Rosai-Dorfman Disease Manifesting as Relapsing Uveitis and Subconjunctival Masses

Hsin-Yuan Tan, MD; Ling-Yuh Kao, MD

Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy, SHML) is a rare, non-hereditary, benign histiocytic proliferative disorder mainly affecting young people with common clinical characteristics such as painless bilateral cervical lymphadenopathy, fever, leukocytosis and polyclonal gammopathy. Extranodal manifestations have been reported in 28-43% of cases. Eye involvement is relatively uncommon (8.5%), and most of cases have presented as lymphoproliferation in the soft tissues of the orbit and eyelids. Uveitis is an even more rare presentation as a review of all the literature. We describe a 63-year-old man with SHML with unusual ophthalmic manifestations of relapsing uveitis and bilateral subconjunctival masses. The results of biopsies were compatible with the characteristic histopathological findings of SHML: focal aggregations of S100-positive foamy histiocytes and the existence of lymphocytophagocytosis. During the clinical course, the patient relapsed but the relapse was relatively benign and the patient showed fair response to topical as well as systemic corticosteroid treatment. Here we describe this unusual presentation of SHML to inform physicians of the possibility for this systemic granulomatous disease to contribute to relapsing uveitis. *(Chang Gung Med J 2002;25;621-5)*

Key words: Rosai-Dorfman disease, uveitis, subconjunctival mass.

Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy, SHML) is a rare, idiopathic, benign proliferative histiocytic disorder, which was first describeed by Rosai and Dorfman in 1969 and 1972, respectively.[1,2] It affects mainly young people with the slight predominance in the male population. The characteristics of Rosai-Dorfman disease are bilateral painless lymphadenopathy, fever, leukocytosis, and polyclonal gammopathy. Extranodal involvement had been reported in 28-43% of the cases with the skin as the most commonly involved site. Ocular involvement is relatively rare (8.5%), and mostly manifested as lymphoproliferation in the soft tissues of the orbit and the eyelids.[1,2] Here we describe an unusual case of SHML with ophthalmic manifestations of relapsing uveitis and bilateral subconjunctival masses.

CASE REPORT

We describe a 63-year-old man who initially presented with congested left eye for 2 months. On examination, bilateral subconjunctival infiltrative lesions were noted (Fig. 1). Under the suggestion of lymphoma, conjunctival biopsies as well as systemic investigations were performed. The results of biopsies showed only infiltration of reactive lymphoid tissue initially. No systemic correlated symptoms such as fever coexisted. Hence, due to the concomitant existence of right-sided post-auricular lymphadenopathy and vocal cord nodule, which was found due to symptom of hoarseness, biopsies for

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Received: Oct. 19, 2001; Accepted: Feb. 25, 2002
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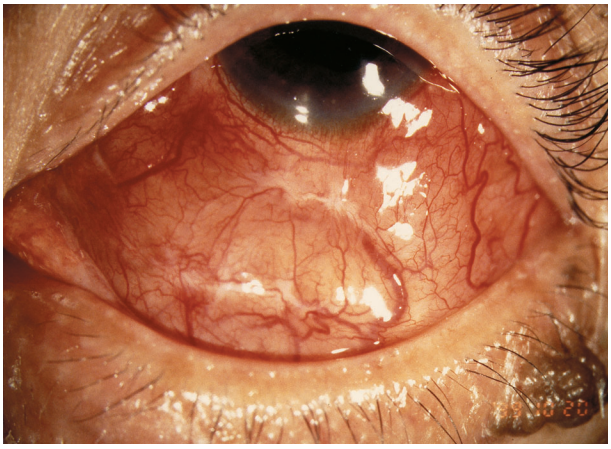

Fig. 1 Salmon-colored lesion is present beneath the conjunctiva of his left eye.

