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Case Report

Moyamoya Syndrome Precipitated by Cranial Irradiation for Craniopharyngioma in Children

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Recently, combination of surgery and radiation therapy (RT) has been recommended in the treatment of craniopharyngioma. RT could be associated with late complications, including vasculopathy. We report two cases of the moyamoya syndrome seen in children with craniopharyngioma who received RT after surgical resection. Thirty-five patients in pediatric age with craniopharyngioma were surgically treated. Fifteen out of 35 patients underwent surgical resection followed by RT or gamma knife surgery. Two of the 15 were found to have symptoms of transient ischemic attack and were diagnosed as moyamoya syndrome through the cerebral angiography. Age at RT was 4 and 13 years, respectively. The latent period for development of the moyamoya syndrome was 27 months and 3 years, respectively, after RT. The RT dose of both patients was 54 Gy. These two patients received bilateral encephaloduroarteriosynangiosis procedures. We report here these two cases of radiation-induced moyamoya syndrome in pediatric craniopharyngioma. Pediatric patients with craniopharyngioma who received RT should be reminded, during follow-up, about the risk of development of the moyamoya syndrome.

Key Words : Moyamoya syndrome · Craniopharyngioma · Radiation · Vasculopathy.

INTRODUCTION

Radiation-induced vasculopathy is one of the late complications of radiation therapy (RT)[3]. The progressive occlusion of the intracranial arterial circulation, such as that occurs in moyamoya syndrome (MMS), is rarely seen[1]. During the past 10 years, the authors experienced 35 cases of craniopharyngioma in pediatric age.

Although total or partial removal of the tumor was performed in all patients, 15 patients followed RT or gamma knife surgery after the surgical resection. During the follow-up, two patients experienced transient ischemic attacks.

In this report, we describe two cases of MMS arising after RT for craniopharyngioma and similar cases in the literature in order to investigate its pathogenesis are reviewed.

CASE REPORT

Case 1

A previously healthy 13-year-old girl presented with progressive visual disturbance. Physical examination revealed bitemporal hemianopsia and pallor of the optic disc, while hormonal investigation showed pan-hypopituitarism. The computed tomography (CT) scan showed a suprasellar and intrasellar cystic mass with calcification. Angiogram showed mild displacement of the both distal internal carotid arteries (ICAs), proximal middle cerebral arteries (MCAs) and anterior cerebral arteries (ACAs). The mass was surgically removed, and pathological examination showed an adamantinomatous type craniopharyngioma. The patient then underwent whole-brain RT with a total of 54 Gy.

Recurrence of the supra- and intra-sellar mass led to revisional surgery. Two years later, a trans-sphenoidal approach was performed for the recurrent intrasellar mass. After this surgery, she experienced episodic attacks of left sided weakness. Angiography showed progressive occlusion of the both distal ICAs. In addition, transdural meningocortical anastomosis between the middle meningeal and superficial temporal arteries was observed (Fig. 1). Finally, the patient underwent right encephaloduroarteriosynangiosis (EDAS). Her condition is currently stable and she is scheduled to undergo left EDAS in a few months.

Case 2

A 4-year-old girl presented with a month-long history of non-localized headaches. Pre-operative CT and magnetic resonance image (MRI) scans revealed a well-demarcated round mass in the suprasellar area, with peripheral rim enhancement and obstructive hydrocephalus (Fig. 2). Hormonal investigation showed

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pan-hypopituitarism. A ventriculo-peritoneal shunt was inserted, after which she underwent subtotal tumor removal. Pathology confirmed the mass as a craniopharyngioma. The follow-up brain MRI scan showed a slight increase in size and decrease in wall thickness of the round cystic mass in the suprasellar area. The patient received post-operative RT with 54 Gy.

Three years after RT, she experienced intermittent bilateral lower extremity weakness brought on by crying. The MRI scan demonstrated bilateral supraclinoidal ICA occlusion, with severe narrowing of the right ACA and MCA. Cerebral angiography revealed bilateral occlusion of the supraclinoidal ICAs, along with basal and leptomeningeal collateral vessels (Fig. 3). The patient underwent bilateral EDAS, which relieved her symptoms. Unfortunately, 7 months after EDAS, she died due to adrenal insufficiency.

