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Emergencies Caused by Pheochromocytoma, Neuroblastoma, or Ganglioneuroma

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This article reviews emergency situations caused by diseases of the sympathetic nervous system. Pheochromocytoma is discussed first and most extensively, because there are numerous reports in the literature on patients with (unsuspected) pheochromocytoma presenting as an emergency. Two other tumors of the sympathetic nervous system are then discussed that less commonly result in endocrine emergencies: neuroblastoma and ganglioneuroma.

Pheochromocytoma

Paragangliomas are rare catecholamine-producing tumors derived from chromaffin cells that can be fatal if left undiagnosed. They occur mainly

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within the adrenal gland, where they are referred to as pheochromocytomas, and less commonly at extra-adrenal sites [1,2]. Because the intra-adrenal and extra-adrenal tumors are histopathologically indistinguishable, the term *pheochromocytoma* is used herein for both extra-adrenal and intra-adrenal tumors. Although most pheochromocytomas occur sporadically without an obvious association with a familial syndrome, as many as 24% have a hereditary basis involving mutations of five different genes associated with different syndromes: the rearranged during transfection proto-oncogene (multiple endocrine neoplasia), the von Hippel-Lindau gene (von Hippel-Lindau disease), the neurofibromatosis type 1 gene (neurofibromatosis), and the genes encoding succinate dehydrogenase enzyme subunits B and D (familial paragangliomas) [3].

Characteristically, patients present with sustained or paroxysmal hypertension, and the triad of headaches, palpitations, and sweating is often seen. There are numerous reports in the literature of unusual presentations of benign or metastatic pheochromocytomas; for this reason, pheochromocytoma is sometimes labeled "the great mimic." Some of these unusual presentations require emergency intervention. In such situations, it is important to establish the correct diagnosis because any surgery in a patient with unsuspected pheochromocytoma carries a high risk for morbidity and mortality.

Emergency situations can occur owing to high levels of catecholamines secreted by the tumor (an overview of the organ-specific responses mediated by adrenergic receptors is shown in Table 1), or they can be the consequence of complications related to a local tumor mass effect. Symptoms related to tumor localization are not discussed herein because they are often nonspecific and similar in management to that of any other tumor at such a location.

The different ways in which a pheochromocytoma can occur as an emergency are discussed according to the following clinical settings: pheochromocytoma multisystem failure, cardiovascular emergencies, pulmonary emergencies, abdominal emergencies, neurologic emergencies, renal emergencies, and metabolic emergencies (Table 2). Treatment for these emergencies in patients with pheochromocytoma is only discussed if it is different from standard practice. In addition, a separate section describes the general perioperative management of patients with pheochromocytoma. Lastly, pheochromocytoma in pregnancy is discussed. This presentation is associated with a high morbidity and mortality if pheochromocytoma is unsuspected.

Multisystem failure

Even though multisystem failure is a rare presentation of pheochromocytoma, with few cases discussed in the literature to date [4–11], this entity is discussed first herein because early detection is crucial to improve the patient's chances of survival. Pheochromocytoma multisystem crisis is defined

Table 1
Organ-specific responses mediated by adrenergic receptors

Adrenergic impulses		Cholinergic impulses	
Effector organs	Receptor type	Responses	Responses
Eye			
Radial muscle, iris	α_1	Contraction (mydriasis) + +	−
Sphincter muscle, iris		−	Contraction (miosis) +++
Ciliary muscle	β_2	Relaxation for far vision +	Contraction for near vision +++
Heart			
SA node	β_1, β_2	Increase in heart rate ++	Decrease in heart rate; vagal arrest +++
Atria	β_1, β_2	Increase in contractility and conduction velocity ++	Decrease in contractility, shortened AP duration +++
AV node	β_1, β_2	Increase in automaticity and conduction velocity +++	Decrease in conduction velocity, AV block +++
His-Purkinje system	β_1, β_2	Increase in automaticity and conduction velocity +++	Little effect
Ventricles	β_1, β_2	Increase in contractility, conduction velocity, automaticity, and rate of idioventricular pacemakers +++	Slight decrease in contractility
Arterioles			
Coronary	α_1, α_2; β_2	Constriction +, dilations ++	Constriction +
Skin and mucosa	α_1, α_2	Constriction +++	Dilation
Skeletal muscle	α; β_2	Constriction ++, dilations ++	Dilation +
Cerebral	α_1	Constriction (slight)	Dilation
Pulmonary	α_1, β_2	Constriction +, dilations	Dilation
Abdominal viscera	α_1, β_2	Constriction +++, dilations +	−
Salivary glands	α_1, α_2	Constriction +++	Dilation ++
Renal	α_1, α_2; β_1, β_2	Constriction +++, dilations +	−
Veins (systemic)	α_1, α_2; β_2	Constriction ++, dilations ++	−
Lung			
Tracheal and bronchial muscle	β_2	Relaxation +	Contraction ++
Bronchial glands	α_1; β_2	Decreased secretion; increased secretion	Stimulation +++

(*continued on next page*)

Table 1 (*continued*)

Adrenergic impulses		Cholinergic impulses	
Effector organs	Receptor type	Responses	Responses
Stomach			
Motility and tone	α_1 α_2; β_2	Decrease (usually) +	Increase ++
Sphincters	α_1	Contraction (usually) +	Relaxation (usually) +
Secretion	Inhibition (?)	Stimulation +++	
Intestine			
Motility and tone	α_1, α_2; β_1, β_2	Decrease +	Increase +++
Sphincters	α_1	Contraction (usually) +	Relaxation (usually) +
Secretion	α_2	Inhibition	Stimulation ++
Gallbladder and ducts	β_2	Relaxation +	Contraction +
Kidney			
Renin secretion	α_1; β_1	Decrease +, increase ++	−
Urinary bladder			
Detrusor	β_2	Relaxation (usually) +	Contraction +++
Trigone and sphincter	α_1	Contraction ++	Relaxation ++
Ureter			
Motility and tone	α_1	Increase	Increase (?)
Uterus	α_1, β_2	Pregnant: contraction (α_1), relaxation (β_2) Nonpregnant: relaxation (β_2)	Variable
Sex organs, male	α_1	Ejaculation ++	Erection +++
Skin			
Pilomotor muscles	α_1	Contraction ++	−
Sweat glands	α_1	Localized secretion +	Generalized secretion +++
Spleen capsule	α_1; β_2	Contraction +++, relaxation +	−
Adrenal medulla		−	Secretion of epinephrine and norepinephrine (primarily nicotinic and secondarily muscarinic)
Skeletal muscle	β_2	Increased contractility, glycogenolysis, K^+ uptake	−
Liver	α_1; β_2	Glycogenolysis and gluconeogenesis +++	−
Pancreas			
Acini	α	Decreased secretion +	Secretion ++
Islets (β cells)	α_2	Decreased secretion +++	−
	β_2	Increased secretion +	−

(*continued on next page*)

Table 1 (*continued*)

Adrenergic impulses		Cholinergic impulses	
Effector organs	Receptor type	Responses	Responses
Fat cells	α_2; β_1, (β_3)	Lipolysis +++ (thermogenesis)	−
Salivary glands	α_1	K^+ and water secretion +	K^+ and water secretion +++
	β	Amylase secretion +	
Lacrimal glands	α	Secretion +	Secretion +++
Nasopharyngeal glands		−	Secretion ++
Pineal gland	β	Melatonin synthesis	−
Posterior pituitary	β_1	Antidiuretic hormone secretion	−

+/− indicates response and its intensity.

Abbreviations: AV, atrioventricular; SA, sinoatrial.

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as multiple organ failure, a temperature often greater than 40°C, encephalopathy, and hypertension or hypotension [4]. Similar to hypertensive crises due to pheochromocytoma, the multisystem crisis may be provoked in a patient with unsuspected and untreated pheochromocytoma by manipulation of the tumor, by anesthetic agents at the induction of anesthesia, or by certain other drugs (corticosteroids, antiemetics [metoclopramide], imipramine). Patients often have pulmonary edema, sometimes necessitating ventilation [6,7,9–11], and acute (anuric) renal failure requiring hemodialysis [5,9,11]. Some patients also have intravascular disseminated coagulation [7,9]. The clinical presentation can be mistaken for septicemia, in which case appropriate treatment is delayed [5,7,10,12–14]. Fever and acute inflammatory symptoms may be due to interleukin-6 production by the tumor [15]; therefore, a pheochromocytoma should be included in the differential diagnosis if a patient with suspected septicemic shock is refractory to fluid and inotropic agents.

If the patient deteriorates despite vigorous medical treatment appropriate for pheochromocytoma, emergency tumor removal is indicated, even if the patient's condition is critical, because this may increase the chances for survival. If the patient can be stabilized, surgery should be delayed to allow adequate medical preparation because this improves survival [16,17]. The prognosis for these patients is grave if diagnosis is delayed.

