

Cerebral Infarction Along the Distribution of Perforating Arteries During Aneurysm Surgery in a Patient With Pheochromocytoma

—Case Report—

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Abstract

A 58-year-old woman with refractory hypertension presented with subarachnoid hemorrhage. Digital subtraction angiography and three-dimensional computed tomography (CT) angiography revealed a ruptured left vertebral artery (VA) aneurysm and an unruptured left middle cerebral artery (MCA) aneurysm. The patient successfully underwent neck clipping of the left VA aneurysm. However, CT obtained just after the operation showed an asymptomatic cerebral infarction along the distribution of medial striate arteries of the right anterior cerebral artery in the caudate nucleus. The pathogenesis of the infarction was unknown. Before clipping surgery of the left MCA aneurysm, detailed examinations to find the cause of her refractory hypertension were performed. Laboratory tests revealed plasma serum level of norepinephrine at 15,521 pg/ml (normal range 100–450 pg/ml). Abdominal magnetic resonance imaging revealed a pheochromocytoma in the right adrenal gland. After preoperative management of the pheochromocytoma, the neck of the left MCA aneurysm was successfully clipped. When the patient awakened from anesthesia, she noticed right hemiparesis and motor aphasia. CT showed cerebral infarction along the distribution of lenticulostriate arteries of the left MCA in the putamen. Her symptoms gradually improved, and the pheochromocytoma was removed by laparoscopic surgery. Sustained severe hypertension and depletion of blood volume resulting from excess catecholamine release from the pheochromocytoma may have caused the complications. Hypervolemic fluid infusion and maintenance of normotensive blood pressure during surgery may avoid such ischemic events.

Key words: cerebral aneurysm, cerebral infarction, complication, perforating artery, pheochromocytoma

Introduction

Pheochromocytomas are rare neuroendocrine tumors with highly variable clinical presentations, including episodes of headaches, pallor, sweating, tachycardia, and hypertension. Of these clinical signs, hypertension is the most common.¹⁵⁾ Previous studies indicate that hypertension accelerates the development of cerebral aneurysms.^{7,8)} However, the association of cerebral aneurysms with pheochromocytoma is extremely rare, with only 5 reported cases.^{2,4–6,9)} We experienced a case of cerebral infarction along the distribution of perforating arteries, which occurred during aneurysm surgery in a patient with pheochromocytoma and discuss the possible pathogenesis of this inexplicable complication.

Case Report

A 58-year-old woman presented with subarachnoid hemorrhage (SAH). She had a 20-year history of refractory hypertension. Computed tomography (CT) showed diffuse, thick SAH, especially in the left cerebellomedullary cistern (Fig. 1A). Digital subtraction angiography (DSA) and three-dimensional CT angiography revealed 2 cerebral aneurysms, located on the left vertebral artery (VA) at its junction with the posterior inferior cerebellar artery (PICA), and at the left middle cerebral artery (MCA) bifurcation (Fig. 1B–D). We decided that the left VA-PICA aneurysm had ruptured based on the subarachnoid clot distribution. No other vascular lesions were found in the bilateral cervical internal carotid arteries (ICAs) and in the intracranial arteries (data not shown). The unruptured left MCA aneurysm was 5 mm in diameter, and had at least one bleb on the dome (Fig. 1D).

