Original Article

Ophthalmic Manifestations of Rosai-Dorfman Disease in Five Patients

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Abstract

Purpose: To report clinical features, pathology characteristics, and treatment outcomes of five patients with Rosai-Dorfman disease (RDD).

Methods: A retrospective case series of patients with RDD from the Ocular Oncology Service of Wills Eye Hospital between 1974 and 2018.

Results: There were six eyes of five patients (3 males, 2 females) with ophthalmic manifestations of RDD. The mean age at the initial presentation was 33 years (median 35, range 10–52 years). Before referral, the tumor was initially suspected to be lymphoma (n = 3), idiopathic orbital inflammation (n = 2), or pterygium (n = 1). The disease was unilateral (n = 4) or bilateral (n = 1). The mean duration of symptoms was 9 months (median 8, range 5–24 months). The disease produced nodules in the conjunctiva (n = 4) or orbit (n = 2). Two patients with conjunctival involvement had corneal involvement. One patient with bilateral conjunctiva lesions demonstrated bilateral orbital involvement and bilateral anterior uveitis. The mean tumor basal dimension was 13 mm (median 9, range 6–27 mm) for conjunctiva lesions and 37 mm (median 37, range 34–40 mm) for orbital lesions. The main symptom (per patient) included proptosis (n = 2), palpable mass (n = 1), and foreign body sensation (n = 2). No patient experienced pain or tenderness. Palpable, nontender lymphadenopathy was detectable in two patients in the cervical and inguinal lymph nodes. Systemic involvement with paranasal sinusitis and mediastinal/pulmonary lymphadenopathy occurred in two patients, both with orbital involvement. Surgical resection was performed for all patients. At a mean follow-up of 31 months (median 12, range, 10–76 months) after the surgery, tumor control was achieved in all six eyes without local recurrence.

Conclusion: In this series of six eyes with RDD, patients with orbital and/or intraocular disease were more likely to demonstrate lymphadenopathy and systemic involvement, while those with unilateral perilimbal conjunctival tumors remained localized.

Keywords: Conjunctiva, Emperipolesis, Eye, Lymph node, Lymphadenopathy, Orbit, Rosai-Dorfman disease, Sinus histiocytosis, Uvea

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Introduction

Rosai-Dorfman disease (RDD) is a rare, non-malignant, histiocytic disorder that was first described in 1969 by Rosai and Dorfman as a new clinicopathological entity, often presenting with painless cervical lymphadenopathy.[1] This pseudo-lymphomatous disorder, also known as "sinus histiocytosis with massive lymphadenopathy," has characteristic histopathologic features of abundant histiocytes, often demonstrating emperipolesis, representing engulfed lymphocytes and lymphoid cells.[1]

The disease has unclear etiology and usually demonstrates a self-limited but prolonged course.[1,2] RDD has been reported worldwide, generally in children and young adults, and less commonly in older adults.[2,3] According to the American Histiocyte Society, RDD is classified as a histiocytic disorder

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characterized by the accumulation of macrophage, dendritic, or monocyte-derived cells in various tissues and organs. Unlike Langerhans cell histiocytosis and Erdheim-Chester disease, RDD does not display BRAF mutation (BRAF V600E) and is typically negative for CD1 marker.[4]

RDD usually manifests inside lymph nodes in the area of the head and neck, but 43% of patients present with extranodal involvement, mostly in skin, upper respiratory tract, bone, periocular, and ocular tissue.[2] Less than 10% of RDD cases have ocular findings,[2,3] and those in the periocular region usually manifest as an orbital mass.[3-9] Other ophthalmic manifestations include epibulbar mass, scleritis, corneal lesion, uveitis, choroidal mass, serous retinal detachment, and lacrimal duct obstruction.[3-13] Herein, we describe a series of six eyes in five patients with biopsy-proven RDD and review the clinical and pathologic features.

Methods

RDD was diagnosed in six eyes of five patients evaluated on the Ocular Oncology Service at Wills Eye Hospital, Philadelphia, PA, USA, between January 1974 and July 2018. Patient data were retrospectively reviewed. Institutional review board approval was obtained from Wills Eye Hospital, and this study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from the patients, patient's parent, or guardian. The diagnosis of RDD was based on clinical and histopathologic examination in all patients.