Cardiovascular emergencies

Pheochromocytomas can present with a variety of life-threatening cardiovascular symptoms, such as hypertensive crisis, shock or profound

Table 2
Emergencies due to pheochromocytoma

Clinical setting	Most prominent symptoms/signs
Pheochromocytoma multisystem crisis	Multiple organ failure, temperature $\geq 40^{\circ}C$, hypertension and/or hypotension [4–12,14]
Cardiovascular	Collapse [180,181]
	Hypertensive crisis
	Upon induction of anesthesia [182–184]
	Medication induced or through other mechanisms [22,25,182,185–190]
	Shock or severe hypotension [8,13,22,24,26–30,87,102,111,191–194]
	Acute heart failure [44]
	Myocardial infarction [69,70,190,195–198]
	Arrhythmia [35–38,40,47]
	Cardiomyopathy [33,50,52,60,65,79,199–203]
	Myocarditis [204,205]
	Dissecting aortic aneurysm [80]
	Limb ischemia, digital necrosis or gangrene [74,77,78]
	Deep vein thrombosis [206]
Pulmonary	Acute pulmonary edema [31,64,83–85,190,207–212]
	Adult respiratory distress syndrome [14,213]
Abdominal	Abdominal bleeding [89,90,97,108,214,215]
	Paralytic ileus [74,95,96,216]
	Acute intestinal obstruction [94,217]
	Severe enterocolitis and peritonitis [99]
	Colon perforation [74,100,218–220]
	Bowel ischemia [50,218,221,222]
	Mesenteric vascular occlusion [223]
	Acute pancreatitis [104,224]
	Cholecystitis [102,103]
	Megacolon [225]
	Watery diarrhea syndrome with hypokalemia [91,226]
Neurologic	Hemiplegia [79,114–117,121]
	General muscle weakness [226,227]
	Generalized seizures [124,125]
Renal	Acute renal failure [33,49,106,109,111]
	Acute pyelonephritis [107]
	Severe hematuria [228]
	Renal artery stenosis by compression of tumor [112,113]
Metabolic	Diabetic ketoacidosis [229]
	Lactic acidosis [230]

Adapted from Brouwers FM, Lenders JW, Eisenhofer G, et al. Pheochromocytoma as an endocrine emergency. Rev Endocr Metab Disord 2003;4:126–8.

hypotension, acute heart failure, myocardial infarction, arrhythmia, cardiomyopathy, myocarditis, dissection of an aortic aneurysm, and acute peripheral ischemia.

Hypertensive crisis

Most patients with pheochromocytoma have hypertension, which can be sustained or paroxysmal. The latter is a result of episodic secretion of catecholamines by the tumor. In 75% of patients, paroxysms with severe

hypertension occur at least weekly [18]. Often, these paroxysms may be precipitated by postural changes, exertion, intake of certain foods or beverages, emotion, and urination. Furthermore, they may be provoked by direct tumor stimulation and the use of certain drugs (eg, histamine, adrenocorticotropic hormone [ACTH], metoclopramide, phenothiazine, tricyclic antidepressants, or anesthetic agents). Intravenous urographic contrast media have also been implicated in such provocation; however, in a small study, the nonionic contrast medium iohexol did not appear to increase catecholamine levels significantly [19]. Blood pressure can reach high values. Such a situation is termed a *hypertensive crisis* when it is life threatening or compromises vital organ function. In all of the previously mentioned situations, the hypertensive crises are the result of a rapid and marked release of catecholamines from the tumor. Hypertensive crises may also develop as a consequence of administration of a beta-adrenoceptor blocker in patients who have a pheochromocytoma who are not on alpha-adrenoceptor blocking agents. In such a situation, unopposed stimulation of alpha-adrenoceptors could lead to a rise in blood pressure.

Patients may experience hypertensive crises in different ways. Some report severe headaches or diaphoresis, whereas others have visual disturbances, palpitations, encephalopathy, acute myocardial infarction, congestive heart failure, or cerebrovascular accidents. It is crucial to start proper antihypertensive therapy immediately.

Treatment of a hypertensive crisis due to pheochromocytoma should be based on administration of phentolamine. This drug is usually given as an intravenous bolus of 2.5 to 5 mg at 1 mg/min. The short half-life of phentolamine allows this dose to be repeated every 3 to 5 minutes until hypertension is adequately controlled. Phentolamine can also be given as a continuous infusion (100 mg of phentolamine in 500 mL of 5% dextrose in water) with an infusion rate adjusted to the patient's blood pressure during continuous blood pressure monitoring. Alternatively, control of blood pressure may be achieved by a continuous infusion of sodium nitroprusside (preparation similar to phentolamine) at 0.5 to 10.0 μg/kg per minute (with the infusion stopped if no results are seen after 10 minutes) [20,21].

Shock and hypotension

Severe hypotension is seen infrequently in patients who have pheochromocytoma and may be preceded by a paroxysm of hypertension. A few patients have been described in whom severe hypotension or shock occurred after treatment with imipramine [22,23], metoclopramide [24,25], or dexamethasone [26]. Hypotension may be accompanied by syncope and may be episodic [27]. In less than 2% of patients, profound shock is the presenting manifestation [28]. In these patients, shock is accompanied by significant abdominal pain, signs consistent with pulmonary edema, intense mydriasis unresponsive to stimulus, profound weakness, diaphoresis, cyanosis, hyperglycemia, and leukocytosis [28].

Although hypotension was thought to occur only in patients with predominantly epinephrine-secreting tumors [29,30], it has also been described in norepinephrine-secreting tumors [31]. The mechanisms that lead to hypotension and shock in patients with pheochromocytoma are not understood. Hypovolemia, impairment of the peripheral response to catecholamines, the ratio of epinephrine and norepinephrine secreted by the tumor (epinephrine-induced vasodilatation), myocardial contractile dysfunction, and baroreflex failure may all contribute to hypotension [27,32].

In some patients, severe hypotension occurs in the postoperative period following resection of a pheochromocytoma. This hypotension is thought to be the result of the sudden depletion of circulating catecholamines in the continuing presence of alpha-adrenoceptor blockade and can be treated by fluid replacement and rarely by intravenous ephedrine or vasopressin [33].

Arrhythmia

Stimulation of beta-adrenoceptors by high levels of catecholamines released from the tumor may result in severe arrhythmia. Although sinus tachycardia occurs most frequently, pheochromocytomas have been associated with a wide variety of arrhythmias, including supraventricular [34], nodal [35], broad complex [36], ventricular tachycardia [37–39], torsade de pointes [40], and Wolff-Parkinson-White syndrome [41]. Furthermore, atrial fibrillation [42] and ventricular fibrillation [5,43,44] have been reported. Because arrhythmias are associated with many other diseases, patients who harbor a pheochromocytoma may undergo multiple tests and examinations by multiple specialists to identify the cause of the arrhythmia. Clinicians should consider a pheochromocytoma if the arrhythmia is paroxysmal, or if it is accompanied with sweating, hypertension, anxiety, nervousness, or pallor.

For rapid control of tachycardia due to atrial fibrillation or flutter, intravenous esmolol, a cardioselective short-acting beta 1 blocker, can be used (0.5 mg/kg intravenously over 1 minute, followed by an intravenous infusion of 0.1–0.3 mg/kg/min [45]). Caution is warranted if alpha blockade has not been achieved before the use of beta blockers, because unopposed alpha-receptor stimulation can result in a hypertensive crisis. Ventricular arrhythmias can be treated with lidocaine [46].

Some patients who have pheochromocytoma present with bradyarrhythmia or asystolic arrest [10,47,48]. These situations are the result of a reflex mechanism in which sinus slowing occurs at the onset of a sudden rise in blood pressure during a paroxysm [48]. Rarely, atrioventricular dissociation and bigeminy [34,40], right bundle branch block [49], and sick sinus syndrome [50] occur in patients with pheochromocytoma. Their treatment is similar to that in patients who do not have pheochromocytoma.

Catecholamine-induced myocarditis and cardiomyopathy

In addition to the previously discussed changes in heart rate and rhythm, hypercatecholemia can also cause sterile myocarditis and cardiomyopathy.

Catecholamine-induced dilating cardiomyopathy is most frequently reported [51–55]; however, some patients may present with a catecholamine-induced obstructive hypertrophic cardiomyopathy [50,56,57]. Acute heart failure or pulmonary edema requires immediate treatment, because the prognosis for patients with pheochromocytoma presenting with acute heart failure is poor, and death due to pulmonary edema may occur within 24 hours of the onset of such complaints [58]. Cardiac changes were found to be reversible in most cases after the institution of appropriate medication or excision of the pheochromocytoma [33,59–63]. Improvement can occur shortly after treatment [53,64,65], but recovery can also be more slow and take over 2 years [57,62]. The mechanisms for catecholamine-induced myocarditis and cardiomyopathy have been studied extensively; the importance of the different factors contributing to myocardial injury is still debated. Myocardial ischemia is thought to be most important, together with direct toxic effects of catecholamine oxidation products [66]. Furthermore, cardiac contractility may be decreased by compensatory downregulation of beta receptors on the heart owing to chronic elevation of epinephrine levels. Cardiac contractility may be further compromised by pheochromocytoma-induced hypocalcemia (through calcium sequestration), resulting in cardiogenic shock [67].

Myocardial ischemia and myocardial infarction

Some patients who have pheochromocytoma present with symptoms associated with myocardial ischemia or myocardial infarction [43,68–70]. They may experience chest discomfort, tachycardia, sweating, and anxiousness. These symptoms are caused by catecholamines, which induce vasoconstriction of the coronary arteries while simultaneously increasing myocardial oxygen demand through stimulation of heart rate and cardiac contractility. The presentation and electrocardiographic changes, such as ST-segment elevation or depression [69,71,72], negative T-waves, and a prolonged QT-interval (present in 7%–35% of patients [40,73]), may resemble those of patients with myocardial ischemia or infarction due to heart disease; however, patients with pheochromocytoma may also have other symptoms due to catecholamine excess, such as severe hypertension or headache, profuse sweating, or intense pallor. A history of episodic attacks is even more helpful. Most importantly, if the coronary arteries appear normal at angiography and no changes over time can be observed in cardiac enzymes despite a severe initial presentation, pheochromocytoma should be suspected [39].

