Endocr (2010) 37:213–219
DOI 10.1007/s12020-009-9303-y

ORIGINAL ARTICLE

Pheochromocytoma crisis after a dexamethasone suppression test for adrenal incidentaloma

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Received: 15 September 2009 / Accepted: 23 November 2009 / Published online: 5 January 2010

Abstract A 61-year-old woman was referred to our department for evaluation of an incidental adrenal mass. An abdominal CT scan revealed a 4.1 cm right adrenal mass. The patient had been diagnosed with hypertension 7 years earlier and had taken antihypertensive medications intermittently. Her physical examination demonstrated a round face, central obesity, and mild hypertension. Serum catecholamines, renin, aldosterone, ACTH and 24-h urine-free cortisol, vanillylmandelic acid levels were within normal limits. However, serum cortisol level was markedly elevated and the circadian rhythm was disturbed. Successive low-dose and high-dose dexamethasone suppression tests were ordered for evaluation of a functioning adrenal incidentaloma. About 2 h after taking the second dose of 2 mg dexamethasone, she suddenly developed nausea and vomiting, palpitations, and anxiety with severe hypertension. On the same day, we measured serum catecholamines, which were markedly elevated. An elective laparoscopic right adrenalectomy was performed and pathologic examination confirmed the diagnosis of pheochromocytoma. One week after surgery, serum and urine catecholamine levels returned to normal. The patient has remained normotensive without any medications and clinically well. Patients with adrenal incidentalomas may have a functional mass that does not always manifest as a full symptomatic disease. During the investigation of adrenal incidentalomas, pheochromocytoma should ideally be ruled out before administering corticosteroids.

Keywords Adrenal incidentaloma · Pheochromocytoma crisis · Steroid

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Introduction

Pheochromocytomas are rare chromaffin cell tumors arising in the adrenal glands that usually produce excess catecholamines leading to paroxysms of hypertension and adrenergic symptoms. Approximately 5.1% of incidental adrenal masses prove to be pheochromocytomas [1] but even clinically silent pheochromocytomas can be lethal [2, 3]. As the condition is often fatal, early diagnosis followed by aggressive and accurate treatment is required to save the patient's life. Pheochromocytoma crisis is a rare, life-threatening condition characterized by deterioration of hemodynamics due to excessive secretion of catecholamines. The crisis can present spontaneously or as a result of unmasking by several factors such as surgery, anesthesia, and drugs. Several classes of drugs may induce a pheochromocytoma crisis in patients with pheochromocytoma. Presentation of pheochromocytoma after administration of steroid is rarely reported [4–12]. In this article, we present a case of a pheochromocytoma crisis induced by a steroid in a patient undergoing a high-dose dexamethasone suppression test (DST) for evaluation of a functioning adrenal incidentaloma and review the literature on steroid-induced pheochromocytoma crisis.

Case report

A 61-year-old normotensive woman was referred to our department with incidentally discovered adrenal tumor during annual health checkup. Abdominal computed tomography scan revealed a 4.1 cm right adrenal mass with low attenuation (Fig. 1).

Her past medical history demonstrated mild hypertension for 7 years, treated periodically with antihypertensive drugs by a family physician. There was no specific family history for a specific disease status including hypertension, tumor/or cancer, and diabetes. The patient was obese with a BMI of 30.1 kg/m^2. Her body temperature was 36.8°C. The blood pressure was 142/90 mmHg, and the pulse rate was 80 beats per minute and regular. The physical examination revealed round face and central obesity. Complete blood cell counts, liver function, renal function, and serum electrolytes revealed no abnormality except hypercholesterolemia (total cholesterol 281 mg/dl). Hormone examination results were as follows: urinary-free cortisol, and vanillylmandelic acid (VMA) levels from 24 h urine sample were 19.12 μg/day (21–85 μg/day) and 7.27 mg/day (normal <8 mg/day), respectively. Serum renin, aldosterone, epinephrine, norepinephrine, and ACTH levels were found to be normal except markedly elevated serum cortisol level (serum cortisol 117.80 μg/dl at 08:00 h) (Table 1). We ordered a two-day low-dose DST administering 0.5 mg orally every 6 h for 2 days based on her laboratory results, and serum cortisol levels were not completely suppressed (Table 2). The first and second days were uneventful and the patient remained normotensive and asymptomatic. A successive high-dose DST, administering 2 mg orally every 6 h for 2 days, was ordered as per an institutional protocol of the Pusan National University Yangsan Hospital, Yangsan, Korea. About 2 h after taking the second dose of 2 mg of dexamethasone, the patient suddenly developed nausea and vomiting, palpitation, and anxiety with severe hypertension (240/140 mmHg), raising our clinical suspicion of a pheochromocytoma crisis. A high-dose DST was halted immediately, and the patient was stabilized after treatment with intravenous bolus of 5 mg pentolamine and continuous intravenous infusion of sodium nitroprusside. We measured serum catecholamines after crisis on the same day, which were markedly elevated as follows: serum epinephrine 1.16 ng/ml (reference range: 0–0.3), serum norepinephrine 1.79 ng/ml (reference range: 0–0.8), 24 h urine metanephrine 3.29 mg/24 h (reference range: 0–1.3). Subsequently, abdominal magnetic resonance imaging performed after crisis revealed a round 3.1×4.1 cm right adrenal mass with high signal intensity on T2-weighted image (Fig. 1). The patient was discharged from our department and was prescribed doxazosin (8 mg/day) and carvediolol (6.25 mg/day). One month later, an elective laparoscopic right adrenalectomy was performed and pathologic examination confirmed the diagnosis of pheochromocytoma

