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Case Report

Intra-arterial chemotherapy for retinoblastoma: Our first experience in Indonesia ☆

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ABSTRACT

Intra-arterial chemotherapy (IAC) has become the mainstay therapy for retinoblastoma group D and E for the past few decades. However, IAC had never been done in Indonesia before. In this report, we present a case of a 2-year-old girl with recurrent Group D retinoblastoma of the left eye that improved significantly after one session of IAC, the first IAC in Indonesia.

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Introduction

Retinoblastoma (RB) is the most common primary intraocular malignancy in children, with an incidence rate of 1 in every 15,000–20,000 live births every year. Forty-three percent of the global burden of RB lives in Asia, and Indonesia is the third country with the most children with RB [1]. For the last few decades, intra-arterial chemotherapy (IAC) has been widely used both as a primary and secondary treatment for RB, and is especially effective in globe salvage for RB group D and E [2]. However, IAC is never done

in Indonesia due to its expensiveness and the drug unavailability [3,4]. Here, we presented a successful IAC for retinoblastoma group D chemoreduction in a 6-month-old infant.

Case illustration

A 6-month-old girl presented to the ophthalmology clinic with leukocoria of both eyes since the age of 2 weeks. From funduscopic examination, there was retinal detachment in the right

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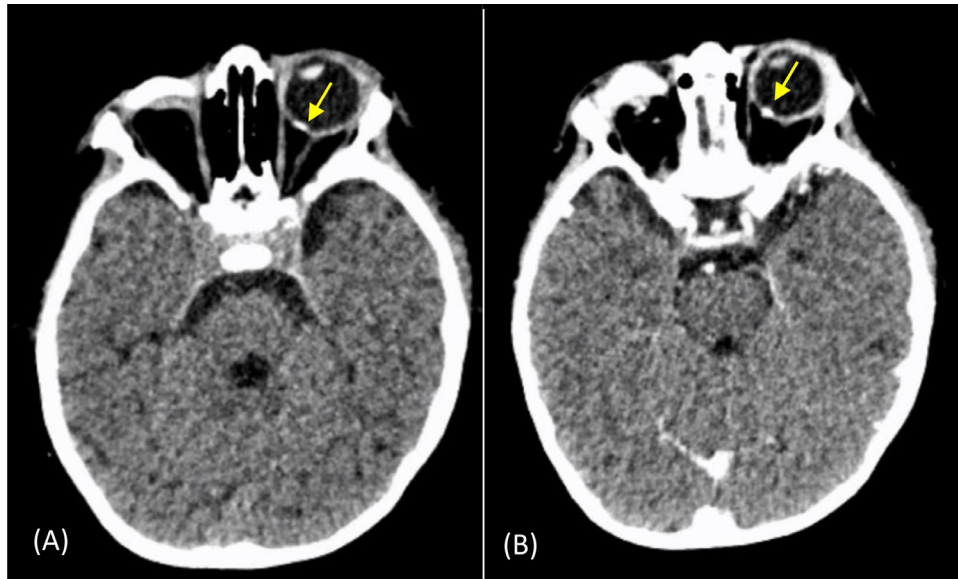


Fig. 1 – Axial CT scan of the orbits. Non-contrast (A) and contrast-enhanced (B) axial CT scan of the orbits show calcification on the posterior wall of the left orbit (arrow).

eye and a 2-cm mass at the orbital apex of the left eye. She was diagnosed with retinoblastoma grade E of the right eye and grade C of the left eye. In the same month, the patient had her right eye enucleated.

The patient underwent intravenous chemotherapy using etoposide, carboplatin, and vincristine. After 9 cycles of chemotherapy, CT scan evaluation showed a lesion with multiple calcifications in the posterior wall of the left orbit (Fig. 1). The patient resumed her treatment with intravenous chemotherapy, TTT, and cryotherapy. After 15 cycles of chemotherapy, eye exam under examination showed a mass in the inferotemporal aspect of the left retina, a calcified lesion in the superotemporal aspect of the retina, and multiple vitreous seedings in the temporal aspect of the retina (Figs. 2A-C). The diagnosis of the patient's left eye became retinoblastoma group D. The patient, now aged 2 years old and weighed 17 kg, was subsequently referred to the interventional radiology division for IAC of the left eye.