Acute peripheral ischemia

In rare instances, pheochromocytoma causes sudden peripheral ischemia, resulting in necrosis or gangrene [74–77]. In most cases, this ischemia is due to extreme vasoconstriction or diffuse arterial vasospasms induced by catecholamine overload. Some patients may already have a history of intermittent claudication [76,78]. Catecholamine-induced vasospasms are easily

overlooked if patients report no other symptoms characteristic for pheochromocytoma. Such patients may undergo extensive operations including amputation [58]. This treatment is very dangerous because any surgery in a patient with unsuspected pheochromocytoma carries a high risk for morbidity and mortality.

Ischemia may also be due to arterial occlusion as a result of embolisms of cardiac thrombi in patients with catecholamine-induced arrhythmia [79]; however, this is a rare event. Occasionally, pheochromocytoma is found during the evaluation or emergency surgery for suspected ruptured aneurysms of the abdominal aorta [76]. Both dissecting and obstructive aneurysms of the abdominal aorta have been found in patients who have pheochromocytoma [80–82].

Pulmonary emergencies

Infrequently, pulmonary edema is the presenting feature of pheochromocytoma [31,83–85]. This event has even been documented following surgery for an unrelated illness [86]. More often, pulmonary edema occurs during the course of the disease and in some patients becomes manifest after tumor resection [43]. Although pulmonary edema is cardiogenic in origin in most patients, some patients have noncardiogenic pulmonary edema [31,84]. This edema is thought to be the result of a catecholamine-induced transient increase in pulmonary capillary pressure owing to pulmonary venoconstriction and increased pulmonary capillary permeability [31,43,87]. Recently, it has been suggested that increased pulmonary neutrophil accumulation caused by catecholamine excess may have a pathophysiologic role in the development of pulmonary edema. Neutrophil-mediated injury would, in turn, lead to increased vascular protein permeability and promote lung edema [85].

Gastrointestinal emergencies

Patients who have pheochromocytomas who present with an acute onset of abdominal symptoms can pose a real challenge. Generally, they experience severe abdominal pain and vomiting. Close monitoring is important, because the abdominal symptoms may indicate hemorrhage of the tumor, which could be accompanied by the excretion of vast amounts of catecholamines. This excretion, in turn, could result in hypertensive crisis [88,89], shock, and rapid deterioration of the patient. Moreover, emergency surgery may be required to stop associated arterial bleeding. Alternatively, angiographic embolization may be employed to stop bleeding [88,90].

Other abdominal catastrophes are the result of prolonged catecholamine excess. Emergency surgery could be indicated if vasoconstriction or spasms of the mesenterial arteries cause bowel ischemia. In other patients, high catecholamine levels seem to affect predominantly gastrointestinal motility. Peristalsis is inhibited through relaxation of the gastrointestinal muscles and contraction of the pyloric and ileocecal sphincters, resulting in constipation.

Conversely, patients with a composite pheochromocytoma that is also secreting vasoactive intestinal polypeptide can present with acute and severe secretory diarrheas, resulting in dehydration, acidosis, and hypokalemia [91].

Patients may also present with intestinal pseudo-obstruction [92,93], abdominal distension [94], severe paralytic ileus [74,89,95,96], dilated small bowel loops [97], or megacolon [94,98]. The latter may be complicated by enterocolitis [98,99], volvulus or colonic rupture [100], and fecal peritonitis [101]. Other abdominal emergencies in patients who have pheochromocytoma include acute cholecystitis [102,103], acute pancreatitis [104], and ruptured aneurysm of the abdominal aorta [82].

Nephrologic emergencies

Rarely, a pheochromocytoma manifests with the clinical presentation of acute renal failure [105,106] or acute pyelonephritis [107]. Acute renal failure is associated with rhabdomyolysis, which may occur after ischemia owing to extreme catecholamine-induced vasoconstriction. The rhabdomyolysis leads to acute myoglobinuric renal failure [105]. More frequently, renal failure occurs as a complication during the course of the disease [5,49,108–111]. Other complications include renal infarction as a consequence of renal ischemia due to (deep) systemic shock, vasoconstriction, or tumor compression of the renal artery [112,113]. In some patients, hemodialysis is required [111].

Neurologic emergencies

Cerebrovascular accidents are most frequently responsible for the neurologic symptoms seen in patients who have pheochromocytoma [79,114–121]. In some patients, cerebral hemorrhage has been reported during paroxysmal attacks of hypertension. In rare cases, subarachnoidal bleeding is found [118]. Hemiparesis, sometimes together with homonymous hemianopsy, is reported most frequently [117]. Cerebral bleeding may be accompanied by seizures [18,116,122,123]. Generalized seizures can also occur as a result of cerebral ischemia caused by vasospasm of the cerebral circulation owing to high levels of circulating catecholamines and may be the presenting symptom [124,125]. In young patients with cerebral hemorrhage without an apparent cause, pheochromocytoma should be suspected. Rarely, neurologic symptoms such as paresis occur due to spinal cord compression by metastases.

Management

Management of pheochromocytoma-related emergencies depends on the symptoms; however, it should always include pharmacologic treatment to block the effects of high levels of circulating catecholamines and prevent life-threatening catecholamine-induced complications.

The most effective drug regimen to prepare patients for surgery has not been established, and, currently, several approaches are used to stabilize

patients and prepare them for (elective) surgery [2]. Patients must be prepared using pharmacologic blockade of adrenoceptors. Phenoxybenzamine is the drug of choice for alpha-adrenoceptor blockade. It is usually given in a starting dose of 10 mg two times a day and is gradually increased up to 1 mg/kg/d given in three to four separate doses [2,126]. Doses higher than 100 mg per day are necessary in a few patients. Adequate alpha-receptor blockade will be achieved within 10 to 14 days. Beta-adrenoceptor blockade (usually, atenolol, 25 mg once daily, or propranolol, 40 mg three times daily) is added after appropriate alpha blockade to prevent reflex tachycardia associated with alpha blockade [2,126]. It can also be indicated if arrhythmia or angina is present after alpha blockade has been achieved. In rare cases, successful selective alpha-adrenoceptor blockade can lead to unopposed beta-adrenergic overactivity that affects multiple organ systems. Patients may experience tachycardia, diastolic dysfunction, diffuse edema (heart), peripheral vasodilatation and hypotension (vascular system), somnolence owing to cerebral hypoperfusion, and oliguria owing to renal hypoperfusion [127]. Treatment consists of beta blockade tapered to alleviate clinical symptoms.

Other approaches to prepare patients for surgery include the use of other alpha 1-adrenoceptor blockers, calcium channel blockers alone or in combination with alpha-receptor blockade [51,128], or labetalol (a combined alpha- and beta-adrenoceptor blocker).

To assess whether a patient is adequately prepared for surgery, the following criteria have been proposed: blood pressure below 160/90 mm Hg for at least 24 hours; the presence of orthostatic hypotension, but with blood pressure in the upright position remaining above 80/45 mm Hg; no more than one ventricular extrasystole every 5 minutes; and no S-T segment changes and T-wave inversions on echocardiography for 1 week [129].

Postoperatively, patients should be monitored closely for 24 hours in an intensive or immediate care unit. Hypotension and hypoglycemia are the two most common major complications seen at this time [2]. Rarely, patients experience pulmonary edema or cardiomyopathy following surgery [43,63].

Pheochromocytoma in pregnancy

Pheochromocytoma in pregnancy warrants special consideration, because it is associated with high morbidity and mortality if pheochromocytoma is unsuspected (40.3% maternal mortality and 56% fetal mortality). Pregnancy-related life-threatening situations can occur owing to tumor stimulation by pressure from the enlarging uterus, by fetal movements, or during labor in a patient with unsuspected pheochromocytoma. If the diagnosis is made antenatal, maternal and fetal mortality can be greatly reduced [130,131]. Nevertheless, in two series, pheochromocytoma remained unrecognized antepartum in 47% to 65% of patients [130,131]. Diagnosis of pheochromocytoma during pregnancy can be difficult because the clinical

presentation may resemble pre-eclampsia. Whereas pre-eclampsia occurs after the twentieth week of gestation and is associated with hypertension in combination with proteinuria, hypertension caused by pheochromocytoma can occur throughout the entire pregnancy, and proteinuria and edema are often absent. Furthermore, pheochromocytoma-associated hypertension can be paroxysmal and may be accompanied by postural hypotension [132].

Hypertensive crisis owing to pheochromocytoma in pregnancy is highly unpredictable. Direct tumor stimulation leading to marked catecholamine release can occur as the result of examination, postural changes, pressure from the uterus, labor contractions, fetal movements, and tumor hemorrhage. It is most frequently seen in the period surrounding delivery. Acute hypertensive crisis may manifest as severely elevated blood pressure, arrhythmia, or pulmonary edema.

The diagnosis can be confirmed biochemically. Biochemical diagnosis can be hindered if the patient is on methyldopa to control blood pressure during pregnancy, because this drug can result in a false-positive test. If pheochromocytoma is suspected, treatment with methyldopa should be suspended or delayed for the measurement of metanephrines.