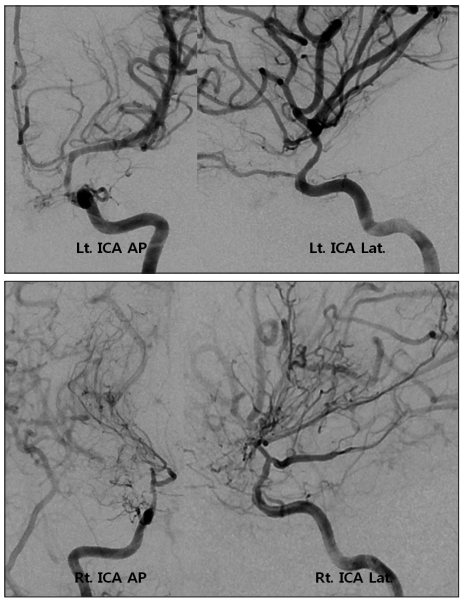

Fig. 1. The ICAs angiogram showing progressive occlusion of the right distal ICA and diffuse narrowing of the left distal ICA, proximal ACA, and MCA compared to the previous angiogram. ICA : internal carotid artery, ACA : anterior cerebral artery, MCA : middle cerebral artery.

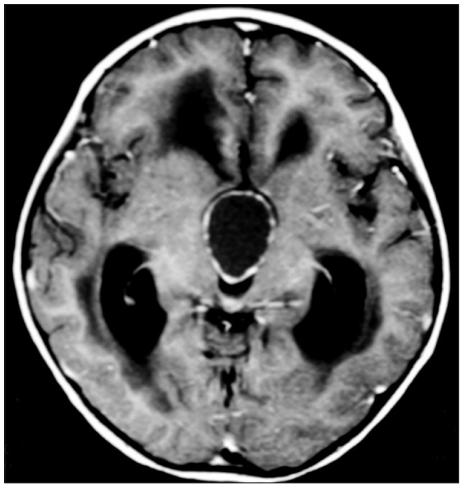

Fig. 2. The T1 weighted enhance MRI scan showing craniopharyngioma with peripheral rim enhancement and central, homogeneous, low-intensity. MRI : magnetic resonance image.

DISCUSSION

The possible side effects of RT include neurocognitive and neuroendocrine disturbances, optic neuropathy, and the risk of a secondary malignant neoplasm[8,9,12]. In both of our presented cases, radiation-induced vasculopathy caused MMS, as seen by cerebral angiogram. Initially, occlusion or tapering off of the distal ICA was not observed on the brain MRA. Furthermore, the patients did not present the symptoms compatible with the moyamoya disease. Therefore, at the time of diagnosis for craniopharyngioma, the probability of moyamoya disease was not considered.

The MMS is a serious complication of cranial irradiation in children, particularly with tumors adjacent to the circle of Willis, such as craniopharyngiomas and optic gliomas[6,8,18,19]. Patients who receive high doses of radiation to the circle of Willis at a young age or who are afflicted with neurofibromatosis type I (NF1) have an increased risk of developing MMS[8,19]. In the vascular complications after radiosurgery, there were several reports showing that ICA stenosis or cerebrovascular accidents with intracranial artery occlusion occurred after gamma knife radiosurgeryfor brain tumor[2,11,14,17].