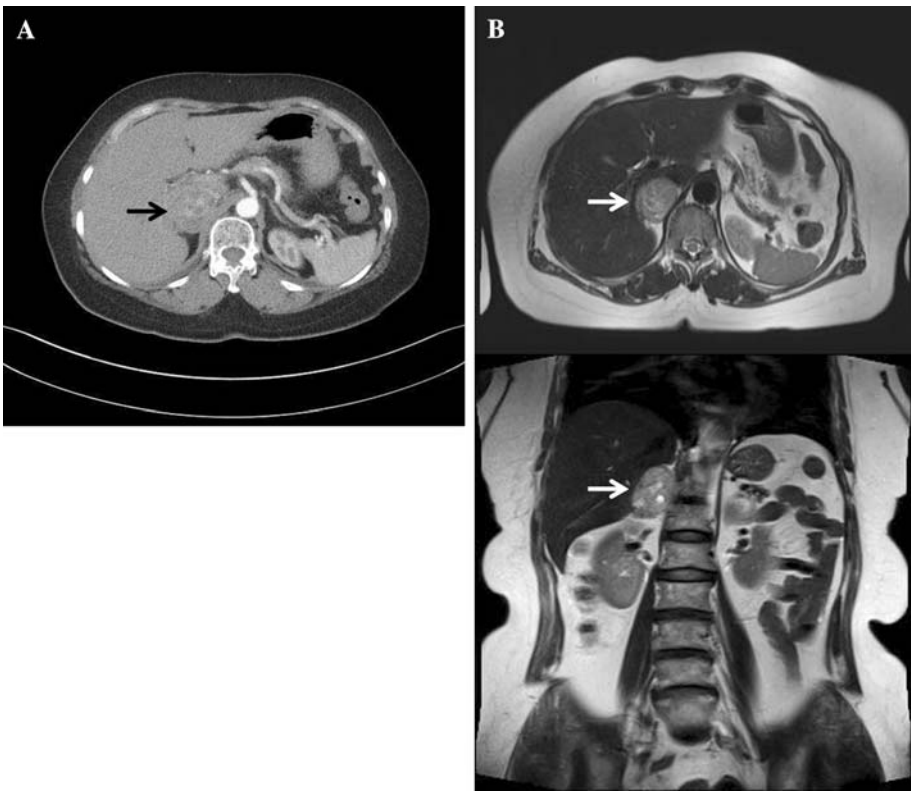

Fig. 1 Imaging studies. **a** Abdominal CT scan shows a round right adrenal mass (*arrow*). **b** Abdominal magnetic resonance imaging shows an abnormal 3.1 × 4.1 cm round mass above the right kidney (*arrow*)

Table 1 Basal hormone data

	Patient	Reference range
Serum		
Renin (ng/ml/hr)	0.28	0.2–2.8
Aldosterone (pg/ml)	58.6	40–310
ACTH (pg/ml)	19.7 (AM)	10–60
	10.5 (PM)	
Cortisol (μg/dl)	117.8 (AM)	8–19
	55.2 (PM)	
Epinephrine (ng/ml)	0.06	0–0.3
Norepinephrine (ng/ml)	0.22	0–0.8
Urine		
Free cortisol (μg/day)	19.12	21–85
VMA (mg/day)	7.27	<8

