The options for treatment of retinoblastoma have gradually changed in recent years from enucleation or external beam radiotherapy to focal conservative methods.\(^1\, 2\) Thermotherapy is one of the newest methods in this regard. When coupled with chemotherapy, it provides satisfactory control in selected cases. The present case was a child with his left eye enucleated previously for retinoblastoma. The multifocal tumors of his right eye were successfully treated by transpupillary thermotherapy (TTT) coupled with chemotherapy.

### Case Report

A two-month-old male visited our hospital on July 1999 with the chief complaint of leukocoria in the left eye. Ocular examination revealed a solid white tumor occupying most of the fundus in the left eye. Retinoblastoma was highly suspected. However, the patient lost follow-up thereafter. When he came to our hospital again five months later, enucleation of the left eye and photocoagulation of the right eye had been performed at another hospital. Pathologic examination confirmed the diagnosis of retinoblastoma without evidence of invasion of the optic nerve and sclera. The tumor progressively increased in size despite photocoagulation treatment.

On ocular examination, the patient can maintain fixation and follow vision in his right eye. There were four separate retinal lesions. The largest one, 6 mm in size and thickness, located at the posterior pole temporal to the macula (Fig. 1A). The second lesion, located superiorty at equator, measured approximately 4.5 mm in size and thickness (Fig. 1B). Another two smaller lesions located near the ora serrata at 2 and 10 o'clock, were visible. The retina was at the tached and vitreous was clear. There were no other ocular abnormalities.

Retinoblastoma has evolved to a new era with a trend toward conservative focal treatment, avoiding enucleation and external beam radiotherapy. An important focal treatment method is thermotherapy. We present a 7-month-old boy of bilateral retinoblastoma with evidence of systemic metastasis. Enucleation of left eye and laser photocoagulation of right eye were done in another hospital. How ever, the tumor of the right eye was progressively enlarged. Transpupillary diode laser thermotherapy was applied twice in two weeks, each was coupled with chemotherapy delivered within 6 hours after thermotherapy. Besides, transscleral cryotherapy was applied to other lesions near the ora serrata and several more courses of chemotherapy were given. Fifteen months after the first treatment, the tumor progressively regressed completely. No major complications and detectable recurrence were found. The advances of thermotherapy and chemotherapy made it possible to preserve both the eye and the vision in children with retinoblastoma.\(^{[Chin Med J (Taipei) 2002;65:41-44]}\)

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**Key Words**
- chemotherapy
- lasers
- retinoblastoma

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**Case Report**

Multifocal Retinoblastomas Treated with Transpupillary Thermotherapy

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nor mal i ties. Or bi tal com put er ized to mog ra phy ex a mi na tion re vealed slightly thick ened en hance ment at the lat er al por tion of the right eye. A com plete blood count, blood chem istries, chest X-ray and ab dom i nal sonography were un re mark able.

The tu mors at the pos te rior pole and equa tor were treated with TTT us ing a spe cially mod i fied in fra red di ode la ser at 810 nm, pro vided by Iris Med i cal In stru -ments. The de li very sys tem was an in di rect oph thal mo -scope with 20-diopter lens. The la ser was ap plied di -rectly to the en tire tu mor sur face un til a light gray color change within the tu mors was seen. To achieve con tin -uous de li very, the la ser cy cle was set at a 9000-msec du ra tion with a 100-msec in ter val. The mean ther -mo -therapy power was 600 mw (range 500-800 mw). To tal cu mu lated ther -mo -therapy time was 10 min utes and 5 min utes for each in di vid ual tu mor lo cated at pos te rior pole and equa tor, re spec tively. There was no ret i nal vas cu lar spasm during treat ment, but hem or rhagic foci on the tu mor sur face were ob served.

Transscleral cryotherapy was se lected for two small per i pheral tu mors. Under in di rect oph thal -moscopic vi su aliza tion with scleral de pres sion, each le -sion was frozen us ing a cryo pro ble at a tem per a ture of ap prox i mately mi nus 65 °C. A tri ple freeze-thaw tech -nie was em ployed.

Sys temic che mo ther apy with vincristine, etopos ide and car bo -platin (VEC) was given with -in 6 hours af ter ther -mo -therapy (Ta ble 1). The pa tient was re as sess -ed un der gen eral an es the sia 2 weeks later. There was no ta -ble shrink age of the two tu mors treated with TTT.

Ther mal onco logists have been seek ing for more ef fec -tive al ter na tives.1-8 One of the most ex cit ing new ap -proaches is ther -mo -therapy. The stan dard man age ment of ret i no blas toma was ei ther pri mary enuclea tion or whole eye ir ra di a tion.1,2 Be cause of the mor bid ity and po ten tial mor tal ity as so -ci ated with these treat ment mo dal i ties, pe di at ric and oc u lar onco logists have been seek ing for more ef fec -tive al ter na tives.1-8 The VEC reg i men was re pe ated ev ery 3 to 4 weeks for 6 times.

The pa tient was fol lowed at reg u lar in ter vals. At the last ex a mi na tion, 15 months af ter the ini tial treat -ment, the tu mors in right eye have com pletely re -gressed (Fig. 2), leav ing lo cal ized atro phic scar with macu lar pres er va tion (Fig. 3).

**Discussion**

The stan dard man age ment of ret i no blastoma was ei ther pri mary enuclea tion or whole eye ir ra di a tion.1,2 Be cause of the mor bid ity and po ten tial mor tal ity as so -ci ated with these treat ment mo dal i ties, pe di at ric and oc u lar onco logists have been seek ing for more ef fec -tive al ter na tives.1-8 One of the most ex cit ing new ap -proaches is ther -mo -therapy.

