

Rosai-Dorfman disease with features of IgG4-related disease in the breast: Cases report and literature review

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Abstract

Background: A proportion of cases of Rosai-Dorfman disease exhibit some histological features consistent with IgG4-related disease (IgG4RD). Several investigators have discussed whether Rosai-Dorfman disease belongs to the spectrum of IgG4RD or is concurrent with it by coincidence.

Objective: To elucidate the relationship between the two diseases, we report key features, including IgG4 and amyloid levels, of four cases of Rosai-Dorfman disease in the breast.

Methods: The histological features of the four cases were analyzed and the numbers of IgG4+ plasma cells and IgG4/IgG ratios were evaluated. Serum IgG4 concentrations were also measured in two recent cases. A literature review was also performed.

Results: Two cases (case 1 and 2) showed features of IgG4RD, including lymphoid follicle formation with regressive changes, obliterative phlebitis, increased number of IgG4+ plasma cells, and increased IgG4/IgG ratio; one of the two had an elevated serum IgG4 level. Amyloidosis was detected in these cases, with amyloid in the stroma and the vessel walls of the lesion. The other two cases (case 3 and 4) only had mild increases in the numbers of IgG4+ plasma cells, while amyloid was deposited in the stroma only.

Conclusions: A subset of Rosai-Dorfman disease may overlap with IgG4RD in the breast. When Rosai-Dorfman disease has features of IgG4RD, amyloidosis could be induced in the lesion.

Keywords: Rosai-Dorfman disease, IgG4-related disease, amyloidosis, sclerosing mastitis, pathology

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Introduction

Rosai-Dorfman disease (RDD), also called sinus histiocytosis with massive lymphadenopathy, was first reported by Destombes in 1965.¹ But Rosai and Dorfman established it as a new entity with two reports in 1969 and 1972.^{2,3} Rosai-Dorfman disease usually occurs at age 20 years or less, but can affect any age. Typical symptoms of Rosai-Dorfman disease are a massive painless bilateral lymph node enlargement in the neck, with fever, anemia, leukocytosis, elevated sedimentation rate, and polyclonal hypergammaglobulinemia in some children.⁴ The skin, upper respiratory tract, and bone are the most frequent extranodal sites and other involved sites include the nasal cavity,

salivary glands, central nervous system, genitourinary tract, and gastrointestinal tract.⁵ But massive lymphadenopathy is usually also present. To date there have been at least 33 identified cases of Rosai-Dorfman disease in the breast purely involving parenchyma.^{6,7,8,9,10,11,12} Histologically, Rosai-Dorfman disease is recognized as a nonmalignant proliferation of histiocytes with abundant cytoplasm and vesicular nuclei and emperipolesis (histiocytes containing intact lymphocytes) in the background of mature lymphocytes and plasma cells. Eighty percent of cases of Rosai-Dorfman Disease may spontaneously resolve without therapy.¹³ Involvement of kidney, tracheobronchial tree, lung

or liver and immunological disease contribute to a poor prognosis. And a significant immune deficiency may cause death in patients with Rosai-Dorfman disease.^{5,14,15}

There has been a reported overlap in the histopathological appearance of Rosai-Dorfman disease and IgG4-related disease (IgG4RD).¹¹ Histopathologically, IgG4RD is characterized by mass-forming lesions due to lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis.¹⁶ An elevated IgG4/IgG cell ratio of >40% is also necessary and serum IgG4 levels of >135 mg/ml might be present but not essential.^{17,18} The concept of IgG4RD was first introduced in 2003, before which many reported cases demonstrated clinicopathological features in accordance with IgG4RD, such as Mikulicz's disease, Riedel thyroiditis, and orbital pseudotumor.¹⁹ It is difficult to accurately estimate the prevalence of IgG4RD, because it may be unrecognized or diagnosed as another disease. Its mean age of presentation is about 60 years with a male predominance. IgG4RD can involve various organs, including the head and neck, salivary glands, liver, lung, pancreatobiliary region, salivary glands, thyroid gland, gastrointestinal tract, and lymph nodes.¹⁸ Mammary involvement has been reported as IgG4-related sclerosing mastitis.^{20,21} Patients with IgG4RD usually have mild symptoms with enlargement of one or more organ and a good clinical outcome. But persistent fibrosis of certain organs may cause organ failure in some cases. Occasionally, the disease can develop malignant lymphoma or carcinoma.²²

Several investigators have discussed a possible association between Rosai-Dorfman disease and IgG4RD, debating whether Rosai-Dorfman disease belongs to the spectrum of IgG4RD or is concurrent with it by coincidence.^{10,11,12} To elucidate the relationship between the two diseases, we report herein four cases of Rosai-Dorfman disease in the breast with features of IgG4RD. We also reviewed the literature to identify cases of Rosai-Dorfman disease with features of IgG4RD involving not only the breast but also other sites.

