Radiation Therapy of the Primary Ocular Melanoma

— A Case Report and Review of Literature —

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Intraocular melanoma is the most common primary occular malignancy in adult above the age of 20.

Before treatment of intraocular melanoma, it is essential to do complete work-ups including LFT (LDH, SGPT), chest X-ray, whole body bone scan. Also, liver-spleen and brain scan will be done if clinically indicated.

Though, malignant melanoma is radioresistant, however, show rapid tumor shrinkage after irradiation with total tumor dose of 7,000 to 8,000 rads in 7-8 weeks.

Key Words: Intraocular melanoma, Radiotherapy

INTRODUCTION

Intracular melanoma constitute the most common primary ocular malignancy in whites over the age of 20, and the reported diagnosis for 80%[1,2] of all primary ocular cancers.

In the United States, the annual incidence rate is 6 cases per one million population, that is, approximately 1,500 new cases each year. Whereas many eye diseases have the potential for loss of vision, ocular melanoma also may result in death of the patients, so, they hold a special significance to the ophthalmologist and oncologist.

Melanoma occur in the uveal tract in the majority of cases, however, can occur on the skin of the lid, on the conjuctiva, and even within the orbit. Reesel reported that seventy-eight percent of uveal melanoma develop at choroid, twelve percent at iris and ten percent of uveal melanoma occur at ciliary body. The pigmented epithelium of above anatomical structures, commonly undergoes non-neoplastic proliferation or reactive hyperplasia in response to various stimuli and, in rare instances, undergoes neoplastic differentiation. The uveal melanocytes[3] originate from the neural crest and are considered the cell of origin for most intraocular pigmented neoplasm.

The major histopathologic types of uveal malignant melanoma have long been recognized. Callender, in 1931, provided the initial data relating the histologic appearance to prognosis. The Callender classification, in somewhat modified form, remains in general use today.

Applying the "simplified classification" they divided into Spindle cell type (A,B) and Non-spindle cell variety (Epithelioid, Mixed, Necrotic), and 45% of them is mixed type melanoma.

Several studies generally confirmed that the best correlation exists between cell type and prognosis. Prognosis would be worse as the epithelioid component increase.[4]

The median age at diagnosis is approximately 55 years and the peak incidence is between 60 and 69 years. The most common presenting symptoms are palpable mass, loss of vision, floating spot sensation according to the anatomical sites. Secondarily they result in cataract, glaucoma, iridocyclitis, and retinal detachment.

With the aid of indirect ophthalmoscopy, orbital CAT scan, fluorescein angiography, 32 P-uptake

test, and A and B mode sonography, 98% of ocular melanoma could be diagnosed. Biopsy of melanomas of the choroid is not acceptable because of a high incidence of consequent orbital spread.

Choice of treatment depends on the location of tumor, size, and preservation of vision on the affected eye. They include surgical management (Enucleation, Exenteration), radiotherapy (Proton beam, Helium ion, Co 60-plaque), cryotherapy and photocoagulation.

CASE REPORT

In September 1985 a 64 year old woman visited to Korea University Hospital for one month history of pain and rapid growing mass on the right orbit. She has been suffered from glaucoma symptoms for eight years. In June 1985 she underwent evisceration of right eye at private clinic. Two months later she underwent reoperation at same clinic due to no apparent symptomatic relief. At that time, they found to have a pedunculated mass which was located in the inferolateral wall of the right orbit and clinically appears to be a malignant, therefore, they referred her to Korea University Hospital with biopsy specimen for further evaluation and treatment. (Fig. 1).

On physical examination at referral, she presents with protruding, very painful hard palpable mass on the right orbit with complete loss of vision. There were no palpable lymphadenopathy and hepatosplenomegaly. Bipsy specimen was reviewed and confirmed malignant melanoma of the choroid. Metastatic work up, including chest x-ray, liver enzyme studies and whole body bone scan were all within normal limits.

Orbital CAT scan was obtained (Fig. 2) and showed right side intraorbital mass which was measured approximately 6cm × 6cm and entire right orbit was filled by tumor and tumor mass was protruding outside of the orbit. Although, the medial wall of the right orbital bone was eroded secondary to tumor pressure.

She was treated by external beam irradiation which consists of an anterior portal with one right oblique portal using the wedge filter for better dose distribution. At the dose of 5,040 cG/5.5 weeks repeat orbital CAT scan (Fig. 3) was obtained and showed that the orbital mass was markedly reduced, so that the treatment field size was reduced and given to a total dose of 7740 cG/8.5 weeks.

