

Giant cell arteritis of the breast: a case report with a review of literatures

Yayoi Kadotani · Yasuyuki Enoki · Naoko Itoi ·
Fumiyoshi Kojima · Genichi Kato · Chol Joo Lee

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Abstract Although giant cell arteritis (GCA), clinically designated as temporal arteritis, is recognized as a systemic disease, the breast may be the primary organ in which it is manifested. GCA of the breast is a rare disease that mainly occurs in postmenopausal elderly women. It manifests as nodules or pain in the breast, with or without tenderness, and is associated with significant constitutional symptoms that resemble those of polymyalgia rheumatica (PMR). These symptoms can be treated with or without prednisone therapy and can improve without the development of organ dysfunction. The clinical manifestations can often be recognized only by retrospective analysis after excisional biopsy. GCA of the breast occasionally mimics carcinoma, and its initial manifestations may be similar to those of other forms of vasculitis involving the breast, such as polyarteritis nodosa and Wegener granulomatosis. Biopsy is indispensable for establishing a definitive diagnosis. Thus far, the findings of imaging procedures, such as mammography and ultrasonography, for patients with mammary GCA have not been reported in detail, and no distinctive findings associated with this condition have been identified. Considering this and the fact that spontaneous remission may occur in some cases, mammary GCA probably often goes undiagnosed or may be misdiagnosed as an ordinary mammary disease. GCA of the breast should

be considered as a potential diagnosis in the case of elderly women presenting with PMR-like symptoms and tenderness, lumps, or pain in the breast. We report a case of GCA affecting the breast and review previous reports on this condition in an attempt to summarize the features that distinguish this disease from other vascular diseases of the breast.

Keywords Giant cell arteritis · Breast · Imaging study · Biopsy · Polymyalgia rheumatica

Abbreviations

GCA	Giant cell arteritis
NSAIDs	Nonsteroidal anti-inflammatory drugs
ESR	Erythrocyte sedimentation rate
WG	Wegener granulomatosis
PAN	Polyarteritis nodosa
MMG	Mammography
US	Ultrasound
CT	Computed tomography
FNA	Fine-needle aspiration
CNB	Core needle biopsy
PMR	Polymyalgia rheumatica

Y. Kadotani (✉) · N. Itoi · C. J. Lee
Department of Breast Surgery,
Japanese Red Cross Kyoto Daiichi Hospital,
15-749 Honmachi, Higashiyama-ku, Kyoto, Japan
e-mail: yayoikadotani2004@yahoo.co.jp

Y. Enoki · F. Kojima · G. Kato
Department of Laboratory Medicine,
Japanese Red Cross Kyoto Daiichi Hospital,
15-749 Honmachi, Higashiyama-ku, Kyoto, Japan

Introduction

Giant cell arteritis (GCA) of the breast is a rare disease that mainly occurs in postmenopausal elderly women. Although it is a systemic disease, it often primarily involves the breast. Since the first case of mammary arteritis reported by Waugh in 1950 [1], some cases of mammary GCA, as either the primary clinical feature or the dominant feature of a generalized disease, have been reported. The

characteristic clinical findings include tender unilateral or bilateral nodules of the breast, significant constitutional symptoms of anorexia, weight loss, myalgia, fever, and arthralgia. These symptoms should be treated rapidly, with or without prednisone therapy, and they can improve without the development of organ dysfunction [1–18]. These typical features suggest that GCA of the breast is a unique syndrome [2].

We present a case of GCA affecting the breast and review previously published reports on this condition in an attempt to summarize the features that distinguish this disease from other vascular diseases of the breast.

Case report

A 74-year-old woman visited our hospital, presenting with tenderness in both breasts, which had persisted for several months, a subjective symptom of swelling, and erythema, which she had recently noticed. She also had mild trismus, but no headaches or visual disturbance. Physical examination confirmed the presence of multiple tender lumps (approximately 1 cm in diameter), diffuse erythema without edema in both breasts, and swollen soft lymph nodes in both axillae. A mammography (MMG) revealed bilateral vascular calcification with dense mammary parenchyma but no evidence of malignancy (Fig. 1). Ultrasonography (US) revealed no mass lesions in the breasts, although the mammary parenchyma appeared slightly hypochoic (Fig. 2).

