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Skin Blood Flow and Plasma Catecholamines during Removal of Pheochromocytoma

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PREOPERATIVE α -adrenergic blockade is thought to reduce perioperative morbidity of patients undergoing removal of pheochromocytoma.¹ In addition, β -adrenergic blockade is also used to control tachycardia and dysrhythmias. However, a sudden decrease in plasma catecholamine concentrations after removal of the tumor often results in marked hypotension.^{1,2} No clinical measure that reflects and monitors rapid changes occurring in plasma levels of catecholamines during manipulation of pheochromocytoma has been available yet, except for the measurement of blood pressure that reflects changes in systemic vascular resistance. Therefore, rapid fluid infusion under careful cardiovascular monitoring, immediately after ligation of adrenal veins or at removal of the tumor, has been recognized as the treatment of choice for this hypotension.¹⁻⁴

In a search for a measure that may correlate with rapidly changing plasma levels of catecholamine, we measured blood pressure, skin blood flow (SBF), and plasma catecholamine concentrations in three patients undergoing removal of pheochromocytoma. Skin blood

flow in the first toe, measured by laser Doppler flowmetry, more closely followed rapid changes in plasma catecholamine concentrations than did blood pressure.

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Case 1

A 50-yr-old, 47-kg man with a 3-month history of headache, nausea, palpitation, hypertension, renal failure secondary to glomerulonephritis, and an episode of cerebral hemorrhage was referred to us. The 24-h urinary catecholamines and the metabolites levels were markedly increased (table 1). Computed axial tomography showed a left adrenal mass of 5.0 cm in diameter, confirming the diagnosis of pheochromocytoma. The patient received 7 mg doxazosin mesilate, 1.5 mg prazosin hydrochloride, and 50 mg atenolol orally for 3 weeks before the operation.

Premedication consisted of 100 mg pentobarbital orally; 10 mg diazepam orally; and 0.3 mg scopolamine subcutaneously. After cannulation of a peripheral vein, a radial artery, and the pulmonary artery, an epidural catheter was inserted through the T9-T10 interspace, and T3-L1 analgesia was achieved 5 min after injection of 15 ml of 2% mepivacaine. Anesthesia was induced with 100 μ g fentanyl, 10 mg midazolam, and 200 mg thiopental, intravenously. Tracheal intubation was facilitated by vecuronium. Anesthesia was maintained with 66% nitrous oxide in oxygen, fentanyl, and epidural mepivacaine. Prostaglandin E₁ was titrated intravenously to maintain systolic arterial pressure between 100 and 130 mmHg. Skin blood flow was monitored at the tip of the right first toe by a laser Doppler flowmeter (ADVANCE, ALF-2100, Tokyo, Japan). The probe, with optic fiber separation of 0.7 mm, was secured to the toe, using double-faced adhesive tape.

Blood pressure (BP) and heart rate increased to 220-250/120-125 mmHg and 130 beats per minute, respectively, during manipulation of the tumor. Hypertension and tachycardia were treated by increasing the infusion rate of prostaglandin E₁, boluses of 0.2-0.4 mg propanolol, and boluses of 1-2 mg phentolamine. Immediately before removal of the tumor, prostaglandin E₁ was discontinued, and 1 l dextran-40 was infused rapidly. However, BP decreased to 80/60 mmHg and then stabilized near 100/70 mmHg. No vasoactive drugs were used. Blood loss was estimated at 640 ml, and blood was not

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Table 1. Preoperative Laboratory Data

Case No.	24-h Urinary					BP (mmHg)
	M (mg)	NM (mg)	VMA (mg)	E (μ g)	N (μ g)	
1	0.15 (0.05-0.23)	21.9 (0.07-0.26)	32.2 (1.5-7.5)			135/80
2				300 (<12)	469 (<90)	140/85
3				21	220	140/75

Values in parentheses are normal ranges.

