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INTERVENTIONAL NEURORADIOLOGY

An alternative technique of the superselective catheterization of the ophthalmic artery for intra-arterial chemotherapy of the retinoblastoma: retrograde approach through the posterior communicating artery to the ophthalmic artery

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Abstract
Introduction Superselective intra-arterial chemotherapy (IAC) in retinoblastoma has recently become a popular treatment option. In this study, we purposed to investigate the effectiveness of the technique of "retrograde approach through the posterior communicating artery to the ophthalmic artery (OA)" for IAC.
Methods A total of 12 unilateral retinoblastomas were treated with IAC in 29 sessions from October 2011 to November 2013. Of the 12 patients, 6 were male and 6 were female, with ages ranging from 12 to 72 months with a median age of 27.6 months. Left-to-right ratio for affected eye was 6/6. In the first 4 patients, we used the ipsilateral internal carotid artery (ICA) to reach the OA of the affected globe (10 sessions). Then, we used the vertebral artery, basilary artery, ipsilateral/contralateral P1 segment of the posterior cerebral artery, and ipsilateral/contralateral posterior communicating artery, respectively, to reach inside the OA at next 15 sessions.
Results At ipsilateral approach, fluoroscopy total time ranged from 16 to 34 min (mean 21.5 min), and the angle between ophthalmic segment of the ICA and proximal segment of the OA was ranged between 34° and 77° with an average angle of 53.4°. At retrograde approach, fluoroscopy total time ranged from 3 to 12 min (mean 7.5 min), and the angle between ophthalmic segment of the ICA and proximal segment of the OA was ranged between 147° and 178° with an average angle of 148.3°.
Conclusion Retrograde approach makes the IAC procedure easier in retinoblastoma patients and shortens the fluoroscopy time.

Keywords Catheterization · Fluoroscopy total time · Intra-arterial chemotherapy · Ophthalmic artery · Retinoblastoma

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Introduction

Superselective intra-arterial chemotherapy (IAC) for the treatment of intraocular retinoblastoma has recently become a popular treatment option. The purpose was to deliver increased local concentration of chemotherapeutic drug to eyes without excessive systemic toxicity, which is not possible with systemic administration. IAC for the treatment of intraocular retinoblastoma was first performed with direct internal carotid artery (ICA) injection of the chemotherapeutic drug in 1954 [1]. Then, "selective ophthalmic artery (OA) infusion technique" was developed where a micro-balloon catheter is positioned at the cervical segment of the ICA just distal to the orifice for the OA in 2004 [2]. "Selective OA infusion

technique" was further developed into "direct intra-arterial (OA) infusion" in 2006 [3]. Besides treatment of intraocular tumor, retinoblastoma-induced total or partial retinal detachment shows resolution of detachment after IAC [4]. Melphalan, topotecan, and carboplatin are the three most commonly used chemotherapeutics. Melphalan has been the most extensively used IAC agent of these [5]. Simultaneous or combined use of these three drugs through sequential intravenous and IAC (bridge chemotherapy) is also applied [6, 7].