Considering inflammatory breast cancer as a potential diagnosis, we performed a needle biopsy and scheduled a follow-up visit. Six days later, she unexpectedly visited the hospital for the second time, presenting with severe pain in both breasts. The physical examination findings had not changed, and loxoprofen sodium, a nonsteroidal anti-inflammatory drug (NSAID), was prescribed. The core needle biopsy (CNB) specimen did not exhibit any specific pathological features.

Eight days later, that is, 16 days after the patient's first visit to the hospital, the erythema in both breasts had disappeared, and the lumps had become slightly softer. However, systemic symptoms, such as general fatigue, low-grade fever, arthralgia, and trismus, were present; this led us to perform a blood examination. The results of the laboratory tests revealed the following values: white blood cell count, 13.3×10^3 cells/ μl ; hemoglobin level, 10.7 g/dl; platelet count, 44.2×10^4 cells/ μl ; C-reactive protein level, 10.0 mg/dl. The serum levels of immunoglobulin G (IgG) and complement factor C3 were slightly elevated, but autoantibody screening, such as antinuclear antibody and rheumatoid factor, proved negative. We did not measure the erythrocyte sedimentation rate (ESR).

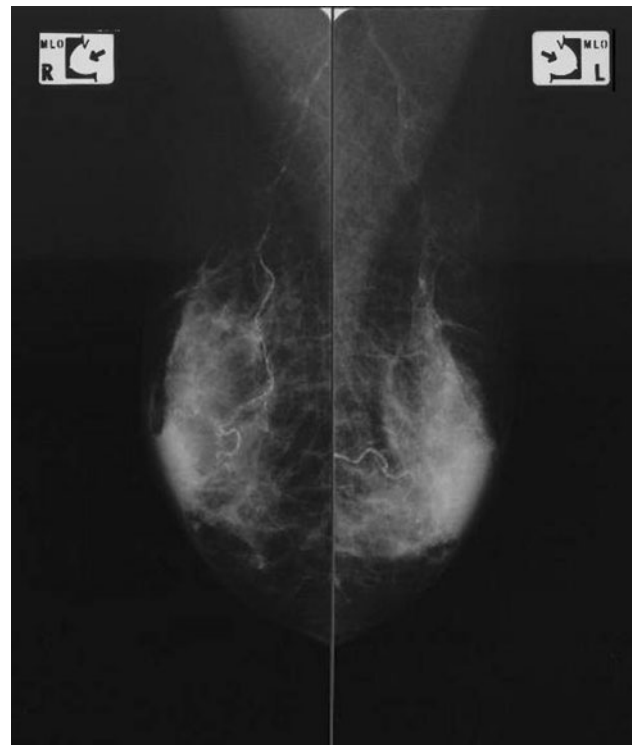


Fig. 1 MMG shows bilateral vascular calcification with dense mammary parenchyma. No mass lesion or malignant calcification is seen

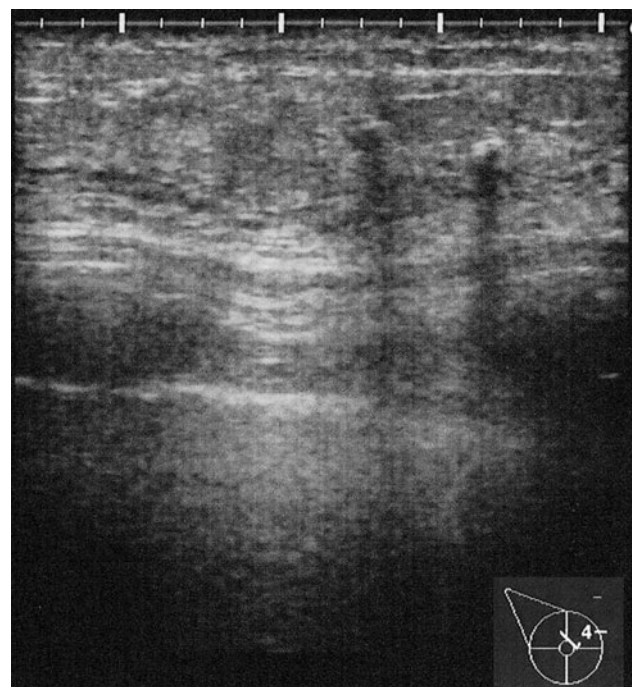


Fig. 2 US shows no mass lesions in the breasts, and the mammary parenchyma appears slightly hypochoic. Vascular calcification is seen accompanied by acoustic shadow