VMA vanillylmandelic acid

Table 2 Two-day low-dose dexamethasone suppression test

	Day 0	Day 1	Day 2
Serum cortisol (μg/dl)	55.21	11.44	9.54
Urine free cortisol (μg/day)	17.59		14.02
17-OHCS (mg/day)	3.15		3.33

17-OHCS 17-hydroxycorticosteroid

(Fig. 2). Postoperative course was uneventful. One week after surgery, serum and urine catecholamine levels returned to normal, and the patient was discharged. We measured basal serum cortisol and urinary-free cortisol at 3 months after surgery. Results were as follows: urinary-free cortisol 32.23 μg/day, serum cortisol 21.19 μg/dl. Serum and urine catecholamine levels were of normal limits. She remained asymptomatic and normotensive without medications.

Discussion

We present a patient with pheochromocytoma who developed the episode of hypertensive crisis after steroid administration. Including the present case, we identified 14 cases of steroid-induced pheochromocytoma crisis in the English literature between 1969 and 2009 (Table 3) [4–12]. There were six men and eight women with the mean age (±SD) of 45.14 ± 13.77 years. The most common presenting symptoms were chest pain, vomiting, and hypertension. In nine (64%) out of 14 patients, serious complications such as congestive heart failure, cardiac arrest, and respiratory failure developed, and among these patients, two had lethal consequences, which reflects high morbidity and mortality of steroid-induced pheochromocytoma crisis. The mean size (±SD) of the tumors was 4.33 ± 1.78 cm, with a slight right-sided predominance, and the size was not constantly associated with severity of complications.

Two deaths occurred in the cases reported here; one occurred during ACTH stimulation test and the other during high-dose DST, which are among the most widely employed endocrine function tests. Dexamethasone and betamethasone, which have high glucocorticoid potency and long duration of action, were responsible for eight cases of crisis, followed by serious complications. The route of steroid administration does not appear to be associated with clinical severity. In addition, there were various intervals ranging 1–72 h between steroid administration and onset of crisis, reflecting heterogeneous and unpredictable nature of pheochromocytoma.

Corticosteroids invoke serious adverse events or even lethal consequences in patients with pheochromocytoma via a variety of mechanisms. They stimulate catecholamine biosynthetic enzymes such as phenylethanolamine-*N*-methyl-transferase, tyrosine hydroxylase, and dopamine *β*-hydroxylase, thereby augmenting the synthesis of catecholamines [13–17]. Corticosteroids administration has also been shown to cause the release of catecholamines from perfused canine adrenal glands [18]. In addition, corticosteroids have permissive effects on potentiating vasoactive responses to catecholamines in peripheral tissues [19, 20]. Administration of ACTH and steroids increases the vasopressor response to infused norepinephrine [19]. Recent evidence suggests that glucocorticoid actions at various sites in the nitric oxide synthase (NOS) pathways may result in elevated blood pressure [21]. These include alterations in L-arginine, NOS2, and NOS3 downregulation, reduced cofactor bioavailability, NOS uncoupling, a concomitant elevation in reactive oxygen species and removal of nitric oxide (NO) from vascular environment, alterations in whole body antioxidant status, and erythropoietin-induced resistance to NO.

The diagnosis of pheochromocytoma is confirmed by demonstration of elevated 24 h urinary or plasma catecholamines and their metabolites. Recent studies suggested the biochemical screening tests such as measurements of plasma-free metanephrines or 24-h urinary total metanephrines and catecholamines [22, 23]. However, the most sensitive screening test still remains a matter of debate. In emergent situation in which pheochromocytoma is suspected, therefore, measurements of both 24-h urine and plasma-free metanephrines should be considered for accurate diagnosis [9].

