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Laparoscopic removal of pheochromocytoma

Why? When? and Who? (Reflections on one case report)

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Abstract. Until now, the need for wide exposure and nonmanipulative dissection of pheochromocytoma has dictated the use of a large intraperitoneal transabdominal approach, which unfortunately results in a significant incidence of morbidity. A unilateral retroperitoneal approach guided by the refinements of new imaging techniques is less invasive but is associated with a small risk of incomplete cure. In one case report, we tested the hypothesis that laparoscopic surgery could combine the beneficial effects of both operative strategies without their respective side effects. We concluded that a laparoscopic approach combined with exclusive intraoperative infusion of nicardipine, a calcium-channel blocker, can be used to surgically remove pheochromocytoma under stable hemodynamic conditions. This provides better exposure of the anatomical structures than open surgery and allows a visual exploration of the entire abdominal cavity to exclude tumor multicentricity or ectopic sites in the case of inconclusive preoperative imaging investigations. Moreover, conversion to open surgery is always possible if needed.

Key words: Pheochromocytoma — Laparoscopy — Adrenalectomy — Calcium-channel blocker

Pheochromocytoma remains a challenging tumor to remove. Owing to continuing improvements in anesthetic management of pheochromocytoma, especially during the past decade, its surgical treatment can now be carried out more safely. In spite of the development and refinements of accurate and noninvasive imaging techniques for localization of pheochromocytoma, most surgeons still recommend a wide intraperitoneal operative approach to explore the entire abdominal cavity [2, 5, 12]. Because of the significant incidence of morbidity associated with the anterior intraperitoneal approach, a lateral retroperitoneal approach was proposed despite a small risk of missing bilateral, metastatic, or extraadrenal tumors [2, 5]. Laparoscopic surgery should theoretically allow an equivalent exposure of the tumor and adequate exploration of the abdominal cavity while decreasing postoperative morbidity. However, increased intraabdominal pressure induces hemodynamic changes [6], particularly in the intraabdominal viscera [1], which may be undesirable in a patient with a pheochromocytoma. Moreover, the effects of pneumoperitoneum on catecholamine release in the case of pheochromocytoma are unknown. In this case report we discuss the feasibility, hemodynamic safety, and potential benefits of laparoscopic adrenalectomy for pheochromocytoma. Guidelines for this surgical approach will be proposed that follow from our results.

Case report and workup

A 32-year-old man (100 kg, 187 cm) was referred for evaluation of severe hypertension, worsening since June 1990, date of the first symptoms. At that time, he complained of severe headache, sweating, palpitations, nervousness, cutaneous flush and pallor of the face, tremor, weakness, fatigue, shortness of breath, and paroxysmal hypertension precipitated by sport activities. Complete cardiac evaluation was normal.

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Morphological and functional exploration of the kidneys remained negative. Thyroid function was normal. Plasma and urine concentrations of catecholamines and their metabolites were normal except for urine excretion of vanillylmandelic acid (VMA), which was slightly elevated (VMA: 5.1 mg/24 h; normal values: 1.4–4.7 mg/24 h). Computerized tomography of the suprarenal glands and nuclear scanning with [^{131}I]-meta iodobenzylguanidin (^{131}I-MIBG) were negative. The review of the family history revealed hypertension in his father and one of his brothers. No endocrine diseases were detected among his immediate relatives. The hypertension considered as essential was therefore symptomatically treated by amlodipin (Amlor), a calcium-channel blocker, enalopril maleas (Renitec), an angiotensin-converting-enzyme inhibitor, and hydrochlorothiazid (Esidrex), a diuretic agent. Hypertension remained, however, poorly controlled, while the associated symptoms persisted and were disabling.

In October 1993, he was admitted to the emergency unit for persistent and intractable hypertension above 300 mmHg accompanied with very severe headache and confusion. Physical examination was normal except for the evidence of excessive sweating, tachycardia, and mild obesity. The skin exhibited no neurofibromatosis, portwine stains or café-au-lait spots. No abdominal tumor was palpable. Symptoms did not seem to be initiated by voiding. No hematuria was noticed. Clinically suspected diagnosis of pheochromocytoma was confirmed by measurements of catecholamines and their metabolites. The plasma concentrations of catecholamines were as follows: epinephrine, 12 ng/l (normal values: 0–100 ng/l); norepinephrine, 10,574 ng/l (normal values: 0–500 ng/l). Twenty-four hour urine excretion of VMA was at 27.7 mg/24 h (normal values: 1.4–4.7 mg/24 h), of epinephrine and norepinephrine was, respectively, 20 μg/24 h (normal values: 3–30 μg/24 h) and 1,929 μg/24 h (normal values: 5–60 μg/24 h), and of normetanephrine, 8,969 μg/24 h (normal values: 0–500 μg/24 h). Dopamine levels were normal [14].