M = metanephrine; NM = normetanephrine; VMA = vanillyl-mandelic acid; E = epinephrine; N = norepinephrine; BP = preoperative blood pressure after treatment.

transfused. The postoperative course was uneventful. The diagnosis was confirmed histologically.

Skin blood flow decreased from 9-12 ml/100 g tissue/min to 3-5 ml during tumor manipulation. Skin blood flow increased promptly after each intravenous bolus of phentolamine. Ligation of veins draining the adrenal gland resulted in some increase in SBF. Within 1 min after removal of the tumor, SBF increased rapidly, from 6-8 ml to 14-17 ml, then continued to increase during the rest of the operation (fig. 1). There were relations between plasma norepinephrine concentration and SBF, as well as BP ($\text{SBF} = -16.8 \times \text{norepinephrine} [\log \text{ ng/ml}] + 28.7$, $r = -0.95$, $P = 0.0002$ [fig. 2] and mean BP [mmHg] = $110 \times \text{norepinephrine} [\log \text{ ng/ml}] - 23$, $r = 0.86$, $P < 0.001$).

Case 2

A 42-yr-old, 46-kg woman with a 6-month history of headache, nausea and vomiting, excessive sweating, palpitation, and hypertension was scheduled for removal of pheochromocytoma. Plasma and 24-h urinary epinephrine and norepinephrine levels were markedly increased. Computed axial tomography showed a right adrenal mass of 3.0 cm in diameter. The patient had been given 2 mg bunazosin hydrochloride orally for 7 weeks before admission.

Anesthetic management was essentially identical to that in case 1. Skin blood flow was measured at the right first toe. Blood loss was estimated at 318 ml. Vasoactive drugs were not administered. Blood was not transfused. The postoperative course was uneventful. The diagnosis was confirmed histologically.

There were relations between SBF and plasma norepinephrine and

epinephrine ($-9.8 \times \text{norepinephrine} [\log \text{ ng/ml}] + 25.0$, $r = -0.95$, $P < 0.0001$ and $-9.8 \times \text{epinephrine} [\log \text{ ng/ml}] + 22.8$, $r = -0.94$, $P < 0.0001$) (fig. 2). The relation of mean BP to plasma norepinephrine was $44 \times \text{norepinephrine} (\log \text{ ng/ml}) + 47$, $r = 0.84$, $P = 0.006$.

Case 3

A 64-yr-old, 56-kg woman with a 3-yr history of headache and palpitation was scheduled for removal of pheochromocytoma. The 24-h urinary catecholamines level was increased. Computed axial tomography showed a right adrenal mass of 3.0 cm in diameter and a cyst in the left kidney of 2.5 cm in diameter. The patient had received 1 mg prazosin hydrochloride orally three times a day for 2 weeks.

Anesthesia management was similar to the previous two cases. An SBF probe was secured to the left first toe. Blood loss was estimated at 1,249 ml. Erythrocytes were transfused. Vasoactive drugs were not used. The procedures performed were removal of right adrenal mass, left radical nephrectomy, and dissection of retroperitoneal lymph nodes. The postoperative course was uneventful. The diagnoses of pheochromocytoma and renal cell carcinoma were confirmed histologically.

There were relations between SBF and plasma catecholamines ($-15.2 \times \text{norepinephrine} [\log \text{ ng/ml}] + 31.5$, $r = -0.98$, $P = 0.0014$ and $-18.5 \times \text{epinephrine} [\log \text{ ng/ml}] + 21.2$, $r = -0.98$, $P = 0.0007$) (fig. 2). There was no relation between mean BP and plasma norepinephrine (mean BP = $28 \times \text{norepinephrine} [\log \text{ ng/ml}] + 82$, $r = 0.54$, $P = 0.3917$).