In the present case, urinary epinephrine and norepinephrine assays are unfortunately not available in our laboratory, but should, if possible, be measured routinely in the investigation of adrenal incidentaloma. We did not measure 24-h urinary metanephrine or catecholamine levels initially, because of a low index of suspicion in view of

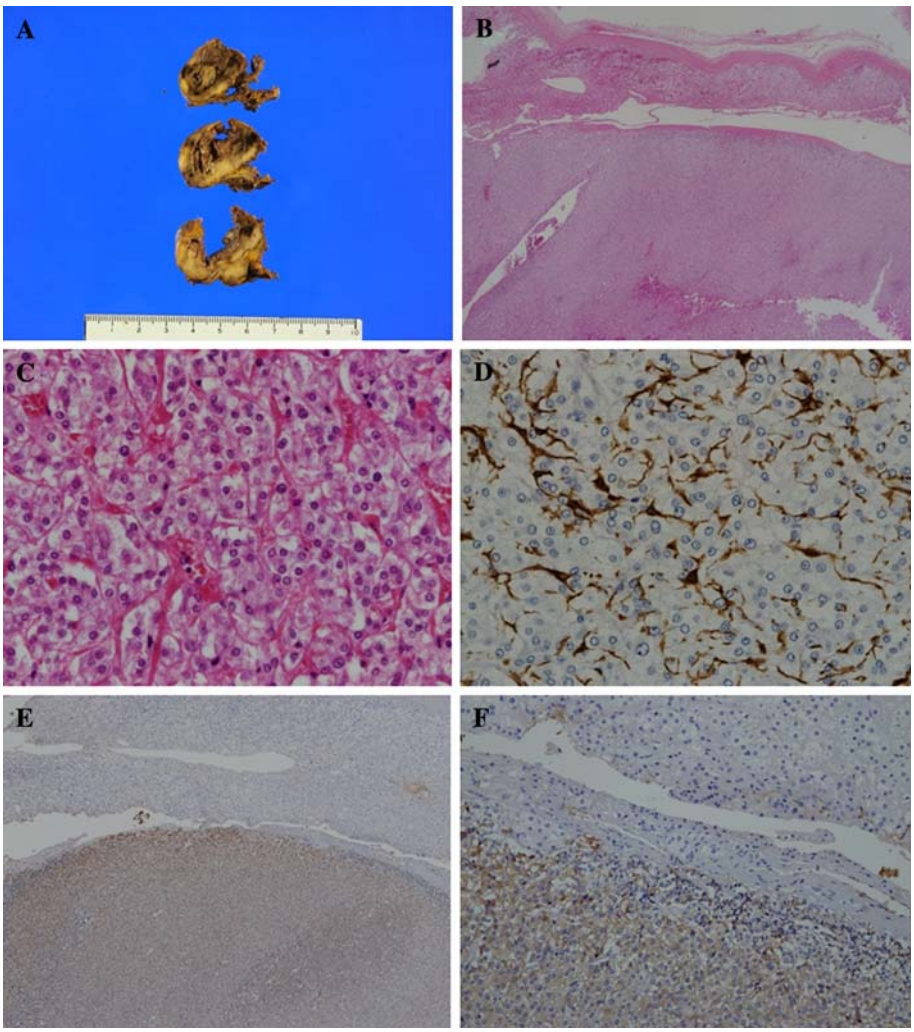

Fig. 2 Pathology. **a** Cross section of a well-demarcated intra-adrenal pheochromocytoma with normal adrenal cortex. **b** Photomicrograph of normal adrenal cortex tissue superiorly and pheochromocytoma tissue inferiorly (×20). **c** Pathology of the adrenal mass compatible with the diagnosis of pheochromocytoma, which shows typical zellballen pattern with nests of cells separated by thin vascular stroma (×400). **d** Immunochemical stain reveals S-100 positive sustentacular cells (×400). **e** and **f** Immunochemical stain reveals chromogranin positive cells (×40 and ×200)

normal urinary VMA and serum catecholamine levels. We included 20 ml of 6 N HCl in the collection container when measuring urinary VMA, which was at the upper limit of normal in this patient. The technique for collection of blood samples for measurement of serum catecholamines requires critical attention, and the quite normal levels in this patient on presentation could reflect inadequate collection technique, a problem with the assay or the truly episodic secretion of the tumor until stimulated by glucocorticoid administration. Kasperlik–Zeluska and colleagues [24] found that four of 19 patients with adrenal incidentalomas had proven pheochrocytomas but normal findings on screening tests. Even when clinically silent, pheochromocytomas can be lethal [2].

Although the optimal diagnostic approach to a patient with an adrenal incidentaloma is debated, most clinicians would agree that the evaluation of the patient should start with a careful history and physical examination focusing on signs and symptoms of adrenal hyperfunctioning and malignancy. Young [1] recommended screening for the following forms of adrenal hyperfunction: 24-h urine for metanephrines and catecholamines, overnight 1 mg dexamethasone suppression test, serum potassium, and plasma aldosterone concentration-to-plasma rennin activity ratio in patients with hypertension. After this case, we changed our protocol for evaluation of adrenal incidentaloma.

