

CASE REPORTS

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Bilateral Dilated Nonreactive Pupils during Surgery in a Patient with Undiagnosed Pheochromocytoma

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A rare but disturbing clinical sign during anesthesia is the appearance of bilateral dilated nonreactive pupils. We recently observed persistent dilated pupils in a patient undergoing a nephrectomy for renal cell carcinoma. A differential diagnosis of the causes for this sign led us to suspect a pheochromocytoma, even though the intraoperative hemodynamic changes, *per se*, did not indicate the presence of this tumor. The following report presents the details of this unusual case and reviews the various causes for dilated pupils.

CASE REPORT

A 39-yr-old man visited his physician because of prolonged influenza-like symptoms. An abdominal mass was discovered, and a diagnosis of renal cell carcinoma was made with a computed tomography-guided needle biopsy. He was scheduled for a radical nephrectomy. On the day before surgery, he was examined in the Anesthesia Clinic. He had abused cocaine and heroin in the past but stated that he had not taken illicit drugs for more than 6 months. On physical examination, he was a well-developed normal man of 82.1 kg with a blood pressure of 150/90 mmHg and a regular heart rate of 80 beats/min. All laboratory values were within the normal range. An electrocardiogram was not obtained.

On the day of surgery, as part of an ongoing investigation of the effects of anesthetics on the pupil,¹ we examined the response of his right pupil to intravenously administered alfentanil (7.5 µg/kg), 1 h before the scheduled time of operation. This showed a large pupil of 6.8 mm diameter, with a normal pupillary light reflex and a normal response to alfentanil.

A 20-G lumbar epidural catheter was then placed, while 2 mg midazolam was administered intravenously for additional sedation. Routine tests for intravenous and subarachnoid catheter placement were negative, and anesthesia was induced with alfentanil (25 µg/kg), thiopental (4.5 mg/kg), and isoflurane (1.5% in oxygen). Intubation of the trachea was facilitated by administration of succinylcholine (1 mg/kg); pancuronium (5 mg) was used to maintain muscle relaxation. During tracheal intubation, the patient's arterial blood pressure increased to 195/100 mmHg, and an additional 100 mg thiopental and 1,000 µg alfentanil were given. Anesthesia was maintained with isoflurane 0.75-2% (end-tidal concentration), nitrous oxide/oxygen (1.5:1 l/min), and an alfentanil infusion (0.3 µg · kg⁻¹ · min⁻¹). Arterial blood pressure de-

creased to 110/70 mmHg. Routine monitoring included arterial blood pressure (oscillometry), pulse oximetry, five-lead electrocardiography, central venous pressure (via a right internal jugular catheter), and central temperature (esophageal stethoscope). Examination of the eyes with a dot comparison pupillometer‡ revealed bilaterally nonreactive 2.3-mm pupils.

After skin incision, the patient's arterial blood pressure increased from 110/60 to 190/100 mmHg, and his heart rate increased from 60 to 72 beats/min. Two percent pH-adjusted lidocaine with epinephrine (1:200,000) was administered epidurally in 5-ml increments (total dose 20 ml). Sixty minutes later, arterial blood pressure had decreased to 150/100 mmHg, and the same dose of lidocaine, along with 2 mg preservative-free morphine, was administered epidurally. Examination of the pupils revealed bilateral nonreactive 8-mm pupils that did not change size after repeated bolus injections of alfentanil (1,000 µg). A 20-G Teflon catheter was inserted into the left radial artery to sample for serum catecholamines (norepinephrine, epinephrine, and dopamine) and blood gases. Laboratory analysis of catecholamines could not be obtained on that day. However, arterial blood gas analysis revealed a pH of 7.4, P_{CO₂} of 37.4 mm Hg, P_{O₂} of 216.8 mmHg, and a base excess of -1.5 mM/l. Arterial blood pressure remained high (150/100 mmHg). Phentolamine 5 mg was given intravenously, and the blood pressure stabilized at 110/65 mmHg; however, the pupils remained dilated. Dissection of the renal blood vessels continued throughout this period.

