

Ruthenium-106 Plaque Radiotherapy for Retinal Vasoproliferative Tumors

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Abstract

Purpose: To evaluate the effect of radiation with Ruthenium-106 (Ru-106) plaques in the control of retinal vasoproliferative tumors

Methods: This study is a retrospective, interventional nonrandomized case series. Seven eyes of seven patients (four males and three females) with retinal vasoproliferative tumors were enrolled. The eyes were treated by Ru-106 plaques with mean apex dose of 39 Gy (range, 38-43 Gy) in low-dose (LD) group (four cases) and 79 Gy (range, 76-81 Gy) in high-dose (HD) group (three cases). Mean (\pm SD) follow-up duration was 18 (\pm 8) months (range, six to 31 months) Main outcome measures were tumor thickness reduction and clinical and visual improvement.

Results: Mean (\pm SD) preoperative logMAR visual acuity improved from 0.92 (\pm 0.49) to 0.85 (\pm 0.71) at the last follow-up ($P=0.50$). Significant exudative retinal detachments, which were presented before brachytherapy in five patients (71.4%), completely reabsorbed following brachytherapy. Radiation retinopathy was seen in three patients during the follow-up period. Tractional rhegmatogenous retinal detachment developed in one patient of LD group which was managed with pars plana vitrectomy and silicon oil tamponade.

Conclusion: Brachytherapy with high-dose Ru-106 plaques is an effective treatment modality for retinal vasoproliferative tumors in terms of functional and anatomic results. Further investigations with enough sample sizes are suggested to identify the optimal apex dose.

Keywords: Retinal Vasoproliferative Tumor, Ruthenium-106, Brachytherapy

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Introduction

Vasoproliferative tumor of retina (VPT or VTR) is a vascularized fundus lesion. It has been recognized as a new clinical entity since 1982, when Baines¹ reported the combination of peripheral telangiectatic nodules and posterior fibro-cellular membrane in five patients. Since then, these tumors have been named in

different ways such as "presumed acquired retinal hemangioma",² "retinal angiomatous mass",³ "hemangioma like masses of the retina",⁴ "acquired retinal angiomas"⁵ to differentiate them from retinal capillary hemangioma.

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However, at the present time "vasoproliferative retinal tumor (VPT)" is the generally accepted term coined by Shields and colleagues.⁶

The exact nature of the VPTs have been remained uncertain, but as demonstrated in different histopathologic reports, they consist of glial cells and a network of vascular proliferations.^{7,8} VPTs are characterized by a globular pinkish to yellowish mass in peripheral retina associated with subretinal exudates (in over 80% of cases),⁶ exudative retinal detachment, retinal and vitreous hemorrhage, retinal pigmented epithelium hyperplasia, preretinal fibrosis and vitreous cells.^{6,7} The lesions lack dilated and tortuous feeder or drainer vessels typically seen in retinal capillary hemangioma, however, retinal vessels with normal or nearly normal calibers may be seen entering the lesions posteriorly.^{6,7,9}

Vasoproliferative tumors may be primary (74%) or secondary (26%) to a preexisting ocular disease and usually present in the third or fourth decades of life and both sexes are affected equally.^{6,7} The majority of the primary types of the lesions are unilateral and solitary which have a predilection for the inferotemporal quadrant.¹⁰ The secondary types are most often associated with intermediate uveitis, retinitis pigmentosa, ocular toxocariasis, Coat's disease, chronic retinal detachment and ocular trauma.¹⁰

The indications and modalities of treatment vary case to case. Although some authors advocate periodic follow-ups for small, asymptomatic lesions,¹⁰ most of them agree that treatment is indicated for lesions associated with a significant amount of exudates and retinal detachment to preserve vision.⁷ These tumors may be managed with cryotherapy, photocoagulation,¹⁰ photodynamic therapy (PDT),¹¹ intravitreal injection of Bevacizumab,¹² plaque radiotherapy¹³ or even surgical removal.¹⁴ There are few reports of brachytherapy with different isotopes for VPTs,^{6,7,12} however there is no consensus regarding the apex dose required for these lesions. Although Bornfeld and his coworkers recommended the apex dose should be 80-100 Gy ideally¹² but Shields and his group showed that brachytherapy with median dose of 40 Gy is able to control the activity of VPTs.¹⁵ In this

study we will report our results with Ruthenium-106 (Ru-106) plaque radiotherapy for symptomatic VPTs with low-dose (40 Gy) versus high-dose (80 Gy) brachytherapy.