Before the procedure, the patient was put under general anesthesia. Topical 0.05% oxymetazoline hydrochloride was sprayed on both nostrils, and topical phenylephrine was given on the ipsilateral periorbital region. Under ultrasonographic guidance, vascular access was made on the right common femoral artery. Cannulation of the ophthalmic artery was done using 1.5 Fr Marathon microcatheter (EV3) and 0.008-inch Mirage microwire (EV3). Diagnostic angiography revealed the left ophthalmic artery and its branches along with an area of hypervascularity. The chemotherapy agent Melphalan (5 mg diluted in normal saline until the volume was 30 ml) was then manually injected into the left ophthalmic artery at the velocity of 1 ml/min for 30 minutes.

After the chemotherapy, diagnostic angiography on the left ophthalmic artery and left internal carotid artery was done to check the patency of the arteries. No stenosis, occlusion, or contrast extravasation were found. All catheters and introducer sheath were then removed from the patient.

No hematoma was found on the vascular access after manual compression.

The patient was evaluated 2 weeks later. From the EUA, there appeared to be a significant decrease in the size of the mass. The amount of vitreous seeding also decreased (Fig. 3).

Discussion

Before the introduction of IAC, almost 80% of advanced RB patients eventually must undergo enucleation to avoid central nervous system involvement and hematogenous spread [5,6]. The effectivity of IAC in globe conservation has been proven in numerous studies. A recent meta-analysis on IAC showed that globe salvage rate were 35% in RB group D and E and 63.3% in RB group A-C [7]. Adverse reactions from systemic therapy can also be avoided, since IAC is administered locally [8]. So far, more than 26 countries have incorporated IAC in the treatment of RB [1,6]. However, IAC had never been done in Indonesia before.

This report illustrates a case of RB group E of the right eye and group C of the left eye. After the enucleation of the right eye, the patient underwent 15 cycles of intravenous chemotherapy along with multiple TTT and cryotherapy sessions of the left eye. However, subsequent EUA evaluation showed that the left eye RB had advanced to group D, indicating tumor recurrence. The indications for IAC are refractory retinoblastoma (group D or E), recurrent tumor (group C or D), bilateral group D or E RB, and primary retinoblastoma (unilateral group C or D) [9]. IAC was therefore indicated in this patient. Contraindications such as vitreous hemorrhage, preseptal or orbital cellulitis, prephthical or phthical eyes, neovascular glaucoma, extraocular RB, trilateral RB, and systemic metastasis [9] were absent.