The findings of chest radiography were normal. A rheumatologist at our institution suspected the condition to be temporal arteritis, but an ophthalmologist rejected this possibility. The persistence of pain and lumps in both the patient's breasts indicated the urgent need for a definitive diagnosis; moreover, the patient herself sought an accurate diagnosis. An excisional biopsy was performed for a representative lump in order to clarify the pathology of the condition.

Continual treatment with loxoprofen sodium for 2 months was prescribed. By the end of the treatment period, the patient's symptoms had completely resolved, and the lumps in her breasts had disappeared. Currently, that is, about 2 years after the biopsy, the patient is in excellent health.

Pathological findings: The biopsy sample obtained from the breast consisted of rubbery fibrous tissue (2×1 cm). Serial sections of this tissue showed a white area with no obvious nodular lesions, and the tissue appeared identical or very similar to normal breast tissue. Microscopic evaluation revealed that the breast tissue mainly comprised fat tissue and was atrophic. Some of the small and medium-sized arteries in the fat tissue showed granulomatous inflammation. Intimal thickening and luminal narrowing were noted in the vessels. The transmural inflammatory infiltrate contained lymphocytes, histiocytes, and several multinucleated giant cells (Figs. 3, 4). Further, the internal elastic lamina was found to be fragmented (Fig. 5). Intimal hyperplasia was present in varying degrees and resulted in obliteration of the vessels due to thrombus formation. No fibrinoid necrosis was detected (Figs. 3, 4).

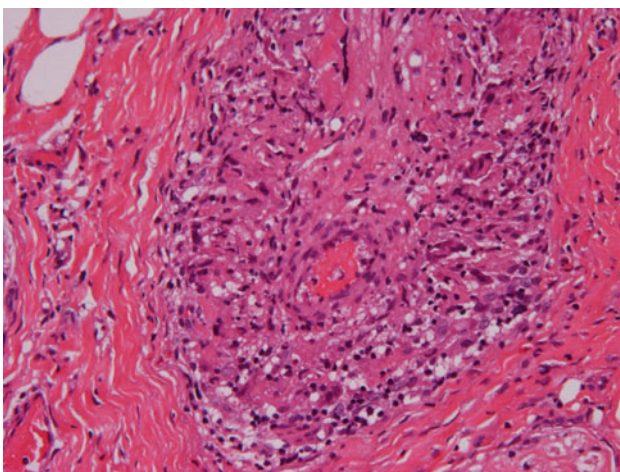


Fig. 3 The breast artery shows transmural inflammatory infiltrates including multinucleated giant cells resulting in luminal obliteration with thrombus. (H&E stain, $\times 100$)

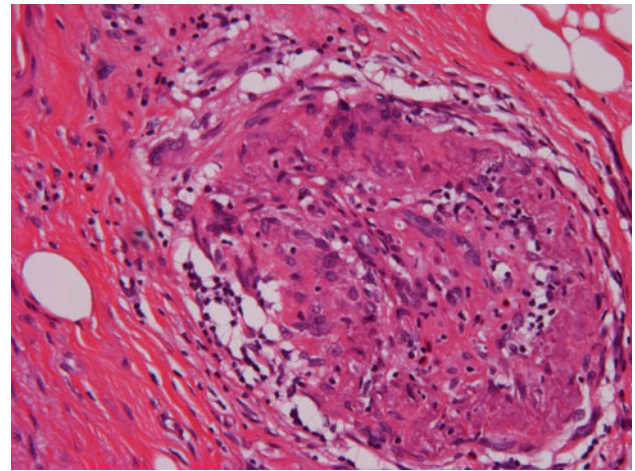


Fig. 4 The lumen of the artery is occluded due to intimal hyperplasia (H&E stain, $\times 100$)