A diagnosis of pheochromocytoma was suggested but considered unlikely by the surgical team because of the preoperative tissue diagnosis of renal cell carcinoma. Nonetheless, we infused a large volume of fluid and prepared vasoactive infusions in anticipation of eventual removal of a pheochromocytoma. Approximately 45 min later, the kidney was removed, revealing a mass on the upper pole that had also invaded the right adrenal gland. There were no significant hemodynamic changes after tumor removal. The pupils slowly constricted to 4-5 mm during closure of the surgical wound. Pathologic analysis of a frozen section intraoperatively indicated anaplastic cells consistent with renal cell carcinoma.

Following surgery, the patient was transferred to the postanesthesia care unit, where he awoke comfortably. Because of the question of pheochromocytoma, he was discharged to the intensive care unit, where analgesia was provided by a continuous infusion of 0.8 mg/h preservative-free epidural morphine. Postoperative tissue diagnosis indicated pheochromocytoma. Serum catecholamine levels drawn during surgery were reported on the second postoperative day (table 1). The patient was discharged on postoperative day 7. A renal cell carcinoma was not found, and there was no explanation for the previous diagnosis.

DISCUSSION

It has been written that for every case of pheochromocytoma that is diagnosed and treated surgically, there

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‡ Larson MD: A New Pupillometer for Operating Room Use. *Anesthesiology Review* 10:23-26, 1978.

TABLE 1. Serum Catecholamine Concentrations Drawn during the Surgical Procedure

	Norepinephrine (pg/ml)	Epinephrine (pg/ml)	Dopamine (pg/ml)
Normal values	110-410	<50	<30
During tumor dissection	7,760	344	102
35 min after tumor removal	1,200	446	138

are two that are missed and discovered only at autopsy.² In an autopsy study of over 40,000 cases, the incidence of pheochromocytoma was 0.13%, and in only 24% of patients was this tumor diagnosed during their lifetimes. In patients in whom the tumor was identified at autopsy, 27% died in the perioperative period from cardiovascular collapse from an unidentified cause.³

Because perioperative morbidity is high in patients with unsuspected pheochromocytoma, it is important to be aware early in the operative course of the clinical signs indicating this tumor. The classical triad of symptoms for pheochromocytoma is headache, palpitations, and diaphoresis.⁴ Our patient had none of these symptoms preoperatively. Neither diaphoresis nor tachycardia was present intraoperatively. Hemodynamic instability occurs intraoperatively in patients with unsuspected pheochromocytoma but often is attributed to other factors.⁵ In the present case, we initially attributed the patient's hypertension and relatively high drug requirements to his history of drug abuse.

Persistent bilateral pupillary dilation as a clinical intraoperative sign for pheochromocytoma has not been observed previously. With some of the older anesthetics, such as diethyl ether and fluroxene, the pupil often was persistently dilated.⁶ With currently used agents, persistent pupillary dilation is unusual because of opioid supplementation of halothane-, isoflurane-, or enflurane-based anesthetics. However, there are certain conditions during which the pupil will remain dilated under the influence of opioids. Certain rare pupillary syndromes such as bilateral Adie's syndrome or the "neuropathic tonic pupil"⁷ prevent the normal miotic response to opioids. Our patient was tested preoperatively and exhibited a normal light reflex and a normal miotic response to alfentanil, thereby eliminating these syndromes as the cause of his persistent pupillary dilation.

Factors that prevent cellular activity within the pupilloconstrictor center or that interfere with the expression of pupilloconstrictor tone *via* the third cranial nerve also may result in persistent pupillary dilation. Examples include an expanding brain mass or hemorrhage into the midbrain,⁸ ganglionic blockade at the ciliary ganglion (as can be produced by trimethaphan⁹), extreme hypothermia,¹⁰ or administration of muscarinic blocking agents (*e.g.*, atropine or scopolamine).¹¹ We had no reason to

suspect an intracranial pathologic process in our patient, who also had none of the other conditions.