The patient underwent emergent neck clipping of the

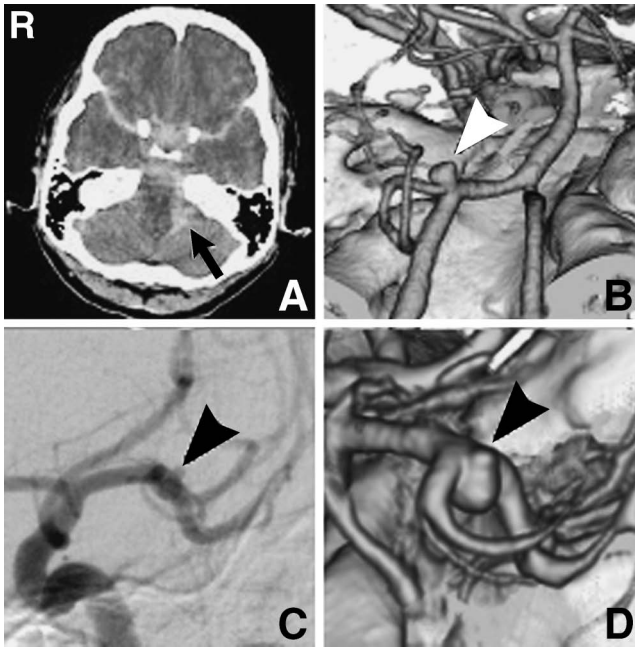


Fig. 1 A: Initial computed tomography (CT) scan showing diffuse thick subarachnoid hemorrhage, especially in the left cerebellomedullary cistern (arrow). B: Three-dimensional CT angiogram showing a left vertebral artery-posterior inferior cerebellar artery aneurysm (arrowhead). C: Digital subtraction angiogram showing the left middle cerebral artery bifurcation aneurysm with a bleb (arrowhead). The wall of the M₁ trunk is very smooth. D: Three-dimensional CT angiogram clearly showing the aneurysm with a bleb (arrowhead).

left VA-PICA aneurysm. During the operation, the systolic blood pressure was maintained between 90 mmHg and 100 mmHg by induced hypotension. She awakened from anesthesia with no neurological deficit, but CT performed just after the operation revealed asymptomatic cerebral infarction along the distribution of medial striate arteries of the right anterior cerebral artery (ACA) in the caudate nucleus, which was not related to the operative field (Fig. 2 left). The pathogenesis of this infarction was unknown.

In our institute, unruptured aneurysms over 5 mm in diameter with blebs are considered to be treatable by microsurgical clip or coil embolization. Therefore, we planned neck clipping of the left MCA aneurysm 3 months after the initial operation. Before the second operation, detailed examinations to find the cause of her refractory hypertension were performed. Laboratory tests revealed plasma serum level of norepinephrine (NE) at 15,521 pg/ml (normal range 100–450 pg/ml). Abdominal magnetic resonance imaging revealed a 4-cm wide mass in the right adrenal gland (Fig. 3). The diagnosis was pheochromocytoma.

After consulting a urologist, we decided that the aneurysm surgery should precede the removal of the pheochromocytoma because the catastrophic hypertension resulting from the acute catecholamine surge during anesthesia induction and surgical manipulation of the pheochromocytoma might trigger aneurysm rupture. Af-

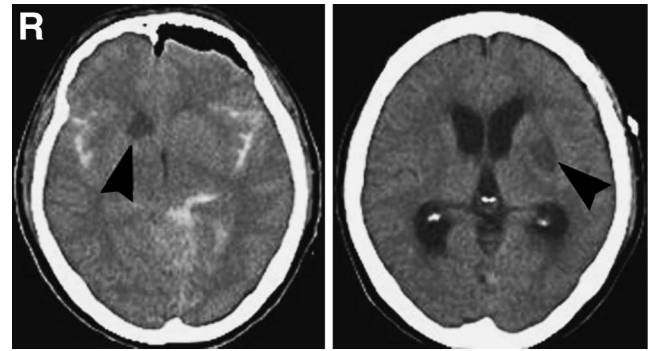


Fig. 2 Left: Computed tomography (CT) scan after the initial operation showing cerebral infarction in the right caudate nucleus (arrowhead). Right: CT scan after the second operation showing cerebral infarction in the left putamen (arrowhead).



Fig. 3 Abdominal T₁-weighted magnetic resonance image showing a 4-cm wide pheochromocytoma in the right adrenal gland (arrowheads).

ter stabilization of the patient's blood pressure by phenox- benzamine administration and adequate intravenous fluid replacement, the patient underwent neck clipping of the left MCA aneurysm. During the surgery, the main trunk of the left MCA was minimally exposed, and the lenticulostriate arteries were minimally manipulated. To avoid premature rupture of the aneurysm, intraoperative systolic blood pressure of the patient was kept between 90 mmHg and 100 mmHg by induced hypotension. When the patient awakened from anesthesia, she noticed right hemiparesis and motor aphasia. CT revealed cerebral infarction along the distribution of lenticulostriate arteries of the left MCA in the putamen (Fig. 2 right). Fortunately, her symptoms gradually improved, and the pheochromocytoma was successfully removed by laparoscopic surgery.