In Desai et al.[4] study of 316 children treated with radiation for primary brain tumors, 54 (17.1%) developed evidence of MMS, including 4 cases of radiation-induced MMS with craniopharyngioma. Liu et al.[8] and Ulrich et al.[19] reported 7 cases of the same phenomenon. Table 1 summarizes the 6 of 11 cases of MMS after RT in craniopharyngiomas reported in the litera-

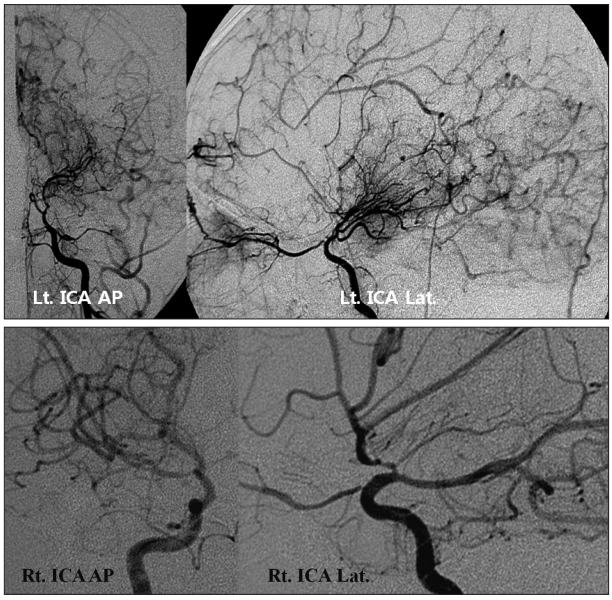

Fig. 3. Post-radiation angiograms showed occlusion of both supraclinoidal ICAs with basal, transdural, and leptomeningeal collateral vessels, characteristic of the moyamoya syndrome. ICA : internal carotid artery, AP : anterior-postrerior view, Lat. : lateral view.

Table 1. Demographic characteristics of craniopharyngioma patients with moyamoya syndrome (review of the literature)

Pt. No.	Age (y)	SEX	OP	Dose (cGy)	U/B
#1	12	M	+	5481	B
#2	?	?	+	5040+1200 (GKS)	B
#3	?	?	+	5400+4400 (GKS)	U
#4	8	F	+	5040	B
#5	5	F	+	5580	U
#6	4	M	+	5400	B

Pt. No. : patient's number, Age : age at diagnosis of craniopharyngioma, OP + : operation was done, Dose : radiation dose to tumor, U/B : unilateral versus bilateral disease, #1 : data from Ullrich et al.[19], #2-#6 : data from Liu et al.[8]

ture. Our analysis showed a more rapid onset of the MMS in patients with NF1 (median 38 vs. 55 months) and in patients who received >5000 cGy of radiation (median 42 vs. 67 months). It has been reported that each 100 cGy increase in radiation dose increased the rate of developing MMS by 7%, while affliction with the NF1 increased it threefold[8,16,19].

Several changes occurring in the weeks after irradiation have been suggested to contribute to the MMS pathogenesis : disruption of the muscle cells, fibrosis of the media, and focal hemorrhage and chronic inflammation of the adventitia[5,7,15]. The main causes of luminal narrowing of the intracranial arteries are probably medial injury, endothelial thickening following repopulation of the endothelium, and perivascular fibrosis[13,15]. Clearly, not only small arteries but also major cerebral arteries may be affected by RT, especially in children[10,12].

To prevent these serious complications, some authors suggest reduced radiation doses in children with parasellar tumors[15]. In general, close follow-up with conventional angiogram is recommended to rule out vasculopathy, especially adjacent to the ICAs that receive high-dose RT. Alternatively, MRI including FLAIR sequences, perfusion images, and MR angiography can be used to detect blood flow disturbances associated with presymptomatic vascular lesions, as well as for a sensitive and quantitative analysis of the vascular changes.

For this report, we reviewed 150 cases of craniopharyngioma, 127 of which were surgically removed at our institute between January 1996 and December 2009. Among these, 33 cases underwent RT. Here, we report 2 cases of MMS occurring after RT in the setting of craniopharyngioma. Despite the low incidence of MMS after RT, early detection and prompt treatment of the vasculopathy are both mandatory, as the consequences of delayed treatment are disastrous in young children. We strongly recommend close follow-up to screen for MMS, in addition to a trial of reduced-dose of RT.

CONCLUSION

Clinicians should remain vigilant for progressive vasculopathy of the distal ICA, which may be precipitated by RT in patients with brain tumors. This holds true especially in cases of tumors adjacent to the ICA.

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