Methods

This study is a retrospective interventional nonrandomized case series to evaluate the effects of radiation dose in brachytherapy for retinal VPTs. We reviewed seven eyes of seven patients in ocular oncology service of Rassoul-Akram Hospital (Iran University of Medical Sciences, Tehran, Iran) who were treated for vasoproliferative tumors of retina by Ru-106 brachytherapy between October 2004 and June 2007. A comprehensive ocular examination including best corrected visual acuity (BCVA) and intraocular pressure (IOP) measurement, slit lamp examination and funduscopy with scleral depression by indirect ophthalmoscopy was done. Tumor size and thickness were determined by A and B scan ultrasonography and whenever possible fluorescein angiography was performed.

Complete systemic evaluation including magnetic resonance imaging (MRI) of the brain, urine analysis and taking the family history were done to rule out Von-Hippel's retinal capillary hemangioma. In addition to specific tumor features such as size, thickness and location, associated retinal findings which were documented included retinal hard exudates, exudative retinal detachment, vitreous hemorrhage, preretinal membrane formation and absence of typical dilated and tortuous feeder or drainer vessels. Four patients had primary (idiopathic) VPT without any preexisting ocular pathology and three patients had history of previous uveitis and Coat's disease which were completely inactive for long times before presentation.

All patients were treated with beta radiation brachytherapy using Ru-106 plaque (Bebig Company, Berlin, Germany). After precise localization of the tumor by indirect ophthalmoscopy, a Ru-106 plaque completely covering the VPT with a safety margin of one millimeter was sutured to sclera over the tumors. The scheduled radiation to the tumor apex was 40 Gy (low-dose) on four patients and three others received about 80 Gy (high-dose). Main outcome measures were tumor thickness reduction, clinical and visual improvement and treatment complications.

Results

Four male and three female consecutive cases were enrolled in this study. Mean age at the time of diagnosis was 27.28 years ranging 14 to 68 years. Mean (\pm SD) follow-up time was 18 (\pm 8) months (range, six to 31 months). Five cases presented with chief complaint of decreased or blurred vision. Floater was presented in one case and in the last one no symptom was reported and VPT was detected during the routine examination. All tumors were located between the equator and ora serrata within the inferotemporal quadrant except for one tumor which was located in inferonasal quadrant of the ocular fundus (Figure 1). Tables 1 and 2 show some of the baseline characteristics of the patients. Significant exudative retinal detachment which was present in five eyes (71.4%) before brachytherapy was reabsorbed completely at the last follow-up. However, different levels of subretinal exudates and pigmentary changes remained.

Mean (\pm SD) preoperative logMAR visual acuity improved from 0.92 (\pm 0.49) to 0.85 (\pm 0.71) at the last follow-up ($P=0.50$). Mean (\pm SD) tumor thickness decreased from 4.25 mm (\pm 1.22 mm) to 2.64 mm (\pm 0.8 mm). The largest mean (\pm SD) basal diameter of the tumors also decreased from 7.91 mm (\pm 2.78) to 5.94 mm (\pm 2.05 mm). Mean applied dose for tumor apex in low-dose and high-dose groups were 39 Gy (38 to 43) and 79 Gy (76 to 81), respectively. One patient experienced

transient vitreous hemorrhage and radiation retinopathy was developed in three patients during the follow-up period. But the most important complication following brachytherapy was development of tractional retinal detachment in one patient of the low dose group. Although it was managed with pars plana vitrectomy and silicone oil tamponade, VA decreased to light perception. The patient had previous Coat's disease with some preretinal fibrous tissues at retinal periphery before brachytherapy.