Discussion

We found that SBF in the first toe increased after epidural block; markedly decreased during manipulation of pheochromocytoma; increased, although transiently, with administration of phentolamine; and increased again after removal of the tumor in all three patients. The SBF increase that followed the removal of pheochromocytoma lasted until the operation was completed. The SBF responses to these interventions

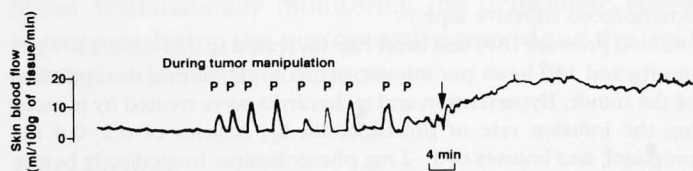


Fig. 1. Changes in skin blood flow in the great toe, measured by laser Doppler flowmetry, during and after removal of pheochromocytoma. P = intravenous phentolamine. Arrow indicates the time when the tumor was removed completely.

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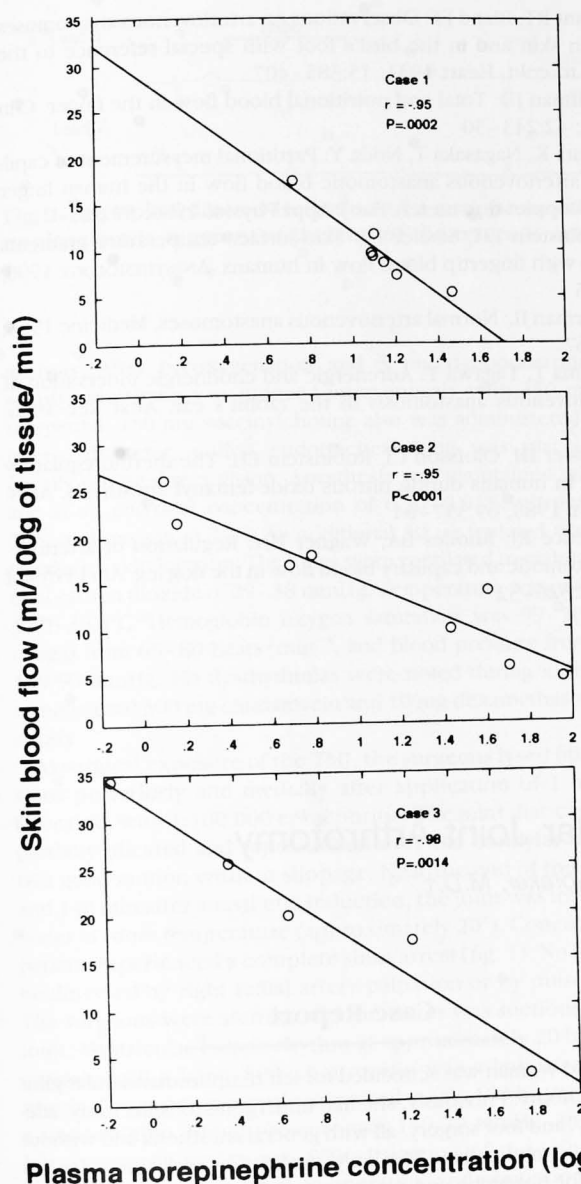


Fig. 2. Relations between skin blood flow in the great toe measured by Doppler flowmetry and plasma norepinephrine concentration during operation.

were rapid. Plasma norepinephrine concentrations from blood samples withdrawn before and after epidural block, immediately before phentolamine administration, and after removal of the tumor correlated more closely with SBF than with mean blood pressure in all patients.

The vascular anatomy of the skin in the fingers and toes is characterized by a highly developed system of arteriovenous anastomoses that regulate body tempera-

ture.^{5,6} Surface skin temperature of the finger has been shown to correlate with total digital blood flow.⁶ It was shown that laser Doppler flowmetry, using a probe with an optic fiber separation between the exciting and receiving fibers of 0.3 mm, detects capillary flow primarily in the outer 0.6–0.8 mm of the skin, but not blood flow through arteriovenous anastomoses located in deeper layers of the skin. However, Hirata *et al.*⁷ showed that a probe with optic fiber separation of 0.7 mm can detect blood flow through both the capillaries and arteriovenous anastomoses in the outer 1.2 mm of the skin. In their study, a close correlation ($r = 0.919$) was found between blood flow in the human finger measured by venous occlusion plethysmography and that measured by laser Doppler flowmetry with an optic fiber separation of 0.7 mm.⁷ Because the probe used in our patients had an optic fiber separation of 0.7 mm, the values obtained in our patients may have reflected blood flow through capillaries and arteriovenous anastomoses in the skin of the toe.

