Most of Intraocular Advanced Retinoblastoma are possible to be cured by the Eye-Preservation Therapy using Selective Ophthalmic Arterial Injections of Melphalan

Akihiro Kaneko,MD Makoto Mohri,MD Department of Ophthalmology Teikyo University Hospital,Tokyo,Japan

Financial Interest

N/A

Purpose

To show 2 cases of successful eye-preservation of intraocular advanced unilateral retinoblastoma using local chemotherapies of melphalan.

Background

Our reports concerning selective ophthalmic arterial injections (SOAI) of melphalan (M) for eye-preservation therapy of retinoblastoma (RB) started in 1989 [1]. However they were not accepted over the world until the confirming papers by Dr.David Abramson in 2008 [2].
We have developed not only SOAI but also vitreous injections (VI) of M [3].
Recently the efficacy and safety of VI has been confirmed by Dr. Francis Munier in Lausanne [4]. As the fathers of local chemotherapies of RB, we have been challenging for eye-preservation of advanced intraocular cases which are grouped as E by the International Classification of Retinoblastoma (ICR) [5] to mean enucleation of the eye.

Patients

Two RB patients of ICR group E without previous treatments were selected for this study.They visited our hospital from 2010 to 2011.
SOAI and VI have been approved at the medicale ethics committee at our university hospital and the parents accepted our eye-preservation therapy for their babies using local chemotherapies by informed consents.

Methods

Principally SOAI was performed as the initial treatment. But when it was not available within one month after the first visit,2 courses of the systemic chemotherapy of VEC according to Shields' report was conducted to prevent progression of the disease in the case 2. When vitreous seeding is remarked, VI was combined with SOAI. Residual tumors after these chemotherapies were treated by diode laser photocoagulation or cryotherapy combined with or independently according to the lesions. Treatments were continued until no active tumor was found for more than one month. Thereafter the patients were followed by close fundus examinations.

Case 1:

Patient:2-month-old, female, one of fraternal twins
C.C: Leucocoria (OD)
History:
No family history of RB
Her parents found leucocoria in her right eye 3 weeks before the first visit at a local hospital.She was diagnosed as retinoblastoma (OD) and enucleation was recommended. But they wished for an eye-preservation therapy and after internet research made contact with the first author.
She visited at our hospital on September 9,2010.

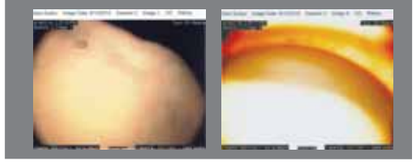
Clinical Findings at the 1st EUA

IOP:OD=13.4mmHg, OS=14.6mmHg
Light Reflex:
OD:slow and weak, OS:prompt
Cornea, Conjunctiva, Anterior chamber, Iris, Lens of OU:no abnormality.
Vitreous:
OD: a yellow and white mass covered with vessels occupies the vitreous space just before the lens except for the nasal periphery.
OS: no abnormality.
Retina:
OD: Except for the nasal periphery, no normal retina is found due to the extensive tumor.
OS:No abnormality.

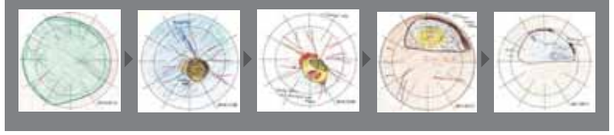
Course of Treatments OD

Sep.14,2010 SOAI (M 3mg, Dexamethasone (D) 1mg)
Oct.12,2010 SOAI (M 3mg, D 1mg)
Nov. 9,2010 SOAI (M 3mg, D 1mg)
Dec. 9,2010 No active tumor
Jan.13,2011 No active tumor
Mar.17,2011 Microphthalmos
Aug.11,2011 MRI revealed phthistic eyeball and no extraocular extension of RB
Dec. 1,2011 Cataract preventing observation of inside of OD
Mar.15,2012 no recurrence

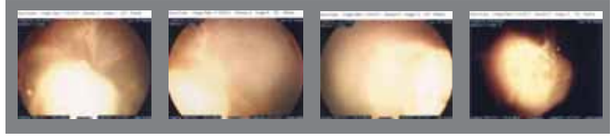
RetCam (2010.09.14)



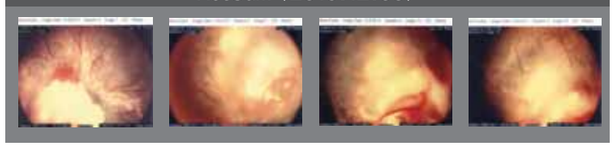
Fundus Chart



RetCam (2010.11.09)



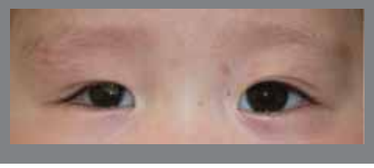
RetCam (2010.12.09)



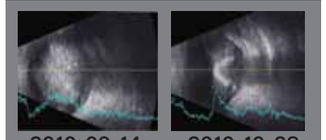
Retcam (2011.03.17)

Retcam (2011.08.11)

(2012.03.15)



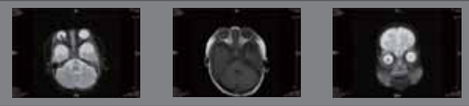
Echogram



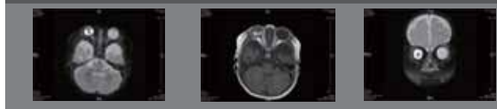
2010.09.14 2010.10.28

SOAI (2011.09.14)