Once the diagnosis of pheochromocytoma is confirmed, appropriate adrenergic blockade should be initiated in all patients regardless of gestational age, because maternal hypertensive crisis is always dangerous for the fetus. Commonly, it results in uteroplacental insufficiency, early separation of the placenta, or fetal death [133]. In situations of hypertensive crisis, intravenous phentolamine as a bolus of 1 to 5 mg or as a continuous infusion of 1 mg/min can be used to control blood pressure. As a final resort, sodium nitroprusside may be used, but this has to be infused at a rate of less than 1 μg/kg/min to avoid fetal cyanide toxicity [134].

To prevent hypertensive crisis or to treat catecholamine-induced high blood pressure in pregnancy, phenoxybenzamine is most commonly used. With the exception of mild perinatal depression and transient hypotension in the newborn, there have been no reports of adverse fetal effects during treatment [135]. If beta blockade is indicated, a selective beta-blocking agent is preferred to lessen the chances of fetal growth retardation.

The timing of tumor excision depends on the duration of pregnancy at the time of diagnosis. Early in pregnancy, the tumor can be resected after suction and curettage or with preservation of the fetus. After the twenty-fourth week of pregnancy, long-term blockade with phenoxybenzamine, combined with a beta blocker if clinically indicated, should be attempted to bring the fetus to term [134,135]. This treatment is not without risks, because blockade does not always prevent acute crisis. Labor and vaginal delivery should be avoided, because this may cause tumor stimulation and further catecholamine secretion with severe hypertensive crisis despite adrenergic blockade. Cesarean section and simultaneous removal of the tumor is the recommended approach [135]. Anesthetic management for this situation is discussed in detail in the article by Dugas and colleagues [136].

Neuroblastoma

Neuroblastomas and ganglioneuroblastomas (a more mature form of neuroblastoma) are tumors that derive from primitive cells (neuroblasts) from the sympathetic nervous system. These tumors comprise the most common malignant disease of childhood and account for 7% to 10% of all childhood cancers [137,138]. The prevalence is uniform throughout the (industrialized) world, occurring in 1 in 7000 live births [137,139]. Neuroblastoma is predominantly a tumor of young children, with a median age at diagnosis of 18 months (40% are diagnosed by 1 year of age, 75% by 4 years of age, and 98% by 10 years of age) [139,140].

Approximately 65% of neuroblastomas are located in the abdomen, most commonly in the adrenal medulla. Other tumor locations are the chest (20%), pelvis (2% to 3%), neck (1% to 5%), and other locations (6% to 12%) [141–143]. The tumor typically spreads to regional lymph nodes, bone, and bone marrow, but can also metastasize to skin, liver, and soft tissues. Approximately 50% of patients have disseminated disease (lymph node involvement outside the cavity of origin) at presentation [143].

Symptoms and signs at presentation depend on the size and location of the primary tumor and on whether the tumor has metastasized. They are often related to a local mass effect of the tumor or metastasis and include paraplegia (paraspinal tumors, sometimes extending through intervertebral foramina [“dumbbell tumors”]), Horner’s syndrome (ie, ptosis, miosis, and anhydrosis owing to cervical masses), ecchymotic proptosis (“raccoon eyes” owing to orbital involvement), and limping (involvement of long bones). Furthermore, in some cases, the tumor is accompanied by remote effects called paraneoplastic phenomena, such as opsoclonus-myoclonus ataxia syndrome caused by an autoimmune process (2% to 3% of patients) [144], or secretory diarrhea if the tumor is producing vasoactive intestinal peptide. Rarely, catecholamines secreted by the tumor (approximately 92% of neuroblastomas have elevated levels of catecholamines) contribute to symptoms and signs at presentation (hypertension or paroxysmal phenomena like flushing or tachycardia). Neuroblastomas are clinically heterogeneous, and disease progression varies widely according to age and disease burden at diagnosis [138].

To stage neuroblastomas, a set of international criteria has been developed—the International Neuroblastoma Staging System (INSS) [145,146]. There are four stages in the INSS classification. The disease is localized in stages 1 to 3, with the stage depending on the extent of lymph node involvement and the presence of midline extension of the disease. In stage 4, the disease is disseminated [146]. Stage 4S is a special subcategory that applies to children under 1 year of age with a distinct pattern of disseminated disease (dissemination limited to skin, liver, or bone marrow) that is associated with spontaneous regression and a high cure rate with or without nonsurgical treatment [147,148].

Prognosis and treatment options are determined predominantly by patient age at diagnosis, INSS stage, tumor histopathology (Shimada system), and biologic features of the tumor, such as the MYCN status (whether or not MYCN amplification is present), the DNA index (near diploid or hyperdiploid karyotype), and the presence or absence of deletions at 1p36 or 11q23 [138,149]. Treatment options include surgery (performed in almost all patients to establish the diagnosis and procure tissue for staging and biologic studies), chemotherapy (the principal treatment modality) with or without supplemental radiotherapy and autologous bone marrow transplantation, radionuclide therapy with ^{131}I-labeled meta-iodo-benzyl-guanidine (^{131}I-MIBG), retinoid therapy, and immunotherapy [140,150].

Emergency conditions related to neuroblastoma

Emergency situations that occur owing to neuroblastomas are not common. When they occur, they are often the result of catecholamine excess, paraneoplastic phenomena, or related to local mass effects of the tumor.

In rare cases, patients who have neuroblastoma experience symptoms and signs owing to catecholamine excess requiring emergency intervention similar to patients with pheochromocytoma. Because the mechanisms behind these conditions are the same as discussed for pheochromocytoma, they are not discussed separately herein. Cardiovascular events are described most frequently as emergency situations owing to catecholamine excess in neuroblastoma. Hypertensive encephalopathy accompanied by seizures [151], cardiogenic shock requiring respiratory ventilation [152], or cardiac failure [153,154] accompanied by coagulopathy and acute renal and hepatic failure [155] have all been described. Furthermore, one patient presented with a condition mimicking sepsis, with hypertension, vasoconstriction, multiorgan failure, and metabolic acidosis [156].

Sometimes paraneoplastic phenomena can lead to emergency conditions. These paraneoplastic manifestations have an immunologic basis and are associated with IgG and IgM antibodies that bind to the cytoplasm of cerebellar Purkinje's cells and to some axons of the peripheral nerves [157]. In one patient with occult neuroblastoma, encephalitis-like features of ataxia, generalized seizures, decreased consciousness, and involuntary movements were seen; however, this patient did not have any signs of opsoclonus-myoclonus at any time during his illness [158]. Less urgent paraneoplastic manifestations of neuroblastoma include paraneoplastic papilloedema with blurring of vision [159] and bilateral ptosis and muscle weakness [160].

A local mass effect of the tumor can also lead to emergency presentations. One patient with a rapidly increasing massive hepatomegaly owing to metastatic infiltration of the liver required mechanical ventilation and urgent surgical decompression for severe respiratory embarrassment [161]. Other treatment options successfully applied to patients with life-threatening abdominal distension owing to liver involvement include chemotherapy and

radiotherapy [150]. Patients may present with leg palsy or weakness of the lower extremities if the tumor involves the spinal cord or results in spinal cord compression [162,163]. Other tumor mass–related presentations include blindness owing to metastatic neuroblastoma [164] and protein-losing enteropathy as the result of lymphatic obstruction [165] or elevated catecholamines [166], resulting in periorbital edema and severe hypoproteinemia.

Early diagnosis of these cases may improve the outcome [162]. For example, the blindness due to metastatic neuroblastoma was reversed by surgery 7 days after onset [164].

Ganglioneuroma

Ganglioneuroma is a rare benign tumor that derives from the sympathetic chain. Controversy exists as to whether it may occur de novo (primary ganglioneuroma) or whether it is a result of maturation and differentiation of neuroblastomas, as suggested by the International Neuroblastoma Pathology Committee [167,168]. Ganglioneuromas occur most frequent in the posterior mediastinum (38%), followed by a retroperitoneal site. As many as half of patients are asymptomatic [169–171], and if patients do experience symptoms, these are often caused by a mass effect of the tumor. Infrequently, patients may have hypertension owing to excessive catecholamine secretion by the tumor (only 20% to 39% of ganglioneuromas are reported to secrete catecholamines or catecholamine metabolites [172–174]), or they can have watery diarrhea owing to the secretion of vasoactive intestinal protein by the tumor [175–177]. Patients can be cured by the complete excision of the tumor; however, even if resection of the ganglioneuroma is incomplete, the prognosis usually remains good.

Endocrine emergencies related to ganglioneuroma are rare. In one patient, a membranous glomerulonephritis resulting in nephrotic syndrome was associated with a ganglioneuroma. A circulating tumor antigen–specific antibody was detected in the patient's serum that cross-reacted with an antigen present on the podocyte membrane of the renal glomeruli [178].

Summary

Pheochromocytoma may lead to important emergency situations. It is vital to think about this disease in any emergency situation when conventional therapy fails to achieve control or symptoms occur that do not fit the initial diagnosis, especially if signs and symptoms occur paroxysmal. The crucial role of keeping this diagnosis in mind is made clear by the fact that, in 50% of patients who have pheochromocytoma, the diagnosis is initially overlooked. When pheochromocytoma is considered, appropriate approaches must be used for its diagnosis and localization. These approaches include measurement of urinary and plasma catecholamines and

metanephrines and imaging techniques such as CT, MRI, and ^{123}I- or ^{131}I-labeled MIBG scintigraphy. Measurement of plasma metanephrines is the biochemical test of choice [179]. MRI is the recommended imaging modality in emergency situations, because it has a high sensitivity for localizing adrenal and extra-adrenal pheochromocytoma.