Material and methods

Four cases were reviewed for their histopathological features. Two patients (case 1 and 2) were seen at the Chinese PLA General Hospital in Beijing, China, in 2012. Positron emission tomography/computed tomography (PET/CT) manifestations in case 2 have been reported previously.⁹ Two patients (case 3 and 4) were seen at the University of Texas MD Anderson Cancer Center in 2007; the histopathological findings of these cases have been reported previously.²³ Additional features of IgG4RD were observed in these two previously reported cases (case 3 and 4). The study was approved by the Ethics Committee of the Chinese PLA General Hospital.

For the current analysis, immunohistochemical staining was performed at MD Anderson on formalin-fixed and paraffin-embedded tissues using a Ventana Autoimmunostain. In all four cases the following antibodies were applied: CD1a (1: 200, O10; Dako), S-100 (1: 2000, polyclonal; Dako), CD68 (1: 100, KP1; Dako), IgG (1: 1000, polyclonal; Dako), IgG4 (1: 100, HP6025; Zymed), Kappa Light Chains (1: 2000, polyclonal; Dako), Lambda Light Chains (1: 2000, polyclonal; Dako), CD3 (1: 100, polyclonal; Dako), CD20 (1: 400, L26; Dako), and AE1/AE3 (1: 100, AE1/AE3; Dako). In case 1 and 2 the following

antibodies were applied: CD21 (1: 150, 1F8; Dako), Bcl-2 (RTU, 124; Dako), CD10 (1: 100, 56c6; Leica), Ki67 (1: 200, MIB-1; Dako) and SMA (1: 100, 1A4; Dako). IgG4+ and IgG+ plasma cells were counted separately using an Olympus BX40 microscope with a DP71 camera and Image-Pro Plus 5.1 computer software. Three high-power fields (HPF) with the maximum number of positive cells were counted, and an average number per HPF was calculated. One HPF covers an area of 0.2375 mm² (×40 objective, ×10 eyepiece, 22 mm field of view). Congo red staining was performed on all four cases. Serum IgG4 and IgG concentrations were also measured for the two recent cases (case 1 and 2).

Results

Case 1

A 65-year-old woman presented with a mass in the right breast for 5 months. The patient had a history of over 20 years of high blood pressure with long-term use of antihypertensive drugs. An excisional biopsy was carried out. Gross examination of the specimen revealed a 1.8×1.5×1.5cm lesion with irregular borders and a grayish-brown cutting surface. Histological sections showed that breast lobules had been replaced by aggregates of large pale cells, mature lymphocytes, and plasma cells, accompanied by lymphoid follicles with germinal centers. Diffuse fibrosis was seen, showing mostly collagen deposition without a fibroblastic component. High power demonstrated features of Rosai-Dorfman disease, large cells containing small round nuclei and abundant cytoplasm with emperipolesis of intact lymphocytes and plasma cells (**Figure 1**). Immunohistochemical features are summarized in **Table 1**. Stains for kappa and lambda light chains showed a polytypic pattern of plasma cells and negative staining for the mesenchyma. Features of IgG4RD were as follows. First, a few veins, outlined by SAM stain, were present, with heavy mural infiltration by lymphocytes and fibrous obliteration of the lumens (**Figure 2**). Second, some lymphoid follicles showed regressed changes with hyalinization of germinal centers and capillaries penetrating

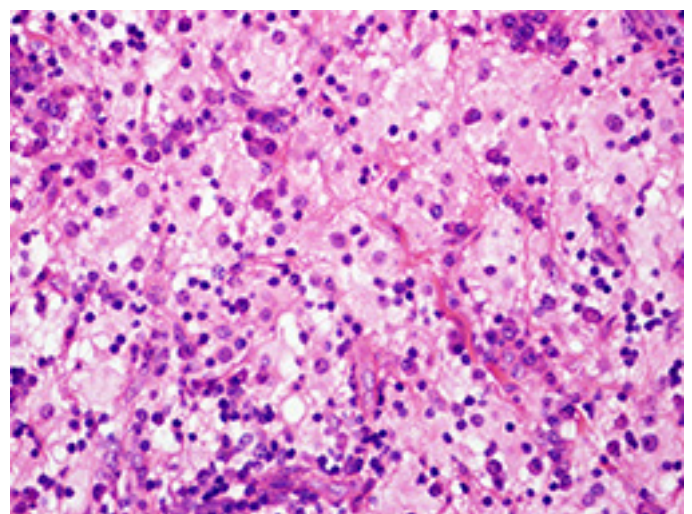


Figure 1. Intact lymphocytes and plasma cells are engulfed by the large histiocytes, a phenomenon known as emperipolesis H&E stain, ×400