We have no explanation for the morning cortisol level being significantly elevated on two occasions preoperatively, while urinary-free cortisol was normal. One explanation would be a methodological problem for either serum or urinary cortisol. Both serum cortisol and urinary-free cortisol were normal postoperatively, consistent with removal of the right adrenal lowering cortisol levels. Since serum ACTH was not suppressed and both ACTH and cortisol exhibited a normal circadian rhythm, autonomous cortisol production by the right adrenal can be excluded. Cushing's disease cannot be excluded, however, since unilateral adrenalectomy can produce a temporary remission in this condition. Round face and central obesity on presentation, incomplete suppression of serum cortisol by

Table 3 The summary of the reported cases of steroid-induced pheochromocytoma crisis

Authors (year of publication)	Age (year)/sex	Tumor side/size	Steroid dose/route	Onset (h)	Clinical features; consequences
Page et al. (1969) [4]	39 M	Right/3.0 cm	ACTH, Hydrocortisone 'injection', Prednisone PO, dose: N/A	After 12 h	Abdominal pain, palpitation, anxiety, HTN, cardiac ischemia, CHF, pulmonary edema; survived
Cowley et al. (1970) [5]	57 M	Left/4.0 cm	ACTH stimulation test (IV) dose: N/A	<48 (2 days later)	Epigastric pain, diaphoresis, anxiety, HTN, cardiogenic shock, bowel infarction; lethal
Daggett et al. (1977) [6]	69 F	Right/N/A	Prednisone 45 mg PO Hydrocortisone 100 mg IV	<72 (within 3 days) 1 h later	Palpitation, tremor, HTN; survived
Kothari et al. (1998) [7]	34 F	Right/4.1 cm	Dexamethasone 16 mg, route: N/A	After 12 h	N&V, CHF, cardiac arrest; survived
	43 F	Left/N/A	Prednisone 60 mg PO	N/A	CHF, cardiac arrest; survived
Takagi et al. (2000) [8]	52 M	Right/3.0 cm	Dexamethasone dose: N/A, intraarticular	12 h later	Chest pain, dyspnea, diaphoresis, CHF, cardiogenic shock, renal insufficiency; survived
Brown et al. (2005) [9]	44 F	Right/6.8 cm	Dexamethasone 2 mg PO tid	Within 24 h	Chest pain, headache, diaphoresis, HTN, myocardial infarction, retroperitoneal hemorrhage; survived
Rosas et al. (2008) [10]	26 F	Right/4.2 cm	Dexamethasone 2 mg PO qid	36	Anxiety, HTN, cardiogenic shock, pulmonary edema; lethal
	39 M	Left/5.5 cm	Betamethasone 6 mg IM	12	Chest pain, headache, N&V, HTN, cardiac arrest, encephalopathy, renal and hepatic insufficiency; survived
	27 M	Metastasis	Methylprednisolone 1.5 g IV	8	Chest pain, N&V, HTN; survived
	39 F	Left/8.0 cm	Dexamethasone 2 mg PO qid	5	Chest pain, headache, N&V, anxiety, HTN, cardiac ischemia; survived
Takahashi et al. (2009) [11]	66 F	Right/3.0 cm	Prednisolone 15 mg PO qd	<48 (2 days later)	Headache, N&V, palpitation, diaphoresis, HTN, rhabdomyolysis; survived
Rashid-Farokhi et al. (2009) [12]	36 M	Left/2.0 cm	Betamethasone 4 mg IM	12	Headache, N&V, palpitation, diaphoresis, anxiety, HTN, respiratory and renal failure[a]; survived
Present case	61 F	Right/4.1 cm	Dexamethasone 2 mg PO qid	14	N&V, palpitation, anxiety, HTN; survived

CHF congestive heart failure, *F* female, *HTN* hypertension, *IM* intramuscularly, *IV* intravenously, *M* male, *N/A* not available, *N&V* nausea and vomiting, *PO* by mouth, *qd* once a day, *qid* four times a day, *tid* three times a day

[a] Respiratory failure was present only in the first episode

low-dose dexamethasone, and serum cortisol falling to normal following unilateral adrenalectomy are all compatible with Cushing's disease. If present, slow, progressive enlargement of the left adrenal would be expected on imaging, as well as slowly rising serum cortisol levels.

