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ORIGINAL ARTICLE

Risk Factors for Development of Rhegmatogenous Retinal Detachment in Patients with Uveitis

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ABSTRACT

Purpose: To describe risk factors for development of rhegmatogenous retinal detachment (RRD) in patients with uveitis.

Methods: We performed a retrospective review of 411 consecutive human immunodeficiency virus-negative patients with uveitis (571 affected eyes) and report on prevalence, risk factors and visual outcomes of patients with RRD.

Results: Prevalence of RRD was 7% of all patients with uveitis. Multivariate analysis revealed that posterior uveitis and panuveitis were associated with RRD ($P = 0.001$). Strong association between RRD development and infectious uveitis was also observed ($P = 0.009$). Acute retinal necrosis (ARN) was firmly associated with RRD development ($P = 0.016$). Although anatomical success was obtained, functional outcome was poor. Poor visual outcomes at 6-month and 1-year follow-up were associated with initial VA < counting fingers ($P = 0.05$, $P = 0.044$).

Conclusions: Prevalence of RRD in uveitis was 7% and development of RRD was encountered in posterior and panuveitis. Infectious uveitis (specifically ARN) formed a high risk for RRD.

Keywords: Prevalence, rhegmatogenous retinal detachment, Thailand, uveitis, visual outcome

Retinal detachment (RD) represents a serious complication of uveitis and is commonly associated with limited visual outcome. All three forms of RD (exudative, rhegmatogenous, and tractional) can develop during the course of uveitis. Previously, the incidence of rhegmatogenous RD (RRD) in uveitis was reported to be 3.1% in contrast to 0.01% of RRD identified in the general population.[1–3]

Development of RRD can be enhanced by inflammatory complications such as posterior vitreous detachment (PVD), morphological changes within vitreous base especially following intermediate uveitis. Inflammation can destroy retinal cells and weaken the intercellular adhesions of the retinal cells and pigment epithelium resulting in higher rate of retinal breaks.[4,5]

The visual prognosis of RRD in uveitis was reported to be worse than RRD without uveitis despite similar surgical treatments, presumably due to multiple factors such as young age, higher prevalence of proliferative vitreoretinopathy (PVR) before and after the surgery as well as the presence of diverse complications of uveitis such as macular edema, glaucoma, hypotony, cataract, and retinal scars.[1,6–10]

The purpose of this study is to report on the risk factors for development of RRD in human immunodeficiency virus (HIV)-negative patients with uveitis as well as to report on the visual outcomes after the surgery.

METHODS

We conducted a retrospective analysis of the medical records of 411 consecutive uveitis patients visiting an outpatient Ophthalmology Department of Chiang Mai

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University Hospital from January 2013 through December 2015. The medical data of all patients were reviewed and patients with RRD were identified. Patients with diagnosis of RRD before the onset of uveitis and patients with HIV infection were not included as the high prevalence of RRD in cytomegalovirus retinitis might strongly affect the results for general uveitis.[11–14] We collected demographic data of the patients including gender, age at onset of RRD, laterality, the interval between the onset of uveitis and the occurrence of RRD, inflammatory activity at the onset of RRD, visual acuity (VA) at onset of RRD, the nature of breaks, the extent of RRD, the presence of PVR, previous intraocular surgery and duration of follow-up. The data concerning uveitis such as its onset, anatomical classification, specific uveitic entities, cause or association with systemic disease were also noted. In addition, surgical technique, visual outcome after surgery and VA after surgery, reattachment rate and complication were registered.

Complete anatomic success was considered if the whole retina was reattached after the operation, and the term "partial success" was used if the retina including the macular area was attached, though the peripheral inferior retina was still detached.

VA was tested using Snellen acuity chart and converted to Early Treatment Diabetic Retinopathy Study (ETDRS) letter scores for all calculations and statistical analyses.[15] Student's *t*-test, Mann–Whitney *U* test, Kruskal–Wallis tests, and ANOVA tests were used for continuous variables and Fisher exact test or Pearson's chi-square test were used for categorical variables by a software package, SPSS 17.0 (SPSS Inc., Chicago, IL, USA). A significance level of 5% was used.

