A rare case of extra-adrenal pheochromocytoma masquerading as an ovarian mass treated by laparoscopic surgery

S. Montemurro[1], E. Ruggieri[1], E. Maselli, A. F. Zito[2], F. Chiumarulo[3], G. Gargano[4]

[1]Department of Surgical Oncology, [2]Department of Pathology, [3]Department of Anesthesiology, [4]Department of Gynecological Oncology
Scientific Institute for Research and Treatment of Cancer "Giovanni Paolo II", Bari (Italy)

Summary

Background. Extra-adrenal pheochromocytoma, or paraganglioma, is a rare tumour arising from paraganglion chromaffin cells of the sympathetic nervous system. In adults, pheochromocytomas are often called the "10% tumor" because approximately 10% occur above the diaphragm, 10% of intraabdominal pheochromocytomas are extra-adrenal, 10% are bilateral, 10% are multiple, 10% are familial, 10% are malignant, and 10% recur postoperatively. In children, instead, this tumor occurs in ectopic sites in 30-40% of the cases. This paper reports the successful laparoscopic resection of an extra-adrenal pheochromocytoma, simulating an ovarian tumor, combined with a laparoscopic cholecystectomy for gallstones.

Case report. The case of a 48-year-old woman affected by an extra-adrenal pheochromocytoma that had been unsuspected for a long time is presented. The patient had some clinical symptoms that had been taken for a climacteric syndrome given her premenopausal age. The atypical and rare location of the pheochromocytoma (parauterine) had contributed to misdiagnosing it as an ovarian tumor. Laparoscopic surgery was chosen for the removal of the tumor because it is a safe technique requiring a shorter hospital stay; a concomitant cholecystectomy was performed due to the presence of gallstones.

Conclusion. Surgical resection is the only treatment option for extra-adrenal pheochromocytomas. With adequate preoperative adrenergic receptor blockers and vascular filling, the laparoscopic approach appears to be a valid alternative to open surgery for paragangliomas. Gynecologists should consider the possibility, although rare, of an extra-adrenal pheocromocytoma when preparing to surgically remove a pelvic mass.

Key Words: Pheochromocytoma; Paraganglioma; Laparoscopic surgery; Catecholamines; Pelvic mass.

Introduction

Pheochromocytoma is a rare tumor arising from the neuroectodermal cells (chromaffin) of the sympathetic nervous system. It may occur in both sexes, with a slight propensity for presentation in women, and at any age, although it is rare after 60 [1, 2].

Chromaffin tissue is more evident in newborns while it tends to regress in adults [3, 4] (Figure 1).

In children 60-70% of pheochromocytomas arise in the adrenal medulla and 30-40% in extra-adrenal sites. In adults, 90% of the tumors are found in the adrenal gland (especially the right gland with an incidence of 3:2 in terms of left to right), and 10% are extra-adrenal (wherever chromaffin tissue is present) [5, 6].

In adults the most frequent extra-adrenal site (70-85%) is the retroperitoneum: along the paraganglia of the sympathetic chain, along the course of the aorta, along the renal vessels, behind the pancreas, at the organ of Zuckerkandl, around the ureter or in the urinary bladder. The parauterine site is extremely rare. Retroperitoneal pheochromocytomas are often functional and malignant (50%). They may also be found in the thorax, in the mediastinum and heart (10-12%). In the neck (2%), they develop along the carotid body. Head and neck pheochromocytomas are usually non-functional and benign [1, 7-9].

In 10% of patients pheochromocytomas are bilateral, multiple, and may also be a part of familial syndromes (MEN, neurofibromatosis, Von Hippel-Lindau disease, Sturge-Weber syndrome and tuberous sclerosis).

The clinical signs and symptoms are extremely variable, depending on the secretion of catecholamines (epinephrine, norepinephrine, dopamine). Since pheochromocytomas sometimes produce and release various hormonal substances responsible for numerous and multifarious clinical manifestations they have been defined as "the great mime" (Table 1) [3, 10].

The presence of this tumor should be suspected in patients with high blood pressure that do not respond to any antihypertensive therapy. Hypertension is often associated with headache, palpitations, sweating and intolerance to carbohydrates or diabetes [1, 11-14]. Other symptoms may be present (Table 2) [11].

In these patients the diagnosis is established by measuring catecholamines and/or the metabolites in the plasma and urine. Once elevated levels of catecholamines have been ascertained, the anatomical localization (adrenal gland or extra-adrenal sites) is determined by computed tomography (CT) or magnetic resonance imaging (MRI). Scintigraphy with meta-iodobenzylguanidine (MIBG) is considered a further useful investigation.