At the dose of 3,000 cG/3.5 weeks, exophthalmos, ocular pain and lid edema was disappeared completely. At the completion of treatment, examination revealed the tearing on the right eye as well as mild erythematous changes on the treatment area but no mass was palpable.

However, one month after completion of irradia-

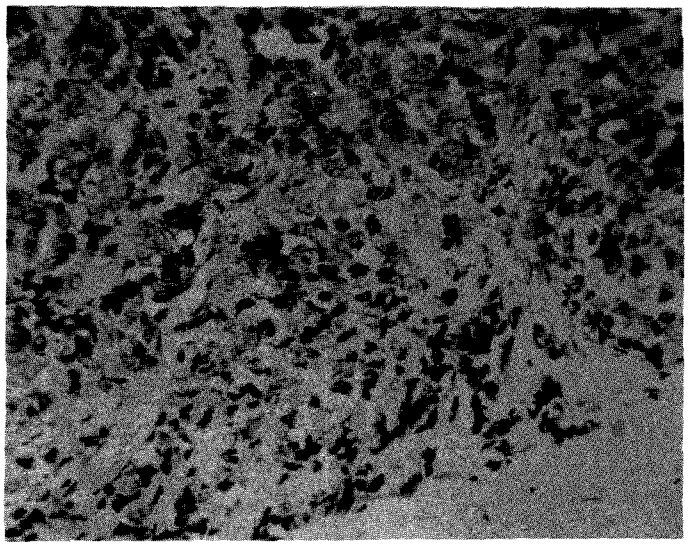

Fig. 1.

tion, she developed anorexia, general weakness and epigastric pain. Physical examination reveals enlarged tender liver and hard mass on the epigastric region. Abdominal and pelvic sonogram was performed and showed multiple liver metastases with a small amount of ascitic fluid in the cul-de-sac area. Concomittantly, ocular sonogram was performed (Fig. 4) and reveals almost complete regression of tumor mass compared to previous CAT scan.

DISCUSSION

The relative efficacy of various modalities used in the treatment of choroidal melanoma is unclear; until prospective, randomized treatment trials are performed, therapeutic decision will be based more on a philosophic opinion than on a secure data base.

However, treatment methods currently in use are surgical management, radiotherapy, photocoagulation and cryotherapy. A[6] number of investigators have questioned the efficacy of enucleation and have suggested other therapies in the treatment of choroidal melanoma. An optimal alternative therapy destroys tumor cells without decreasing vision.

As long ago as 1882, Fuchs[7] wrote that all eyes containing a uveal melanoma were treated by enucleation. Already in 1900, Powel[7] emphasized that every uveal melanoma not treated by enucleation definitely would prove fatal. This conviction was repeated by Stallard[7] in 1964. For a century, enucleation has remained the accepted practice, the only exceptions occuring in cases where the patients have refused enucleation or cases where a melanoma has been diagnosed in the only functioning eye. So, they reported 10-year follow-up data on large series of patients whose enucleated eyes harbored a melanoma varying between 40% and 60%.[8] Also, Raivio[9] found a 20-year corrected survival rate of 43% in 214 patients.

Occasionally, the effectiveness of enucleation was doubted. Von Hippel and Zimmerman[10] concluded that there was not enough evidence that early enucleation would save noticeably more lives than later enucleation. They stressed that extended follow-up periods were necessary to evaluate the

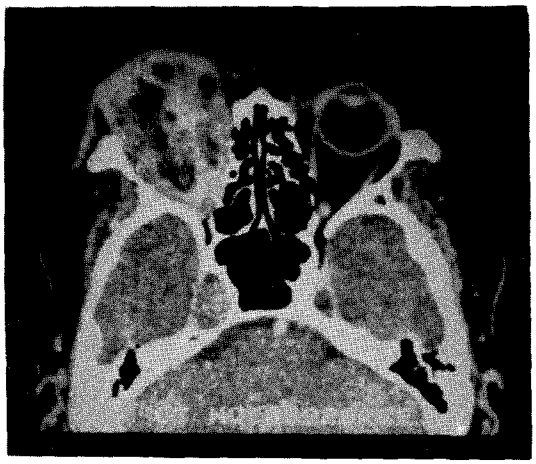

Fig. 2.