Methods and results

A total of 12 unilateral retinoblastomas were treated with IAC in 29 sessions from October 2011 to November 2013. Our local institutional review board has approved these treatments, and informed consent was obtained from the parents. Of the 12 patients, 6 were male and 6 were female, with ages ranging from 12 to 72 months with a median age of 27.6 months. Left-to-right ratio for affected eye was 6/6. IAC session was repeated every 4 weeks, if complete regression was not documented with any sign of tumor or seed viability. Number of session per patient was 2.4. One patient was group C and the others were group D or group E based on international classification of retinoblastoma. All the procedures are performed under general anesthesia with all patients requiring intubation. The common femoral artery (right side) is accessed under ultrasonography guidance and the patient is then anticoagulated with a standard dose of heparin (50 IU/kg). In the first 4 patients, we used the ipsilateral ICA to reach to the OA of the affected globe (10 sessions). Two of these were in the right side and the other 2 were in the left side. In these cases, after puncture of the femoral artery, a 4-French arterial long sheath was placed in the ipsilateral common carotid artery (CCA). Anteroposterior and lateral arteriograms were taken to visualize cerebral vasculature and to select the best approach, showing the path of the OA from the ICA. Then, a Prowler 10 microcatheter with straight tip (Codman Neurovascular, Miami Lakes, FL) with an X-Pedion-10 guidewire (Covidien, Neurovascular, Irvine, CA) was guided into the ipsilateral ostium of the OA using fluoroscopic guidance and roadmapping. Then, superselective angiography of the OA was performed to detect whether contrast reflux occurs and to visualize angiographic anatomy. Fluoroscopy total time ranged from 16 to 34 min (mean 21.5 min). The selective catheterization of the OA was sometimes very challenging due to a small caliber OA, OA that was making an acute angle off the ICA, or OA treated with IAC before that had stenosis at the proximal portion. So, we investigated an alternative technique to catheterize the OA. We realized that the retrograde approach by posterior communicating artery (PComA) that located just opposite the wall of the ICA or anterior communicating artery (AComA) seemed easier and reasonable. On this way, there was an obtuse angle between the paraophthalmic segment of the ICA and OA (Fig. 1a, b). At retrograde approach, a 4-French arterial long sheath was placed in the V1 segment of the left vertebral artery (VA). Then, we used the VA, basilary artery (BA), ipsilateral/contralateral P1 segment of the posterior cerebral artery (PCA), and ipsilateral/contralateral PComA, respectively, to reach inside the OA at 15 sessions (Fig. 2). These routes allowed a more direct angle of access to the origin of the OA. Fluoroscopy total time ranged from 3 to 12 min (mean 7.5 min). At ipsilateral approach, the angle between ophthalmic segment of the ICA and proximal segment of the OA was ranged between 34° and 77° with an average angle of 53.4°. At retrograde approach, the angle between ophthalmic segment of the ICA and proximal segment of the OA was ranged between 147° and 178° with an average angle of 148.3°. At 4 sessions, we used the anterior communicating artery to reach the contralateral OA (Fig. 3a, b). After catheterization of the OA, melphalan with or without topotecan and carboplatin were infused according to the dose schemes related with patient age and weight. After infusion of the melphalan was completed, fluoroscopy was

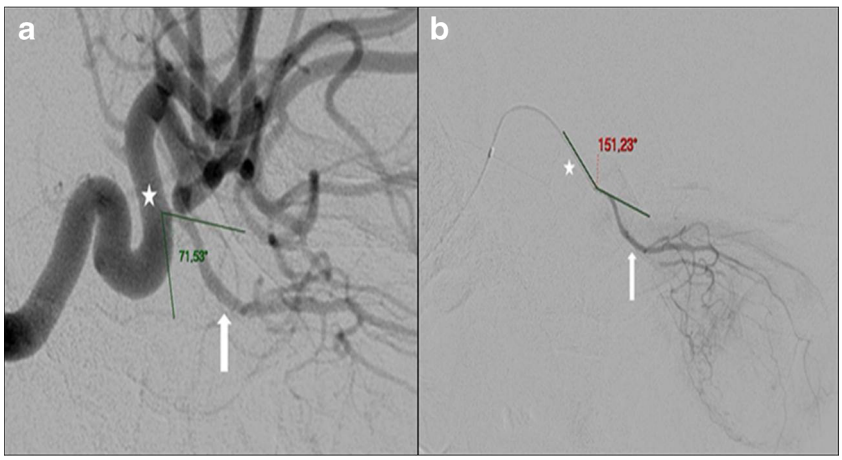

Fig. 1 **a** Lateral digital subtraction angiography (DSA) image shows an acute angle between paraophthalmic segment of the ICA and OA. **b** Otherwise, the angle between paraophthalmic segment of the ICA and OA becomes obtuse when we use a retrograde approach to the OA through the PComA (*arrow* indicate OA, *star* indicate paraophthalmic segment of the ICA)

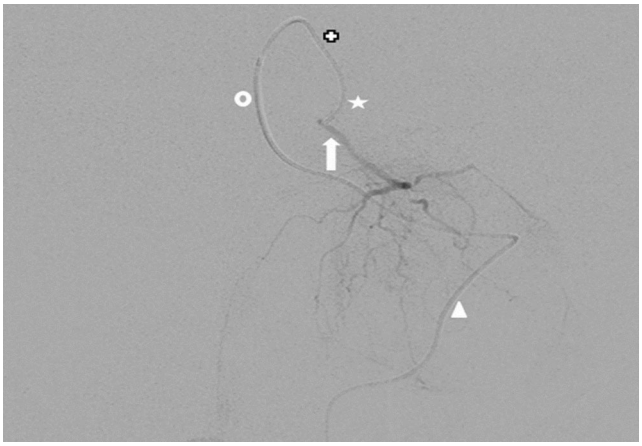

Fig. 2 Posteroanterior DSA image shows the retrograde approach to the OA through the PComA (*arrowhead* indicate V3 segment of the VA, *circle* indicate BA, *plus sign* indicate PComA, *star* indicate paraophthalmic segment of the ICA, *arrow* indicate OA)