Revised manuscript accepted for publication February 26, 2007

Table 1. — *Principal hormonal substances produced by pheochromocytoma.*

Epinephrine	Norepinephrine	Dopamine
ACTH	Beta-endorphine	Somatostatin
VIP	Substance P	Interleukin-6
PTH-Related Protein	Neuropeptide Y	Calcitonin
Metenkephalin	Serotonin	Gastrin
Neurotensin	IGF-II	Pancreastatin

Data from Goldfien A., 1995 [10].

After adequate pharmacological preparation with adrenergic receptor blockers and vascular filling, surgical resection of the tumor is the only treatment modality for these cases.

The histological examination is unable to distinguish between benign and malignant pheochromocytomas. Evidence for local invasion and/or presence of distant metastases (bone, liver, lymph nodes and lungs) may establish malignancy [1, 9, 14-19].

This paper reports the successful laparoscopic resection of an extra-adrenal pheochromocytoma, simulating an ovarian tumor, combined with a laparoscopic cholecystectomy for gallstones.

Case Report

In September 2002, a 48-year-old woman was admitted to another hospital because she had been suffering from type 2 diabetes mellitus and hypertension for two years which had been unsuccessfully treated with oral hypoglycemic drugs and ACE inhibitors. Based on ultrasonography of the abdomen and pelvis an ovarian neoplasm was suspected so the patient was submitted to laparoscopy. Resection could not be performed because of early dangerous bleeding associated with severe hypertensive crises and the patient was then referred to the Surgical Department of our hospital for further investigation and treatment.

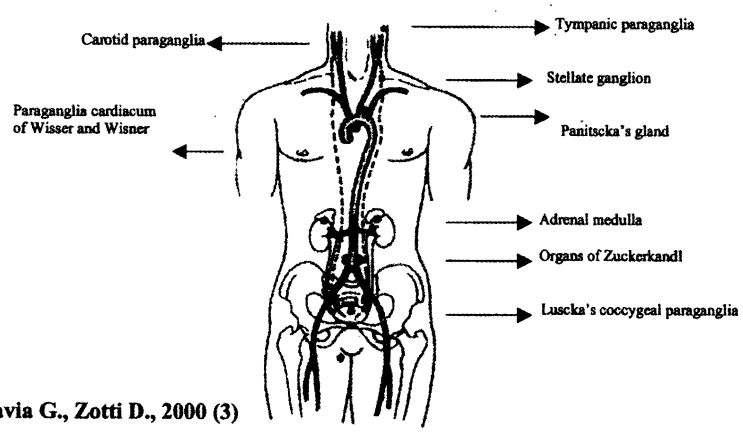
The patient reported experiencing some hypertensive crises (240/120 mmHg) preceded by palpitations, sweating, headache and hyperglycemic peaks (over 400 mg/100 ml). Blood chemistry tests showed hyperglycemia, anemia caused by iron deficiency, and normal tumor marker values (CEA, alpha-FP, CA 125, CA 15/3, CA 19/9, CA 72/4); 24-hour urinary catecholamine measurements revealed high levels of epinephrine and norepinephrine. Normal values of serum calcium, parathyroid hormone and calcitonin ruled out polyendocrine syndrome.

Table 2. — *Frequency of symptoms in 100 patients with pheochromocytoma.*

Symptoms	%
Headache	80
Excessive perspiration	71
Palpitation (with or without tachycardia)	64
Pallor	42
Nausea (with or without vomiting)	42
Tremor or trembling	31
Weakness or exhaustion	28
Nervousness or anxiety	22
Epigastric pain	22
Chest pain	19
Dyspnea	19
Flushing or warmth	18
Numbness or paresthesia	11
Blurring of vision	11
Tightness of throat	8
Dizziness or faintness	8
Convulsions	5
Neck-shoulder pain	5
Extremity pain	4
Flank pain	4
Tinnitus	3
Dysarthria	3
Gagging	3
Bradycardia	3
Back pain	3
Coughing	1
Yawning	1
Syncope	1
Unsteadiness	1
Hunger	1

Data from Thomas J.E., Rooke E.D., Kvale W.F., 1974 [11].

Abdominal-pelvic MR and aortography detected an 8 cm solid and nonhomogeneous parauterine mass at the bifurcation between the left internal and external iliac arteries. The mass was hypervascular in the arterial phase with persistent enhance-



Data from D'Amico D., Favia G., Zotti D., 2000 (3)

Figure 1. — Distribution of chromaffin tissue in adults.