The study was approved by the Ethics Committee of Chiang Mai University Hospital and performed in agreement with the Declaration of Helsinki.

RESULTS

Our study included 411 patients (571 eyes affected by uveitis) consisting of 205 females (49.9%) and 206 males (50.1%). The patient demographics and specific uveitis entities are given in Tables 1 and 2. The prevalence of RRD in patients with uveitis was 7% (28/411; 5%; 29/571 of affected eyes). RRD occurred within a year after diagnosis of uveitis in all patients and in 23/28 patients (82%) within 3 months.

Total RRD was present in 21/28 patients (75%) and 5 patients (18%) developed proliferative vitreoretinopathy before surgery. We encountered a horseshoe tear in 15/29 eyes (52%) and atrophic round holes in atrophic and/or necrotic retina in 14/29 eyes (48%). Multiples retinal breaks were observed in 11/29 eyes (38%) whilst 18/29 eyes (62%) had 1 or 2 retinal breaks. Majority of retinal breaks were located in the peripheral retina (26/29, 90%). We found primary RRD in 23/29 eyes (79%) and secondary RRD (retinal breaks induced by traction which) in 6/29 eyes (21%).

Active inflammation at time of RRD onset was present in 21/29 RRD eyes (72%). The VA at the first presentation was worse in RRD group ($P < 0.001$). Previous cataract surgery was performed in 2/29 eyes; 7% of RRD group and in 35/542 eyes; 7% of non-RRD uveitis patients. Previous diagnostic vitrectomy was performed in 15 eyes, all of which were in non-RRD patients.

Using univariate analysis, we found that posterior uveitis ($P = 0.038$; OR 2.86 CI 1.192–6.859) and panuveitis ($P < 0.001$; OR 5.239 CI 2.3–11.937) were associated with RRD. In addition, infectious uveitis and specifically acute retinal necrosis (ARN) were associated with the development of RRD ($P = 0.009$; OR = 2.938, CI 1.353–6.379 and $P = < 0.001$; OR = 11.385, CI 4.234–30.608, respectively).

TABLE 1. General characteristics of uveitic patients with and without rhegmatogenous retinal detachment.

	Uveitic RRD	Uveitis without RRD	*P*-value
Patients ($n = 411$)	28	383	–
Laterality (unilateral:bilateral)	27:1	224:159	–
Eyes ($n = 571$)	29	542	–
Location ($n = 411$)			
- Anterior uveitis ($n = 177$)	1(3.6%)	**176 (46%)**	**$P < 0.001$[a]**
- Posterior uveitis ($n = 55$)	**8 (28.6%)**	47 (12.3%)	**$P = 0.038$[b]**
- Intermediate uveitis ($n = 50$)	0	**50 (13%)**	**$P = 0.036$[b]**
- Panuveitis ($n = 129$)	**19 (67.8%)**	110 (28.7%)	**$P < 0.001$[a]**
Median age (years) at onset of uveitis ($n = 411$)	44.5 (range 13–78)	46 (range 3–83)	$P = 0.589$[c]
Male/female ratio	15:13	191:192	0.845[d]
Mean follow-up (months)	16	N/A	–

RRD, rhegmatogenous retinal detachment
[a]Continuity correction.
[b]Fisher's exact test.
[c]Mann–Whitney test.
[d]Pearson chi-square test.

TABLE 2. Specific entities in patients with and without rhegmatogenous retinal detachment in uveitis.