It is of utmost importance to rule out pheochromocytoma first in dealing with adrenal incidentalomas using the most sensitive biochemical test available, because a missed diagnosis can lead to devastating complications. Moreover, clinicians should be alert to the presence of clinically and biochemically silent pheochromocytomas [1, 24–27]. If hypertension is paroxysmal, measurements of catecholamines and metabolites in plasma and urine may be normal during normotensive periods. Decreased renal function and low urine acidity can reduce urinary catecholamine metabolite levels [28]. A recent study proposed that ^{131}I-metaiodobenzylguanidine (MIBG) scintigraphy could be a very sensitive tool in the patients with the clinical symptoms of pheochromocytoma and normal catecholamine levels [29].

In summary, vigorous investigations including thorough clinical history, appropriate biochemical tests and imaging studies are prerequisite for adequate diagnosis of pheochromocytoma in a patient with an adrenal incidentaloma. If corticosteroid suppression test is necessary before ruling out a pheochromocytoma, a low-dose DST (1 mg given orally at night) should be used; no cases of pheochromocytoma crisis have been reported with this dose. Higher doses of corticosteroids must be used with great caution in any patient with an adrenal incidentaloma even in the absence of clinical and biochemical evidence of pheochromocytoma. When needed, a high-dose DST has to be obtained, once the measurement of plasma or urinary metanephrines rules out a pheochromocytoma. Clinicians should suspect a pheochromocytoma crisis in any patient who presents with sudden adrenergic symptoms or severe hypertension associated with corticosteroid administration. It is crucial to detect a pheochromocytoma crisis promptly and prevent devastating consequences with intensive treatment.

Acknowledgment This work was supported for two years by Pusan National University Research Grant.

References

1. W.F. Young Jr, Management approaches to adrenal incidentalomas. A view from Rochester, Minnesota. Endocrinol. Metab. Clin. North Am. **29**, 159–185 (2000)
2. M.G. Sutton, S.G. Sheps, J.T. Lie, Prevalence of clinically unsuspected pheochromocytoma. Review of a 50-year autopsy series. Mayo Clin. Proc. **56**, 354–360 (1981)
3. E.L. Bravo, R. Tagle, Pheochromocytoma: state-of-the-art and future prospects. Endocr. Rev. **24**, 539–553 (2003)
4. L.B. Page, J.W. Raker, F.R. Berberich, Pheochromocytoma with predominant epinephrine secretion. Am. J. Med. **47**, 648–652 (1969)
5. D.J. Cowley, D.A. Montgomery, R.B. Welbourn, Management of paroxysms of hypertension in patients with phaeochromocytomas. Br. J. Surg. **57**, 832–834 (1970)
6. P. Daggett, S. Franks, Steroid responsiveness in phaeochromocytoma. Br. Med. J. **1**, 84 (1977)
7. S.N. Kothari, W.A. Kisken, Dexamethasone-induced congestive heart failure in a patient with dilated cardiomyopathy caused by occult pheochromocytoma. Surgery **123**, 102–105 (1998)
8. S. Takagi, S. Miyazaki, T. Fujii, S. Daikoku, Y. Sutani, I. Morii, S. Yasuda, Y. Goto, H. Nonogi, Dexamethasone-induced cardiogenic shock rescued by percutaneous cardiopulmonary support (PCPS) in a patient with pheochromocytoma. Jpn. Circ. J. **64**, 785–788 (2000)
9. H. Brown, P.A. Goldberg, J.G. Selter, H.S. Cabin, N.J. Marieb, R. Udelsman, J.F. Setaro, Hemorrhagic pheochromocytoma associated with systemic corticosteroid therapy and presenting as myocardial infarction with severe hypertension. J. Clin. Endocrinol. Metab. **90**, 563–569 (2005)
10. A.L. Rosas, A.A. Kasperlik-Zaluska, L. Papierska, B.L. Bass, K. Pacak, G. Eisenhofer, Pheochromocytoma crisis induced by glucocorticoids: a report of four cases and review of the literature. Eur. J. Endocrinol. **158**, 423–429 (2008)
11. N. Takahashi, T. Shimada, K. Tanabe, H. Yoshitomi, Y. Murakami, Y. Ishibashi, R. Kikkawa, S. Yano, A. Araki, A. Inoue, Steroid-induced crisis and rhabdomyolysis in a patient with pheochromocytoma: a case report and review. Int. J. Cardiol. doi: 10.1016/j.ijcard.2008.12.183 (2009)
12. F. Rashid-Farokhi, A. Cheraghvandi, M.R. Masjedi, Pheochromocytoma crisis due to glucocorticoid administration: a case report and review of the literature. Arch. Iran. Med. **12**, 190–194 (2009)
13. J. Axelrod, Purification and properties of phenylethanolamine-*N*-methyl transferase. J. Biol. Chem. **237**, 1657–1660 (1962)
14. R.J. Wurtman, Control of epinephrine synthesis in the adrenal medulla by the adrenal cortex: hormonal specificity and dose-response characteristics. Endocrinology. **79**, 608–614 (1966)
15. R. Goodman, D. Edgar, H. Thoenen, W. Wechsler, H. Herschman, Glucocorticoid induction of tyrosine hydroxylase in a continuous cell line of rat pheochromocytoma. J. Cell Biol. **78**, R1–R7 (1978)
16. A.S. Tischler, R.L. Perlman, G.M. Morse, B.E. Sheard, Glucocorticoids increase catecholamine synthesis and storage in PC12 pheochromocytoma cell cultures. J. Neurochem. **40**, 364–370 (1983)
17. A. McMahon, E.L. Sabban, Regulation of expression of dopamine beta-hydroxylase in PC12 cells by glucocorticoids and cyclic AMP analogues. J. Neurochem. **59**, 2040–2047 (1992)
18. J.A. Critchley, C.G. Henderson, L.E. Moffat, A. Ungar, J. Waite, C.P. West, Proceedings: The release of catecholamines from perfused canine adrenal glands by corticosteroids. J. Physiol. **254**, 30–31 (1976)
19. G.S. Kurland, A.S. Freedberg, The potentiating effect of ACTH and of cortisone of pressor response to intravenous infusion of L-nor-epinephrine. Proc. Soc. Exp. Biol. Med. **78**, 28–31 (1951)
20. M.E. Ullian, The role of corticosteroids in the regulation of vascular tone. Cardiovasc. Res. **41**, 55–64 (1999)
21. J.A. Whitworth, C.G. Schyvens, Y. Zhang, M.C. Andrews, G.J. Mangos, J.J. Kelly, The nitric oxide system in glucocorticoid-induced hypertension. J. Hypertens. **20**, 1035–1043 (2002)
22. J.W. Lenders, K. Pacak, M.M. Walther, W.M. Linehan, M. Mannelli, P. Friberg, H.R. Keiser, D.S. Goldstein, G. Eisenhofer, Biochemical diagnosis of pheochromocytoma: which test is best? JAMA **287**, 1427–1434 (2002)