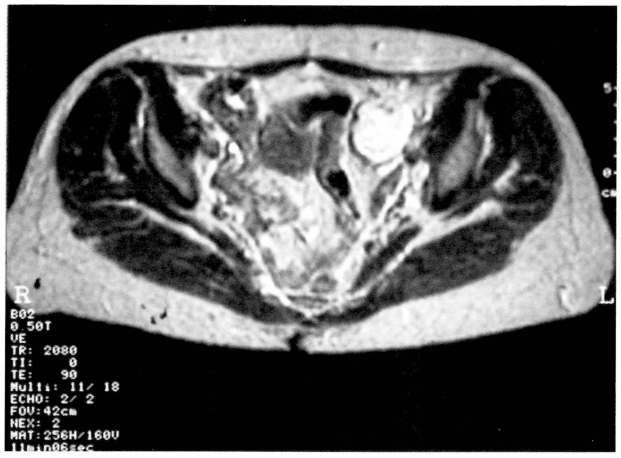


Figure 2. — MR image: a persistently enhanced a solid mass (8 cm) is evident in the pelvis.

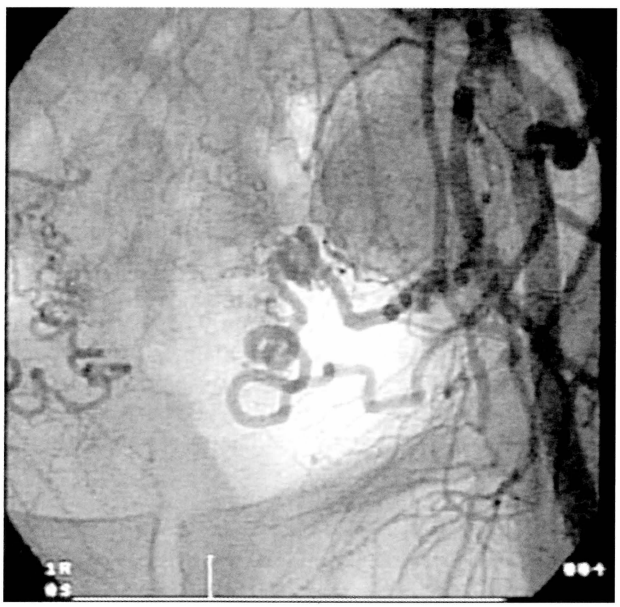


Figure 3. — Angiography: the mass, with its neovasculature, is located between the left internal and external iliac vessels.

ment and presence of neovasculature (Figures 2 and 3). Gallbladder stones were also found while no renal artery stenosis or subdiaphragmatic adenopathies were present. The (^{131}I) metaiodo MIBG scan showed a positive uptake and no other distant localizations.

The patient was treated with insulin and alpha-adrenergic receptor blockers (doxazosin 4 mg/daily) for three weeks.

After two weeks of treatment her 24-hour blood pressure readings were normal. An electrocardiogram (ECG) showed normal sinus rhythm.

In the preoperative period, vascular filling was performed with plasma expanders and lactated Ringer's solution.

The patient was premedicated with midazolam and fentanyl and general anesthesia was induced with fentanyl, thiopental and cisatracurium IV. Orotracheal intubation was performed and anesthesia was maintained with N2O, O2, sevoflurane and supplementary doses of fentanyl and cisatracurium. Hemodynamic (HR, BP, CPV) and respiratory (ETCO2,SO2) parameters were monitored throughout the surgical procedure.

After induction of general anesthesia the patient was placed in the Trendelenburg position. The laparoscopic procedure was started by introducing a Veress needle to obtain a pneumoperitoneum; the first 10-mm trocar was then placed in the umbilical region and, under laparoscopic guidance with a 30° lens, a second 10-mm trocar was positioned in the suprapubic region and a third 5-mm trocar in the left flank thus forming a triangle. The pelvic mass appeared lumpy, dark-bluish and hypervascular, surrounded by large varicose veins and was very close to the left ovary and tube. It was supplied by anomalous branches of the left ovarian blood vessels in the upper side and of the left uterine blood vessels in lower side. The anomalous blood vessels feeding into the neoplasm were doubly clipped and then divided. After sharp dissection from the left ovary and tube, the tumor was resected and placed into a retrieval bag (EndopouchPRO®-Ethicon ENDO-SURGERY) and removed. Another 10-mm trocar was inserted in the left hypochondriac region for the cholecystectomy.

Finally, a pelvic drain was positioned and, after adequately controlling any bleeding, the pneumoperitoneum was evacuated. The overall surgical time was 204 minutes and blood loss was 50 ml.

Frozen section histology confirmed the diagnosis of extra-adrenal pheochromocytoma and the definitive histology demonstrated focal invasion of the tumor capsule and blood vessels (Figures 4 A and B).

Short-lasting, slight blood pressure elevations (180/100 mmHg) occurred at the induction of anesthesia and before resection of the mass, but not such as to require medication. Unremarkable hypotension (90/60 mmHg) appeared during clamping of the blood vessels and in the early postoperative period. It was treated with vasoactive catecholamines (norepinephrine) and albumin infusion until normalization of blood pressure. The heart rate was regular, without tachy- or arhythmia. Administration of insulin was unnecessary during both the intra- and postoperative periods because blood glucose levels were normal.