Table 1. Histopathological features and serum IgG4 of 4 cases in our cohort

| case | Features specific for RDD | | Features specific for IgG4RD | | | | | Features for both diseases | | | |
|--------|----------------------------------|------------------------|------------------------------|-----------|-----------|-------------------------|--------------|----------------------------|---|--|----------------------------------|
| | S-100+ histiocytes emperipolesis | Obliterative phlebitis | Regressive lymphoid follicle | IgG4+/HPF | IgG4/IgG% | Serous IgG4 level mg/dl | Plasma cells | Lymphocytes | Stromal fibrosis | Amyloidosis | ADH |
| Case 1 | +++ | + | + | 172 | 82 | 150 | +++ | +++ | Diffuse fibrosis without fibroblastic component | +, the vessel walls and the mesenchyma of the lesion | A duct with ADH, measuring 1.8mm |
| Case 2 | +++ | + | + | 118 | 53 | 18 | +++ | +++ | Fibroblast-rich, storiform fibrosis | +, the vessel walls and the mesenchyma of the lesion | - |
| Case 3 | ++ | - | - | 15 | 10 | Unknown | + | +++ | Dense fibrous bands without myofibroblastic proliferation | +, the mesenchyma of the lesion | - |
| Case 4 | ++ | - | - | 22 | 24 | Unknown | +++ | +++ | Collagen-rich, patchy fibrosis | +, the mesenchyma of the lesion | - |

+, few; ++, moderate; +++, many;

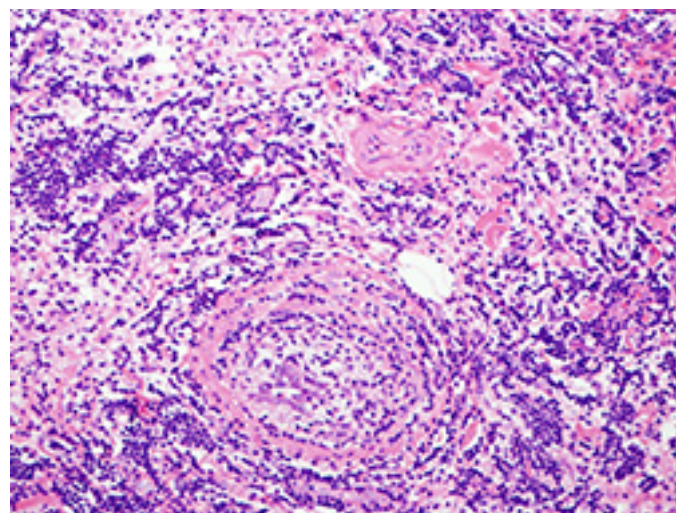


Figure 2. An obliterated vein (obliterative phlebitis) in case 1 creates an inflammatory nodule next to a patent artery H&E stain, ×200

follicles, resembling the follicle in Castleman disease. The residual ducts could only be identified by immunohistochemical stain for AE1/AE3. A duct with atypical ductal hyperplasia (ADH), measuring 1.8 mm, could be found in the mid portion of the lesion. The surrounding breast parenchyma showed no epithelial hyperplasia and atypical hyperplasia.

The average number of IgG4+ cells was 172/HPF and the IgG4/IgG ratio was 82% (Figure 3). Congo red stain showed amyloid deposits in the stroma and vessel walls of the lesion demonstrating apple-green birefringence in polarized light. Serum IgG4 level was 150 mg/dL (normal, 8 to 140 mg/dL) on the 7th day after surgery. We therefore concluded that the patient had both Rosai-Dorfman disease and IgG4RD.

Pre-op thyroid ultrasonography showed multiple nodules and suggested nodular goiter with elevated levels of serum antithyroglobulin antibody (113.1 IU/ml) and thyroperoxidase antibody (1300.0 IU/ml). The patient had no evidence of extramammary Rosai-Dorfman disease or IgG4RD. At 40 months of clinical follow-up there has been no progressive disease or recurrence.

Case 2

A 78-year-old Chinese woman presented complaining of chest congestion. The patient had a history of chronic bronchitis without long-term medication history. Chest computed tomography (CT) scan showed multiple masses in bilateral lungs. As reported previously,⁹ PET/CT scan revealed a nodule in the right breast, multiple irregular nodules of the lungs bilaterally and lightly increased fluoro-deoxyglucose uptake of the cervical lymph nodes. Surgical excision of the breast nodule was performed, followed by a CT-guided needle biopsy of lung masses on the 4th day after operation and ultrasound-guided needle biopsy of the right cervical lymph node on the 9th day after operation.

The excised specimen of the breast showed a 3x2x2 cm well-defined firm lesion. The histological and immunohistochemical features summarized in Table 1 supported the diagnosis of Rosai-Dorfman disease. Some interspersed lymphoid follicles