Concomitant assays for parathormone and calcitonin in search of multiple endocrine neoplasia were within normal ranges. Although these important biochemical disturbances strongly suggested the diagnosis of a pheochromocytoma, nuclear scanning with ^{131}I MIBG still failed to demonstrate any tumoral process. Position emission tomography (PET scan) using C-11 hydroxyephedrine and nuclear magnetic resonance (NMR), however, clearly localized a 4-cm-diameter tumor in the right suprarenal gland (Fig. 1) No additional tumor was found in the contralateral suprarenal gland or in an ectopic position such as along the paraspinal axis from the diaphragm to pelvis.

Fig. 1. Position emission tomography (PET scan, using C-11 hydroxyephedrine) of the right adrenal tumor.

Materials and methods

Preoperative preparation

Previous treatment was modified and implemented to control hypertension. Antihypertensive medications included atenonol (Tenormin), a β-blocking agent; amlodipin (Amlor) and pinacidil (Therapress), two calcium-channel blockers; and prazosine chlorydrate (Minipress), a specific α_1-receptor blocker. This treatment was maintained until the day of operation.

Anesthesia and intraoperative management

Premedication consisted of 75 mg hydroxyzine and 1 mg alprazolam orally 1 h before induction of anesthesia. A large-bore intravenous catheter was inserted in an antecubital vein and the left radial artery was cannulated for direct determination of blood pressure prior to the induction of anesthesia. Routine monitoring consisted of two-lead electrocardiogram, oscillometric arterial blood pressure, capnography, and pulse oximetry (AS/3, Datex, Helsinki, Finland). Nicardipine infusion was started 15 min before the induction of anesthesia at a rate of 1 $\mu g\ kg^{-1}\ min^{-1}$. Anesthesia was induced with 0.2 mg/kg etomidate and 0.5 μg/kg sufentanil. Orotracheal intubation was facilitated with 0.5 mg/kg atracurium. After the induction of anesthesia, a flow-directed pulmonary artery catheter (Swan-Ganz, Baxter) was inserted via the right internal jugular vein.

Anesthesia was maintained with 0.25 $\mu g\ kg^{-1}\ h^{-1}$ sufentanil and N_2O/O_2 (1:1). Muscle relaxation was provided by a continuous infusion of 0.3 mg/kg atracurium. Hemodynamic parameters (mean arterial pressure [MAP], right atrial pressure [RAP], pulmonary artery pressure [PAP] were continuously monitored on the AS/3 Datex monitor. Pulmonary capillary wedge pressure (PCWP) and cardiac output were measured at the end of the expiratory cycle, using the AS/3 monitor. Nicardipine infusion was adjusted to keep systolic arterial pressure between 150 and 120 mmHg. If heart rate increased above 100 beats per min, 5 mg acebutolol, a β-blocking agent, was administered intravenously. Arterial blood samples were collected for determination of plasma concentrations of epinephrine and norepinephrine before induction of anesthesia (T1), after induction of anesthesia (T2), after tilting the patient in the lateral position and before peritoneal insufflation (T3), 5, 15, and 30 min after peritoneal insufflation (T4, T5, T6), during adrenal gland manipulation (T7), after the clamping of the right adrenal vein (T8), after gland resection (T9), and at the end of surgery (T10). Hemodynamics were measured at the same time points except before induction of anesthesia since the pulmonary artery catheter was not inserted yet.

Plasma and urine concentrations of epinephrine and norepinephrine were measured using high-pressure liquid chromatography with electrochemical detection [14].

Coelioscopic operative approach

After the induction of anesthesia, the patient was turned gently to the left lateral position. A firm pillow was placed beneath the left