Results

The postoperative course was smooth and uneventful and the patient was discharged from hospital on postoperative day 5.

At her follow-up visit after 48 months the patient was asymptomatic and free from tumor recurrence but with a slight glucose intolerance which is being treated with oral hypoglycemic drugs.

Discussion

Extra-adrenal pheochromocytoma is a tumor with extremely variable clinical manifestations which may even be asymptomatic (17% of cases) [1, 2, 20]. Some tumors tend to excrete lesser amounts of catecholamines thus compounding the difficulty of making a correct diagnosis [21]. Tohya *et al.* described a clinical case of a patient whose symptoms did not suggest an excess of catecholamines. The initial diagnosis was an ultrasonographically detected ovarian mass which later proved to be a pheochromocytoma upon surgical removal [22].

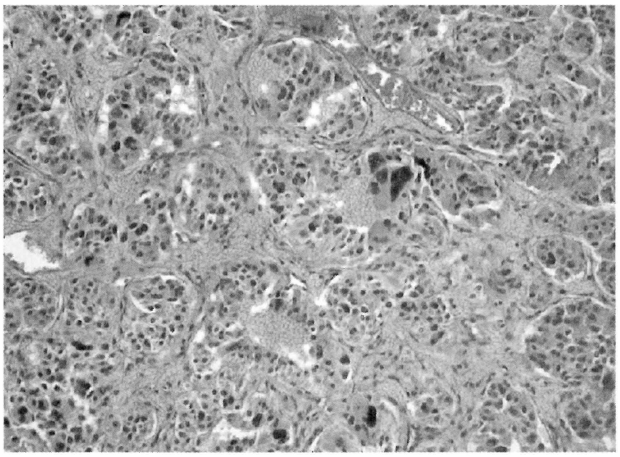


Figure 4 A. — Distinct nets of tumor cells surrounded by dilated sinusoids; some cells show pleomorphic nuclei.

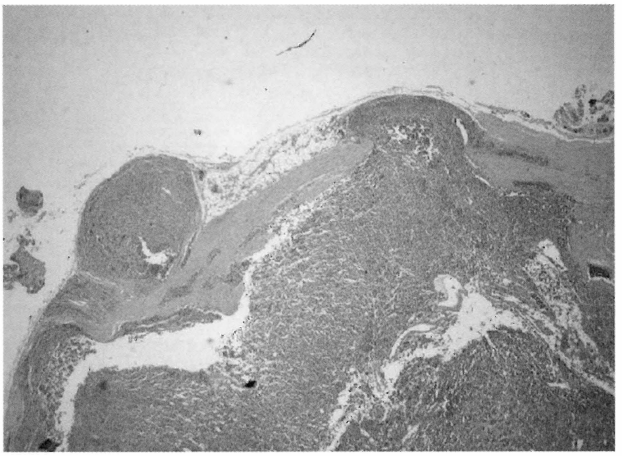


Figure 4 B. ·— The tumor is surrounded by a thick fibrous capsule penetrated by neoplastic cells.

About 30-60% of pheochromocytomas are found unexpectedly at post-mortem examination [1, 20].

Pheochromocytoma should always be suspected before surgery when a retroperitoneal mass is found as it may be a life-threatening condition for the patient. Rabii *et al.* reported the case of a 60-year-old man with an unsuspected paraganglioma who died after surgery. Ultrasonography (US) and CT had detected a retroperitoneal mass and the patient had complained of right lumbar pain but presented no other signs or symptoms. Surgical resection of the mass was performed without adequate preparation and during the procedure ventricular fibrillation occurred followed by bradycardia and irreversible cardiac arrest [23].

Pregnancy complicated by a pheochromocytoma is a dangerous and potentially fatal condition. An unsuspected pheochromocytoma is associated with maternal and fetal mortality rates of 58% and 50%, respectively, because it is often confused with pre- or eclampsia; even with an established diagnosis, maternal and fetal mortality rates have been reported to be 17% and 40%, respectively [1, 2, 16, 24-26].

When clinical manifestations of pheochromocytoma are present hypertension is frequently observed. In the study by O'Riordain *et al.*, concerning 66 patients operated on due to functional extra-adrenal paragangliomas, 83% of the patients were hypertensive. Other frequent symptoms were headache, palpitations and sweating [14].

Sometimes, extra-adrenal pheochromocytomas present with other symptoms that are related to the specific location of the tumor and may help localize it (e.g., micturition and hematuria in bladder paragangliomas, or cranial nerve deficits in intra-cranial paragangliomas, etc.) [16].

If the presence of a pheochromocytoma is suspected, biochemical and instrumental tests are required to establish a definite diagnosis and detect the location of the tumor.

In all diagnostic protocols, the first step is to measure the levels of plasma and urinary catecholamines and/or their metabolites. Measurement of urinary catecholamines has a higher specificity (100%) and sensitivity (97%) than that of plasma catecholamines [1, 17, 21, 27-29]. In our clinical case both urinary and plasma catecholamines were elevated.

