamen H, Andrew CJ, Homsi S (2015) Polyarteritis nodosa presenting as digital gangrene and breast lesion following exposure to silicone breast implants. Case Rep Rheumatol. https://doi.org/10.1155/2015/765170
25. Reddy SM, Pui JC, Gold LI, Mitnick HJ (2005) Postirradiation morphea and subcutaneous polyarteritis nodosa: case report and literature review. Semin Arthritis Rheum 34(5):728–734. https://doi.org/10.1016/j.semarthrit.2004.11.004
26. Kafantari E, Sotiropoulou M, Sfikakis P, Dimitrakakis K, Zagouri F, Mandrekas K, Dimopoulos S, Dimopoulos MA, Papadimitriou CA (2008) Giant cell arteritis of the breast and breast cancer: paraneoplastic manifestation or concomitant disease? A case report. Onkologie 31(12):685–688. https://doi.org/10.1159/000165055
27. Hinze S, Hart YM, Adams RF (2011) Lumpy breasts and headache—a crucial ultrasound. Br J Radiol 84(1000):386–387. https://doi.org/10.1259/bjr/23418860
28. Lee JY, Joo M (2017) Isolated breast vasculitis manifested as breast edema with suggestive sonographic findings: a case report with imaging findings. J Med Ultrason 44(2):191–195. https://doi.org/10.1007/s10396-016-0753-6
29. Anim JT, van Herk EJ (2004) Giant cell arteritis of the breast. Med Princ Pract 13(4):234–236. https://doi.org/10.1159/000078322
30. Kim KH, Yang WI, Choi IJ (1990) Giant cell arteritis of the breast—a case report. Yonsei Med J 31(1):80–84. https://doi.org/10.3349/ymj.1990.31.1.80
31. Allende DS, Booth CN (2009) Wegener's granulomatosis of the breast: a rare entity with daily clinical relevance. Ann Diagn Pathol 13(5):351–357. https://doi.org/10.1016/j.anndiagpath.2009.04.005
32. Georgescu R, Podeanu MD, Colcer I, Grigorescu G, Coros MF, Moldovan C, Ilyes A, Barsan I, Moncea D, Stolnicu S (2015) Wegener's granulomatosis of the breast with peculiar radiological aspect mimicking breast carcinoma. Breast J 21(5):550–552. https://doi.org/10.1111/tbj.12458
33. Mengoli MC, Ragazzi M, Lococo F, Mengoli MA, Balli MC, Marchioni A, Rossi G (2017) Breast granulomatosis with polyangiitis mimicking breast cancer. Pathologica 109(4):405–407
34. Lee MXW, Teng GG, Raju GC, Lim AYN (2017) Catastrophic subarachnoid hemorrhage in eosinophilic granulomatosis with polyangiitis without asthma. Int J Rheum Dis 20(12):2127–2131. https://doi.org/10.1111/1756-185x.12594
35. Zardawi IM, Barker BJ, Clark DA, Davies DJ (2004) ANCA-positive vasculitis of the breast. Pathology 36(4):370–373. https://doi.org/10.1080/00313020410001721645