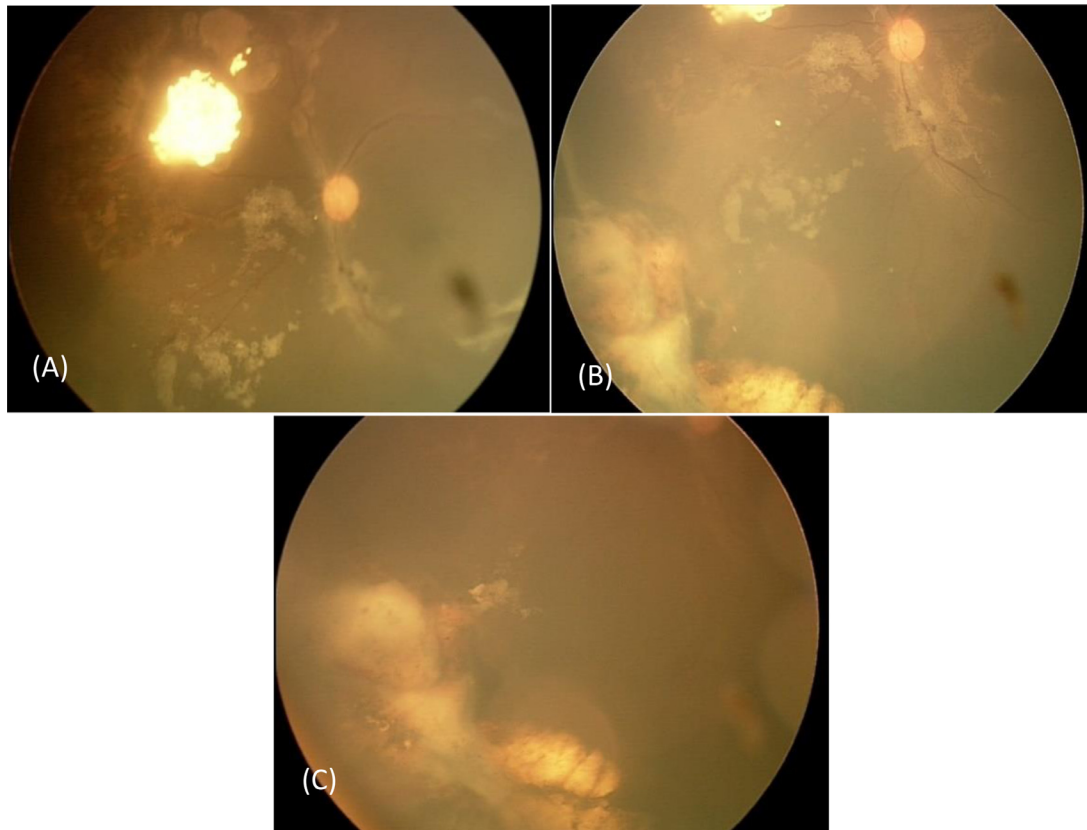


Fig. 2 – Retinal camera (RetCam) images of the patient’s left eye before IAC. RetCam images (A-C) show a mass in the inferotemporal aspect of the left retina, a calcified lesion in the superotemporal aspect of the retina, and multiple vitreous seedings in the temporal aspect of the retina.

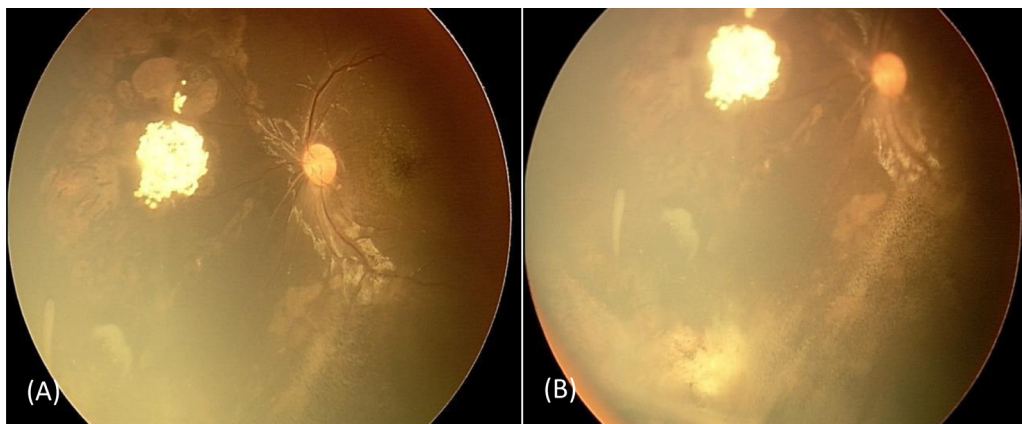


Fig. 3 – RetCam Images of the patient’s left eye 2 weeks after the first IAC session (A and B). These images show decreased mass size and vitreous seeding.

This patient used the chemotherapeutic agent melphalan, which is the most used agent for IAC. Melphalan for injection is available commercially in a powder form and must be diluted before use. Other chemotherapeutic agents include topotecan and carboplatin. Topotecan can be used as an alternative if the RB is unresponsive to melphalan, whereas carboplatin is usually added for triple therapy if single- or double-

agent IAC failed [9]. IAC is usually done 3 times every 4 weeks [2].

Super selective catheterization was done to deliver melphalan to the left ophthalmic artery. Ocular complications that could happen were retinal detachment, retinopathy, palpebral edema, and choroidal occlusion. Systemic complications include neutropenia, cardiorespiratory disturbances,

and nausea or vomiting [6]. This patient showed neither ocular nor systemic complications. RetCam images 2 weeks after the procedure showed that the patient responded well to IAC. Therefore, enucleation can be delayed in the meantime as future IAC sessions are planned.

Although IAC for chemoreduction to delay enucleation was successful, the opportunity for another IAC in Indonesia is slim. Because there are several problems that Indonesia must face. As a developing country Indonesia also has a National Health Insurance System called *Jaminan Kesehatan Nasional* (JKN). Most primary care services are paid through capitation, while only some hospital care can reimburse based on necessity [10]. IAC is a very expensive procedure and not listed in JKN, patients must pay out-of-pocket for the procedure. Because of that IAC cannot be considered as a treatment option in most cases [3,11]. The other problem only the oral form of melphalan is commercially available in Indonesia [4]. In this case, melphalan powder for injection was imported from India. Therefore, we hope this case report could contribute as a cornerstone for developing IAC in Indonesia.

Patient consent

The authors have obtained consent from the patient for their data, including their medical history and imaging studies, to be published in this case report.

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