Sometimes an asymptomatic or paucisymptomatic pheochromocytoma may be first found at US, a common non-invasive diagnostic examination [30].

Once increased catecholamine levels have been ascertained, CT or MRI are needed to detect the adrenal or ectopic locations. These examinations have a high sensitivity (98%) and specificity (98%) [1, 31-36].

Scintigraphy after administration of I^{131} MIBG is considered a further useful test for the diagnosis and the follow-up of pheochromocytomas with a sensitivity of 90% and specificity of 100% [1, 35-37]. The combination of a MIBG scan with an MRI examination is able to locate even smaller sized neoplasms [35].

In a recent Swedish study, Trampal et al. evaluated 19 patients with suspected adrenal pheochromocytomas by carbon 11 hydroxyephedrine (HED) positron emission tomography (PET). The HED-PET outcomes were validated and confirmed by surgical and histopathological evaluation. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of HED-PET in the detection of pheochromocytomas were 92%, 100%, 100%, 87.5% and 95%, respectively. The authors concluded that HED-PET may be useful in the detection of pheochromocytomas, providing a high level of accuracy [38].

Since the first report by Gagner *et al.* in 1992 [39] laparoscopic adrenalectomy has been used as a valid alternative technique to open surgery, also for functional endocrine tumors.

Currently, laparoscopic ultrasonography may be relied on to provide details substituting the tactile information acquired at open surgery. It may define the anatomical relations and vascularization of the tumor, and verify whether the mass is contained in its capsule so that the surgeon may remove it maintaining its integrity [40-42]. Hence, laparoscopic surgery has the advantage of reducing morbidity and hospital stay. There is a vast literature describing this type of surgery for adrenal pheochromo-

cytomas [39, 43-48], because the adrenal gland is the most common site. Conversely, there are few papers on the rarer extra-adrenal pheochromocytomas. Furthermore, laparoscopic procedures need to be adapted and changed according to the location and relation the neoplasm has with the neighbouring organs and vascular structures [40, 42, 49, 50].

In any case, before open or laparoscopic surgery, hematocrit and blood volume values will have to be normalized and alpha-adrenergic receptor blockers administered to counter the hemodynamic effects triggered by the excess of circulating catecholamines secreted by the tumor in the pre- and intraoperative period. Beta-blockers, nitrate and calcium antagonists should be at hand during surgery in case hypertensive spikes occur because of tumor manipulation, and resorting to norepinephrine may be necessary if there is a drop in blood pressure after clamping of the blood vessels and tumor removal [51, 52].

Surgically, clamping of the blood vessels before tumor dissection is important to avoid the release of catecholamines.

According to some authors, the CO_2 pneumoperitoneum induced to perform laparoscopic surgery may theoretically represent a stimulus for the release of catecholamines because of hypercapnea and increased abdominal pressure [53, 54]. In our case, as well as in other cases described in the literature, there was no evidence of such a reaction [40-50].

Some reports have shown an association between chromaffin tumors and cholelithiasis which may be due to hypercalcemia with normal parathyroid hormone values sometimes observed in these cases [1, 55, 56].

Another association which has often been described is that of renal artery stenosis due to fibromuscular hypertrophy and consequent arterial hypertension caused by multiple factors [3, 57, 58].

Histopathological discrimination for prognostic purposes is often problematic since invasion of the capsule, nuclear atypicality, cellular pleomorphism and mitosis may be present in benign neoplasms [59]. The only indicative signs of malignancy are invasion of adjacent structures or presence of distant metastases (lymph nodes, liver, bone, lungs) [1, 9, 14-19].

Early diagnosis is important not only because these tumors represent a serious danger (an unexploded bomb) for the patient's life but also because they are frequently malignant when they are larger than 5 cm [14].

Long-term follow-up is particularly useful for extra-adrenal pheochromocytomas, which tend to be more malignant (50%) than adrenal tumors (10%) [60].

Although a lesion may be considered to be benign when first resected, the possibility of further surgery is 10% within 20 years [15, 18, 19, 61].

Conclusion

Gynecologists should consider the possibility, although rare, of an extra-adrenal pheocromocytoma when preparing to surgically remove a pelvic mass.

The occurrrence of a parauterine tumor associated with hypertensive crises with signs and symptoms related to an excess of circulating catecholamines may suggest this diagnosis.

Not long ago laparoscopic surgery was contraindicated in the treatment of the extra-adrenal pheochromocytoma. Currently, due to improved diagnostic methods and laparoscopic techniques, this approach represents a valid alternative to traditional laparotomy. Laparoscopic surgery, preceded by adequate administration of adrenergic receptor blockers and vascular filling, can avert disruption of hemodynamic stability because of lesser tumor manipulation; it also requires smaller doses of postoperative analgesics, a shorter hospital stay and favors a better cosmetic outcome.