Occasionally, neuroblastoma and ganglioneuroma may cause emergency situations. These situations are related to catecholamine excess, paraneoplastic phenomena, or local tumor mass effects. Diagnosis of neuroblastoma can be confirmed by biopsy and measurement of urinary catecholamines [146]. Many imaging modalities are used for localization and assessment of the extent of the disease, including MRI or CT and ^{123}I- or ^{131}I-labeled MIBG scintigraphy [140,146,150].

References

[1] Manger WM, Gifford RW Jr, Hoffman BB. Pheochromocytoma: a clinical and experimental overview. Curr Probl Cancer 1985;9:1–89.
[2] Lenders JW, Eisenhofer G, Mannelli M, et al. Phaeochromocytoma. Lancet 2005;366: 665–75.
[3] Bryant J, Farmer J, Kessler LJ, et al. Pheochromocytoma: the expanding genetic differential diagnosis. J Natl Cancer Inst 2003;95:1196–204.
[4] Newell KA, Prinz RA, Pickleman J, et al. Pheochromocytoma multisystem crisis: a surgical emergency. Arch Surg 1988;123:956–9.
[5] Gordon DL, Atamian SD, Brooks MH, et al. Fever in pheochromocytoma. Arch Intern Med 1992;152:1269–72.
[6] Moran ME, Rosenberg DJ, Zornow DH. Pheochromocytoma multisystem crisis. Urology 2006;67(4) 846e19–20.
[7] Herbland A, Bui N, Rullier A, et al. Multiple organ failure as initial presentation of pheochromytoma. Am J Emerg Med 2005;23:565–6.
[8] De Wilde D, Velkeniers B, Huyghens L, et al. The paradox of hypotension and pheochromocytoma: a case report. Eur J Emerg Med 2004;11:237–9.
[9] Caputo C, Fishbane S, Shapiro L, et al. Pheochromocytoma multisystem crisis in a patient with multiple endocrine neoplasia type IIB and pyelonephritis. Am J Kidney Dis 2002;39: E23.
[10] Kizer JR, Koniaris LS, Edelman JD, et al. Pheochromocytoma crisis, cardiomyopathy, and hemodynamic collapse. Chest 2000;118:1221–3.
[11] Kolhe N, Stoves J, Richardson D, et al. Hypertension due to phaeochromocytoma—an unusual cause of multiorgan failure. Nephrol Dial Transplant 2001;16:2100–4.
[12] Fred HL, Allred DP, Garber HE, et al. Pheochromocytoma masquerading as overwhelming infection. Am Heart J 1967;73:149–54.
[13] Ford J, Rosenberg F, Chan N. Pheochromocytoma manifesting with shock presents a clinical paradox: a case report. CMAJ 1997;157:923–5.
[14] Mok CC, Ip TP, So CC. Phaeochromocytoma with adult respiratory distress syndrome mimicking septicaemic shock. Med J Aust 1997;166:634–5.
[15] Kang JM, Lee WJ, Kim WB, et al. Systemic inflammatory syndrome and hepatic inflammatory cell infiltration caused by an interleukin-6 producing pheochromocytoma. Endocr J 2005;52:193–8.
[16] Ulchaker JC, Goldfarb DA, Bravo EL, et al. Successful outcomes in pheochromocytoma surgery in the modern era. J Urol 1999;161:764–7.
[17] Kobayashi T, Iwai A, Takahashi R, et al. Spontaneous rupture of adrenal pheochromocytoma: review and analysis of prognostic factors. J Surg Oncol 2005;90:31–5.

[18] Manger WM, Gifford RW Jr. Pheochromocytoma: current diagnosis and management. Cleve Clin J Med 1993;60:365–78.
[19] Mukherjee JJ, Peppercorn PD, Reznek RH, et al. Pheochromocytoma: effect of nonionic contrast medium in CT on circulating catecholamine levels. Radiology 1997;202: 227–31.
[20] Bravo EL, Gifford RW Jr. Pheochromocytoma. Endocrinol Metab Clin North Am 1993; 22:329–41.
[21] Pacak K, Chrousos GP, Koch CA, et al. Pheochromocytoma: progress in diagnosis, therapy and genetics. In: Margioris AN, Chrousos GP, editors. Adrenal disorders. Totowa (NJ): Humana Press; 2001. p. 379–413.
[22] Ferguson KL. Imipramine-provoked paradoxical pheochromocytoma crisis: a case of cardiogenic shock. Am J Emerg Med 1994;12:190–2.
[23] Brown K, Ratner M, Stoll M. Pheochromocytoma unmasked by imipramine in an 8-year-old girl. Pediatr Emerg Care 2003;19:174–7.
[24] Maxwell PH, Buckley C, Gleadle JM, et al. Nasty shock after an anti-emetic. Nephrol Dial Transplant 2001;16:1069–72.
[25] Leow MK, Loh KC. Accidental provocation of phaeochromocytoma: the forgotten hazard of metoclopramide? Singapore Med J 2005;46:557–60.
[26] Takagi S, Miyazaki S, Fujii T, et al. Dexamethasone-induced cardiogenic shock rescued by percutaneous cardiopulmonary support (PCPS) in a patient with pheochromocytoma. Jpn Circ J 2000;64:785–8.
[27] Ueda T, Oka N, Matsumoto A, et al. Pheochromocytoma presenting as recurrent hypotension and syncope. Intern Med 2005;44:222–7.
[28] Bergland BE. Pheochromocytoma presenting as shock. Am J Emerg Med 1989;7:44–8.
[29] Richmond J, Frazer SC, Millar DR. Paroxysmal hypotension due to an adrenaline-secreting phaeochromocytoma. Lancet 1961;2:904–6.
[30] Hamrin B. Sustained hypotension and shock due to an adrenaline-secreting phaeochromocytoma. Lancet 1962;2:123–5.
[31] de Leeuw PW, Waltman FL, Birkenhager WH. Noncardiogenic pulmonary edema as the sole manifestation of pheochromocytoma. Hypertension 1986;8:810–2.
[32] Ramsay ID, Langlands JHM. Phaeochromocytoma. Lancet 1962;2:126–8.
[33] Augoustides JG, Abrams M, Berkowitz D, et al. Vasopressin for hemodynamic rescue in catecholamine-resistant vasoplegic shock after resection of massive pheochromocytoma. Anesthesiology 2004;101:1022–4.
[34] Sode J, Getzen LC, Osborne DP. Cardiac arrhythmias and cardiomyopathy associated with pheochromocytomas: report of three cases. Am J Surg 1967;114:927–31.
[35] Lydakis C, Hollinrake K, Lip GYH. An unusual cause of palpitations requiring atrioventricular node ablation and pacemaker therapy. Blood Press 1997;6:368–71.
[36] Tzemos N, McNeill GP, Jung RT, et al. Post exertional broad complex tachycardia in a normotensive patient: a rare presentation of phaeochromocytoma. Scott Med J 2001; 46:14–5.
[37] Petit T, de Lagausie P, Maintenant J, et al. Thoracic pheochromocytoma revealed by ventricular tachycardia: clinical case and review of the literature. Eur J Pediatr Surg 2000; 10:142–4.
[38] Michaels RD, Hays JH, O'Brian JT, et al. Pheochromocytoma associated ventricular tachycardia blocked with atenolol. J Endocrinol Invest 1990;13:943–7.
[39] Brilakis ES, Young WF Jr, Wilson JW, et al. Reversible catecholamine-induced cardiomyopathy in a heart transplant candidate without persistent or paroxysmal hypertension. J Heart Lung Transplant 1999;18:376–80.
[40] Shimizu K, Miura Y, Meguro Y, et al. QT prolongation with torsade de pointes in pheochromocytoma. Am Heart J 1992;124:235–9.
[41] Gurlek A, Erol C. Pheochromocytoma with asymmetric septal hypertrophy and Wolff-Parkinson-White syndrome. Int J Cardiol 1991;32:403–5.

