

Pituitary Apoplexy: A Complication of Cardiac Surgery

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ABSTRACT Pituitary apoplexy occurred in 3 patients in the immediate postoperative period following cardiac operation with cardiopulmonary bypass. In this setting, this complication is extremely rare and not widely recognized.

Precipitating factors may be related to the extracorporeal bypass apparatus, anticoagulation, low cerebral blood flow, and even anesthetic agents.

Neurosurgical decompression can be safely performed in the early postoperative period following open-heart operations.

Pituitary apoplexy is a clinical syndrome related to pituitary hemorrhage, necrosis, or both. Signs and symptoms are due to sudden expansion of a preexisting tumor with compression of the optic chiasm and parasellar structures, which results in ophthalmoplegia, visual loss, and headache. Acute apoplexy occurs in about 9% of patients with pituitary adenomas, although the proportion increases to 16.5% when cases of asymptomatic hemorrhage are included [1].

Apoplexy often occurs within a previously silent tumor. Pituitary apoplexy can occur spontaneously but has been associated with a variety of conditions including radiotherapy, anticoagulation therapy, the mechanical respirator, angiography, and head trauma [2, 3]. Although an association between open-heart operation and pituitary apoplexy has been described in the literature [4-6], this complication is not widely recognized.

We report the cases of 3 patients having pituitary apoplexy following an open-heart procedure, and discuss the possible mechanisms involved.

Material and Methods

Case Reports

PATIENT 1. A 63-year-old man with a history of hypertension, unstable angina, and severe triple-vessel coronary artery disease was admitted for coronary artery bypass grafting (CABG) operation. He had no history suggestive of endocrine disorders. The results of the preoperative neurological examination were normal.

A left internal mammary artery graft and three aortocoronary saphenous vein grafts were placed. Car-

diopulmonary bypass was terminated uneventfully. Anticoagulation was reversed with protamine sulfate, and satisfactory hemostasis was obtained. There was neither hemodynamic instability nor evidence of a perioperative myocardial infarction (Table).

Twelve hours after the operation, the patient was noted to have a dilated left pupil, which was unresponsive to light. There were ptosis of the left lid and paralysis of the left extraocular muscles, but no other abnormal neurological findings. Treatment with dexamethasone was begun. A computed axial tomogram (CAT) of the head showed a left parasellar mass with suprasellar extension and bony destruction, with inferior extension to the left side of the sphenoidal sinus. Carotid angiograms showed no evidence of an aneurysm.

The ophthalmoplegia gradually improved. Two weeks after the CABG procedure, a transsphenoidal hypophysectomy was performed, and a large necrotic hemorrhagic chromophobe adenoma was removed. The patient was placed on a regimen of hormone replacement therapy, and the ophthalmoplegia resolved over the following two months.

PATIENT 2. A 62-year-old man was referred for mitral and aortic valve replacement because of severe and symptomatic rheumatic valvular disease. He had been treated with thyroxine for hypothyroidism for the previous ten years, and four months prior to this admission he was found to have panhypopituitarism. A CAT revealed a large pituitary tumor with no suprasellar extension. Treatment with prednisone and testosterone was begun. On admission, the patient had a normal neurological examination. It was decided that the cardiac operation should precede resection of the pituitary tumor. Steroids were given preoperatively and intraoperatively.

Aortic and mitral bioprosthetic valves were implanted. Cardiopulmonary bypass was terminated uneventfully. Anticoagulation was reversed with protamine, and satisfactory hemostasis was obtained. There was no hemodynamic instability or evidence of perioperative myocardial infarction (see Table).

Twelve hours postoperatively, the patient was noted to have a dilated right pupil, unresponsive to light. Neurological examination revealed right ptosis and complete right ophthalmoplegia, decreased visual acuity in the right eye, and bitemporal visual field deficits; other findings were normal. A CAT suggested presence of hemorrhage within an intrasellar tumor.