References

[1] Landsberg L., Young J.B.: "Catecholamines and the adrenal medulla: Pheochromocitoma". In: Wilson & Foster (eds) "Williams' textbook of endocrinology", Philadelphia, W.B. Saunders, 1985, 932.

[2] Keiser H.R.: "Pheochromocytoma and other diseases of the sympathetic nervous system". In: Becker K.L. (ed) "Principles and Practice of Endocrinology and Metabolism", 2nd ed. Philadelphia, J.B. Lippincott, 1995, 763.

[3] Favia G., Lumachi F.: "Feocromocitoma e Paragangliomi". In: Società Italiana di Chirurgia (ed) "La chirurgia del surrene", Roma, Collana Monografica 13, S.I.C., 2000, 42.

[4] Coupland R.E.: "The natural history of the chromaffin cell", London, Longmans, Green, 1965, 192.

[5] Gifford R.W. Jr., Manger W.M., Bravo E.L.: "Pheochromocytoma". *Endocrinol. Metab. Clin. North. Am.,* 1994, *23*, 387.

[6] Stackpole R.H., Melicow M.M., Uson A.C.: "Pheochromocytoma in children: report of 9 cases and review of the first 100 published cases with follow-up studies". *J. Pediatr.*, 1992, *63*, 315.

[7] Whalen R.K., Althausen A.S., Daniel G.H.: "Extra-adrenal pheochromocytoma". *J. Urol.* 1992, *147*, 1.

[8] Richards M.L., Schwesinger W.H.: "An incidental paracaval mass". *Current Surgery*, 2001, *58*, 299.

[9] Zidi B., Bouziani A., Ben Hamadi F., Tissaoui K., Manaa J., Louzir B. *et al.*: "Le phèochrocytome extrasurrènalien. A propos de trois observations et revue de la littèrature". *Rev. Med. Interne*, 1995, *16*, 102.

[10] Goldfien A.: "Adrenal Medulla". In: Greenspan F.S. "Basic and Clinical endocrinology". Appleton & Lange, East Norwalk, 1995, 370.

[11] Thomas J.E., Rooke E.D., Kvale W.F.: "The neurologist's experience with pheochromocytoma: a review of 46 cases". *J. Urol.* 1974, *111*, 715.

[12] Isles C.G., Johnson J.K.: "Pheochromocytoma and diabetes mellitus: further evidence that alpha 2 receptors inhibit insulin release in man". *Clin. Endocrinol. (Oxf)*, 1983, *18*, 37.

[13] Balestrieri P.G., Spandrio S., Romanelli G., Giustina G.: "Diabetes mellitus as presenting feature in extra-adrenal pheochromocytoma: report of a case". *Acta Diabetol. Lat.*, 1990, *27*, 261.

[14] O'Riordain D.S., Young W.F. Jr., Grant C.S., Carney J.A., van Heerden J.A.: "Clinical spectrum and outcome of functional extraadrenal paraganglioma". World. J. Surg., 1996, *20*, 916.

[15] Werbel S.S., Ober K.P.: "Pheochromocytoma: update on diagnosis, localization and management". *Med. Clin. North. Am.*, 1995, *79*, 131.

[16] Atiyeh B.M., Barakat A.J., Abumrad N.N.: "Extra-adrenal pheochromocytoma". *J. Nephrol.*, 1997, *10,* 25.

[17] Klingler H.C., Klingler P.J., Martin J.K., Smallridge R.C., Smith S.L., Hinder R.A.: "Pheochromocytoma". *Urology*, 2001, 57, 1025.

[18] Mori S., Okura T., Kitami Y., Takata., Nakamura M., Watanabe S. *et al.*: "A case of metastatic extra-adrenal pheochromocytoma 12 years after surgery". *Hypertens. Res.*, 2002, *25*, 141.