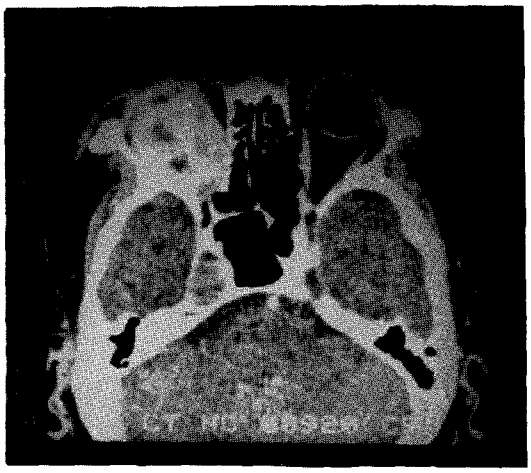

Fig. 3.

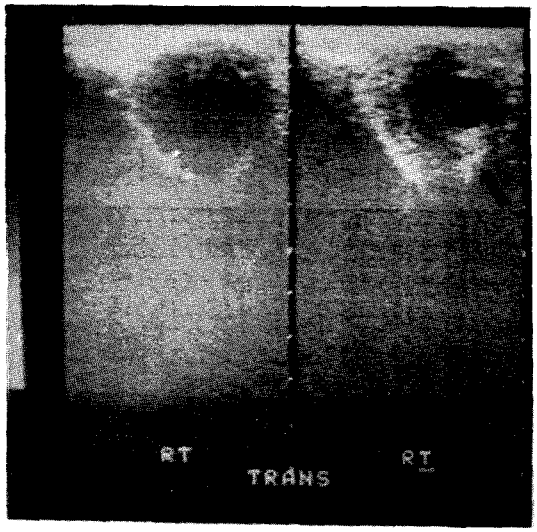

Fig. 4.

results of the operation. And they also said that the mortality rate before enucleation is low, estimated at 1% per year, however, the mortality rate rises abruptly following enucleation, reaching a peak of about 8% during the second year after operation; and that approximately two thirds of the fatalities could be attributed to the dissemination of tumor emboli at the time of enucleation. So recently, many surgeons reported "no-touch"[11] technique to prevent tumor spread from occuring secondary to ocular manipulation during operation. This technique avoids intraocular pressure above 15 mmHg before freezing completely occurs around the tumor, thereby prevents flow of fluid and blood to or from the tumor prior to the manipulation necessary for enucleation.

The treatment of small sized choroidal melanoma is still controvertial. Some favor early enucleation, whereas others favor observation carefully because very small tumor have rarely been associated with a fatal outcome. Minimum[7] follow-up of 5 years with small choroidal melanoma patients(32), only ten of thirty-two were enucleated eventually and one of ten patients who were enucleated was died due to tumor.

Photocoagulation (Fig. 5) and radioactive plaques (Fig. 6) are two traditional options used in the management of choroidal melanomas. There are number of disadvantages to each of these

Table 1. Anatomic Sites of Malignant Melanoma Lesions

Sites of Metastasis	All (N=86)		Ocular (n=9)		Monocular (n=73)		Unknown Sites (n=4)	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Liver	58	67	9	100	48	66	1	25
Lung	68	79	5	55	59	81	4	100
Bone	45	52	5	55	40	55	0	0
Kidney	48	56	4	44	42	57	2	50
Brain	51	59	2	22	48	66	1	25

[From Zakka et al., 1980]

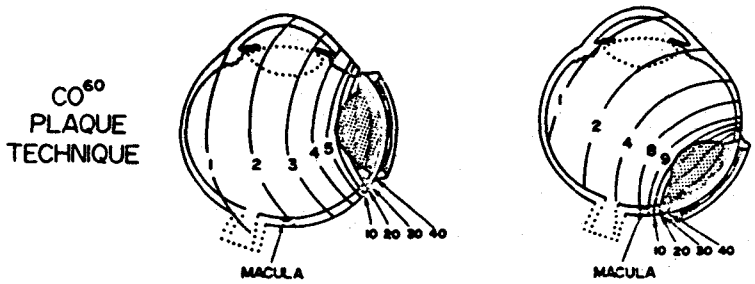

Fig. 5.