The patient underwent transsphenoidal resection of the tumor 9 hours after the onset of the neurological

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Intraoperative Variables in Pituitary Apoplexy following Cardiac Operations

| Patient No. | Anesthetic Agents | Anticoagulation | Blood Prime Solution | Aortic Blood Flow (ml/kg/min) | Total Cross-clamp Time (min) | Duration Bypass (min) | Hypothermia (°C) | Volume of Cardioplegic Solution (ml) | Mean Arterial Pressure (mm Hg) | Hematocrit (%) | |
|-------------|------------------------------------|-----------------|----------------------|-------------------------------|------------------------------|-----------------------|------------------|--------------------------------------|--------------------------------|----------------|-------|
| | | | | | | | | | | Before | After |
| 1 | Morphine, halothane, nitrous oxide | Heparin | Crystalloid | 55 | 66 | 114 | 26 | 1,650 | 45-70 | 33 | 29.3 |
| 2 | Fentanyl, halothane | Heparin | Crystalloid | 68 | 109 | 161 | 24 | 4,800 | 47-98 | 37 | 24 |
| 3 | Sufentanil citrate, droperidol | Heparin | Crystalloid | 60 | 73 | 101 | 27 | 1,100 | 37-75 | 36 | 24 |

deficit. Light microscopy of the tumor showed a sclerosing adenoma with calcification and hemorrhages. Hormone replacement therapy was instituted. On discharge three weeks postoperatively, the patient was well, aside from a resolving sixth cranial nerve paresis and slight right ptosis.

PATIENT 3. A 55-year-old man was admitted for a CABG procedure. He was known to have had a borderline low serum level of L-thyroxine for six months. A left internal mammary artery graft was placed to bridge two sites in the left anterior descending distribution, and a sequential aortocoronary saphenous vein graft was constructed to two posterolateral circumflex arteries. Cardiopulmonary bypass was terminated uneventfully, and cardiac function appeared normal. Anticoagulation was reversed with protamine, and satisfactory hemostasis was obtained. There was no hemodynamic instability or evidence of perioperative myocardial infarction (see Table).

On arrival in the intensive care unit, the patient was noted to have a dilated right pupil, unreactive to light. He was unresponsive because of the effect of the anesthetic. Pituitary apoplexy was considered, and treatment with hyperventilation, mannitol, and dexamethasone was begun for possible increased intracranial pressure. Three hours later, the patient was awake enough to permit a full neurological examination. Mentation was appropriate, and the only new findings were ptosis of the right lid and paralysis of the right extraocular muscles; the right pupil remained dilated and unreactive. A CAT made 4 hours postoperatively showed a large pituitary mass with suprasellar extension (Figure). The patient's neurological status remained unchanged, and 18 hours after CABG, he underwent an uneventful transphenoidal removal of the pituitary tumor, which proved to be a prolactin- and follicle-stimulating, hormone-secreting adenoma with neither hemorrhage nor necrosis seen in the specimen. Hormone replacement therapy was instituted, and the postoperative course was uncomplicated.

Partial resolution of the right ptosis and ophthalmoplegia had occurred by the eighth postoperative day, when he was discharged from the hospital. Slight ptosis was still present when he was seen two months after operation.

Comment

Surgical operations requiring cardiopulmonary bypass appear to constitute a specific risk for pituitary apoplexy. The literature has reports of 6 patients, including our 3, who sustained pituitary apoplexy during an open-heart operation. Five of these patients had an asymptomatic pituitary tumor, and 1 had a known tumor. An association between an operation on the heart and necrosis of a normal pituitary gland has also been described in the literature [6].

Cardiopulmonary bypass and the setting of a cardiac operation could induce pituitary apoplexy by several mechanisms: edema, tissue ischemia, and hemorrhage.



Sector computed axial tomogram of sella in Patient 3. The sella is expanded and eroded, and contains necrotic tumor (arrow).

Edema

As measured by weight gain, edema is commonly associated with cardiopulmonary bypass. The administration of intravenous fluids does not affect the edema, which appears to result from diverse causes.

Hemodilution with crystalloid is commonly used during cardiac operations to minimize the use of donor blood and to improve perfusion during bypass. In our patients, the pump-oxygenator and tubing were primed with crystalloid. On initiation of bypass, there is an abrupt dilution of plasma protein and a resulting decrease in the colloid osmotic pressure (COP). The COP typically decreases to 45% of the initial value and, on the average, increases to 84% of the initial value after 1 hour; the COP is usually normal 24 hours after bypass [7]. Presumably, the use of large amounts of crystalloid cardioplegic solution, which is drained into the venous circulation, will contribute to more sustained reduction in COP. With abrupt hemodilution, the increase in interstitial fluid pressure is more rapid in tissues having low compliance. Under these conditions, the increase in interstitial fluid pressure in a pituitary adenoma may be extreme, because, to a variable degree, the tumor is constrained within the pituitary fossa.