Another possible cause of pupillary dilation is "total spinal" anesthesia. Pupillary dilation is one indicator of total spinal anesthesia.¹² However, we thought catheter migration into the subarachnoid space in this case to be unlikely since we could not aspirate cerebrospinal fluid through the catheter. In addition, the patient's arterial blood pressure did not require continued support with vasoactive agents, as would be expected in the presence of total spinal anesthesia.

By a process of exclusion, we therefore determined that interference with the parasympathetic mechanism was not the cause of the dilated pupils and that perhaps the sympathetic (dilator) muscle had become strong enough to overpower the parasympathetic (sphincter) mechanism. Both the labile blood pressure and the location of the surgery contributed to our conclusion that the patient's tumor was secreting large doses of catecholamines and this was the mechanism of the persistent dilation of the pupils. Although moderate doses of α_1 -adrenergic agonists do not dilate the pupil, it is known that high blood concentrations of these agonists (*e.g.*, dopamine¹³ or topical phenylephrine¹⁴) can lead to a dilated and nonreactive pupil during anesthesia.

The most puzzling aspect of the case was that phentolamine decreased the blood pressure, but the pupils remained dilated. A review of the unique pharmacology of the iris later revealed that phentolamine does not block the adrenergic receptor of the dilator muscle in cats.¹⁵ Because the pupil remained dilated after phentolamine in the present case, it is possible that this is true also for humans. Usually, patients scheduled for resection of pheochromocytoma are pretreated with phenoxybenzamine, an agent that produces a long-lasting block of all α_1 -adrenergic receptors, including the dilator muscle of the iris.¹⁵ Consequently, the pupils remain small during elective surgery for pheochromocytoma.

In summary, we observed dilated nonreactive pupils in a patient undergoing a radical nephrectomy. An analysis of the case provided us with a tentative diagnosis of pheochromocytoma and allowed us to establish an appropriate anesthetic plan. Although it is more common for the dilated pupil to result from interference with the parasympathetic innervation of the iris, markedly increased concentrations of circulating catecholamines should be suspected as well. Clearly, an understanding of the physiology of the pupil can be beneficial to the anesthesiologist.

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§ Koss MC: Adrenergic control of the iris (abstract). 19th Pupil Colloquium, Falmouth, Massachusetts, September 12-14, 1991.

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Successful Cardiopulmonary Resuscitation of Two Patients in the Prone Position Using Reversed Precordial Compression

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Standard precordial cardiac massage was developed for cardiac arrest with the patient in the supine position. On rare occasions cardiac massage is required for patients in the prone position during anesthesia. These occurrences may be catastrophic. Resuming the supine position is usually recommended for effective cardiac massage. However, there are some drawbacks. Changing position is usually time-consuming and delays the initiation of cardiac massage. If intracranial or spinal cord surgery is in progress, moving the patient without proper protection into

the supine position may injure the brain or spinal cord. To date we know of no previous report or description of cardiac massage for patients in whom cardiac arrest occurred while they were in the prone position. We therefore report the successful resuscitation of two patients while in the prone position who suffered cardiac arrest during posterior cranial fossa and cervical spine surgery. We call our resuscitation technique for these patients "the reverse precordial compression maneuver (reversed precordial compression)."

CASE REPORTS

Case 1. A 14-yr-old girl who sustained an open occipital fracture in a motorcycle accident was scheduled for an emergency posterior fossa craniectomy. She had been unconscious after the accident. Neurologic examination revealed a Glasgow coma scale of 8. Her pupils were small and equal, and the light reflex was sluggish. Computerized tomographic scan of the head revealed a left intracerebellar hematoma measuring 3 × 3.5 cm, a reduction in size of both lateral ventricles, and a depressed occipital fracture. In the operating room she was monitored with electrocardiogram, pulse oximeter (SpO₂), direct radial arterial blood pressure, and central venous pressure *via* right internal jugular vein. Following induction of anesthesia, she was placed in the prone position with her head supported by a Mayfield head clamp. Anesthesia was maintained with oxygen-nitrous oxide-fentanyl.

The patient's vital signs were stable for 75 min (blood pressure = 90/

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