An ophthalmology examination and systemic history were taken at the initial consultation. Data from medical records were extracted, including patient age at diagnosis (years), race (White, African American, Hispanic, or Asian), sex (males or females), ocular symptoms, cutaneous or other extraocular lesions, and prior ocular treatment. The complete ophthalmological examination included Snellen visual acuity measurement, intraocular pressure, anterior segment examination by slit-lamp biomicroscopy, and posterior segment examination by indirect ophthalmoscopy at each visit. Baseline tumor features such as location, laterality, number of tumors, and tumor size (largest basal diameter and thickness in millimeters) were recorded. For patients with orbital involvement, imaging of the tumor was performed with magnetic resonance imaging (MRI) or computed tomography (CT).

Treatment modalities included incisional or excisional biopsy, adjunctive corticosteroids (topical, periocular, and oral), and/or chemotherapy. Tumor response (regression, stable, or progression) and tumor recurrence after treatment were recorded.

Results

Five patients with ocular RDD were identified over this 43-year period. There were three males and two females, with unilateral ($n = 4$) or bilateral ($n = 1$) involvement. Mean patient age at presentation was 33 years (median 35 years, range 10–52 years). The mean duration of symptoms before treatment was 9 months (median 9 months, range 5–24 months). Patient demographics are listed in Table 1. The case reports are given below separately.

Case #1

A 22-year-old White female noted a nodule on the right eye. Despite treatment with topical prednisone, the mass persisted. On referral, visual acuity was 20/30 in the affected right eye. There was a non-pigmented, vascular conjunctival mass measuring 6 mm in diameter and 2 mm in thickness, located superiorly at the limbus with limited corneal stromal invasion for 2 mm. There was no lymphadenopathy. Excisional biopsy revealed inflammatory infiltration with lymphocytes, plasma cells, and histiocytic cells and demonstrating positive staining for CD68, CD163, and S-100 protein, and negative staining for CD1a. Rare emperipolesis was noted in the small specimen. On examination 12 months after surgery, the corneal infiltration improved, and visual acuity was 20/25 [Figure 1a and b].

Case #2

A 35-year-old White male presented with left eye irritation, redness, and conjunctival mass for 1 month that did not respond to topical corticosteroids. On referral, visual acuity was 20/25, and the left eye revealed a non-pigmented, vascular conjunctival mass measuring 6 mm in diameter and 2 mm in thickness, located inferiorly at the limbus with 4 mm of corneal stromal invasion, leading to stromal lipid deposition. There

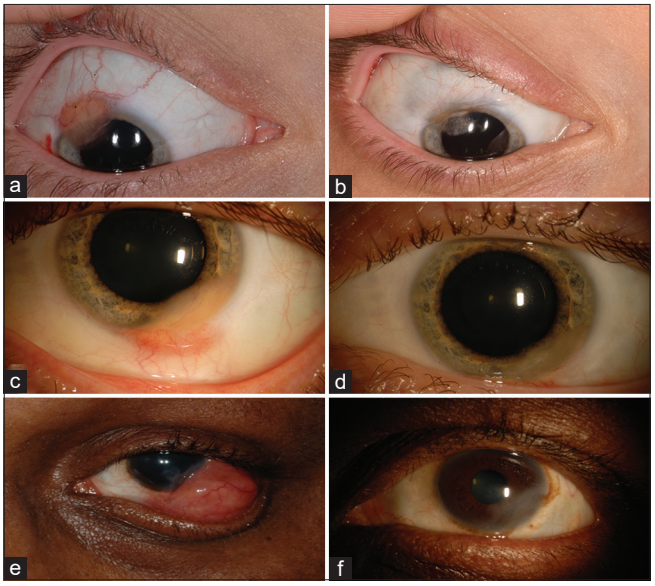

Figure 1: (a) Slit-lamp photograph of right eye in 22-year-old woman (case #1) showing pink elevated limbal nodule with cornea stromal keratitis. (b) Twelve months after surgery, there was no evidence of recurrence. (c) Elevated, pink, conjunctival lesion of the left eye in 35-year-old man (case #2) with corneal stromal lipid infiltration. (d) Slit-lamp photograph of same eye after resection showing minor corneal opacity. (e) Bilateral asymmetric conjunctival tumors in 45-year-old man (case #3). (f) Following resection and sub-tenon triamcinolone, the tumor remained under control at 4 years

Table 1: Summary of five cases of Rosai-Dorfman disease with ophthalmic involvement