Ther -mo -therapy is a method which de li vers heat to tis sue us ing ul tra sound, mi cro waves or in fra red ra di a -tion to raise lo cal tem per a ture to cyto toxic lev els caus -ing tu mor cell death.9 It can be used as a pri mar y treat -ment or as an ad ju vant treat ment by sen si tiz ing tu mor cells to ra dio ther apy or che mo ther apy. When em ploy-
ing thermotherapy alone, the ideal tissue temperature is 45 °C to 60 °C, a temperature that is below the coagulative threshold, therefore, spares the retinal vessels. When coupling with other treatment modalities, the tissue temperature may be slightly lower, ranging from 42 °C to 44 °C, so as to decrease the risk of local heat-related complications.¹

Recently, a number of researchers have become interested in the application of thermotherapy for retinoblastoma coupling with intravenous chemotherapy, termed thermochemotherapy.¹²⁴⁵ It has been reported that heat increases the binding of platinum to tumor DNA in the transgenic murine retinoblastoma cell line.¹⁰ Thermochemotherapy was thus applied based on the synergistic effect of platinum-containing chemotherapeutic agents and hyperthermia. In a retrospective, uncontrolled study by Murphree et al, thermochemotherapy was 100% effective for patients with Reese-Ellsworth group I and II caner. Only 2 of 4 patients with Reese-Ellsworth group III responded and all group Vb patients failed in response.¹¹ These results suggest the need to develop other methods for advanced stage of the disease.⁷

Chemoreduction is a technique which uses chemotherapy over a short course to reduce tumor size so that subsequent conservative adjuvant treatment can be applied for ultimate tumor control.¹³ It has evolved into an important component of the initial management of intraocular retinoblastoma. The agents for chemoreduction varied among pediatric oncologists. However, vincristine, etoposide and carboplatin have been most commonly used in recent studies.¹³⁷¹² Fo cal adjuvant treatments were usually delivered after the second or third cycle of chemotherapy. Shields and associates found that the ocular salvage rate in Reese-Ellsworth group V patients was 78% by using chemoreduction (VEC for 6 cycles) and adjuvant treatment.¹²

The decision to choose either thermotherapy, thermochemotherapy or preceding chemoreduction depends on many factors including age, tumor size, location, and the presence of subretinal or vitreous seeds.¹³ In general, tumors less than 3 to 4 mm in size and located posterior to the equator are treated with thermotherapy alone. However, larger tumors with or without metastatic seeds of ten necessitate chemotherapy, before or coupled with thermotherapy.¹

The visual outcome after thermotherapy depends on the tumor size and location. Gregg has reported cases of macular retinoblastoma with satisfactory visual acuity preservation following chemotherapy and laser hyperthermia.¹³ The main complications of thermotherapy are focal iris atrophy and focal lens opacity resulting from heat damage to pigmented iris
tissue and lens. In rare instances, retinal traction, retinal vascul ar obstruction, transient s e reous retinal detachment and corneal scarring were noted.1

Other local treatment modalities, such as cryotherapy and laser photoagulation, are also accepted treatment means for small retinoblastomas. Cryotherapy is use ful for man ag ing pe riph eral tu mors, while photoagulation is suit able for le sions at the pos te rior pole. La ser photoagulation is a method that coagulates all blood sup ply to the tu mor and in duces is ch e mi nec ne cross. The tu mor size and lo ca tion is im por tant for the ef- fect of photoagulation. Thus small tumors, usually 4.5 mm or less in base and 2.5 mm or less in thickness, are re ported to have better re sponse to the treat ment.2,14 If a tumor is located near the optic disc or macula, photoagulation must be ex tremely cau tious and pre- cise be cause the re sul tant scar may dis tort the ret ina in the macular area.15

The left eye of this case had been enucleated for a large retinal no blas toma. Our treat ment was tar geted, most im por tantly, to save the child’s life, and sec ondly to pre- serve his sec ond eye and vi sion if pos si ble. The ma jor mass in his right eye was near the macula with a rel a- tively large tu mor vol ume. The white color of the tu mor sur face sug gested the lower ab il ity of tu mor to ab sorb the en ergy of photo coagulation. Be sides, thermo therapy fo cuses on di rect ap pli ca tion and deep pen e- tration of la- ser into tu mors rather than in di rect co ag u lates of the feeder ves sels as photoagulation.9,14 It ap peared that tu mor con trol can be achieved with less dam age to the retina and re tinal pig ment epithelium with ther- mo- therapy.14 For these rea sons we used phototherapy for the tu mors at the pos te rior pole in stead of ar gon la ser photo coagulation. The re sponse to therapy was sat isfac tory with out ma jor com plications.

In conclu sion, the ma- nage ment of retinal no blas toma has evolved to a new era, with a trend to ward con ser va- tive fo cal treat ment to pre serve the eye and im prove the vi sual prog no sis. TTT is the new est fo cal method to con- trol se lected small re tinoblas tomas lo cated pos te rior to the equa tor. When com bined with che mo ther apy, it pro- vides a sat is fac to ry tu mor con trol leav ing the child with a rea son ably small scar and a better vi sion. Al though we have only one case of retinal no blas toma treated with TTT com bined with che mo ther apy, the re sult is very en cour- aging. Fur ther study and longer follow-up will be needed to eval u ate its use ful ness.

References

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