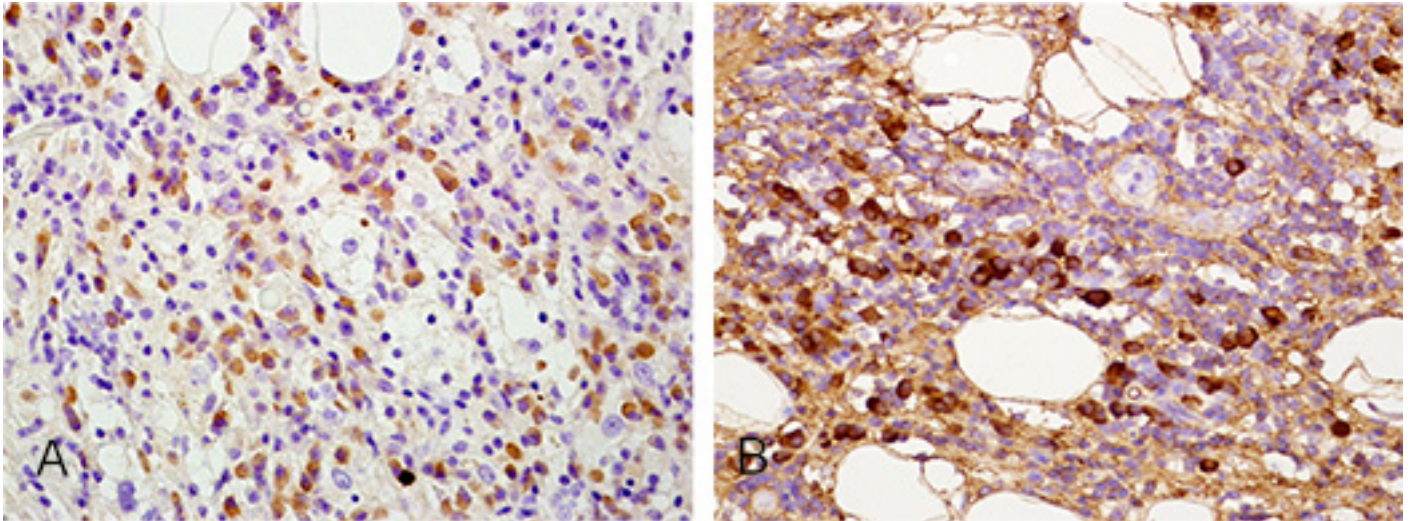


Figure 3. Immunostaining for IgG and IgG4 in the lesion of case 1. **A.** Immunostaining for IgG4 shows many IgG4+ plasma cells in the stroma. **B.** The IgG-stained section shows that the ratio of IgG4 to IgG is about 82%. H&E stain, ×400

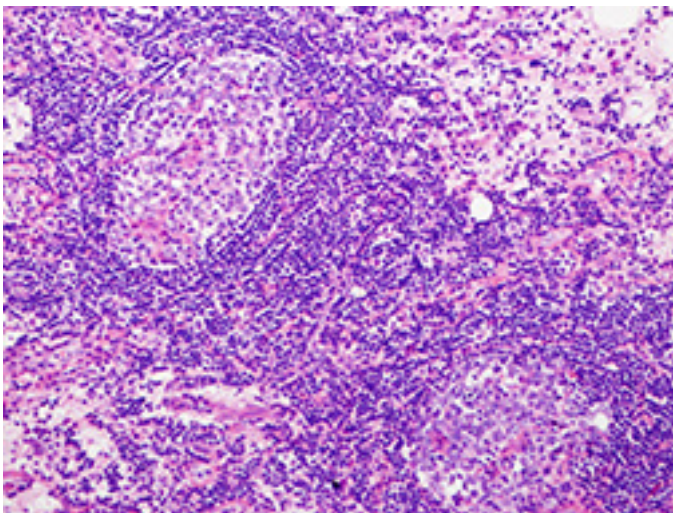


Figure 4. The lymphoid follicles are penetrated by hyalinized venules, which resembles Castleman disease in case 2. H&E stain, ×200

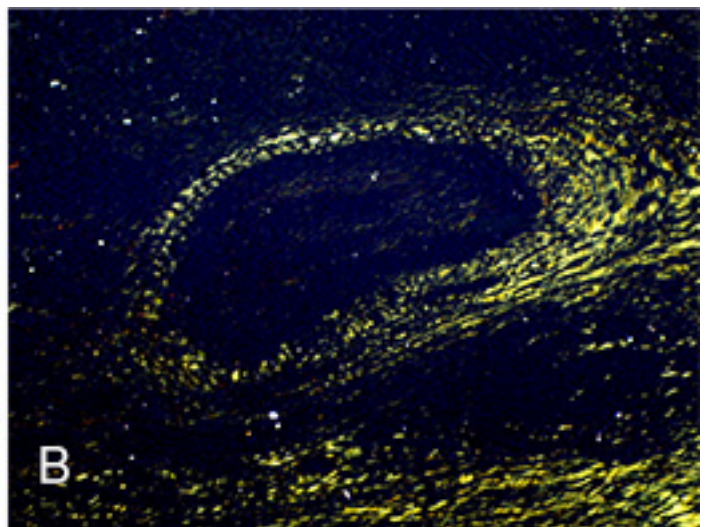
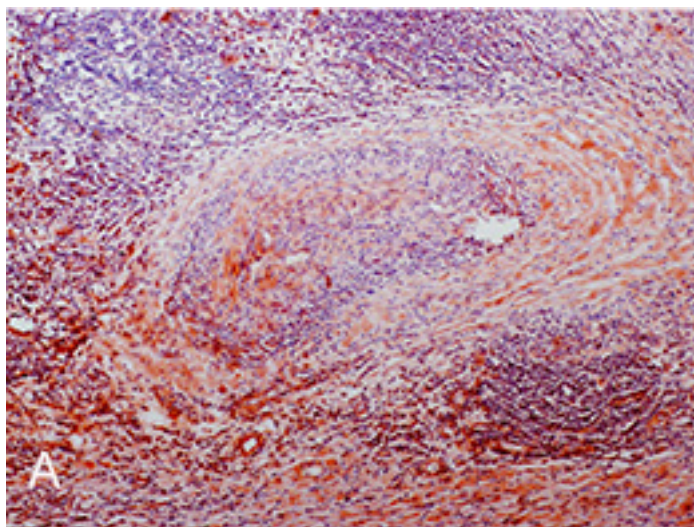