Blood flow through arteriovenous anastomoses ranges from negligible to 80% of the total flow.⁸ The diameter of arteriovenous anastomoses may be 10 μ m at vasoconstriction but 100 μ m at vasodilation, and blood flow through a unit length of an arteriovenous anastomosis with a diameter of 100 μ m at vasodilation is estimated to be 10,000 times greater than that through a capillary of 10 μ m in diameter.⁹ Subsequently, Iijima and Tagawa¹⁰ showed that, in the rabbit's ear, thick-walled intermediate sections of arteriovenous anastomoses had dense adrenergic innervation; small arteries and arterial segments had moderate adrenergic innervation; and small veins and venous segments had only a few innervations. The increase in the total SBF in the toe that occurred soon after epidural block in our patients suggests that the increase was due largely to dilatation of arteriovenous anastomoses secondary to sympathetic nerve blockade.^{11,12} The marked decrease in the total SBF in the toe observed during manipulation of the tumor was interrupted by phentolamine. The decrease in the blood flow during tumor manipulation and the rapid increase in SBF after removal of the tumor were inversely and linearly related to the plasma norepinephrine levels in all patients and to the epinephrine levels in two patients.

Our finding suggests that the changes in SBF, measured in the big toe of our patients under epidural anesthesia, appear to reflect the changes in circulating catecholamine concentrations. Skin blood flow measurement may be a useful marker for the changes that occur in the concentrations of plasma catecholamines during removal of pheo-

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chromocytoma, and may indicate more correctly the complete removal of the tumor than does blood pressure.

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Asystole during Temporomandibular Joint Arthrotomy

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MOST anesthesiologists are aware that compression of the eye or traction on the extraocular muscles can cause oculocardiac reflex. Perhaps less well known is that noxious stimulation of trigeminal divisions other than the ophthalmic division (V_1) can also trigger life-threatening dysrhythmia and asystole. We present a case of asystole after stimulation of the mandibular division of the trigeminal nerve (V_3).

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Key words: Complications: asystole. Ophthalmology: oculocardiac reflex. Surgery: temporomandibular joint arthrotomy. Trigeminal nerve. Trigeminal reflex.

Case Report

A 41-yr-old woman was scheduled for left temporomandibular joint (TMJ) arthrotomy. Previously, she had undergone tonsillectomy, adenoidectomy, and foot surgery, all with general anesthesia and without any known complication. Her only medication was ibuprofen, as necessary, for headache and preauricular pain.

Preoperative vital signs were: blood pressure of 125/50 mmHg, pulse of 72 beats \cdot min $^{-1}$, oral temperature of 36.4°C, and respiratory rate of 18 breaths \cdot min $^{-1}$. Physical examination revealed an obese woman who weighed 111 kg and was 150 cm tall. She had healthy teeth, a 28-mm mandibular opening, a normal-appearing jaw, clear lungs, unremarkable heart sounds, and normal cranial nerve function and extremity strength. Hematocrit was 35%. Electrocardiogram demonstrated normal sinus rhythm at 67 beats \cdot min $^{-1}$, normal axis and intervals, and no dysrhythmias.

Preoperatively, the patient was extremely anxious, and wept. She was reassured, and 5 mg midazolam and 100 μ g fentanyl were administered in divided doses. Four percent lidocaine with 1:100,000 epinephrine was administered as an aerosol into both nares. Intraoperative monitoring included continuous electrocardiogram (limb lead III and precordial lead V_5), blood pressure, temperature, chest auscultation by esophageal stethoscope, pulse oximetry, and respiratory gas