[19] Suzuki K.: "Surgical management of pheochromocytoma". Biomed & Pharmacother, 2000, *54* (Suppl.1), 150.
[20] Sutton M.G., Sherps S.G., Lie J.T.: "Prevalence of clinically unsuspected pheochromocytoma: review of a 50-year autopsy series". *Mayo Clin. Proc.*, 1981, *56*, 354.
[21] Sinclair D., Shenkin A., Lorimer A.R.: "Normal catecholamine production in a patient with a paroxysmally secreting pheochromocytoma". *Ann. Clin. Biochem.*, 1991, *28*, 417.
[22] Tohya T., Yoshimura T., Honda Y., Miyoshi J., Okamura H.: "Unsuspected extra-adrenal pheochromocytoma simulating ovarian tumor". *Eur. J. Obst. & Gynecol. and Rep. Biol.*, 1999, *82*, 217.
[23] Rabii R., Idali B., Joual A., Sarf I., Naciri K., Hafiani M. *et al.*: "Phèochromocytome extrasurrènalien dècouvert en peropèratoire". *Ann. Urol.*, 2001, 35, 13.
[24] Schenker J.G., Chowers I.: "Pheochromocytoma and pregnancy: review of 89 cases". *Obstet. Gynecol. Surv.*, 1971, *26*, 739.
[25] Harper M.A., Murnaghan G.A., Kennedy L., Hadden D.R., Atkinson A.B.: "Pheochromocytoma in pregnancy: five cases and review of the literature". *Br. J. Obstet. Gynaecol.*, 1989, *96*, 594.
[26] Demirkesen O., Cetinel B., Yaycioglu O., Uygun N., Solok V.: "Unusual case of early preeclampsia: bladder paraganglioma". *Urology*, 2000, *56*, 28.
[27] Stewart M.F., Reed P., Weinkove C., Moriarty K.J., Ralston A.J.: "Biochemical diagnosis of pheochromocytoma: two instructive case reports". *J. Clin. Pathol.*, 1993, *46*, 280.
[28] Bravo E.L.: "Evolving concepts in the pathophysiology, diagnosis and treatment of pheochromocytoma". *Endocr. Rev.*, 1994, *15*, 356.
[29] Shawar L., Svec F.: "Pheochromocytoma with elevated metanephrines as the only biochemical finding". *J. La State Med. Soc.*, 1996, *148*, 535.
[30] Schwerk W.B., Gorg C., Gorg K., Restrepo I.K. "Adrenal pheochromocytomas: a broad spectrum of sonographic presentation". *J. Ultrasound Med.*, 1994, *13*, 517.
[31] Stewart B.H., Bravo E.L., Haaga J., Meaney T.F., Tarazi R.: "Localization of pheochromocytoma by computed tomography". *N. Engl. J. Med.*, 1978, *299*, 460.
[32] Rozenblit A., Morehouse H.T., Amis E.S. Jr.: "Cystic adrenal lesions: CT features". *Radiology*, 1996, *201*, 541.
[33] Doppman J.L., Reinig J.W., Dwyer A.J., Frank J.P., Norton J., Loriaux D.L., Keiser H.: "Differentiation of adrenal masses by magnetic resonance imaging". *Surgery*, 1987, *102*, 1018.
[34] Belden C.J., Powers C., Ros P.R.: "MR demonstration of a cystic pheochromocytoma". *J. Magn. Reson. Imaging*, 1995, *5*, 778.
[35] Van Gils A.P.G., Falke T.H.M., van Erkel A.R., Arndt J.W., Sandler M.P., van der Mey A.G., Hoogma R.P.: "MR imaging and MIBG scintigraphy of pheochromocytoma and extra-adrenal functioning paragangliomas". *Radiograph.*, 1991, *11*, 37.
[36] Maurea S., Cuocolo A., Reynolds J.C., Neumann R.D., Salvatore M.: "Diagnostic imaging in patients with paragangliomas. Computed tomography, magnetic resonance and MIBG Scintigraphy comparison". *Q. J. Nucl. Med.*, 1996, *40*, 365.
[37] Sisson J.C., Frager M.S., Valk T.W., Gross M.D., Swanson D.P., Wieland D.M. *et al.*: "Scintigraphic localization of pheochromocytoma". *N. Engl. J. Med.*, 1981, *305*, 12.
[38] Trampal C., Engler H., Juhlin C., Bergstrom M., Langstrom B.: "Pheochromocytomas: detection with 11C hydroxyephedrine PET". *Radiology*, 2004 Feb., *230*, 423.
[39] Gagner M., Lacroix A., Bolte E.: "Laparoscopic adrenalectomy in Cushing' syndrome and pheochromocytoma". *N. Engl. J. Med.*, 1992, *327*, 1003.
[40] Kercher K.W., Heniford B.T., Marroum M.C., Greene F.L.: "Laparoscopic intraoperative ultrasonic localization and resection of an extra-adrenal pheochromocytoma". *J. Laparoendosc. Adv. Surg. Tech.*, 1999, *9*, 511.
[41] Pautler S.E., Choyke P.L., Pavlovich C.P., Daryanani K., Walther M.M.: "Intraoperative ultrasound aids in dissection during laparoscopic partial adrenalectomy". *J. Urol.*, 2002, *168*, 1352.