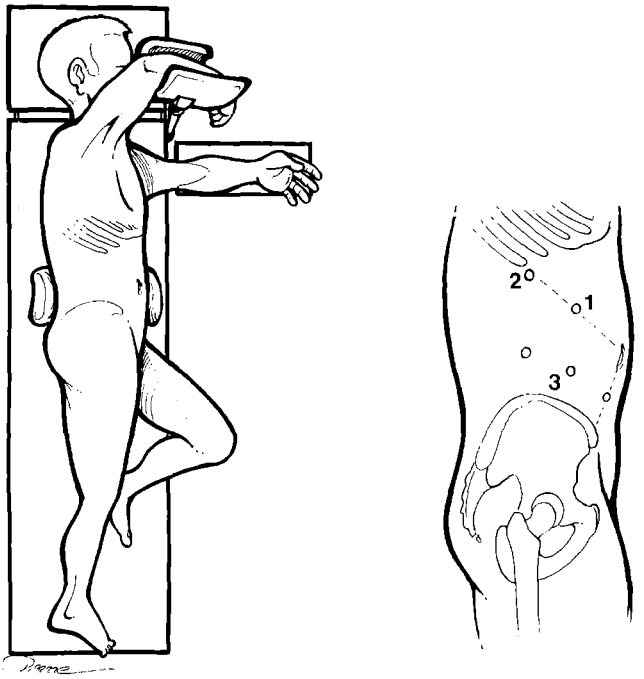

Fig. 2. Schematic representation of the insertion sites of the video camera (*1*), the hepatic retractor (*2*), and the other hand laparoscopic instruments (*3*).

flank to extend the operative area on the right flank (Fig. 2). Intraperitoneal CO_2 insufflation was carried out through a small periumbilical incision. Pneumoperitoneum was automatically maintained at 14 mmHg. The camera system was inserted in the middle of a line joining the umbilic and the tip of the 12th rib. A liver retractor was inserted through a small incision just below the costal roof. Irrigation-suction device, electrocautery, and other hand instruments were introduced in the abdomen through small incisions around the video camera (Fig. 2). This transabdominal approach allowed a thorough examination of the general abdominal cavity. The hepatic flexure of the colon was then mobilized and the second part of the duodenum was freed by dividing its lateral avascular reflection (Kocher maneuver). Both organs spontaneously sagged downward and fell away from the retroperitoneum area, without any need for retraction because of the patient position and the pneumoperitoneum. Posterior peritoneal attachments of the liver were then incised and right lobe was gently retracted upward. This maneuver largely exposed the underlying vena cava and the pheochromocytoma of the right adrenal gland overlying the superior pole of the kidney. Leaves of the peritoneum and Gerota's fascia were then dissected off the tumor. Surrounding fascial attachments of the fat lateral and superior portions and fascial fixation to the kidney were divided using the electrocauter. The vena cava was then rolled away, exposing the adrenal vein, which was secured by metal clips. The pheochromocytoma was then removed from the abdominal cavity, using a specimen retrieval plastic bag introduced through a 10-mm trocar and secondarily exteriorized by a 3-cm incision of the abdominal wall in the right iliac fossa. No drainage was required at the end of the surgical procedure, which lasted less than 2.5 h.

Postoperative management

The patient woke up in the operating room. Strict attention was then paid to fluid management by careful monitoring of the pulmonary capillary wedge pressure. Blood pressure was supported, if needed, using fluid infusion (polygelinum, Haemaccel, Behring, Marburg, Germany) rather than vasopressors.

Results

Hemodynamic data during the operation

In this patient, three events resulted in the release of catecholamines: induction of anesthesia, induction of pneumoperitoneum, and adrenal gland manipulation. Norepinephrine plasma concentrations were increased by 25%, 33%, and 100%, respectively, as compared with preoperative value. The use of a continuous infusion of nicardipine allowed one to markedly attenuate the hemodynamic changes secondary to these catecholamine releases. Systolic arterial blood pressure (SAP) remained below 160 mmHg, i.e., less than 20% above preoperative SAP (142 mmHg) during the whole surgical procedure except during the last adrenal manipulation when the gland was retracted to expose and dissect the adrenal vein. During this manipulation, SAP rose up to 195 mmHg, which required an increase in the infusion rate of nicardipine to 6 $\mu g\ kg^{-1}\ min^{-1}$ and the administration of 5 mg acebutolol. The effect of the treatment was very effective since SAP decreased below 180 mmHg within 5 min. It should be noted that during the dissection phase (T4–T6), catecholamine plasma concentrations and hemodynamics remained stable. No ventricular arrhythmias were observed. No vasoconstrictive drug nor inotropic agent was needed. Infusion of only 1,000 ml colloid solution (polygelinum, Haemaccel) and 500 ml lactated-Ringer's solution was required intraoperatively. No significant bleeding occurred. As an average, nicardipine was infused at a rate of $2\mu g\ kg^{-1}\ min^{-1}$. Infusion was stopped immediately after ligation of the adrenal vein.