Figure 5. Congo red stain in case 2. **A.** Amyloid in vessel wall with obliterative phlebitis is stained brick-red. **B.** Amyloid in vessel wall and peripheral stroma is apple green when viewed with fully polarized light. H&E stain, ×100

were present with regressive changes, without the onion-skin pattern in the mantle zone (**Figure 4**). Occasional obliterative phlebitis was found. The two features suggested the possibility of IgG4RD. The average number of IgG4+ cells was 118/HPF and the IgG4/IgG ratio was 53%. Congo red stain showed amyloid deposits in the stroma and vessel walls in the lesion (**Figure 5**).

Histologically, the biopsy of the lung mass showed sparsely cellular, homogeneous pink material demonstrating apple-green birefringence under polarized light after Congo red stain. Only a few fibrocytes and histiocytes positive for CD68 and vimentin were embedded within the amyloid.

Histological sections of the biopsy of the right cervical lymph node showed normal reactive follicular hyperplasia. There were amyloid deposits in both intranodal and extranodal areas including vessel walls and the stroma.

The anti-SSA and anti-SSB antibodies were detected in the serum before surgery. Serum IgG4 level was 18 mg/dL (normal, 8 to 140 mg/dL) on the 5th day after surgery. Serum immunoglobulin levels increased on the 9th day after surgery as follows:

IgA 485 mg/dL (normal, 70 to 400 mg/dL), IgG 2030 mg/dL (normal, 700 to 1600 mg/dL), Ig light-chain kappa 432 mg/dL (normal, 170 to 370 mg/dL), and Ig light-chain lambda 249 mg/dL (normal, 90 to 210 mg/dL). The patient showed no evidence of extramammary Rosai-Dorfman disease or IgG4RD. No progressive disease or recurrence was detected at 39 months of clinical follow-up.

Case 3

Our group has previously reported the case of a 53-year-old African American woman with a 1.5-cm mass in the left breast.²³ A needle core biopsy was diagnostic of Rosai-Dorfman disease. After almost 4 years, the lesion was excised. To assess for the presence of IgG4RD, morphological features of IgG4RD were evaluated and immunohistochemical stains for IgG and IgG4 were performed. No obliterative phlebitis and no regressive lymphoid follicles were seen in the lesion. The average number of IgG4+ cells was 15/HPF and the IgG4/IgG ratio was 10%. These results, in conjunction with the morphological features, excluded a possible IgG4RD. The histological and immunohistochemical features of Rosai-Dorfman disease are summarized in **Table 1**. Congo red stain showed amyloid deposits in the stroma of the lesion and the vessel walls were uninvolved.

The patient showed no evidence of extramammary Rosai-Dorfman disease or IgG4RD. No progressive disease or recurrence occurred during the 155 months of total clinical follow-up.

Case 4

Our group has previously reported the case of a 45-year-old African American woman with a solid lesion in the left breast.²³ This patient had a history of type 2 diabetes with metformin treatment. Needle-localized excisional biopsy showed the lesion lacked the characteristic histopathological features of IgG4RD including obliterative phlebitis, regressive lymphoid follicles, an elevated IgG4 number and IgG4/IgG ratio. The average number of IgG4+ cells was 22/HPF and the IgG4/IgG ratio was 24%. Histopathological features were consistent with a diagnosis of Rosai-Dorfman disease (**Table 1**). Congo red stain showed amyloid deposits in the stroma of the lesion and the vessel walls were negative.

The patient showed no evidence of extramammary Rosai-Dorfman disease or IgG4RD. At 86 months of clinical follow-up, there has been no progressive disease or recurrence.