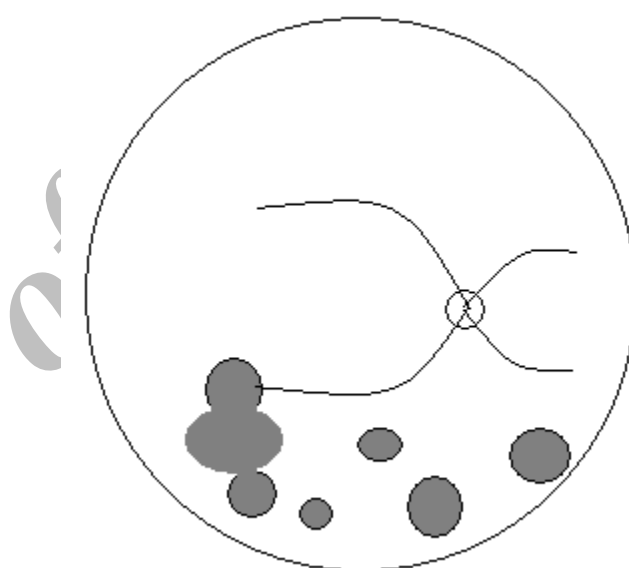


Figure 1. Schematic diagram of the tumor location in the ocular fundus

Table 1. Basic characteristics of the patients

Age, mean (range)	27.28 yr (14-68)
Male/Female	3/4
Mean largest tumor basal diameter (range)	7.91 mm (5-12)
Mean tumor thickness (range)	4.25 mm (2-5.7)
Mean visual acuity	0.92 (SD 0.61)
Macular hard exudates	6/7 (85.7%)
Submacular hemorrhage	1/7 (14.3%)
Macular epiretinal membrane	1/7 (14.3%)
Vitreous hemorrhage	1/7 (14.3%)
Exudative retinal detachment >2 DD around tumor	5/7 (71.4%)
Secondary glaucoma	0/7 (0%)
Idiopathic VPT	4/7 (57.1%)
Secondary VPT	
to uveitis	2/7 (28.6%)
to Coat's disease	1/7 (14.3%)

Table 2. Patients' characteristics

No.	Sex	Age	Preoperative							Postoperative			
			Initial BCVA	Largest base (mm)	Thickness (mm)	SRF	Primary or secondary	Radiation Time (hour)	Radiation dose to Apex (Gray)	FU Period (months)	BCVA In last FU	Largest base (mm)	Thickness (mm)
1	M	24	20/160	5.8	5.7	Yes	sec. to uveitis	132	38	31	1.5 m CF	4	2.5
2	F	68	20/30	5.2	2	No	primary	23	38	20	20/30	5	1
3	M	22	20/50	12	3.5	Yes	sec. to coat's	19	38	22	HM	8	2.6
4	M	24	2 m CF	7.4	5.3	No	primary	75	43	18	20/30	4	2.7
5	M	19	2 m CF	8.4	4.5	Yes	primary	129	76	20	20/200	7	3
6	F	14	20/200	11.5	4.2	Yes	primary	42	81	12	20/60	9	2.9
7	F	20	20/200	5	4.5	Yes	sec. to uveitis	102	80	6	20/60	4.6	3.8

BCVA: Best corrected visual acuity, sec.: Secondary, FU: Follow-up

Discussion

Although management of vasoproliferative tumors of the retina is still controversial, the results of our study showed that Ru-106 plaque radiotherapy, particularly with high dose radiation, is an effective method in treating VPTs with extensive exudative retinal detachment.

The natural course of retinal VPT is variable and it may be stable for long times or even regress spontaneously. However, most authors agree that treatment is indicated for those lesions with progressive enlargement and increasing exudation and vitreous hemorrhage.¹⁰ In cases of cryotherapy or photocoagulation failure and those with lesions thickness of two mm or more, plaque radiotherapy may be considered.^{7,9,13} This treatment modality has been applied with Ru-106 and Iodine-125 (I-125) plaques. Following cryotherapy and photocoagulation, immediate direct tumor vascular damage occurs which may subsequently lead to exudation and hemorrhage.⁷ Meanwhile, most of the radiation-related side effects are delayed complications that may develop a few months or years after plaque radiotherapy.¹⁶ The main advantage of using Ru-106 rather than I-125 is delivering high-dose radiation with lower complications such as radiation papillopathy and maculopathy.¹⁶

The exact dose required for the apex of tumor in brachytherapy for VPTs has not been determined yet.⁷ In our study, a significant visual loss (two lines or more) was seen in 28% (two of seven) of cases which is comparable with 14% in Bornfeld and colleagues report¹³ and 27% in Shields' study.¹⁵ Exudative retinal detachment which was presented in 71.4% of our cases resolved completely after treatment. Similar results have been reported in other studies.^{7,13} Machemer and coworkers¹⁷ have discussed the pathogenesis of tractional retinal detachment in different retinal capillary hemangiomas (RCHs) and Coat's disease. He suggested that membrane growth is due to proteinaceous exudates released by the vascular abnormality. As Bornfeld and colleagues¹³ have reported, the main reason for significant visual loss following plaque radiotherapy is development of epiretinal gliosis. This process has resulted in tractional retinal detachment and severe visual loss in one of our patients in the low-dose group. However, it is impossible to determine whether this complication was secondary to VPT itself or was a side effect of plaque radiotherapy.

The small number of patients in our series was the major limitation for interpreting the

results. Although mean follow-up period was 18 months, but it is possible that some patients will develop more radiation complications with more follow-ups and this may affect the long-term results in the treated patients.

Conclusion

Although the treatment outcomes of

brachytherapy were promising for vasoproliferative tumors, it was not possible to establish a dose-effect relation due to small patients sample size. Successful results of plaque radiotherapy merits further investigations with enough sample size to identify the optimal dose of radiation to achieve the tumor regression associated with lower side effects.

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