Pathology

Cut section of the tumor was typically pink-tan in color, with foci of hemorrhage, calcification, necrosis, and gelatinous change. Microscopically, the tumors cells were arranged in a cordlike pattern in a very vascular stroma. No mitotic figures and no microscopic evidence of intravascular or extracapsular extension were shown.

Patient outcome

The postoperative course was uneventful. The patient remained normotensive with no antihypertensive drugs, confirming successful removal of the pheochromocytoma. He deambulated and ate normally on the 1st postoperative day. His solely complaint was moderate shoulder-tip pain for a few days, related to pneumoperitoneum. On the 3rd postoperative day, 24-h urine excretion for catecholamines and metanephrines was normal (epinephrine: 4 μg/24 h, norepinephrine: 34 μg/24 h, normetanephrine: <350 μg/24 h). The patient was discharged on the 4th postoperative day.

Discussion

Is there yet a need for broad surgical exploration?

Until now, the surgical removal of pheochromocytoma required a wide abdominal incision to allow wide and rapid exposure of the adrenal vein without manipulative dissection, and to explore the entire abdominal cavity because of the potential multicentricity and anatomic variability of the tumors encountered in approximately 10% of patients [2, 5, 12]. Abdominal and thoracoabdominal approaches, while providing an excellent exposure, are, however, associated with a significant incidence of morbidity [2, 5, 13]: wound infection, evisceration, ileus, urinary retention, splenectomy, peritoneal adhesions, pleural effusion, pneumonia, need for blood transfusions, and long hospital stay. Development of methods for accurate, reliable, and noninvasive preoperative localization of the tumor such as CT scan, ^{131}I-MIBG scintigraphy, NMR [4, 8, 11], or, more recently in our experience, PET scan, led some authors to propose a direct approach of most pheochromocytomas through a unilateral retroperitoneal flank approach. This approach reduces the incidence of morbidity as compared with transabdominal broad surgical exploration but increases the risk of missing synchronous tumors [2, 5]. In defining the proper operative strategy for excision of pheochromocytoma, we wondered if the laparoscopic approach could meet the requisites of safety and complete cure, and at the same time decrease postoperative morbidity.

Does laparoscopic approach provide some advantages?

Like Gagner et al. [3], we used laparoscopic minimal invasive surgery for adrenalectomy [9]. Patients were operated in the lateral position, which provides an excellent and wide exposure of the adrenal gland. Indeed, in this position and with pneumoperitoneum, the hepatic flexure of the colon and the second part of the duodenum in case of right adrenalectomy, or the splenic flexure of the colon in case of adrenalectomy, is easily mobilized and freed, and subsequently sags spontaneously downward away from the retroperitoneal area. No additional device other than a smooth hepatic or splenopancreatic retractor is needed to largely expose the superior pole of the kidney and the adrenal gland. In this lateral position, the entire abdominal cavity including the periaortic regions can be adequately examined, but not the contralateral uninvolved adrenal gland. If preoperative imaging techniques do not demonstrate a normal-sized contralateral adrenal gland, the supine position must be preferred to enable examination of both adrenal glands. On the other hand, because of the tightness and precision of the laparoscopic graspers or scissors, the large exposure permitted by this laparoscopic approach, and the excellent view secondary to the magnification of the video camera, the fat surrounding the adrenal gland rather than the capsule can be gradually dissected away from the tumor. Therefore, laparoscopic surgery of pheochromocytoma allows one "to dissect the patient away from the tumor" [12] more easily than in open surgery, especially in obese patients, minimizes direct manipulation of the tumor, and thus reduces the release of catecholamines. The superior, inferior, medial, and posterior aspects of the gland are successively freed in order to progressively and finally pediculize the gland on the main adrenal vein. Small clips and unipolar electrocautery are used for the hemostasis of the many fine arterial twigs that pass into the periphery of the gland from the surrounding fat. Accordingly, in our patient, catecholamine plasma concentrations and hemodynamics remained stable during the dissection phase. Catecholamines and SAP increased when the vena cava was rolled away and the adrenal gland was retracted to expose the adrenal vein to be secured by metal clips. Clamping of the adrenal vein is much easier when the adrenal gland is completely freed and pediculized on the adrenal vein, as during the laparoscopic approach. On the contrary, during open surgery, the prerequisite for quick control of the venous effluent of a minimally dissected adrenal gland, particularly right sided, always remains a challenge. Finally, the possibility of easily converting laparoscopy to open surgery is another advantage of this approach.

Are hemodynamics influenced by laparoscopic approach?