Discussion

Evaluation of four cases of Rosai-Dorfman disease revealed two cases with features of IgG4RD and another two cases that lacked these features. Rosai-Dorfman disease in the breast should be differentiated from granulomatous mastitis, Langerhans' cell histiocytosis, non-hodgkin lymphoma, fibrous histiocytoma, inflammatory myofibroblastoma, and Erdheim-Chester disease. The morphological appearance of classical Rosai-Dorfman disease (**Table 1**) in our four cases and immunoreactivity of the histiocytes to S-100 and negativity to CD1a confirmed the diagnosis. Among the 33 reported cases of Rosai-Dorfman disease in the breast with follow-up ranging from 2 to 70 months, one patient died of disseminated Rosai

-Dorfman disease 2 months after excision,²⁴ and one patient had local recurrence.⁶ Our four patients have had no progressive disease or recurrence at 39–155 months of clinical follow-up.

Our study showed that the histological features of case 1 and 2 (**Table 1**) met the criteria for IgG4-related sclerosing mastitis, a new member of IgG4RD which is characterized by mass-forming infiltration of lymphocytes and IgG4+ plasma cells, obliterative phlebitis, lymphoid follicle formation, loss of breast lobules, and severe fibrosis.^{20,21} Increased numbers of IgG4+ plasma cells (>50 / HPF) and the IgG4/IgG ratio (>40%) of case 1 and 2, and the elevated serum IgG4 (>135 mg/dl) of case 1, were also highly suggestive of IgG4RD in accordance with the consensus statement.¹⁸ In accordance with reports,^{20,21} case 1 and 2 showed a favorable outcome with no recurrence at follow-up of 40 and 39 months respectively.

Only one case of Rosai-Dorfman disease has ever been reported focusing on increased IgG4+ plasma cells involving the breast.⁷ Hereby we reviewed the literature on Rosai-Dorfman disease with features of IgG4RD involving not only the breast but also other sites (**Table 2**). Similar to previous reports, case 1 and 2 demonstrated the characters specific for Rosai-Dorfman disease and IgG4RD (**Table 1**) and met the morphological criteria for Rosai-Dorfman disease with features of IgG4RD. We found that IgG4RD shares some histological features seen in Rosai-Dorfman disease, including lymphoplasmacytic infiltrate, lymphoid follicle formation, and stroma fibrosis. But the lymphoid follicle in IgG4RD shows regressive changes, a capillary penetrating into the germinal center and hyalinization of the germinal center. Compared to case 3 and 4, case 1 and 2 showed regressive lymphoid follicles and obliterative phlebitis (**Table 1**), which were not present in all reported cases (**Table 2**). Therefore, we speculate that regressive lymphoid follicles and obliterative phlebitis may be characteristic histopathological features of Rosai-Dorfman disease with features of IgG4RD involving the breast, excluding increased IgG4+ plasma cells and IgG4/IgG ratio, dense lymphoplasmacytic infiltrate, and fibrosis. Some investigators have suggested that the increased number of IgG4+ cells in Rosai-Dorfman disease are coincidental.^{11,12} The isolated increase in IgG4+ cells and IgG4/IgG ratio, which these reports concentrated on, is not sufficient to establish a diagnosis of Rosai-Dorfman disease with features of IgG4RD; the diagnosis requires the coexistence of increased IgG4+ plasma cells, the characteristic histopathological appearance, and clinical context.¹⁸

Amyloidosis was detected in all cases in our study. In case 3 and 4, amyloid was deposited in the stroma of the lesion. In contrast, amyloid was also deposited in the vessel walls of the lesion in case 1 and 2. In case 2, amyloidosis resulted in the formation of pulmonary nodules and amyloid deposits in both intranodal and extranodal areas including the vessel walls and the stroma of the cervical lymph node. As far as we know, this is the first report describing the concurrence of amyloidosis in Rosai-Dorfman disease with features of IgG4 RD (**Table 2**). The vessel walls and stroma of case 1, 2, and 3 did not stain for lambda (λ) or kappa (κ) light chains. And the ratio between the serum κ and λ light chains ($432/249=1.73$) of case 2 was not in the range (0.26-1.65) that is diagnostic for immunoglobulin light-chain (AL) amyloidosis.³³ Therefore, we can rule out the

Table 2. Histopathological features and serum IgG4 of reported cases of Rosai-Dorfman Disease overlapping with IgG4RD