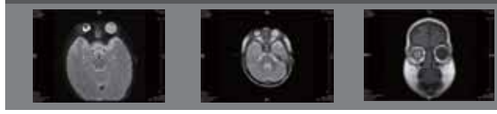
MRI (2010.09.30)



MRI (2011.01.13)



MRI (2011.08.10)



Case 2

Patient:19-month-old, female
C.C: Eye-preservation therapy of unilateral RB
History:
No family history of RB
At the 6-month-old health check, her left leucocoria was recognized.
She was referred to a local university hospital.
Unilateral retinoblastoma with extensiva total retinal detachment was diagnosed and removal of the eye was recommended.
Her parents wished for eye-preservation therapy at our hospital.
We accepted their offer, but SOAI was not available because of a long waiting list. Therefore the first treatment was conducted at the pediatric department of Jikei University Hospital using 2 courses of VEC systemic chemotherapy. Her retinoblastoma responded very well to VEC but residual tumors and flat total retinal detachment were found.

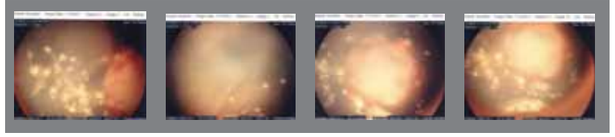
Treatments

Jun.8, 2011~ June 27,2011
Systemic Chemotherapy:2 courses of VEC
Jul.19, 2011
SOAI: M 5mg,D 1mg
Aug.23, 2011
SOAI: M 3mg, D 1mg, Diode Laser Thermotherapy, VII: M 20μg
Sep.20, 2011
SOAI: M 3mg,D 2mg, Dode Laser Thermotherapy, VI: M 20μg
Oct.18
SOAI: M 3mg,D 1mg, Diode Laser Thermotherapy
Nov.18,2011
SOAI: M 3mg, D 1mg
Dec.6
SOAI:SOAI: M 3mg, D 1mg, Dode Laser Thermotherapy
Jan.19,2012
Diode Laser Thermotherapy
Mar.15,2012
No recurrence

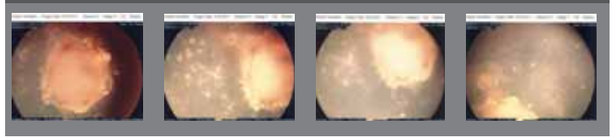
SOAI (2010.07.19)

Fundus Charts

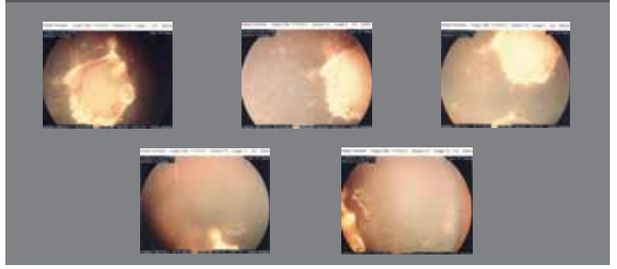
RetCam (2010.07.19)



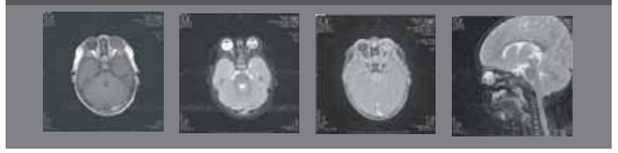
RetCam (2011.09.20)



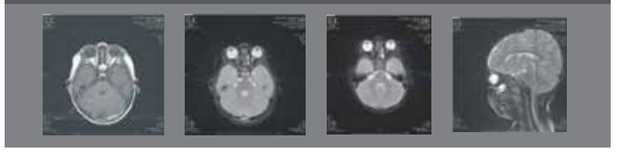
RetCam (2012.02.19)



MRI before treatment



MRI after treatment (Nov. 2011)



Discussion

1) Local chemotherapies using M are very effective and safe in eye-preservation therapy of RB. After extensive treatments of the case 1 ,the eyeball has become very soft and rather arophic.
The causes of this change are estimated to be severe inflammation by a large amount of necrotized tumor cells and vitreous seeds.
And the eyeball of this 2-month-old baby might be very vulnerable compared with these of older children.
2) The value of eyeballs without visual function is controversial.
We think these eyeballs are more valuable than prosthesis, esthetically and psychologically. If a vey thin prosthesis is inserted on the phthisical eyeball, it moves more naturally than those prosthetic eyes with a movable orbital implant . Of course more careful procedures to prevent phthisis must be considered for the treatment of very young babies.

Conclusion

1,Local chemotherapies using melphalan are safe and effective for eye-preservation therapy of RB.
2,Most of ICR E eyes might be able to be preserved by the local chemotherapies without external beam radiotherapy.
3,When patients are very young infants, their ICR E eyes must be carefully treated to prevent phthisis during eye-preservation therapies.

References

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3) Kaneko A. et al : Eye-preservation treatment of retinoblastoma with vitreous seeding.Jpn J Clin Oncol.2003;12:601-607
4) Munier F. : A keynote lecture at the International Congress of Ocular Oncology at Buenos Aires in 2011.
5) Murphree AL.: Intraocular retinoblastoma : the case for a new group classification. Ophthalmol Clin North Am. 2005;18:41-53.

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Correspondence

E-mail : akikaneko@jcom.home.ne.jp
TEL:+81-90-1703-6112