performed to demonstrate the patency of the OA and cerebral circulation in all cases. After the femoral sheath was removed, hemostasis of the femoral artery was achieved by manual compression. OA stenosis and occlusion were confirmed on fluoroscopy in 3 and 2 cases, respectively, at repeating sessions. Only 1 in 12 patients required enucleation. In 91 % of patients, eye preservation was achieved.

Procedural complications

There was no significant groin hematoma. No allergic reaction to iodinated contrast, and bronchospasm was observed. There were no neurological complications. In one patient, blue toe syndrome occurred due to distal embolus, which was treated successfully with low-molecular-weight heparin [8]. In two patients that we treated three times before, we could not achieve to catheterize the OA due to occlusion.

Discussion

Retinoblastoma is the most common primary intraocular malignancy in childhood. The good prognosis depends on early detection and advanced treatments. IAC has been a therapeutic challenge to avoid enucleation and to preserve vision in eyes with advanced retinoblastoma alternative or complementary to intravenous chemotherapy, laser ablation, thermoablation, cryoablation, or radiotherapy [9–11]. The goal for delivery of chemotherapy by an intra-arterial route is to provide a higher local concentration and thereby achieve a greater biological effect at the site of interest while minimizing systemic side effects. A small chemotherapy dose, few necessary sessions, and 1-day delivery are most prominent benefits of IAC. The efficacy and safety were documented in preliminary studies [3, 12, 13]. This technique is challenging and requires a physician experienced in interventional neuroradiology. In this paper, we aimed to emphasize the importance of the retrograde approach through the PComA or AComA to the OA. Pham et al. firstly announced PComA technique in two cases [14]. Unlike that study, we represented our experiences of 19 sessions. Moreover, we also used AComA for the same purpose. The AComA and both of the PComAs are patent in newborn and childhood. The mean fluoroscopy time was shorter in the retrograde approach through the PComA to the OA via the VA than that in the ipsilateral approach through the ICA. Because of shorter fluoroscopy time, radiation dose that patient was exposed to would decrease.

Conclusions

The technique of retrograde approach through the posterior communicating artery to the OA for intra-arterial chemotherapy in retinoblastoma patients is safe and effective. The lower

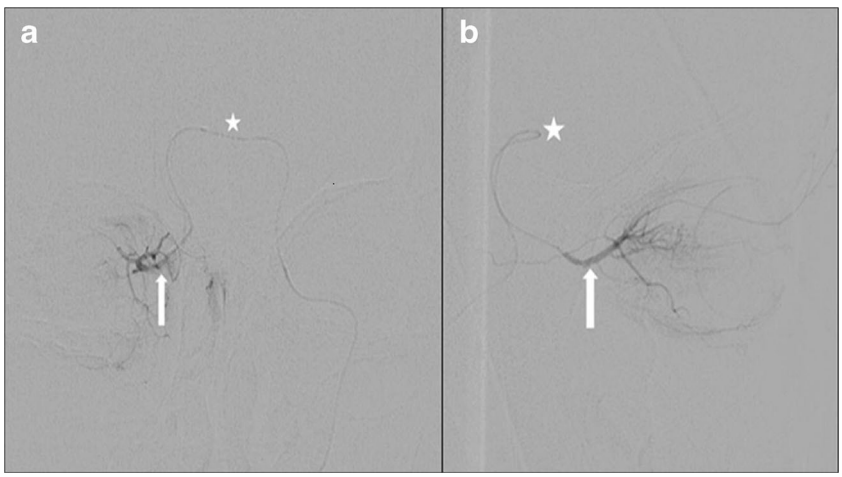

Fig. 3 **a** Posteroanterior, **b** lateral DSA images show the retrograde approach to the OA through the AComA via the contralateral ICA (*star* indicate location of the AComA, *arrow* indicate OA)

fluoroscopy time is the most prominent benefit of the technique.

Ethical standards and patient consent We declare that all human and animal studies have been approved by the Istanbul University Cerrahpasa Ethics Committee, 19451483/1125-A23 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare that all patients gave informed consent prior to inclusion in this study.

Conflict of interest We declare that we have no conflict of interest.

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