[42] Hicks RJ, Wood B, Kalff V, et al. Normalization of left ventricular ejection fraction following resection of pheochromocytoma in a patient with dilated cardiomyopathy. Clin Nucl Med 1991;16:413–6.
[43] Cohen CD, Dent DM. Phaeochromocytoma and acute cardiovascular death (with special reference to myocardial infarction). Postgrad Med J 1984;60:111–5.
[44] Gill PS. Acute heart failure in the parturient—do not forget phaeochromocytoma. Anaesth Intensive Care 2000;28:322–4.
[45] Nicholas E, Deutschman CS, Allo M, et al. Use of esmolol in the intraoperative management of pheochromocytoma. Anesth Analg 1988;67:1114–7.
[46] Manger WM, Gifford RW. Pheochromocytoma. J Clin Hypertens (Greenwich) 2002;4: 62–72.
[47] Zweiker R, Tiemann M, Eber B, et al. Bradydysrhythmia-related presyncope secondary to pheochromocytoma. J Intern Med 1997;242:249–53.
[48] Forde TP, Yormak SS, Killip T 3rd. Reflex bradycardia and nodal escape rhythm in pheochromocytoma. Am Heart J 1968;76:388–92.
[49] Hamada N, Akamatsu A, Joh T. A case of pheochromocytoma complicated with acute renal failure and cardiomyopathy. Jpn Circ J 1993;57:84–90.
[50] Grossman E, Knecht A, Holtzman E, et al. Uncommon presentation of pheochromocytoma: case studies. Angiology 1985;36:759–65.
[51] Serfas D, Shoback DM, Lorell BH. Phaeochromocytoma and hypertrophic cardiomyopathy: apparent suppression of symptoms and noradrenaline secretion by calcium-channel blockade. Lancet 1983;2:711–3.
[52] Schaffer MS, Zuberbuhler P, Wilson G, et al. Catecholamine cardiomyopathy: an unusual presentation of pheochromocytoma in children. J Pediatr 1981;99:276–9.
[53] Lam JB, Shub C, Sheps SG. Reversible dilatation of hypertrophied left ventricle in pheochromocytoma: serial two-dimensional echocardiographic observations. Am Heart J 1985;109:613–5.
[54] Shapiro LM, Trethowan N, Singh SP. Normotensive cardiomyopathy and malignant hypertension in phaeochromocytoma. Postgrad Med J 1982;58:110–1.
[55] Velasquez G, D'Souza VJ, Hackshaw BT, et al. Phaeochromocytoma and cardiomyopathy. Br J Radiol 1984;57:89–92.
[56] Jacob JL, da Silveira LC, de Freitas CG, et al. Pheochromocytoma with echocardiographic features of obstructive hypertrophic cardiomyopathy: a case report. Angiology 1994;45: 985–9.
[57] Huddle KR, Kalliatakis B, Skoularigis J. Pheochromocytoma associated with clinical and echocardiographic features simulating hypertrophic obstructive cardiomyopathy. Chest 1996;109:1394–7.
[58] Sardesai SH, Mourant AJ, Sivathandon Y, et al. Phaeochromocytoma and catecholamine induced cardiomyopathy presenting as heart failure. Br Heart J 1990;63:234–7.
[59] Quigg RJ, Om A. Reversal of severe cardiac systolic dysfunction caused by pheochromocytoma in a heart transplant candidate. J Heart Lung Transplant 1994;13:525–32.
[60] Wood R, Commerford PJ, Rose AG, et al. Reversible catecholamine-induced cardiomyopathy. Am Heart J 1991;121:610–3.
[61] Imperato-McGinley J, Gautier T, Ehlers K, et al. Reversibility of catecholamine-induced dilated cardiomyopathy in a child with a pheochromocytoma. N Engl J Med 1987;316: 793–7.
[62] Mishra AK, Agarwal G, Kapoor A, et al. Catecholamine cardiomyopathy in bilateral malignant pheochromocytoma: successful reversal after surgery. Int J Cardiol 2000;76: 89–90.
[63] Gordon RY, Fallon JT, Baran DA. Case report: a 32-year-old woman with familial paragangliomas and acute cardiomyopathy. Transplant Proc 2004;36:2819–22.
[64] Kaye J, Edlin S, Thompson I, et al. Pheochromocytoma presenting as life-threatening pulmonary edema. Endocrine 2001;15:203–4.

[65] Salathe M, Weiss P, Ritz R. Rapid reversal of heart failure in a patient with phaeochromocytoma and catecholamine-induced cardiomyopathy who was treated with captopril. Br Heart J 1992;68:527–8.
[66] Ganguly PK, Beamish RE, Dhalla NS. Catecholamine cardiotoxicity in pheochromocytoma. Am Heart J 1989;117:1399–400.
[67] Olson SW, Deal LE, Piesman M. Epinephrine-secreting pheochromocytoma presenting with cardiogenic shock and profound hypocalcemia. Ann Intern Med 2004;140:849–51.
[68] Murai K, Hirota K, Niskikimi T, et al. Pheochromocytoma with electrocardiographic change mimicking angina pectoris, and cyclic change in direct arterial pressure—a case report. Angiology 1991;42:157–61.
[69] Mirza A. Myocardial infarction resulting from nonatherosclerotic coronary artery diseases. Am J Emerg Med 2003;21:578–84.
[70] Darze ES, Von Sohsten RL. Pheochromocytoma-induced segmental myocardial dysfunction mimicking an acute myocardial infarction in a patient with normal coronary arteries. Arq Bras Cardiol 2004;82:178–80, 175–7.
[71] Yoshinaga K, Torii H, Tahara M. A serial echocardiographic observation of acute heart injury associated with pheochromocytoma crisis. Int J Cardiol 1998;66:199–202.
[72] Liao WB, Liu CF, Chiang CW, et al. Cardiovascular manifestations of pheochromocytoma. Am J Emerg Med 2000;18:622–5.
[73] Stenstrom G, Swedberg K. QRS amplitudes, QTc intervals and ECG abnormalities in pheochromocytoma patients before, during and after treatment. Acta Med Scand 1988; 224:231–5.
[74] Januszewicz W, Wocial B. Clinical and biochemical aspects of pheochromocytoma: report of 110 cases. Cardiology 1985;72:131–6.
[75] Radtke WE, Kazmier FJ, Rutherford BD, et al. Cardiovascular complications of pheochromocytoma crisis. Am J Cardiol 1975;35:701–5.
[76] Krane NK. Clinically unsuspected pheochromocytomas: experience at Henry Ford Hospital and a review of the literature. Arch Intern Med 1986;146:54–7.
[77] Tack CJ, Lenders JW. Pheochromocytoma as a cause of blue toes. Arch Intern Med 1993; 153:2061.
[78] Scharf Y, Nahir M, Plavnic Y, et al. Intermittent claudication with pheochromocytoma. JAMA 1971;215:1323–4.
[79] Dagartzikas MI, Sprague K, Carter G, et al. Cerebrovascular event, dilated cardiomyopathy, and pheochromocytoma. Pediatr Emerg Care 2002;18:33–5.
[80] Triplett JC, Atuk NO. Dissecting aortic aneurysm associated with pheochromocytoma. South Med J 1975;68:748–53.
[81] Cabot. Case 27022. N Engl J Med 1941;224:77–9.
[82] Ehata T, Karasawa F, Watanabe K, et al. Unsuspected pheochromocytoma with abdominal aortic aneurysm—a case report. Acta Anaesthesiol Sin 1999;37:27–8.
[83] Naeije R, Yernault JC, Goldstein M, et al. Acute pulmonary oedema in a patient with phaeochromocytoma. Intensive Care Med 1978;4:165–7.
[84] Takeshita T, Shima H, Oishi S, et al. Noncardiogenic pulmonary edema as the first manifestation of pheochromocytoma: a case report. Radiat Med 2005;23:133–8.
[85] Sukoh N, Hizawa N, Yamamoto H, et al. Increased neutrophils in bronchoalveolar lavage fluids from a patient with pulmonary edema associated with pheochromocytoma. Intern Med 2004;43:1194–7.
[86] Fahmy N, Assaad M, Bathija P, et al. Postoperative acute pulmonary edema: a rare presentation of pheochromocytoma. Clin Nephrol 1997;48:122–4.
[87] Baxter MA, Hunter P, Thompson GR, et al. Phaeochromocytomas as a cause of hypotension. Clin Endocrinol (Oxf) 1992;37:304–6.
[88] Hendrickson RJ, Katzman PJ, Queiroz R, et al. Management of massive retroperitoneal hemorrhage from an adrenal tumor. Endocr J 2001;48:691–6.

[89] Hatada T, Nakai T, Aoki I, et al. Acute abdominal symptoms caused by hemorrhagic necrosis of a pheochromocytoma: report of a case. Surg Today 1994;24:363–7.
[90] Park JH, Kang KP, Lee SJ, et al. A case of a ruptured pheochromocytoma with an intratumoral aneurysm managed by coil embolization. Endocr J 2003;50:653–6.
[91] Van Eeckhout P, Shungu H, Descamps FX, et al. Acute watery diarrhea as the initial presenting feature of a pheochromocytoma in an 84-year-old female patient. Horm Res 1999; 52:101–6.
[92] Khafagi FA, Lloyd HM, Gough IR. Intestinal pseudo-obstruction in pheochromocytoma. Aust N Z J Med 1987;17:246–8.
[93] Turner CE. Gastrointestinal pseudo-obstruction due to pheochromocytoma. Am J Gastroenterol 1983;78:214–7.
[94] Bernstein A, Wright AC, Spencer D. Phaeochromocytoma as a cause of gastrointestinal distension. Postgrad Med J 1967;43:180–3.
[95] Noguchi M, Taniya T, Ueno K, et al. A case of pheochromocytoma with severe paralytic ileus. Jpn J Surg 1990;20:448–52.
[96] Sawaki D, Otani Y, Sekita G, et al. Pheochromocytoma complicated with refractory paralytic ileus dramatically improved with intravenous administration of alpha-adrenergic receptor antagonist, phentolamine. J Clin Gastroenterol 2003;37:194.
[97] Lee PH, Blute R Jr, Malhotra R. A clinically "silent" pheochromocytoma with spontaneous hemorrhage. J Urol 1987;138:1429–32.
[98] Rosati LA, Augur NA Jr. Ischemic enterocolitis in pheochromocytoma. Gastroenterology 1971;60:581–5.
[99] Fee HJ, Fonkalsrud EW, Ament ME, et al. Enterocolitis with peritonitis in a child with pheochromocytoma. Ann Surg 1977;185:448–50.
[100] Mazaki T, Hara J, Watanabe Y, et al. Pheochromocytoma presenting as an abdominal emergency: association with perforation of the colon. Digestion 2002;65:61–6.
[101] Mullen JP, Cartwright RC, Tisherman SE, et al. Pathogenesis and pharmacologic management of pseudo-obstruction of the bowel in pheochromocytoma. Am J Med Sci 1985;290: 155–8.
[102] Mishra AK, Agarwal G, Agarwal A, et al. Cystic phaeochromocytoma presenting as an acute abdomen with shock. Eur J Surg 2001;167:863–5.
[103] Cho YU, Kim JY, Choi SK, et al. A case of hemorrhagic gallbladder paraganglioma causing acute cholecystitis. Yonsei Med J 2001;42:352–6.
[104] Dugal Perrier NA, van Heerden JA, Wilson DJ, et al. Malignant pheochromocytoma masquerading as acute pancreatitis—a rare but potentially lethal occurrence. Mayo Clin Proc 1994;69:366–70.
[105] Shemin D, Cohn PS, Zipin SB. Pheochromocytoma presenting as rhabdomyolysis and acute myoglobinuric renal failure. Arch Intern Med 1990;150:2384–5.
[106] Gillett MJ, Arenson RV, Yew MK, et al. Diagnostic challenges associated with a complex case of cystic phaeochromocytoma presenting with malignant hypertension, microangiopathic haemolysis and acute renal failure. Nephrol Dial Transplant 2005;20:1014.
[107] Winter C, Schmidt-Mutter C, Cuny R, et al. Fatal form of phaeochromocytoma presenting as acute pyelonephritis. Eur J Anaesthesiol 2001;18:548–53.
[108] Evans JP, Bambach CP, Andrew S, et al. MEN type 2a presenting as an intra-abdominal emergency. Aust N Z J Surg 1997;67:824–6.
[109] Takabatake T, Kawabata M, Ohta H, et al. Acute renal failure and transient, massive proteinuria in a case of pheochromocytoma. Clin Nephrol 1985;24:47–9.
[110] Scully RE, Mark EJ, McNeely BU. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 6–1986. A 34-year-old man with hypertension and episodes of flushing, nausea, and vomiting. N Engl J Med 1986;314:431–9.
[111] Raman GV. Phaeochromocytoma presenting with cardiogenic shock and acute renal failure. J Hum Hypertens 1987;1:237–8.