Case	Age/race/sex	Symptoms duration (month)	Laterality	Visual acuity	Location	Uveitis	Lymph nodes involvement	Systemic involvement	Treatment	Emperipolesis	Follow-up duration (month)	Recurrence
1	22/W/female	4	Right eye	20/25	Conjunctiva and cornea	Absent	Absent	Absent	Excision and STK	Negative	12	None
2	35/W/male	1	Left eye	20/30	Conjunctiva and cornea	Absent	Absent	Absent	Excision and STK	Negative	10	None
3	45/AA/male	24	Both eyes	20/30	Conjunctiva and orbit	Yes	Cervical and Inguinal	Sinusitis and lung	Excision, chemotherapy and STK	Strongly positive	47	None
4	10/W/male	8	Right eye	20/40	Orbit	Absent	Absent	Absent	Excision and STK	Positive	76	None
5	52/W/female	10	Right eye	20/40	Orbit	Absent	Cervical	Sinusitis	Excision and STK	Strongly positive	10	None

W: White, AA: African American, STK: Sub-Tenon Kenolag

was no lymphadenopathy. Excisional biopsy revealed mixed inflammatory cells, rich in histiocytes, positive for CD68, CD163, and S-100 protein, and negative for CD1a. Classic emperipolesis was not detected in the small specimen, but other findings were consistent with RDD. Ten months after surgery, the visual acuity was 20/20, and the corneal stromal lipid deposits had decreased substantially [Figure 1c and d].

Case #3

A 45-year-old African-American male presented with a painless elevated forniceal nodule on both eyes for 2 years, with no response to topical corticosteroids. On referral, visual acuity was 20/25 in both eyes. Each eye demonstrated a non-pigmented, vascular conjunctival mass in the inferotemporal fornix, extending into the orbit and measuring 6 mm in diameter and 4 mm in thickness. There was no corneal invasion. There was bilateral lymphadenopathy of the neck and groin. Ten months before presentation, a biopsy of the left groin mass revealed RDD. Excisional biopsy of the tumors on each eye revealed RDD with obvious emperipolesis and histiocytic cells with positive reactivity for CD68, CD163, and S-100 protein, and negative for CD1a. One year after the presentation, the patient developed severe nasal congestion and dyspnea with voice alterations. Chest and neck CT revealed a 4 cm nasal mass, 3.5 cm mediastinal mass with tracheal compression, and 8 cm mass encasing the aortic arch, believed to represent systemic RDD. Intravenous rituximab (6 cycles) and chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone were delivered, with tumor control. Two years after the initial presentation, the conjunctival/orbital tumors were controlled, but uveitis developed in both eyes with anterior chamber keratic precipitates and inflammatory cells. This was treated with sub-Tenon's triamcinolone and topical prednisone in both eyes. At 4 years following initial surgery, visual acuity was 20/25 in both eyes, and there was no further recurrence of active uveitis [Figure 1e and f].

Case #4

A 10-year-old White male developed 9 months of painless right eyelid swelling that failed systemic corticosteroids. On referral, visual acuity was 20/30 in the right eye, and the globe was intact without inflammation. There was 4 mm right proptosis from a firm, fixed, and nontender lacrimal gland mass, depicted on MRI with enhancement [Figure 2a and b]. Laboratory studies revealed normal complete blood count (CBC), normal erythrocyte sedimentation rate, and negative testing for Lyme, Bartonella, and Tuberculosis. Excisional biopsy revealed a firm encapsulated mass with histopathologic evaluation demonstrating diffuse mixed inflammatory infiltration with variable fibrosis and emperipolesis. Occasional multinucleated giant cells were positive for CD68 and S-100, and negative for CD1a. At 6 years after surgery, the visual acuity remained 20/20 with no further local recurrence or systemic disease.

Case #5

A 52-year-old White female noted 10 months history of a lump on her right upper eyelid and multiple lumps in her neck