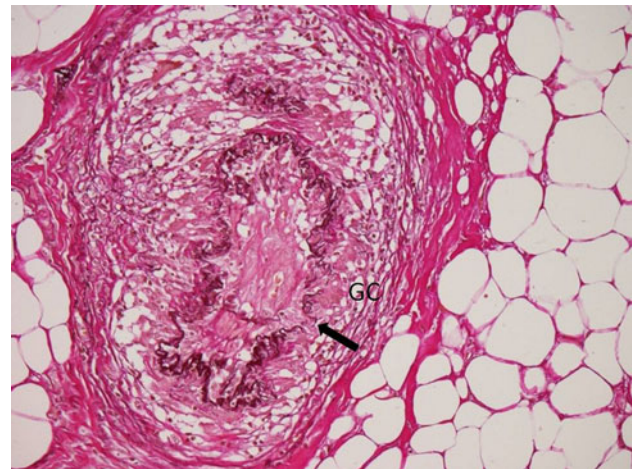


Fig. 5 A giant cell (GC) lies adjacent to the fragmented internal elastic lamina (arrow) (Elastic van Gieson stain, $\times 100$)

Discussion

Arteritis that manifests itself in the mammary glands, with symptoms such as pain and/or lumps in the breast as the chief complaint, as noted in our case, has been rarely reported [1–23]. Arteritis of the breast is pathologically classified as conditions such as GCA, Wegener granulomatosis (WG), and polyarteritis nodosa (PAN).

The pathology of GCA typically involves fragmentation of the elastica, in association with giant cell infiltration, intimal proliferation, and narrowing of the vascular lumina. Because of these clinical features, GCA is usually recognized as temporal arteritis, polymyalgia rheumatica (PMR), large-vessel arteritis, and Takayasu's arteritis [24, 25]. PAN clinically presents multisystemic panarteritis involving medium-sized and small arteries; it is accompanied by

fibrinoid deposition in the vessel wall, dense inflammatory infiltration, and occasionally luminal occlusion due to narrowing and/or thrombosis. Localized forms of PAN can affect various organs, such as the skin [26], gallbladder [27], and cervix [28]. PAN of the breast is a rare disease that usually does not involve other organs [19, 20]. WG is characterized by distinct clinical and pathological features that include necrotizing granulomatous vasculitis of the arteries and veins in the upper and lower respiratory tracts, accompanied by glomerulonephritis. WG may affect the skin, joints, and eyes, and it rarely affects only the breasts [21]. It has been reported that in eight of ten patients, WG acquires breast involvement during its clinical course [22]. This condition can usually be distinguished from granulomatous mastitis or sarcoidosis on the basis of the organs involved and the clinical course. Such discrimination can typically be achieved by performing an excisional biopsy.

In our review of English medical literature, we encountered only 20 cases [1–18] of GCA, including the present case (Table 1). In all of the cases, the patients were elderly women (median age, 65 years; range, 52–79 years). The mammary involvement was bilateral in 50% of the cases [1, 3, 6–9, 13–15, 18], and the onset of the condition was heterochronic in two of these cases [1, 13].

With regard to symptoms indicative of breast involvement, lumps due to arteritis were present in 80% of the cases (16 of 20 patients) [1–9, 13–16, 18], and redness and tenderness, in the absence of lumps, were noted in 10% (2 of 20 patients) [12, 17]. Further, in 10% (2) of the cases [10, 11], breast carcinoma and arteritis were unexpectedly identified in contiguous segments of the same specimens. These patients had lumps, but no redness or pain in their breasts. It was difficult to determine whether the lumps were due to breast carcinoma or arteritis, and none of the reviewed reports have described the relationship between these two conditions. Many of the patients had multiple lumps in both breasts; however, of 16 patients who had palpable arteritis-related lumps, 4 had only a single lump in one breast [2, 4, 8, 14]. Spontaneous breast pain and tenderness were the chief complaints in 85% (17) of the cases [1–5, 7–9, 13–18]. The condition was suspected to be inflammatory carcinoma in four [12–14] of seven cases, including the present case in which redness was noted on the skin of the breasts. Further, breast cancer was strongly suspected in three cases [1, 6, 15] because the nipples had retracted and/or were fixed to the skin and the adjacent tissue; in one case [1], mastectomy was required because of these symptoms.