Edema may also result from a generalized inflammatory process associated with activation of complement. Complement activation occurs as a result of the contact of blood with the synthetic materials of the extracorporeal circuit [8]. Complement may also be activated by the complexes formed when anticoagulation with heparin is reversed by administration of protamine; this is found to occur *in vitro*, but there is evidence against this effect under clinical conditions [9].

There are other potential sources of generalized edema in association with cardiac operations. Edema may result from histamine release caused by administration of large doses of morphine [10], which was used as an anesthetic in Patient 1. Allergic reactions may occur to the drugs used, and the reactions to protamine in particular are notably common and severe [11]; such reactions were not seen in our 3 patients. Finally, increased venous pressure is a common cause of edema, and can result from either inadequate drainage during bypass or cardiac dysfunction following bypass.

Tissue Ischemia

Perfusion during bypass to tissues that, because of a pathological process, have merely adequate perfusion under normal hemodynamic conditions has not been studied. It seems likely that such tissues become ischemic under conditions common during cardiopulmonary bypass.

Hemodilution to a hematocrit of 20%, mean arterial pressures transiently as low as 30 mm Hg, and flows less than 2.2 L/min/m² may occur during bypass. This alteration in normal physiology appears to cause little ischemia of normal tissues [12]. However, under such conditions, compensatory mechanisms such as increased

oxygen extraction and preferential redistribution of blood flow toward the brain are required [13].

Pituitary adenomas may have a compromised blood supply because of compression of the meningeohypophyseal trunks, although the importance of this mechanism is debated [14]. In other instances, the vasculature within the tumor itself seems inadequate [15–17]. Thus, the reduced perfusion during bypass may be a factor in initiating ischemic necrosis of pituitary tumors.

Ischemia may also occur because of embolization. Antifoam agents (used in Patient 1), plastic fragments, aggregates of formed elements from the blood, and bubbles are emboli that arise in the extracorporeal circuit [18, 19]. In the case reports presented here, the effects of such possible emboli were minimized by the use of a 20- μ filter at the arterial outflow line of the bypass apparatus. Other emboli may arise within the patient's circulation during the course of the operation. Fragments of atheroma dislodged from the aorta, tissue or fragments of calcifications from valves, air ejected from cardiac chambers that have been opened, and clots present within the cardiac chambers are all potential sources of emboli in cardiac operations. Microembolization to a pituitary adenoma may be among the events precipitating pituitary apoplexy after bypass.

Hemorrhage

The vasculature of pituitary adenomas is often fragile, and anticoagulation has precipitated pituitary apoplexy [3, 20]. In patients undergoing cardiopulmonary bypass, anticoagulation is achieved before the initiation of bypass by the administration of heparin, and supplemental heparin is administered during bypass. After bypass, protamine is administered to reverse the effects of heparin. In the absence of major blood loss, the levels of clotting factors are usually adequate for normal coagulation. However, some abnormality of hemostasis occurs in virtually all patients after cardiopulmonary bypass. Heparin reversal is incomplete in up to 52% of patients [21]. Bleeding, related to fibrinolysis, may occur in some patients. The most frequent abnormalities of hemostasis are a reduction in the platelet count during bypass and partial platelet dysfunction [22]. Usually, abnormalities of hemostasis resolve within 24 hours following bypass.

Two of our 3 patients did not have hemorrhage within the tumor. These findings have been observed previously [20], which suggests that ischemia and edema may play a more important role than hemorrhage in the pathogenesis of apoplexy under these circumstances.

In the majority of patients, pituitary operation is recommended immediately after pituitary apoplexy [23, 24]. In our experience, neurosurgery can be safely performed in the early postoperative period following an open heart procedure.

In 1 of our patients, the presence of the pituitary adenoma was known preoperatively. Should such a circumstance occur again, it might be possible to reduce the risk of pituitary apoplexy by the use of a colloid-

containing solution to prime the bypass apparatus, by maintaining a higher hematocrit during bypass, by specifically avoiding low flows and pressures, and by prophylactic administration of antifibrinolytic agents and platelets after bypass. However, since patients with known pituitary adenomas rarely are seen for cardiac procedures, the effectiveness of such measures will remain unknown. More practically, the prompt diagnosis and the timely surgical treatment of these lesions appear to minimize the disability resulting from pituitary apoplexy as a complication of cardiopulmonary bypass.

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