Surgery is the mainstay of the treatment of pheochromocytoma since it is the only treatment that can result in cure. However, it has been associated with perioperative hemodynamic instability and arrhythmias. Preoperative preparation with α-adrenergic blocking agents allows one to partially control intraoperative hypertension during surgery. Since the recent demonstration of the beneficial effects of nicardipine, a calcium-channel blocker, on the hemodynamic stability during removal of pheochromocytoma [10], all our patients have been adequately managed using this drug. In a series of five consecutive pheochromocytomas treated by transperitoneal open surgery, we only observed small changes in blood pressure and heart-rate changes despite release of catecholamines, owing to the direct vasodilatation induced by nicardipine [7]. Using the same protocol for intraoperative nicardipine administration, we studied the hemodynamics and fluid and drug requirements during laparoscopic removal of a pheochromocytoma. Patient hemodynamics remained very stable. Arterial blood pressure slightly increased when the patient was turned in the operative position but this change was not related to an increase in catecholamine plasma concentration. On the other hand, peritoneal insufflation resulted in a rapid increase (~10%) of catecholamine plasma concentrations. Although this increase might be considered insignificant when expressed in percent of preinsufflation value, the actual increase (~1,000 ng/ml)

Table I. Intraoperative hemodynamic data and catecholamines release[a]

Parameters	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
MAP (mmHg)	86	76	85	90	94	113	116	72	66	65
HR (beats/min)	59	44	47	47	47	56	88	64	61	58
RAP (mmHg)	—	10	13	15	19	20	14	15	14	12
PCWP (mmHg)	—	7	12	16	16	21	11	14	12	12
CI ($l \cdot min^{-1} \cdot m^{-2}$)	—	2.82	2.49	3.00	3.11	4.18	5.78	4.34	3.07	3.59
SVR (dynes · s cm^{-5})	—	886	1076	936	903	831	662	493	630	551
PVR (dynes · s cm^{-5})	—	67	88	94	71	102	74	67	75	51
nicardipine (μg kg^{-1} min^{-1})	—	1	2	2	2	2	6	4	0	0
Catecholamine plasma levels										
Epinephrine (ng/ml)	116	71	61	113	297	942	2,083	316	145	233
Norepinephrine (ng/ml)	7,803	9,581	9,365	10,407	10,168	10,811	15,925	13,328	12,010	4,653

[a] T1, before induction of anesthesia; T2, after induction of anesthesia, T3, after tilting the patient in the left lateral position; T4, 5 min after peritoneal insufflation; T5, 15 min after peritoneal insufflation; T6, 30 min after peritoneal insufflation; T7, tumor manipulation; T8, adrenal vein clamping; T9, 10 min after tumor removal; T10, end of surgery.
MAP, mean arterial blood pressure; HR, heart rate; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance

represents two times the upper normal limit of norepinephrine and could induce substantial hemodynamic effects. The use of nicardipine infusion, however, prevented these hemodynamic changes. We must therefore be aware that pneumoperitoneum can induce catecholamine release by the pheochromocytoma and be ready to respond to this release to reduce or prevent its secondary hemodynamic effect using a vasodilatator agent. The use of nicardipine probably explains why systemic vascular resistance, expected to increase during penumoperitoneum, did not rise (Table 1) [6]. As during open surgery, nicardipine proved to be very effective in preventing or correcting the hemodynamic changes. Despite a twofold increase of norepinephrine, plasma concentration, which in this case corresponded to a concentration 25 times superior to normal value, only small hemodynamic disturbances, quickly reversible, were observed during adrenal manipulation and just before clamping of the adrenal vein. Blood loss was minimal and no transfusion was necessary. Only plasma expanders were required intra- and postoperatively (total amount of 2.8 l/24 first h).

Is laparoscopic surgery the future for removal of pheochromocytoma?

This case report suggests the feasibility and safety of laparoscopic removal of pheochromocytoma using intraoperative infusion of nicardipine. Given the reliability of imaging techniques to precisely localize pheochromocytoma, the possibility of extensive visual exploration under laparoscopy, and the ease of intraoperative conversion to open surgery, we consider that the laparoscopic approach might be considered for the treatment of most pheochromocytomas, even bilateral, but more particularly when preoperative imaging suggests a normal-sized contralateral adrenal gland. In this latter case, the patient can be immediately tilted to the lateral position, which allows easier tumor exposure for removal. On the other hand, preoperative demonstration of an extraadrenal mass should not be considered a contraindication for the laparoscopic approach. Nevertheless, further studies are needed to confirm this strategy and to define precisely the indications for laparoscopic surgery in pheochromocytoma.

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