		Uveitic RRD (n = 28)	Uveitis without RRD (n = 383)
Infectious uveitis			
Viral (n = 81)	Herpetic AU (n = 33)	0	33 (8.6%)
	ARN (n = 21)	8 (28.6%)	13 (3.4%)
	CMVR (n = 27)	1 (3.6%)	26 (6.8%)
Parasitic (n = 37)	Toxoplasma (n = 27)	2 (7.1%)	25 (6.5%)
	Toxocara (n = 9)	3 (10.7%)	6 (1.6%)
	Cysticercus (n = 1)	1 (3.6%)	0
Bacterial (n = 5)	Tuberculosis (n = 5)	0	5 (1.3%)
Total (n = 123)		**15 (53.6%)**	**108** (28.2%)
Non-infectious uveitis			
Diagnosis	Lymphoma (n = 3)	2 (7.1%)	1 (0.3%)
	Behcet disease (n = 40)	1 (3.6%)	39 (10.2%)
	VKH (n = 31)	2 (7.1%)	29 (7.6%)
	HLA-B27 (n = 24)	0	24 (6.3%)
	Sarcoidosis (n = 8)	0	8 (2.1%)
	Fuchs uveitis (n = 13)	0	13 (3.4%)
	Sympathetic ophthalmia (n = 3)	0	3 (0.8%)
	Eales' disease (n = 8)	0	8 (2.1%)
	Undetermined (n = 158)	8 (28.6%)	150 (39.2%)
Total (n = 288)		**13 (46.4%)**	**275** (71.8%)

RRD, rhegmatogenous retinal detachment; AU, anterior uveitis; ARN, acute retinal necrosis; CMVR, cytomegalovirus retinitis; VKH, Vogt–Koyanagi–Harada; HLA-B27, human leukocyte antigen B27.

Posterior and panuveitis associated with RRD exhibited retinal vasculitis in 7/29 eyes (24%), choroiditis 3/29 eyes (10%), granuloma 3/29 eyes (10%), neovascularization at disk or elsewhere in the retina in 3/29 eyes (10%), and necrotic retinal lesions 12/29 eyes (41%). Prior intravitreal injections were more common in the RRD group (5/29 eyes; 17% versus 34/542 eyes; 6%; P = 0.04; OR = 3.113, CI 1.118–8.668).

Multivariate analysis revealed that posterior uveitis (P = 0.001; OR 34.022 CI 4.060–285.092), panuveitis (P = 0.001; OR 29.559 CI 3.830–228.136), and ARN (P = 0.016; OR = 5.057, CI 1.354–18.885) were risk factors of RRD in patients with uveitis. Patients with posterior and panuveitis had 10 times greater risk to develop RRD compared to patients with anterior uveitis (OR = 10.034, 95% CI 3.655–245.524 and OR = 10.922, 95% CI 4.013–230.300, consecutively). Age, sex and prior ocular surgery were not associated with the RRD development. Using the multivariate analysis, the association between the RRD and prior intravitreal injections disappeared.

In patients with RRD, infectious etiology was present in 54%, with ARN being the most common entity (8/28, 29% of all; 8/15, 53% of infection; 8/21, 38% of all with ARN) followed by toxocariasis (3/28, 11% of all; 3/15, 20% of infection; 3/9, 33% of all with toxocariasis) and toxoplasmosis (2/28, 7.1% of all; 2/15, 13.3% of infection; 2/27, 7.4% of all with toxoplasmosis). The remainder of RRD patients had mostly uveitis of undetermined origin (8/28, 28.6% of all; 8/13, 61.5% of not proven infectious origin; 8/158, 5.1% of all with undetermined cause of uveitis).

All 29 eyes with RRD underwent pars plana vitrectomy (PPV), with addition of scleral bucking in 10 eyes and silicone oil tamponade in 19 eyes. During surgery, oral steroid treatment was given to 18/28 (64%) patients and one patient received immunosuppressive therapy. Visual outcome is shown in Table 3. Although anatomical success at 1-year follow-up was obtained in 90% of eyes, almost 75% of patients became legally blind (VA less than 20/200). Six out of 19 eyes (32%) had to retain long-term silicone oil tamponade due to either hypotony and/or recurrence of RRD. However,

TABLE 3. Visual outcome of rhegmatogenous retinal detachment in uveitis.