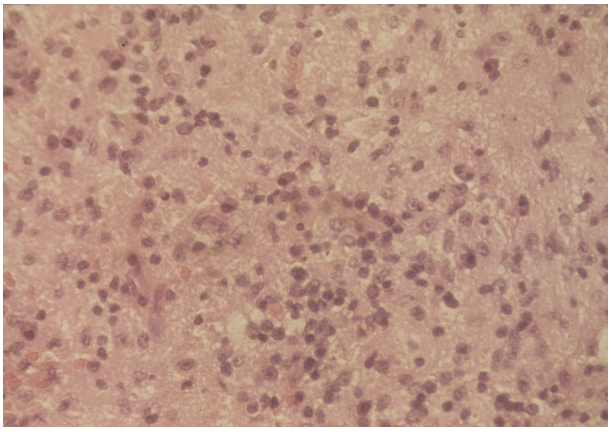

Fig. 2 The biopsy specimen contains aggregates of histiocytes, plasma cells and small lymphocytes with existence of lymphocytophagocytosis (hematoxylin and eosin ¡ 100).

were performed thereafter. The pathological result showed infiltration of foamy and granular histiocytes along with aggregation of plasma cells and lymphocytes, with the existence of lymphocytophagocytosis. In addition, immunohistochemical studies showed positive results for S100 protein and CD68, all which were compatible with the histopathological characteristics of SHML. Therefore, another conjunctival biopsy was performed and the pathological and immunohistochemical reports confirmed the diagnosis of SHML (Fig. 2). Laboratory investigation results including hemogram, erythrocyte sedimentation rate (ESR), serologic tests, and abdominal computed tomography scan, showed positive results of minimal leukocytosis (10200/mm^3), mildly elevated ESR level (17 mm/hr), weakly positive anti-nuclear-antibody titer (1:40), and elevated Epstein-Barr virus IgG titer (1:640), without typical polycloncal gammopathy. Meanwhile, several episodes of anterior as well as posterior uveitis developed in his left eye during follow-up with manifestations of keratic precipitates, cell/flare in anterior chamber, and vitreous cell/opacity (Fig. 3), which showed fair response to systemic oral and topical corticosteroid. Recurrence of bilateral conjunctival masses was also noted during the 2-year follow-up period. Cataract surgery and subsequent vitrectomy for cystoid macular edema were performed in his left eye during the follow-up period. At the last visit, the best corrected visual acuity was 0.9 (od) and 0.4 (os), respectively without signs of uveitis or subconjunctival masses noted.

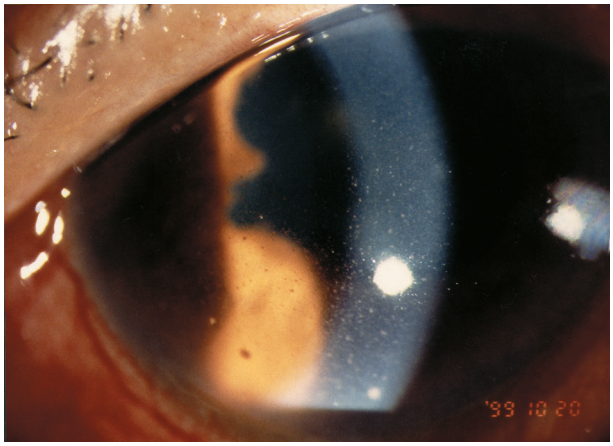

Fig. 3 Numerous mutton-fat keratic precipitates are noted in his left eye.

DISCUSSION

SHML is a rare, idiopathic, benign proliferative histiocytic disorder, which was established as a clinical entity by Rosai and Dorfman in 1969 and 1972, respectively.[1,2] It affects predominantly young people with the mean age at onset of 20 years.[3] Compared with the mean age, our patient is relatively old (63 years old). The characteristics of SHML are bilateral painless lymphadenopathy (90%), fever, leukocytosis and polyclonal gammopathy.[3] The eti-