[112] Crowe AV, Jones NF, Carr P. Five ways to be fooled by phaeochromocytoma—renal and urological complications. Nephrol Dial Transplant 1997;12:337–40.
[113] Kuzmanovska D, Sahpazova E, Kocova M, et al. Phaeochromocytoma associated with reversible renal artery stenosis. Nephrol Dial Transplant 2001;16:2092–4.
[114] Hill JB, Schwartzman RJ. Cerebral infarction and disseminated intravascular coagulation with pheochromocytoma. Arch Neurol 1981;38:395.
[115] Moritani H, Sakamoto M, Yoshida Y, et al. Pheochromocytoma of the urinary bladder revealed with cerebral hemorrhage. Intern Med 2001;40:638–42.
[116] Chuang HL, Hsu WH, Hsueh C, et al. Spontaneous intracranial hemorrhage caused by pheochromocytoma in a child. Pediatr Neurosurg 2002;36:48–51.
[117] Goswami R, Tandon N, Singh B, et al. Adrenal tumour, congestive heart failure and hemiparesis in an 18-year-old male: a clinical-pathological conference. Int J Cardiol 1995;49: 233–8.
[118] Beatty OL, Russell CF, Kennedy L, et al. Phaeochromocytoma in Northern Ireland: a 21 year review. Eur J Surg 1996;162:695–702.
[119] Favia G, Lumachi F, Polistina F, et al. Pheochromocytoma, a rare cause of hypertension: long-term follow-up of 55 surgically treated patients. World J Surg 1998;22:689–93.
[120] Plouin PF, Duclos JM, Soppelsa F, et al. Factors associated with perioperative morbidity and mortality in patients with pheochromocytoma: analysis of 165 operations at a single center. J Clin Endocrinol Metab 2001;86:1480–6.
[121] Fox JM, Manninen PH. The anaesthetic management of a patient with a phaeochromocytoma and acute stroke. Can J Anaesth 1991;38:775–9.
[122] Wilkenfeld C, Cohen M, Lansman SL, et al. Heart transplantation for end-stage cardiomyopathy caused by an occult pheochromocytoma. J Heart Lung Transplant 1992;11:363–6.
[123] Thomas JE, Rooke ED, Kvale WF. The neurologist's experience with pheochromocytoma: a review of 100 cases. JAMA 1966;197:754–8.
[124] Leiba A, Bar-Dayan Y, Leker RR, et al. Seizures as a presenting symptom of phaeochromocytoma in a young soldier. J Hum Hypertens 2003;17:73–5.
[125] Reichardt P, Apel TW, Domula M, et al. Recurrent polytopic chromaffin paragangliomas in a 9-year-old boy resulting from a novel germline mutation in the von Hippel-Lindau gene. J Pediatr Hematol Oncol 2002;24:145–8.
[126] Pacak K, Linehan WM, Eisenhofer G, et al. Recent advances in genetics, diagnosis, localization, and treatment of pheochromocytoma. Ann Intern Med 2001;134:315–29.
[127] Kantorovich V, Pacak K. A new concept of unopposed beta-adrenergic overstimulation in a patient with pheochromocytoma. Ann Intern Med 2005;142:1026–8.
[128] Proye C, Thevenin D, Cecat P, et al. Exclusive use of calcium channel blockers in preoperative and intraoperative control of pheochromocytomas: hemodynamics and free catecholamine assays in ten consecutive patients. Surgery 1989;106:1149–54.
[129] Roizen MF, Schreider BD, Hassan SZ. Anesthesia for patients with pheochromocytoma. Anesthesiol Clin North America 1987;5:269–75.
[130] Harper MA, Murnaghan GA, Kennedy L, et al. Phaeochromocytoma in pregnancy: five cases and a review of the literature. Br J Obstet Gynaecol 1989;96:594–606.
[131] Oishi S, Sato T. Pheochromocytoma in pregnancy: a review of the Japanese literature. Endocr J 1994;41:219–25.
[132] Schenker JG, Chowers I. Pheochromocytoma and pregnancy: review of 89 cases. Obstet Gynecol Surv 1971;26:739–47.
[133] Brunt LM. Phaeochromocytoma in pregnancy. Br J Surg 2001;88:481–3.
[134] Molitch ME. Endocrine emergencies in pregnancy. Baillieres Clin Endocrinol Metab 1992; 6:167–91.
[135] Ahlawat SK, Jain S, Kumari S, et al. Pheochromocytoma associated with pregnancy: case report and review of the literature. Obstet Gynecol Surv 1999;54:728–37.
[136] Dugas G, Fuller J, Singh S, et al. Pheochromocytoma and pregnancy: a case report and review of anesthetic management. Can J Anaesth 2004;51:134–8.

[137] Gurney JG, Ross JA, Wall DA, et al. Infant cancer in the US: histology-specific incidence and trends, 1973 to 1992. J Pediatr Hematol Oncol 1997;19:428–32.
[138] Maris JM. The biologic basis for neuroblastoma heterogeneity and risk stratification. Curr Opin Pediatr 2005;17:7–13.
[139] Brodeur GM. Neuroblastoma: biological insights into a clinical enigma. Nat Rev Cancer 2003;3:203–16.
[140] Brodeur GM, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, editors. Principles and practice of pediatric oncology. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 895–939.
[141] Brossard J, Bernstein ML, Lemieux B. Neuroblastoma: an enigmatic disease. Br Med Bull 1996;52:787–801.
[142] Castleberry RP. Biology and treatment of neuroblastoma. Pediatr Clin North Am 1997;44: 919–37.
[143] Haase GM, Perez C, Atkinson JB. Current aspects of biology, risk assessment, and treatment of neuroblastoma. Semin Surg Oncol 1999;16:91–104.
[144] Rudnick E, Khakoo Y, Antunes NL, et al. Opsoclonus-myoclonus-ataxia syndrome in neuroblastoma: clinical outcome and antineuronal antibodies—a report from the Children's Cancer Group Study. Med Pediatr Oncol 2001;36:612–22.
[145] Brodeur GM, Seeger RC, Barrett A, et al. International criteria for diagnosis, staging, and response to treatment in patients with neuroblastoma. J Clin Oncol 1988;6:1874–81.
[146] Brodeur GM, Pritchard J, Berthold F, et al. Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment. J Clin Oncol 1993;11:1466–77.
[147] Evans AE, Baum E, Chard R. Do infants with stage IV-S neuroblastoma need treatment? Arch Dis Child 1981;56:271–4.
[148] Evans AE, Chatten J, D'Angio GJ, et al. A review of 17 IV-S neuroblastoma patients at the Children's Hospital of Philadelphia. Cancer 1980;45:833–9.
[149] Attiyeh EF, London WB, Mosse YP, et al. Chromosome 1p and 11q deletions and outcome in neuroblastoma. N Engl J Med 2005;353:2243–53.
[150] Kushner BH. Neuroblastoma: a disease requiring a multitude of imaging studies. J Nucl Med 2004;45:1172–88.
[151] El-Hayek M, Trad O, Hardy D, et al. The triad of seizures, hypertension, and neuroblastoma: the first described case. J Pediatr Hematol Oncol 2004;26:523–5.
[152] Chauty A, Raimondo G, Vergeron H, et al. Discovery of a neuroblastoma producing cardiogenic shock in a 2-month-old child. Arch Pediatr 2002;9:602–5.
[153] Sendo D, Katsuura M, Akiba K, et al. Severe hypertension and cardiac failure associated with neuroblastoma: a case report. J Pediatr Surg 1996;31:1688–90.
[154] Kedar A, Glassman M, Voorhess ML, et al. Severe hypertension in a child with ganglioneuroblastoma. Cancer 1981;47:2077–80.
[155] Steinmetz JC. Neonatal hypertension and cardiomegaly associated with a congenital neuroblastoma. Pediatr Pathol 1989;9:577–82.
[156] Lindner W, Behnisch W, Kunz U, et al. Congenital neuroblastoma mimicking early onset sepsis. Eur J Pediatr 2001;160:436–8.
[157] Russo C, Cohn SL, Petruzzi MJ, et al. Long-term neurologic outcome in children with opsoclonus-myoclonus associated with neuroblastoma: a report from the Pediatric Oncology Group. Med Pediatr Oncol 1997;28:284–8.
[158] Yeung WL, Li CK, Nelson EA, et al. Unusual neurological presentation of neuroblastoma. Hong Kong Med J 2003;9:142–4.
[159] Scott JX, Moses PD, Somashekar HR, et al. Paraneoplastic papilloedema in a child with neuroblastoma. Indian J Cancer 2005;42:102–3.
[160] Tatli B, Saribeyoglu ET, Aydinli N, et al. Neuroblastoma: an unusual presentation with bilateral ptosis. Pediatr Neurol 2004;30:284–6.
[161] Lee EW, Applebaum H. Abdominal expansion as a bridging technique in stage IV-S neuroblastoma with massive hepatomegaly. J Pediatr Surg 1994;29:1470–1.