23. A.M. Sawka, R. Jaeschke, R.J. Singh, W.F. Young Jr, A comparison of biochemical tests for pheochromocytoma: measurements of fractionated plasma metanephrines compared with the combination of 24-hour urinary metanephrines and catecholamines. J. Clin. Endocrinol. Metab. **88**, 553–558 (2003)
24. A.A. Kasperlik-Zeluska, E. Rosłonowska, J. Słowinska-Srzednicka, B. Migdalska, W. Jeske, A. Makowska, H. Snochowska, Incidentally discovered adrenal mass (incidentaloma): investigation and management of 208 patients. Clin. Endocrinol. (Oxf) **46**, 29–37 (1997)
25. A. Miyajima, J. Nakashima, S. Baba, M. Tachibana, K. Nakamura, M. Murai, Clinical experience with incidentally discovered pheochromocytoma. J. Urol. **157**, 1566–1568 (1997)
26. L. Barzon, C. Scaroni, N. Sonino, F. Fallo, M. Gregianin, C. Macrì, M. Boscaro, Incidentally discovered adrenal tumors: endocrine and scintigraphic correlates. J. Clin. Endocrinol. Metab. **83**, 55–62 (1998)
27. N.B. Tütüncü, O. Gedik, Adrenal incidentaloma: report of 33 cases. J. Surg. Onco. **70**, 247–250 (1999)
28. W.M. Manger, R.W. Gifford Jr., Pheochromocytoma: current diagnosis and management. Cleve. Clin. J. Med. **60**, 365–378 (1993)
29. U. Guller, J. Turek, S. Eubanks, E.R. Delong, D. Oertli, J.M. Feldman, Detecting pheochromocytoma: defining the most sensitive test. Ann. Surg. **243**, 102–107 (2006)