	6-month follow-up (n = 22)	1-year follow-up (n = 19)
Anatomical success		
- Complete	16 (72.8%)	14 (73.7%)
- Partial	3 (13.6%)	3 (15.8%)
- Recurrent RRD	3 (13.6%)	2 (10.5%)
Visual outcome		
- Improved	14 (63.7%)	10 (52.6%)
- Stable	5 (22.7%)	6 (31.6%)
- Worse	3 (13.6%)	3 (15.8%)
Visual outcome*		
- BCVA ≥ 20/200	6 (27.3%)	5 (26.3%)
- BCVA ≤ CF	8 (36.4%)	12 (63.2%)

BCVA, best-corrected visual acuity; CF, counting fingers; RRD, rhegmatogenous retinal detachment.

*Initial VA (n = 29): VA ≥ 20/200 in 5 (17.2%), VA ≤ CF in 23 (79.3%).

some visual improvement after surgery occurred in 50–60% of eyes (Table 3).

Complication rate increased with the longer duration of follow-up. Out of the 19 eyes, which could be evaluated at 1-year follow-up, cataract occurred in 42% and ocular hypertension or glaucoma in 37%; one eye developed phthisis.

Visual outcomes of less than counting fingers at 6-month and 1-year follow-up were associated with poor VA at presentation with RRD (P = 0.05; OR 1.75 CI 1.112–2.755 and P = 0.044; OR 2.167 CI 1.204–3.898, respectively)

DISCUSSION

In our study, the prevalence of RRD in uveitis population was 7% and the risk factors for development of RRD included posterior and panuveitis locations as well as infectious origin of uveitis, with ARN being the most common single uveitis entity.

The RRD prevalence in uveitis of 7% is higher than in normal population and seems also higher than 3.1% reported earlier in uveitis population in Europe.[1–3] This difference might be explained by a possible higher prevalence of infectious uveitis in developing countries.[11,16–23] The prevalence of infectious uveitis was 30% in this study whilst 15–23% was documented in previous the study from United States and Europe. [1,24–26] Infectious uveitis (especially viral infections) is usually associated with retinal necrosis and subsequent atrophy combined with vitreous degeneration, fibrosis, and traction, resulting in development of retinal holes and finally detachment. In addition, patients in Thailand possibly attended the ophthalmologists in the later stage, which is illustrated by the fact that 75% of patients with RRD had total RD and 80% of these patients had VA of counting fingers or less at first presentation with RRD. Posterior and panuveitis were the risk factors for RRD development. The posterior location of inflammation may lead to structural alterations of the vitreous, and vitreous gel shrinkage[4] as well as to development of tractional forces especially at poorly perfused areas with, all of which might be associated with development of retinal tears.

ARN was the most common single uveitis entity found in patients with uveitis and RRD. In our study, the incidence of RRD in ARN was 38%, which is consistent with recent studies that indicate the RRD occurrence from 20% to 85% of eyes.[27–32]

Prior intravitreal injections might form a predisposing factor for RRD development. This was already noted in previous reports[33,34] which hypothesized that intravitreal injection might induce PVD and thereby increase a risk of retinal tears. In our study, with the application of multivariate analysis, we cannot confirm this association. The intravitreal injections in uveitis are mostly given to patients with posterior and panuveitis, whilst posterior and panuveitis also form a high-risk factor for RRD. When solely patients with posterior and panuveitis were compared for the number of prior intravitreal injections, no differences were observed in patients with and without RRD (P = 0.078).

The visual prognosis of RRD complicating uveitis was in our series poor despite the anatomical success obtained in the majority of patients. Silicone oil was used in majority of patients and though this tamponade induces retinal stability, silicone oil itself decreases visual function and increases complication such as cataract, glaucoma, band keratopathy.

The limitations of our study include its retrospective character, limited number of patients, and a possible selection bias towards more severe. Due to the limited number of patients, the efficacy of specific treatment approaches cannot be evaluated.

In conclusion, our data show that uveitis itself is a risk factor for the development of RRD, especially posterior uveitis and panuveitis. Infectious uveitis and specifically ARN were associated with the development of RRD.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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