[42] Hwang J.J., Shoaf G., Uchio E.M., Watson J., Pacak K., Linehan W.M., Walther M.M.: "Laparoscopic management of extra-adrenal pheochromocytoma". *J. Urol.*, 2004, *171*, 72.
[43] Gagner M., Pomp A., Heniford B.T., Pharand D., Lacroix A.: "Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures". *Ann. Surg.*, 1997, *226*, 238.
[44] Stuart R.C., Chung S.C.S., Lau J.Y.W., Chan A.C.W.: "Laparoscopic adrenalectomy". *Br. J. Surg.*, 1995, *82*, 1498.
[45] Smith C.D., Weber C.J., Amerson J.R.: "Laparoscopic adrenalectomy: new gold standard". *World J. Surg.*, 1999, *23*, 389.
[46] Suzuki K., Ushiyama T., Ihara H., Kageyama S., Mugiya S., Fujita K.:"Complications of laparoscopic adrenalectomy in 75 patients treated by same surgeon". *Eur. Urol.*, 1999, *23*, 825.
[47] Henry J.F., Defechereux T., Raffaelli M., Lubrano D., Gramatica L.: "Complications of laparoscopic adrenalectomy: result of 169 consecutive procedures". *World J. Surg.*, 2000, *24*, 1342.
[48] Terachi T., Matsuda T., Terai A., Ogawa O., Kakehi Y., Kawakita M. *et al.*: "Transperitoneal laparoscopic adrenalectomy: experience in 100 patients". *J. Endourol.*, 1997, *11*, 361.
[49] Janetschek G., Finkenstedt G., Gasser R., Waibel U.G., Peschel R., Bartsch G., Neumann H.P.: "Laparoscopic surgery for pheochromocytoma: adrenalectomy, partial resection, excision of paragangliomas". *J. Urol.*, 1998, *160*, 330.
[50] Edwin B., Kazaryan A.M., Mala T., Pfeffer P.F., Tonnessen T.I., Fosse E.: "Laparoscopic and open surgery for pheochromocytoma". BMC Surg., 2001, *1*, 2.
[51] Sprung J., O'Hara J.F., Gill I.S., Abdelmalak B., Sarnaik A., Bravo E.L. "Anesthetic aspects of laparoscopic and open adrenalectomy for pheochromocytoma". *Urology*, 2000, *55*, 339.
[52] Baraka A., Siddik-Sayyid S., Jalbout M., Yaacoub C.: "Variable hemodynamic fluctuations during resection of multicentric extraadrenal pheochromocytomas". Can. J. Anesth., 2002, *49*, 682.
[53] Fernandez-Cruz L., Taura P., Saenz A., Benarroch G., Sabater L.: "Laparoscopic approach to pheochromocytoma: hemodynamic changes and catecholamine secretion". *World J. Surg.*, 1996, *20*, 762.
[54] Fernandez-Cruz L., Saenz A., Taura P., Benarroch G., Sabater L., Astudillo E., Fontanals J.: "Helium and carbon dioxide pneumoperitoneum in patients with pheochromocytoma undergoing laparoscopic adrenalectomy". *World J. Surg.*, 1998, *22*, 1250.
[55] Gluvic Z., Rasic-Milutinovic Z.: "Pheochromocytoma associated with cholelithiasis". *Med. Pregl.*, 2001, 54, 383.
[56] Stewart A.F., Hoecker J.L., Mallette L.E., Segre G.V., Amatruda T.T. Jr, Vignery A.: "Hypercalcemia in pheochromocytoma. Evidence for a nouvel mechanism". *Ann. Intern. Med.*, 1985, *102*, 776-9.
[57] Lance Pickard J., Ross G., Silver D.: "Coexisting extra-adrenal pheochromocytoma and renal artery stenosis: a case report a review of the pathophysiology". *J. Pediatr Surg.*, 1995, *30*, 1613.
[58] Monnier G., Guerard S., Godon P., Van de Walle J.P., Brion R.: "Paraganglioma associated with renal artery stenosis : unusual cause of secondary arterial hypertension. A case report and review of the literature". *Ann. Cardiol. Angeiol.* (Paris), 2000, *49*, 168.
[59] Schlumberger M., Gicquel C., Lumbroso J., Tenenbaum F., Comoy E., Bosq J. *et al.*: "Malignant pheochromocytoma: clinical, biological, histologic, and therapeutic data in a series of 20 patients with distant metastases". J. Endocrinol. Invest., 1992, *15*, 631.
[60]Sclafani L.M., Woodruff J.M., Brennan M.F.: "Extraadrenal retroperitoneal paragangliomas: natural history and response to treatment". *Surgery*, 1990, *108*, 1124.
[61] Tanaka S., Ito T., Tomoda J., Higashi T., Yamada G., Tsiji T.: "Malignant pheochromocytoma with hepatic metastasis diagnosed 20 years after resection of the primary adrenal lesion". *Intern. Med.*, 1993, *32*, 789.

Address reprint requests to:
S. MONTEMURRO, M.D.
Scientific Institute for Research
and Treatment of Cancer
"Giovanni Paolo II"
Department of Surgical Oncology
Via Hahnemann, 10
70126 Bari (Italy)