Of the reviewed cases of mammary GCA, MMG, US, and/or computed tomography (CT) were performed in eight cases [3, 12–15, 17, 18], including our case; however, no mass lesions or any other specific findings were noted in any of these cases. Moreover, no specific

findings were noted for two breast carcinoma patients [10, 11], for whom imaging procedures should have been performed. All these patients had either multiple lumps in both breasts or no lumps; none of them had only one lump. In our case, MMG did not reveal any mass lesions, but indicated that the breast tissue was rather dense for the patient's age; hence, we considered that small nodules may have been hidden within the tissue. However, US revealed that the breast tissue was homogeneous; this finding suggested that the pathogenesis of the condition was characterized by features such as multiple small nodules and diffuse erythema in both breasts. It is possible that localized breast lesions present specific findings in MMG and US.

In all the reviewed cases except one [1], analysis of the excisional biopsy specimens or the resected tissues provided crucial information that led to a definitive diagnosis. In the one exceptional case, a diagnosis of GCA was established before the biopsy, on the basis of the systemic symptoms, and the lumps in the breast were considered to be associated with systemic GCA. A diagnosis could not be achieved using a small amount of tissue, for example, the amount obtained by fine-needle aspiration (FNA) [12, 15, 16] or core-needle biopsy (CNB) [16] in any of the cases. Similarly, in our case, the CNB-derived sample did not contain the vessels required for the evaluation. This suggests that a considerable amount of tissue is required to achieve a diagnosis of GCA of the breast.

Symptoms not related to the mammary glands, such as low-grade fever, arthralgia, myalgia, anorexia, and those suggestive of PMR, were present in 65% (13) of the cases [2–4, 6, 7, 9–11, 13, 14, 16, 18]. Biochemical tests revealed an increase in the ESR, a mild increase in the white blood cell count, slight anemia, and the absence of autoantibodies, such as antinuclear antibodies and rheumatoid factors in almost all cases in which these parameters were examined. In our case, biochemical test and PMR-like manifestations led our rheumatologist to suspect the condition to be temporal arteritis, but unfortunately, our ophthalmologist rejected this possibility because of the absence of visual disturbance. Visceral organ involvement was not observed in any of the cases, and the prognosis was good in all cases. However, one patient [10] developed reversible visual disturbance as a possible complication of temporal arteritis, which is a typical clinical feature of GCA. With regard to the clinical course of the condition, spontaneous remission occurred in 30% (6) of the cases [1, 5, 6, 8, 15, 17] after removal of the lumps or even without any treatment. In 60% (12) of the cases [2–4, 7, 9–14, 16, 18], the condition improved with prednisone treatment and in 10% (2) of the cases [14], including our case, with NSAID treatment. A previous report has described the case of one patient with PAN [23] where the painful mass of mammary

Table 1 Clinical features of reported cases with giant cell arteritis affecting the breasts

