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 underwent 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 progres-

sive 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. 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 encephalo-duroarteriosynangiosis (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...
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.

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 cranio-pharyngioma, 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 radiosurgery for 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-
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. 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. The main causes of luminal narrowing of the intracranial arteries are probably medial injury, endothelial thickening following repopulation of the endothelium, and perivascular fibrosis. Clearly, not only small arteries but also major cerebral arteries may be affected by RT, especially in children.

To prevent these serious complications, some authors suggest reduced radiation doses in children with parasellar tumors. In general, close follow-up with conventional angiogram is recommended to rule out vasculopathy, especially adjacent to the ICA 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.

**References**

1. Aoki S, Hayashi N, Abe O, Shirouzu I, Ishigami K, Okubo T, et al.: Radiation-induced arteritis: thickened wall with prominent enhancement on cranial MR images report of five cases and comparison with 18 cases of Moyamoya disease. *Radiology* 223: 683-688, 2002.

2. Barani K, Grow A, Brem S, Dagnow E, Sloan AE: Vascular complications after radiosurgery for meningiomas. *Neurosurg Focus* 22: E9, 2007.

3. Bitzer M, Topka H: Progressive cerebral occlusive disease after radiation therapy. *Stroke* 26: 131-136, 1995.

4. Desai SS, Paulino AC, Mai WY, Tch BS: Radiation-induced moyamoya syndrome. *Int J Radiat Oncol Biol Phys* 65: 1222-1227, 2006.

5. Kalapurakal JA, Goldman S, Hsieh YC, Tomita T, Marymont MH: Clinical outcome in children with craniopharyngioma treated with primary surgery and radiotherapy deferred until relapse. *Med Pediatr Oncol* 40: 214-218, 2003.

6. Kang JK, Song JU: Results of the management of craniopharyngioma in children. An endocrinological approach to the treatment. *Childs Nerv Syst* 4: 135-138, 1988.

7. Komotar RJ, Roguski M, Bruce JN: Surgical management of craniopharyngiomas. *J Neurosurg* 92: 283-296, 2009.

8. Liu AK, Bagrosky B, Fenton LZ, Gaspar LE, Handler MH, McNatt SA, et al.: Vascular abnormalities in pediatric craniopharyngioma patients treated with radiation therapy. *Pediatr Blood Cancer* 52: 227-230, 2009.

9. Merchant TE: Craniopharyngioma radiotherapy: endocrine and cognitive effects. *J Pediatr Endocrinol Metab* 19 Suppl 1: 439-446, 2006.

10. Minniti G, Esposito V, Amichetti M, Enrici RM: The role of fractionated radiotherapy and radiosurgery in the management of patients with craniopharyngioma. *Neurosurg Rev* 32: 125-132; discussion 132, 2009.

11. Pollock BE, Stafford SL: Results of stereotactic radiosurgery for patients with imaging defined cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys* 62: 1427-1431, 2005.

12. Regine WF, Mohiuddin M, Kramer S: Long-term results of pediatric and adult craniopharyngiomas treated with combined surgery and radiation. *Radiother Oncol* 27: 13-21, 1993.

13. Robertson RL, Chavali RV, Robson CD, Barnes PD, Eldredge EA, Burrows PE, et al.: Neurologic complications of cerebral angiography in childhood moyamoya syndrome. *Pediatr Radiol* 28: 824-829, 1998.

14. Roche PH, Régis J, Dufour H, Fournier HD, Delsanti C, Pellet W, et al.: Gamma knife radiosurgery in the management of cavernous sinus meningiomas. *J Neurosurg* 93 Suppl 3: 68-73, 2000.

15. Rudolz MS, Regine WF, Langston JW, Sanford RA, Kornar EH, Kun LE: Multiple causes of cerebrovascular events in children with tumors of the parasellar region. *J Neurooncol* 37: 251-261, 1998.

16. Servo A, Puranen M: Moyamoya syndrome as a complication of radiation therapy. Case report. *J Neurosurg* 48: 1026-1029, 1978.

17. Stafford SL, Pollock BE, Foote RL, Link MJ, Gorman DA, Schomberg PJ, et al.: Meningioma radiosurgery: tumor control, outcomes, and complications among 190 consecutive patients. *Neurosurgery* 49: 1029-1037; discussion 1037-1038, 2001.

18. Tanaka Y, Takemae T, Kobayashi S, Sakai K, Miyahara T, Ishizaka S, et al.: A clinical analysis of treatment and long-term outcome in 56 craniopharyngiomas. *No Shinkei Geka* 35: 887-893, 2007.

19. Ulrich NJ, Robertson R, Kinnannon DD, Scott RM, Kieran MW, Turner CD, et al.: Moyamoya following cranial irradiation for primary brain tumors in children. *Neurology* 68: 932-938, 2007.