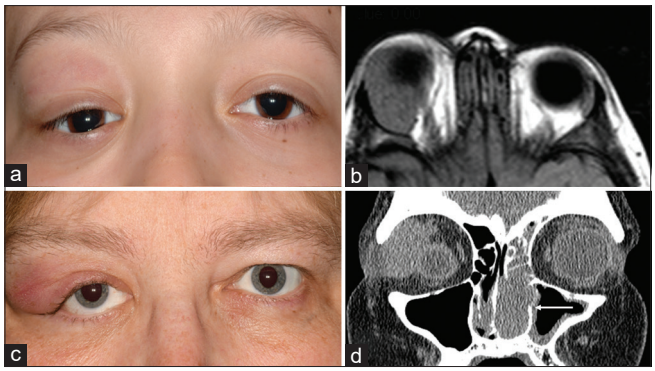

Figure 2: Orbital presentation of Rosai-Dorfman disease. (a) External photograph of 10-year-old male (case #4) with right upper eyelid mass, showing blepharoptosis and inferolateral globe displacement. (b) Axial T1 magnetic resonance imaging showing large, well-defined mass in the lacrimal gland region of the orbit. (c) External photograph of 52-year-old woman (case #5), showing erythematous right upper eyelid mass, blepharoptosis, and mild proptosis. (d) Coronal orbital computed tomography scan showing a large homogeneous lesion in lacrimal gland region of the orbit. White arrow shows involvement in para nasal sinuses

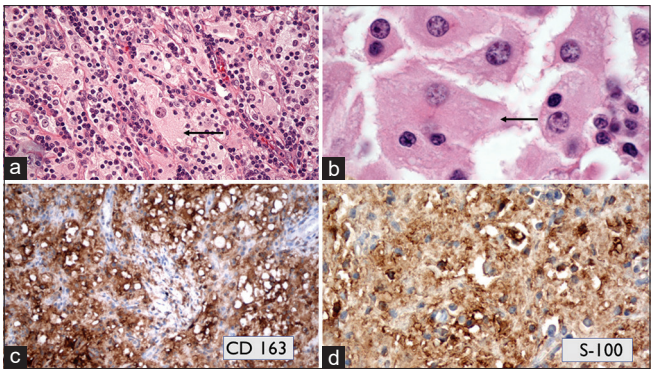

Figure 3: (a) Photomicrographs of the orbital mass show plump histiocytes surrounded by mature lymphocytes and plasma cells (H and E, ×40). (b) Higher magnification shows engulfed lymphocytes (emperipolesis, arrow) that can be found within the cytoplasm of some of the enlarged histiocytes (H and E, ×100). (c) CD163 cytoplasmic positivity in histiocytes with negative stain for lymphocytes and plasma cells (d) immunohistochemical staining of histiocytes is strongly positive for S-100 protein (Photograph courtesy of Dr. Tatyana Milman, Department of Ophthalmic Pathology, Wills Eye Hospital, Philadelphia, PA, USA)

and submandibular region, shown on fine-needle aspiration biopsy to have atypical mature lymphocytes. She also noted nasal congestion and epistaxis for 4 months. On referral, visual acuity was 20/40 in the affected right eye, and the globe was intact. There was a large mass fixed to orbital rim superotemporally that demonstrated marked enlargement of the right lacrimal gland and opacification of the fronto-ethmoidal sinuses [Figure 2c and d]. Laboratory examination showed normal CBC. Following surgical excision, histopathology revealed large histiocytes with copious eosinophilic cytoplasm, positive for CD68, CD163, and S-100 protein [Figure 3], and negative for CD1a, consistent with RDD. The histiocytes showed prominent emperipolesis. Subsequent sinus mucosal biopsy revealed features of RDD. Ten months after surgery, the visual acuity was 20/30, and there was no recurrence.

Discussion

It is estimated that there are fewer than 100 cases of RDD in the United States each year.[13] The first reports of RDD were mostly in the African-American population, and subsequent studies revealed that this disease has no specific predilection for geographic location or race.[2] This tumor is usually benign, asymptomatic, and it takes years to develop.[9] The clinical course of RDD is chronic and unpredictable with episodes of exacerbation alternating with periods of remission.[2] Foucar *et al*. reported progressive disease in only 1%, spontaneous regression in 21%, and stable disease in 78% of patients.[2]

The precise etiology of RDD remains unknown; however, certain etiologic factors have been suspected including bacterial (*Klebsiella*), virus (parvovirus B 19 or Epstein-Barr virus), or an aberrant response to an unspecified antigen such as human herpes virus 6.[14-16] The increased incidence of serum autoreactive antibodies during active disease, presence of characteristic histiocytes derived from circulating mononuclear cells, and a long history of disease suggest a possible pathogenic correlation with an immune dysregulatory process.[14]