Reference	Year	Age(years)/sex	Breast examination	Breast imaging study	Other features	Biopsy of temporal artery	ESR (mm/h)	Method of definitive diagnosis (other methods)	Presumptive diagnosis	Treatment
Waugh [1]	1950	64/F	Bilateral (heterochronic), right: a lump, 1.3 cm, left: a lump, 3 by 2 cm, tender, fixed to the skin	Not described	None	Not described	40	R: mastectomy L: radial elliptical incision	Carcinoma	R: mastectomy L: lumpectomy No drugs
McCarty [3]	1968	66/F	Bilateral painful multiple masses, size of a plum, reddened and warm skin	MMG: no malignancy	Headaches, dizziness, burning sensation in hands, diagnosed as temporal arteritis before the presence of mammary manifestations	Not described	Normal	Excisional biopsy	Not described	Prednisone 60 mg/d, isonicotinic acid hydrazide, high calcium diet, potassium supplements
Dega [4]	1974	72/F	Left a firm, tender, 2 × 3 cm lump	Not described	PMR-like syndrome after breast biopsy, weakness, pain in extremities, night sweats, weight loss, temp. 38.6°C continued, biopsy of triceps muscle: necrotizing panarteritis	Normal	112	Excisional biopsy	Not described	Prednisone 40 mg/d
Chaitin [5]	1981	54/F	Left two tender nodules 0.2 cm and 1.5 cm	Not described	Not described	Not described	Not described	Excisional biopsy	Not described	No specific treatment
Potter [6]	1981	59/F	Bilateral, right: a fixed 4.0 cm lump with retracted nipple, palpable axillary nodes Left:a similar fixed lump	Not described	PMR-like symptoms for 2 weeks, a swollen painful left ankle	Not described	98	Excisional biopsy	Carcinoma	No specific treatment
Thaell [7]	1983	72/F	Bilateral, multiple 1 × 2 cm tender lumps, an enlarged tender lymph node in the left axilla	Not described	Temp. 38.3°C weight loss	Not described	124	Excisional biopsy	Not described	Prednisone 40 mg/d
Nirodi [8]	1985	68/F	Left a 3–4 cm painful lump	Not described	None	Not described	60 (a month after biopsy)	Excisional biopsy	Not described	Resection of the lump, no specific treatment
Stephenson [9]	1986	62/F	Bilateral, slightly tender masses	Not described	Anorexia left thyroid lobectomy: adenoma and GCA	Not described	85	Excisional biopsy	Carcinoma	Prednisone 40 mg/d
Clement [10]	1987	68/F	Right a 0.5 cm lump (coexist with ductal carcinoma)	Not described	Shoulder and neck pain, leg stiffness, history of possible scotoma in the right eye	Normal (biopsy was performed 5 months after presentation)	65	Excisional biopsy → quadrantectomy with axillary lymph node resection	Not described	Quadrantectomy and a right axillary lymph node resection, radiation, Prednisone 30 mg/d × 3 days → Diclofenac 50 mg × 3 daily

Table 1 continued

Reference	Year	Age(years)/sex	Breast examination	Breast imaging study	Other features	Biopsy of temporal artery	ESR (mm/h)	Method of definitive diagnosis (other methods)	Presumptive diagnosis	Treatment
Home [11]	1987	79/F	Right a 2.5 cm lump (coexist with breast cancer)	Not described	A diagnosis of PMR was made, joint pain and stiffness	GCA	70 → 82	Mastectomy with axillary lymph node resection	Breast cancer and PMR	Prednisone 60 mg/d
Cook [12]	1988	52/F	Right no lump, burning pain, erythema	MMG: no evidence of architectural distortion, calcification or nipple deformity	No symptoms suggestive of PMR	Not described	94	Excisional biopsy (FNA; benign ductal epithelial cells)	Inflammatory breast carcinoma	Prednisone 40 mg/d
Kim [13]	1990	69/F	Bilateral (hererochronic), painful, tender, multiple lumps fixed to the deep tissue, ecchymotic area of the skin	US: no mass, several enlarged heterogeneous mixed echogenicities CT: not stated about the breast	Chronically ill Temp. 37°C	Not described	60	Excisional biopsy	Inflammatory breast carcinoma	Steroid 15 days
McKendry [14]	1990	64/F	Bilateral tender lumps, largest measuring 3 × 3 cm, erythematous skin	MMG: very mild fibrocystic dysplasia	No other symptoms of GCA	Not described	Not described	Excisional biopsy	Not described	Phenybutazone, pethidine, and ice packs
McKendry [14]	1990	60/F	Left a painful, erythematous lump	Not described	Anorexia, weight loss, low grade fever, bone pain	Not described	56	Excisional biopsy	Breast cancer	Prednisone 60 mg/d
Susmano [2]	1990	58/F	Left a painful lump, a longitudinal hard 5–6 cm	Not described	Cough, headaches, fever (temp. 39.4°C), drenching night sweats, myalgias, arthritis biopsy of the skin (left calf) and the muscle (gastrocnemius): normal	Normal	139	Excisional biopsy	Mondor	Prednisone 30 mg/2d
Pappo [15]	1992	67/F	Bilateral tender lumps measuring 6–8 cm, fixed to the underlying fascia, the skin was retracted and the nipples were inverted	MMG: no evidence of malignancy	The physical findings otherwise was normal, healing of the surgical wounds took about 8 weeks	Not described	Normal after bilateral incisional biopsies	Bilateral incisional biopsies (FNA: slight atypia of epithelial cells)	Malignancy	No specific treatment
Lau [16]	1996	75/F	Right multiple tender inflamed-looking lumps, a tender enlarged axillary lymph node	Not described	Febrile (temp. 38°C), malaise, bilateral knee discomfort	Not described	126	Excisional biopsy (FNA: chronic inflammatory cells, true cut biopsy: medium-sized artery with fibrinoid necrosis)	Carcinoma or mastitis	Prednisone 30 mg/d