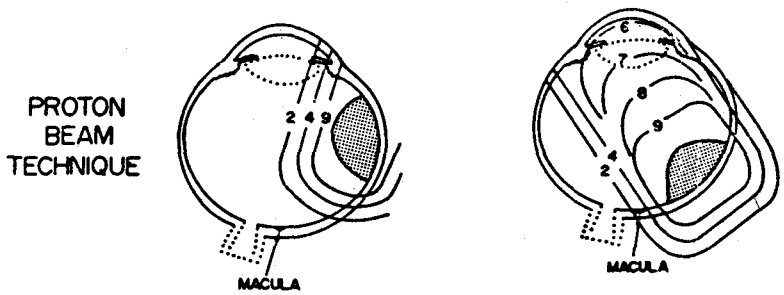

Fig. 6.

modalities. Photocoagulation has limited applicability; ocular morbidity is a substantial problems with most types of radioactive plaques. Almost 40% of choroidal melanomas treated with either approach require enucleation because of treatment complications or continued tumor growth.[12]

Charged-particle irradiation may be a more effective form of therapy in the management of choroidal melanomas. There are both physical dose distribution and biologic advantages[6,13,14,15] associated with helium ions and heavier charged particles. All charged particles have a characteristic Bragg peak that deposits the maximum dose at the end of the particle range. This and a sharp lateral dose fall-off allow the radiation to be localized to the tumor-containing portion of the eye, the result of which is a lower potential for radiation retinopathy in areas distant from the tumor. A second advantage of charged particle is the uniform dosage, which is not possible with radioactive plaques.

Regression of uveal melanomas after proton beam irradiation is a delayed process, and occasionally more than a year is required before the onset of tumor shrinkage is observed clinically. This is in contrast to retinoblastoma that regresses to an inert scar usually within weeks. So, additional radiation after proton beam irradiation should be considered only for tumors that increase in size after treatment.

By Devron et al,[6] forty patients with choroidal melanomas received radiotherapy with Helium ion charged-particle and thirty-six of them either remained stable or demonstrated tumor shrinkage. Seventeen of eighteen patients followed for at the last one year after therapy demonstrated tumor regression, with a mean tumor shrinkage of approximately 40%.

However, there are a numbler of unresolved issues[15] regarding the use of charged-particle irradiation in the management of choroidal melanoma. Prospective, controlled clinical trials will be necessary to determine the relative efficacy of this form of therapy vs enucleation or other forms of therapy.

But in spite of various treatment modalities, malignant ocular melanoma show frequent metastases. By Wagoner's[17] large survey to evaluate the preoperative presence of metastases, twenty-nine (2.47%) of 1,214 patients were found to have metastases prior to surgical manipulation of the globe. The most common site of distant metastases was liver by Wagoner and Zakka[18] (Table 1). And his data also lend support to previous observation that preoperative metastases can be expected to be greater in older patients(mean age: 63.4) and in those with large tumors. So there must be complete evaluation for metastases and these includes liver function enzyme test (GPT, LDH) and chest X-rays. But the addition of a bone, brain or CT scan in the absence of a clear clinical indication does not seem to increase the detection rate of metastases in malignant ocular melanoma patients.

Finally, patients with a small choroidal melanoma which growth is documented, patients with a large or medium melanomas with good vision, patients with tumors in their only functioning eye, and those patients who refuse enucleation are suitable for radiotherapy.

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=국문초록=

원발성 안구 흑색종의 방사선 치료 및 증례보고

고려대학교 의과대학 치료방사선과 학교실

반 성 범·최 명 선

원발성 안구 흑색종은 20세이상의 성인에서 가장 많이 발생되는 안구의 악성종양이지만 한국에서의 발생빈도는 그리 흔하지 않은 것으로 되어 있다.

안구 흑색종의 치료전에는 문진, 이학적검사, 기본적인 혈액상검사와, 특히 간, 폐, 골에 세심한 주의를 하여야 하며, 그래서 흉부 X-선과 LDH, SGPT, Transpeptidase를 포함한 간기능 검사등을 시행하여야 하고 만약 임상적으로 증상이 있거나 위의 검사상 비정상적인 소견을 보일 때에는 전신뼈 스캔, 간—지라 스캔을 시행하여야 한다.

일반적으로 악성 흑색종은 방사선 치료에 대해 치료효과가 나쁜 것으로 알려져 있지만 때로는 총 종양조사선량 7,000~8,000 cG/8~9주로 매우 빠른 종괴의 감소를 보여 주기도 한다.

그리하여 저자등은 외부방사선조사로 빠른 치료방응을 보인 원발성 안구 흑색종의 치료와 문헌고찰을 보고하는 바이다.