The differential diagnosis of RDD includes Langerhans cell histiocytosis, lymphoma, and inflammatory pseudotumor. The diagnosis of RDD depends on histopathologic and immunohistochemical testing.[2] Classically, there is a population of histiocytes with prominent vesicular nucleoli and abundant pale cytoplasm that often manifest entire imbibed lymphocytes, plasma cells, and neutrophils, termed "emperipolesis."[2] Furthermore, RDD tissue shows immunoreactivity for CD163 [Figure 3c], CD68 and S-100 [Figure 3d] but negative for CD1a, a feature of Langerhans cell histiocytosis. Nuclear atypia and mitotic figures are rare [Figure 3a and b].[2,17]

Foucar *et al*.[2] reviewed a large series of RDD in 423 patients and noted extranodal manifestations of this disease to involve the skin, upper respiratory tract, and bone. They also documented 36 (8.5%) cases with periocular involvement including orbit (n = 26), eyelid (n = 5), uvea (n = 4), and conjunctiva (n = 1).[2] Others have shown that orbital involvement is the most common site for the ophthalmic manifestation of RDD.[3-9] Orbital RDD typically involves the soft tissue of intraconal space, as opposed to other xanthogranulomatous disorders, which tend to be extraconal or involve anterior orbital spaces.[9] In a report, between 34 cases of RDD, 24 had an orbital mass, 6 of which were confined to the lacrimal gland.[9] While the majority of patients with orbital involvement have concurrent lymphadenopathy, some may present with an orbit as the sole extranodal site without the synchronous nodal disease.[3] A minority of these patients may include other extranodal sites such as skin or paranasal sinuses at the same time.[3] In our series of five

patients, three had orbital involvement (cases 3, 4, and 5), and of those, two (cases 3 and 5) had synchronous regional lymphadenopathy with concurrent paranasal sinusitis.

Tran *et al*.[18] reviewed 20 cases of RDD reported with an epibulbar mass. They described the mass as pink, red, or salmon-color and fleshy appearance. Unilateral involvement was seen in 70% (n = 14) and concurrent lymphadenopathy in 15% (n = 3).[18] These lesions typically arose at the limbus and occasionally extended onto the cornea causing inflammatory keratitis. A lack of endothelial or anterior chamber inflammation was documented.[19] Fernandes *et al*. reviewed 9 cases of RDD with limbal involvement, and only 2 demonstrated lymphadenopathy.[20] In our series, there were 3 cases of conjunctival involvement, 2 with unilateral perilimbal tumor (cases 1 and 2) and no nodal involvement, and 1 with bilateral forniceal tumors with orbital invasion (case 3) and systemic involvement.

The involvement of RDD within the eye is exquisitely rare. Choi *et al.* evaluated four patients with intraocular involvement (retinal detachment, ciliary body mass, scleritis, and anterior uveitis) and noted that they all demonstrated multi-organ disease, including lymph nodes, sinusitis, renal, and lung involvement.[4] In our series, there was one patient (case 3) with bilateral anterior uveitis, and he additionally demonstrated chronic sinusitis and cervical, inguinal, and mediastinal lymphadenopathy from RDD. Based on these findings, we believe that patients with intraocular and/or bilateral RDD are at risk for systemic involvement as compared to those with limbal tumor who are very low to no risk.

Regarding therapy, Foucar *et al*. have documented that approximately 50% of patients require intervention including surgical excision (if surgically accessible), corticosteroids, chemotherapy, and radiotherapy.[2] Surgical excision is generally first-line therapy for orbital[21] and perilimbal lesions,[20] leading to often curative results with low recurrence rate.[20,21] Radiotherapy has been reported with doses ranging from 1000 to 5000 cGy.[21] Komp found that 10 of 34 (30%) patients with RDD that were treated with radiotherapy showed some improvement, but only 1 patient achieved complete response.[21] Recurrent orbital disease or significant residual lesion after surgical debulking may be treated with systemic corticosteroids, chemotherapy, or radiotherapy. Chemotherapy also has been used for multi-organ involvement or sight-threatening optic nerve compression.[22] Other reports have shown the positive response of Rituximab in the treatment of systemic RDD.[23,24] The pathogenic mechanism responsible for rituximab response is unclear, but it may be due to inhibition of immuno-modulatory signals or indirect targeting of the precursor cells supporting the plasmacytic infiltrate.[24]