Discussion

Pheochromocytomas are catecholamine-producing neuroendocrine tumors originating from chromaffin cells of the adrenal medulla or extra-adrenal paraganglia. Approx-

imately 80–85% of pheochromocytomas originate from the adrenal medulla, whereas approximately 15–20% originate from the extra-adrenal chromaffin tissue.¹⁵⁾ Almost all pheochromocytomas produce either epinephrine (EPI) or NE.¹³⁾ EPI is a circulating hormone with potent action on the β_2 -adrenergic receptors of the skeletal muscle vasculature, causing vasodilation that results in hypotension.¹⁰⁾ In contrast, NE released locally from sympathetic nerve endings within the vasculature causes α_1 -adrenoceptor-mediated vasoconstriction, resulting in hypertension and depletion of blood volume.^{3,10)}

Our patient experienced cerebral infarction twice during each aneurysm surgery, both times along the distribution of the perforating arteries. The maximum size of infarction during the initial and second operations was 14.4 mm and 19.3 mm in diameter, respectively. The former was categorized as lacunar infarction,¹¹⁾ which was caused by occlusion of a single medial striate artery of the right ACA. In contrast, the latter was thought to be caused by occlusion of multiple lenticulostriate arteries of the left MCA, because the infarction was larger than 15 mm.

Preoperative DSA indicated that the arterial walls of the bilateral cervical ICAs and main trunks of the intracranial vessels including the right ACA and the left MCA were so smooth that branch atheromatous disease or artery-to-artery embolism could be excluded from the pathogenesis of occlusion of the perforating arteries.

A number of possible mechanisms can be proposed for the pathogenesis of cerebral infarction along the perforating arteries. Her longstanding, refractory hypertension may have affected the perforating arteries and predisposed to the development of microatheroma and lipohyalinosis, which are the most frequent etiologies for perforating artery occlusion.¹¹⁾ In addition, she had the potential risk of depletion of blood volume due to excess catecholamine release from the pheochromocytoma,¹⁴⁾ and this chronic hypovolemic condition may also be a risk factor for cerebral ischemia along the affected perforating arteries.

Both ischemic events occurred during aneurysm surgery, so the surgery, the surgical technique, and anesthetic management during surgery may have been involved in the ischemic events. One possible pathogenesis during surgery is kinking or stretching of the perforating arteries by brain sinking due to removal of the cerebrospinal fluid. The “affected” perforating arteries might be prone to occlusion by kinking or stretching.

In the initial ischemic event, the surgical technique was completely innocent because the operative field was located in the infratentorial area and the cerebral infarction was in the caudate nucleus, far from the operative field. In the second ischemic event, the surgical technique is probably also innocent because the end of the left M_1 was exposed only for the width of the temporary clip blade, and the lenticulostriate arteries were barely manipulated.

According to anesthetic management during surgery, the patient’s blood pressure was maintained hypotensive compared with her daily value. Decreased cerebral perfusion pressure due to this induced hypotension, and the chronic hypovolemic condition together might have been

responsible for cerebral infarction along the distribution of the “affected” perforating arteries. Intraoperative fluid infusion volume was maintained at 3 ml/kg/hr.

Data obtained from general outpatient clinics show that the prevalence of pheochromocytoma in hypertensive patients is 0.1–0.6%.^{1,12)} Pheochromocytoma has not been identified as a causative factor for hypertension because of this low incidence and highly variable clinical presentations. However, we would like to emphasize that the presence of pheochromocytoma should never be overlooked in patients with unruptured cerebral aneurysms who will undergo planned surgical intervention by neck clipping or coil embolization, because these patients may suffer hypertensive crisis during the induction of anesthesia or during the surgery,¹³⁾ and this crisis may induce premature rupture of aneurysms.

The main objective of preoperative management of a patient with pheochromocytoma is to normalize the blood pressure, heart rate, and functions of other organs; restore blood volume depletion; and to prevent surgery-induced catecholamine storm and its consequences on the cardiovascular system.¹³⁾ Any patient with pheochromocytoma and their families should be informed about the risks of various complications including cerebral infarction during aneurysm surgery. Despite careful preoperative management of pheochromocytoma, our patient developed cerebral infarction during the second aneurysm surgery. Considering the possible mechanisms of this complication, hypervolemic fluid infusion and maintenance of normotensive (not hypotensive) blood pressure during surgery may avoid such ischemic events.

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