ology of SHML remains unknown, may be a reactive process to infection such as Epstein-Barr virus, etc.[3] In our patient, we found only a possible correlation in increased levels of IgG anti-Epstein-Barr-virus (1:640). The diagnosis of SHML is histopathologic, based on the characteristics of the proliferation of foamy histiocytes with round vesicular nuclei and abundant, pale cytoplasm, showing lymphocytophagocytosis,[3] and a S100 immunophenotype protein.[4] The prevalence of extranodal involvement have been reported in 28-43% of cases, including the skin, upper respiratory tract, salivary glands, epidural space, bone and ocular adnexa. Ocular involvement is rare. In the largest series of 243 cases reported by Foucar in 1990, the eye was involved in 36 cases (8.5%) and was highly associated with nasal sinuses involvement. Soft tissue of the orbit and the eyelids infiltrations were the most common manifestations of ocular involvement.[3,5] In addition, infiltration of the lacrimal system, conjunctiva/subconjunctiva, cornea, uveal tract, and optic nerve, have all been reported.[1-3,5-11] Uveitis was present in six cases as found in a literature reviewed: three isolated anterior uveitis,[3,5,6,10] one with coexistent corneal infiltration,[11] one with coexistent papilledema,[12] and one diagnosed pathologically after enucleation due to post-traumatic uveitis.[3,5] Five cases had lymphadenopathy[3,5,6,11,12] and one had only cutaneous involvement.[10] It had been proposed as the expression of a proliferative process involving the uveal tract (pseudouveitis). There was only one case histopathologically confirmed with typical histiocytic infiltration in the uveal tract after enucleation because of post-traumatic uveitis. The rest were not histopathologically proven because it was unnecessary to perform an ocular biopsy for such a benign course. In our patient, the diagnosis was made using histopathologic confirmation by biopsies of conjunctival lesions, lymph node, and vocal cord nodule. Although intraocular biopsy were not performed either, the concomitant existence of several documented involving sites convinced us of the correlation of his relapsing uveitis and underlying SHML.

The natural course of SHML is highly variable but relatively benign and self-limiting, usually with spontaneous regression after years.[3,13] Therefore the indications for treatment remain obscure. Most often, an excisional biopsy is required to establish the diagnosis. Surgery, radiotherapy, and chemotherapy including vinca alkaloid, alkylating agents, and corticosteroids are all options of treatment for those life-threatening or function-threatening conditions, although the treatment might not always be effective.[13,14] Excision of epibulbar lesion has both diagnostic and therapeutic effects. Unlike our case, no recurrence ever occurred after tumor excised in previous reports.[7-9] Regarding the treatment of uveitis, the results seem less efficient, as in our case. Topical and systemic corticosteroids were administered in most cases with fair results. Recurrence occurred in three cases, including our case. Several episodes of recurrence developed in our patient during the 2 years of follow up, with fair response to corticosteroids. In spite of the setbacks, the disease course was relatively benign.

In conclusion, we presented an unusual case of SHML with ophthalmic manifestation as recurrent uveitis and subconjunctival masses, which showed fair response to corticosteroid therapy. The clinical course relapsed but was relatively benign. The subsequent lymphadenopathy drew our attention to the fact that the systemic granulomatous disease might contribute to the unusual presentation of relapsing uveitis and subconjunctival masses.

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Rosai-Dorfman病：以復發性的葡萄膜炎及結膜下腫瘤表現

譚欣媛　高玲玉

Rosai-Dorfman病是種罕見的組織球細胞增生疾病，主要好發於年輕族群。其主要臨床表徵爲出現雙側性的頸部淋巴腫。出現淋巴結外病灶的機率約爲28-43%。而出現眼部表徵的機會較爲稀少，通常是以侵犯眼窩組織及眼瞼爲主。而以葡萄膜炎爲表現又更爲稀少。我們提出一位63歲Rosai-Dorman病的個案，以罕見的復發性葡萄膜炎以及結膜下腫瘤作爲其臨床表徵。病理結果符合Rosai-Dorfman病的特徵：出現S100陽性反應的組織球聚集以及淋巴球聚嗜現象。病患臨床病程是復發性但屬良性病程，對於類固醇治療有不錯的反應。我們提出這罕見的病例藉以提醒這全身性的疾病－Rosai-Dorfman病可能會以復發性的葡萄膜炎作爲其臨床表徵。(長庚醫誌 2002;25:621-5)

關鍵字：Rosai-Dorfman病；葡萄膜炎；結膜下腫瘤。

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