Table 1 continued

Reference	Year	Age(years)/sex	Breast examination	Breast imaging study	Other features	Biopsy of temporal artery	ESR (mm/h)	Method of definitive diagnosis (other methods)	Presumptive diagnosis	Treatment
Anim [17]	2004	56/F	Left tender, no lump	MMG and US: no definite masses or changes to suggest malignancy	None	Not described	67 (after operation)	Wedge excision	No abnormality (the patient was concerned about the possibility of cancer)	No specific treatment (referred to the rheumatologist)
Marie [18]	2008	56/F	Bilateral tender lumps	MMG/CT: normal	Low grade fever, asthenia, weight loss, headache, PMR-like symptoms	Not described	114	Surgical biopsy	Malignancy	Steroid 0.7 mg/kg
Kadotani (present case)	2008	74/F	Bilateral tender lumps, erythematous skin, bilateral soft axillary lymph nodes swelling	MMG: dense breast US: no mass	General fatigue, low grade fever, arthralgias, trismus	Not done	Not done	Excisional biopsy (CNB: no specific findings)	Bilateral inflammatory breast cancer?	Loxoprofen

ESR erythrocyte sedimentation rate, PMR polymyalgia rheumatica, MMG mammography, US ultrasound, CT computed tomography, FNA fine-needle aspiration, CNB core-needle biopsy

tissue developed central necrosis after surgical debridement, and this eventually led to ulceration of the breast skin; however, no such case has been reported for patients with GCA.

A temporal artery biopsy was performed in 20% (4) [2, 4, 10, 11] of the reviewed cases; analysis of the biopsy specimen indicated the condition to be GCA in only one of these cases, but revealed the artery to be normal in the other cases. In another case [9], the condition was definitively diagnosed as GCA of the thyroid artery after a thyroid lobectomy had been performed for adenomatous goiter. GCA generally occurs in branches of the cranial arteries such as the temporal artery; therefore, it is reasonable to assume that it can also develop in branches of the carotid artery, such as the thyroid artery, or in branches of the subclavian artery, such as the internal mammary artery and the external thoracic artery (i.e., in the breasts). Furthermore, considering that spontaneous remission may occur in some cases, mammary GCA probably often goes undiagnosed. Moreover, GCA of the breast can be mistaken for an ordinary mammary disease if no distinctive features are noted in imaging studies.

Prednisone treatment has proven effective for mammary GCA, and it improves both the general and breast-specific manifestations of the disease. Therefore, this treatment is considered essential for patients with severe symptoms. However, because of the adverse side effects associated with long-term steroid therapy [2–4, 12, 18], a definitive diagnosis should be established by performing a biopsy before the initiation of prednisone treatment. In cases of mammary GCA mimicking breast cancer (e.g., [6]), a biopsy could eliminate the need for mastectomy. A definitive diagnosis of GCA is a welcome relief for both patients and their physicians because of the associated expectation that the symptoms will gradually improve with NSAID or prednisone treatment. Interestingly, some cases of WG [22, 23] have been reported, wherein the breast seemed to be the first organ involved and the manifestations resembled those of mammary GCA. In such cases, where subclinical manifestations are present in organs other than the breasts, delayed diagnosis and inadequate initial treatment may give rise to lethal conditions, including organ failure; therefore, it is important to establish an accurate early differential diagnosis by performing a biopsy.

Conclusion

GCA of the breast may be misdiagnosed as an ordinary mammary disease. Physicians should consider the possibility of vasculitis or even GCA of the breasts among patients with pain or lumps in the breasts. Further, the

importance of biopsy for ensuring adequate treatment should be recognized.

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