| Reference | No. Cases | Site | Features specific for RDD | | Features specific for IgG4RD | | | Features for both diseases | | | |
|--------------------------------|-----------|---------------|----------------------------------|-----------|--|-------------|------------------------|----------------------------|----------------------------|------------------|-------------|
| | | | S-100+ histiocytes emperipolesis | Phlebitis | Regressive lymphoid Follicle | IgG4+/- HPF | IgG4/IgG% | Serous IgG4 level mg/dl | Lymphoplasmic Infiltration | Stromal fibrosis | Amyloidosis |
| Kuo TT et al ²⁵ | 12 | skin | + 12/12* | - , 12/12 | Geminal center without regressive change | 21- 204 | 16-51 | 385, 38.5, 2/12 | + , 12/12 | + , 12/12 | Unknown |
| Roberts SS et al ²⁶ | 1 | lung | + | Unknown | - | 10-30 | Unknown | Unknown | + | + | Unknown |
| El-Kersh K et al ²⁷ | 1 | lung | + | - | - | Unknown | significant proportion | 26 | + | + | Unknown |
| Chen TD et al ²⁸ | 1 | Parotid Gland | + | - | - | 121 | 33.4 | Unknown | + | + | Unknown |
| Wimmer DB et al ²⁹ | 1 | colon | + | - | - | 164 | 51 | 37 | + | +, Storiform | Unknown |
| Cha YJ et al ⁷ | 1 | breast | + | - | Diffusely scattered lymphoid follicles without regressive change | 100.2 | 56.7 | Unknown | + | +, Storiform | Unknown |
| Park BH et al ³⁰ | 1 | Lymph node | + | - | Unknown | 200 | Unknown | 356 | + | - | Unknown |
| Mudhar HS et al ³¹ | 1 | orbita | + | - | - | Unknown | >40 | Unknown | + | +, Storiform | Unknown |

+12/12*: 12 of 12 cases are positive

diagnosis of AL amyloidosis and presume that the amyloid deposits of case 1 and 3 are AA amyloidosis and that case 2 is systemic AA amyloidosis. Röcken et al. reported a patient suffering from Rosai-Dorfman disease, followed by generalized AA amyloidosis 5 years later.³⁴ Kato et al. reported a patient with primary sclerosing cholangitis (PSC) complicated by systemic AA amyloidosis.³⁵ They also considered that a sustained acute phase response, owing to Rosai-Dorfman disease or PSC, might be a sufficient cause of AA amyloid deposits. Therefore we hypothesize that the amyloidosis that occurred in our four cases may have been induced by chronic inflammatory stimuli. It is also possible that the obliterate phlebitis in case 1 and 2 caused the amyloid to deposit in the vessel walls of the lesions.

Conclusions

We report four cases of Rosai-Dorfman disease, of which two showed features of IgG4RD including S-100+ large histiocytes, dense lymphoplasmacytic infiltrate, obliterate phlebitis, storiform fibrosis, increased IgG4+ plasma cells and IgG4/IgG ratio, and elevated serum IgG4. Lymphoid follicle formation with regressive changes and obliterate phlebitis could be characteristic histopathological features of Rosai-

-Dorfman disease with features of IgG4RD in the breast. We suggest that a subset of Rosai-Dorfman disease could overlap with IgG4RD in the breast, which might possibly induce amyloidosis in the lesion.

Conflict of interest

The authors declare no conflict of interest relevant to this manuscript.

References

1. Destombes P. Adenitis with lipid excess, in children or young adults, seen in the Antilles and in Mali (4 cases). Bull Soc Pathol Exot Filiales. 1965;58: 1035-1039.
2. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinicopathological entity. Arch Pathol. 1969;87:63-70.
3. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a pseudolymphomatous benign disorder. Analysis of 34 cases. Cancer. 1972;30:1174-1188.
4. Suvatte V, Mahasandana C, Tanphaichitr VS, Sukpanichnant S. Sinus histiocytosis with massive lymphadenopathy: the first three cases reported in Thailand. Asian Pac J Allergy Immunol. 1990;8: 127-32.
5. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol. 1990;7:19-73.