In summary, we report a series of six eyes in five patients demonstrating the variety of ophthalmic manifestations in RDD. Those with multi-organ disease were typically associated with orbital and/or intraocular involvement, whereas those with only localized disease showed perilimbal tumor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol 1969;87:63-70.
2. 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.
3. Foucar E, Rosai J, Dorfman RF. The ophthalmologic manifestations of sinus histiocytosis with massive lymphadenopathy. Am J Ophthalmol 1979;87:354-67.
4. Choi MB, Salomão DR, Smith WM, Pulido JS, Garrity JA. Ophthalmic findings of Rosai-Dorfman disease. Am J Ophthalmol 2018;188:164-72.
5. Friendly DS, Font RL, Rao NA. Orbital involvement in sinus histiocytosis a report of four cases. Arch Ophthalmol 1977;95:2006-11.
6. Childs HA 3rd, Kim RY. Radiation response of Rosai-Dorfman disease presenting with involvement of the orbits. Am J Clin Oncol 1999;22:526-8.
7. Vemuganti GK, Naik MN, Honavar SG. Rosai Dorfman disease of the orbit. J Hematol Oncol 2008;28:7.
8. McClellan SF, Ainbinder DJ. Orbital Rosai-Dorfman disease: A literature review. Orbit 2013;32:341-6.
9. Mohadjer Y, Holds JB, Rootman J, Wilson MW, Gigantelli JW, Custer PL. The spectrum of orbital Rosai-Dorfman disease. Ophthal Plast Reconstr Surg 2006;22:163-8.
10. Pivetti-Pezzi P, Torce C, Colabelli-Gisoldi RA, Vitale A, Baccari A, Pacchiarotti A. Relapsing bilateral uveitis and papilledema in sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Eur J Ophthalmol 1995;5:59-62.
11. Vermeulen TL, Isaacs TW, Spagnolo D, Amanuel B. Rosai-Dorfman disease presenting as choroidal melanoma: A case report and review of the literature. Graefes Arch Clin Exp Ophthalmol 2013;251:295-9.
12. Yuen HK, Cheuk W, Leung DY, Tse RK, Chan N. Atypical presentation of Rosai-Dorfman disease in the lacrimal gland mimicking malignancy. Ophthalmic Plast Reconstr Surg 2006;22:145-7.
13. Albini TA, Evans M, See R, Rao NA, Marback E, de Souza MM. Rosai-Dorfman disease: Isolated epibulbar masses in two adult patients. Br J Ophthalmol 2005;89:241-3.
14. McClain KL, Natkunam Y, Swerdlow SH. Atypical cellular disorders. Hematology Am Soc Hematol Educ Program 2004;1:283-96.
15. Mehraein Y, Wagner M, Remberger K, Füzesi L, Middel P, Kaptur S, *et al*. Parvovirus B19 detected in Rosai-Dorfman disease in nodal and extranodal manifestations. J Clin Pathol 2006;59:1320-6.
16. Harley EH. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) in a patient with elevated Epstein-Barr virus titers. J Natl Med Assoc 1991;83:922-4.
17. Sarwal R, Tu E, Mendelblatt FI, Sugar J, Gross SA, Pulido JS, *et al*. Atypical ocular presentations of Rosai-Dorfman disease. Ocul Immunol Inflamm 2008;16:9-15.
18. Tran HM, Chinichian S, Storkersen K, Tokuhara K. An unusual case of extranodal Rosai-Dorfman disease manifesting as an epibulbar mass. Case Rep Ophthalmol 2015;6:351-5.

19. AlWadani S, Robinson S, Myers R, Akpek EK, Eberhart CG. No increase in IgG4-positive plasma cells in limbal Rosai-Dorfman disease. Cornea 2014;33:844-7.
20. Fernandes BF, Brazuna A, Moura LR, Ayres B, Nakamura P, Al-Kandari AA, *et al*. Extranodal Rosai-Dorfman disease presenting as an epibulbar tumor. Cornea 2008;27:378-81.
21. Komp DM. The treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Semin Diagn Pathol 1990;7:83-6.
22. Horneff G, Jürgens H, Hort W, Karitzky D, Göbel U. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): Response to methotrexate and mercaptopurine. Med Pediatr Oncol 1996;27:187-92.
23. Alqanatish JT, Houghton K, Bond M, Senger C, Tucker LB. Rituximab treatment in a child with Rosai-Dorfman disease and systemic lupus erythematosus. J Rheumatol 2010;37:1783-4.
24. Pagel JM, Lionberger J, Gopal AK, Sabath DE, Loeb K. Therapeutic use of Rituximab for sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Am J Hematol 2007;82:1121-2.