6. Tenny SO, McGinness M, Zhang D, Damjanov I, Fan F, Breast J. Rosai-Dorfman disease presenting as a breast mass and enlarged axillary lymph node mimicking malignancy: a case report and review of the literature. *Breast J*. 2011;17:516-20.
7. Cha YJ, Yang WI, Park SH, Koo JS. Rosai-Dorfman Disease in the breast with increased IgG4 expressing plasma cells: a case report. *Korean J Pathol*. 2012;46:489-93.
8. Baladandapani P, Hu Y, Kapoor K, Merriam L, Fisher PR. Rosai-Dorfman disease presenting as multiple breast masses in an otherwise asymptomatic male patient. *Clin Radiol*. 2012;67:393-5.
9. Fu L, Liu M, Song Z, Xu B, Tian J. 18F-fluoro-deoxyglucose positron emission tomography/computed tomography scan findings in Rosai-Dorfman disease with IgG4-positive plasma cell infiltration mimicking breast malignancy: a case report and literature review. *J Med Case Rep*. 2012;30:6: 411.
10. Zhang X, Hyjek E, Vardiman J. A subset of Rosai-Dorfman disease exhibits features of IgG4-related disease. *Am J Clin Pathol*. 2013;139: 622-32.
11. Menon MP, Evbuomwan MO, Rosai J, Jaffe ES, Pittaluga S. A subset of Rosai-Dorfman disease cases show increased IgG4-positive plasma cells: another red herring or a true association with IgG4-related disease? *Histopathology*. 2014;64:455-9.
12. Liu LI, Perry AM, Cao W, Smith LM, Hsi ED, Liu X, et al. Relationship between Rosai-Dorfman disease and IgG4-related disease: study of 32 cases. *Am J Clin Pathol*. 2013;140:395-402.
13. Pulsoni A, Anghel G, Falcucci P, Matera R, Pescarmona E, Ribersani M, et al. Treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): report of a case and literature review. *Am J Hematol*. 2002;69:67-71.
14. Foucar E, Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. An analysis of 14 deaths occurring in a patient registry. *Cancer*. 1984;54:1834-40.
15. Maric I, Pittaluga S, Dale JK, Niemela JE, Delsol G, Diment J, et al. Histologic features of sinus histiocytosis with massive lymphadenopathy in patients with autoimmune lymphoproliferative syndrome. *Am J Surg Pathol*. 2005;29:903-11.
16. Okazaki K, Umehara H. Current Concept of IgG4-Related Disease. *Curr Top Microbiol Immunol*. 2016;Dec 28. [Epub ahead of print]
17. Cheuk W, Chan JK. IgG4-related sclerosing disease: a critical appraisal of an evolving clinicopathologic entity. *Adv Anat Pathol*. 2010;17:303-32.
18. Khosroshahi A, Wallace ZS, Crowe JL, Akamizu T, Azumi A, Carruthers MN, et al. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. *Arthritis Rheumatol*. 2015;67: 1688-99.
19. Kamisawa T, Zen Y, Pillai S, Stone JH. IgG4-related disease. *Lancet*. 2015; 385:1460-71.
20. Cheuk W, Chan AC, Lam WL, Chow SM, Crowley P, Lloyd R, et al. IgG4-related sclerosing mastitis: description of a new member of the IgG4-related sclerosing diseases. *Am J Surg Pathol*. 2009;33:1058-64.
21. Chougule A, Bal A, Das A, Singh G. IgG4 related sclerosing mastitis: expanding the morphological spectrum of IgG4 related diseases. *Pathology*. 2015;47:27-33.
22. Divatia M, Kim SA, Ro JY. IgG4-related sclerosing disease, an emerging entity: a review of a multi-system disease. *Yonsei Med J*. 2012;53:15-34.
23. Morkowski JJ, Nguyen CV, Lin P, Farr M, Abraham SC, Gilcrease MZ, et al. Rosai-Dorfman disease confined to the breast. *Ann Diagn Pathol*. 2010;14:81-7.
24. Green I, Dorfman RF, Rosai J. Breast involvement by extranodal Rosai-Dorfman disease: report of seven cases. *Am J Surg Pathol*. 1997;21:664-8.
25. Kuo TT, Chen TC, Lee LY, Lu PH. IgG4-positive plasma cells in cutaneous Rosai-Dorfman disease: an additional immunohistochemical feature and possible relationship to IgG4-related sclerosing disease. *J Cutan Pathol*. 2009;36:1069-73.
26. Roberts SS, Attanoos RL. IgG4+ Rosai-Dorfman disease of the lung. *Histopathology*. 2010;56:662-4.
27. El-Kersh K, Perez RL, Guardiola J. Pulmonary IgG4+ Rosai-Dorfman disease. *BMJ Case Rep*. 2013;10:2013.
28. Chen TD, Lee LY. Rosai-Dorfman disease presenting in the parotid gland with features of IgG4-related sclerosing disease. *Arch Otolaryngol Head Neck Surg*. 2011;137:705-8.
29. Wimmer DB, Ro JY, Lewis A, Schwartz MR, Caplan R, Schwarz P, et al. Extranodal rosai-dorfman disease associated with increased numbers of immunoglobulin g4 plasma cells involving the colon: case report with literature review. *Arch Pathol Lab Med*. 2013;137:999-1004.
30. Park BH, Son da H, Kim MH, Shim TS, Lee HJ, Huh J. Rosai-Dorfman Disease: Report of a Case Associated with IgG4-Related Sclerotic Lesions. *Korean J Pathol*. 2012;46:583-6.
31. Mudhar HS, Duke R. A case of orbital Rosai-Dorfman disease with IgG4 positive plasma cells. *Orbit*. 2013;32:315-7.
32. Beyer G, Schwaiger T, Lerch MM, Mayerle J. IgG4-related disease: a new kid on the block or an old acquaintance? *United European Gastroenterol J*. 2014;2:165-72.
33. Palladini G, Russo P, Bosoni T, Verga L, Sarais G, Lavatelli F, et al. Identification of amyloidogenic light chains requires the combination of serum-free light chain assay with immunofixation of serum and urine. *Clin Chem*. 2009;55:499-504.
34. Röcken C, Wieker K, Grote HJ, Müller G, Franke A, Roessner A. Rosai-Dorfman disease and generalized AA amyloidosis: a case report. *Hum Pathol*. 2000;31:621-4.
35. Kato T, Komori A, Bae SK, Migita K, Ito M, Motoyoshi Y, et al. Concurrent systemic AA amyloidosis can discriminate primary sclerosing cholangitis from IgG4-associated cholangitis. *World J Gastroenterol*. 2012;18:192-6.