[162] Christiansen GM, Pulley SA. Two cases of neuroblastoma presenting to the emergency department. J Emerg Med 1999;17:265–8.
[163] Nejat F, Zabihyan Sigarchi S, IzadYar M. Congenital dumbbell neuroblastoma mimicking birth trauma. J Neurol Neurosurg Psychiatry 2005;76:143–4.
[164] McGirt MJ, Cowan JA Jr, Gala V, et al. Surgical reversal of prolonged blindness from a metastatic neuroblastoma. Childs Nerv Syst 2005;21:583–6.
[165] D'Amico MA, Weiner M, Ruzal-Shapiro C, et al. Protein-losing enteropathy: an unusual presentation of neuroblastoma. Clin Pediatr (Phila) 2003;42:371–3.
[166] Gerdes JS, Katz AJ. Neuroblastoma appearing as protein-losing enteropathy. Am J Dis Child 1982;136:1024–5.
[167] Shimada H, Ambros IM, Dehner LP, et al. The International Neuroblastoma Pathology Classification (the Shimada system). Cancer 1999;86:364–72.
[168] Shimada H, Ambros IM, Dehner LP, et al. Terminology and morphologic criteria of neuroblastic tumors: recommendations by the International Neuroblastoma Pathology Committee. Cancer 1999;86:349–63.
[169] Stowens D. Neuroblastoma and related tumors. Arch Pathol 1957;63:451–3.
[170] Radin R, David CL, Goldfarb H, et al. Adrenal and extra-adrenal retroperitoneal ganglioneuroma: imaging findings in 13 adults. Radiology 1997;202:703–7.
[171] Carpenter WB, Kernohan JW. Retroperitoneal ganglioneuromas and neurofibromas: a clinicopathological study. Cancer 1963;16:788–97.
[172] Geoerger B, Hero B, Harms D, et al. Metabolic activity and clinical features of primary ganglioneuromas. Cancer 2001;91:1905–13.
[173] Hamilton JP, Koop CE. Ganglioneuromas in children. Surg Gynecol Obstet 1965;121: 803–12.
[174] Lucas K, Gula MJ, Knisely AS, et al. Catecholamine metabolites in ganglioneuroma. Med Pediatr Oncol 1994;22:240–3.
[175] Hansen LP, Lund HT, Fahrenkrug J, et al. Vasoactive intestinal polypeptide (VIP)-producing ganglioneuroma in a child with chronic diarrhea. Acta Paediatr Scand 1980;69: 419–24.
[176] Scheibel E, Rechnitzer C, Fahrenkrug J, et al. Vasoactive intestinal polypeptide (VIP) in children with neural crest tumours. Acta Paediatr Scand 1982;71:721–5.
[177] Koch CA, Brouwers FM, Rosenblatt K, et al. Adrenal ganglioneuroma in a patient presenting with severe hypertension and diarrhea. Endocr Relat Cancer 2003;10:99–107.
[178] Wadhwa NK, Gupta M, Afolabi A, et al. Membranous glomerulonephritis in a patient with an adrenal ganglioneuroma. Am J Kidney Dis 2004;44:363–8.
[179] Lenders JW, Pacak K, Walther MM, et al. Biochemical diagnosis of pheochromocytoma: which test is best? JAMA 2002;287:1427–34.
[180] Spencer E, Pycock C, Lytle J. Phaeochromocytoma presenting as acute circulatory collapse and abdominal pain. Intensive Care Med 1993;19:356–7.
[181] Preuss J, Woenckhaus C, Schwesinger G, et al. Non-diagnosed pheochromocytoma as a cause of sudden death in a 49-year-old man: a case report with medico-legal implications. Forensic Sci Int 2006;156:223–8.
[182] Jones SE, Redfern N, Shaw IH, et al. Exaggerated cardiovascular response to anaesthesia—a case for investigation. Anaesthesia 1999;54:882–4.
[183] Diamond JA. Pheochromocytoma in a symptomatic patient with severe hypertension upon anesthesia induction. Am J Hypertens 2001;14:729–30.
[184] Myklejord DJ. Undiagnosed pheochromocytoma: the anesthesiologist nightmare. Clin Med Res 2004;2:59–62.
[185] Achong MR, Keane PM. Pheochromocytoma unmasked by desipramine therapy. Ann Intern Med 1981;94:358–9.
[186] Montminy M, Teres D. Shock after phenothiazine administration in a pregnant patient with a pheochromocytoma: a case report and literature review. J Reprod Med 1983;28: 159–62.

[187] Raisanen J, Shapiro B, Glazer GM, et al. Plasma catecholamines in pheochromocytoma: effect of urographic contrast media. AJR Am J Roentgenol 1984;143:43–6.
[188] Korzets A, Floro S, Ori Y, et al. Clomipramine-induced pheochromocytoma crisis: a near fatal complication of a tricyclic antidepressant. J Clin Psychopharmacol 1997; 17:428–30.
[189] Pineda Pompa LR, Barrera-Ramirez CF, Martinez-Valdez J, et al. Pheochromocytoma-induced acute pulmonary edema and reversible catecholamine cardiomyopathy mimicking acute myocardial infarction. Rev Port Cardiol 2004;23:561–8.
[190] Brown H, Goldberg PA, Selter JG, et al. Hemorrhagic pheochromocytoma associated with systemic corticosteroid therapy and presenting as myocardial infarction with severe hypertension. J Clin Endocrinol Metab 2005;90:563–9.
[191] Delaney JP, Paritzky AZ. Necrosis of a pheochromocytoma with shock. N Engl J Med 1969;280:1394–5.
[192] Mohamed HA, Aldakar MO, Habib N. Cardiogenic shock due to acute hemorrhagic necrosis of a pheochromocytoma: a case report and review of the literature. Can J Cardiol 2003;19:573–6.
[193] Guzik P, Wykretowicz A, Wesseling IK, et al. Adrenal pheochromocytoma associated with dramatic cyclic hemodynamic fluctuations. Int J Cardiol 2005;103:351–3.
[194] Schifferdecker B, Kodali D, Hausner E, et al. Adrenergic shock—an overlooked clinical entity? Cardiol Rev 2005;13:69–72.
[195] Zangrillo A, Valentini G, Casati A, et al. Myocardial infarction and death after caesarean section in a woman with protein S deficiency and undiagnosed phaeochromocytoma. Eur J Anaesthesiol 1999;16:268–70.
[196] Biccard BM, Gopalan PD. Phaeochromocytoma and acute myocardial infarction. Anaesth Intensive Care 2002;30:74–6.
[197] Dinckal MH, Davutoglu V, Soydinc S, et al. Phaeochromocytoma-induced myocarditis mimicking acute myocardial infarction. Int J Clin Pract 2003;57:842–3.
[198] Katechis D, Makaryus AN, Spatz A, et al. Acute myocardial infarction in a patient with pheochromocytoma and neurofibromatosis. J Invasive Cardiol 2005;17:331–3.
[199] Gatzoulis KA, Tolis G, Theopistou A, et al. Cardiomyopathy due to a pheochromocytoma: a reversible entity. Acta Cardiol 1998;53:227–9.
[200] Mootha VK, Feldman J, Mannting F, et al. Pheochromocytoma-induced cardiomyopathy. Circulation 2000;102:E11–3.
[201] Dalby MC, Burke M, Radley-Smith R, et al. Pheochromocytoma presenting after cardiac transplantation for dilated cardiomyopathy. J Heart Lung Transplant 2001;20: 773–5.
[202] Attar MN, Moulik PK, Salem GD, et al. Phaeochromocytoma presenting as dilated cardiomyopathy. Int J Clin Pract 2003;57:547–8.
[203] Vahdat A, Vahdat O, Chandraratna PA. Pheochromocytoma presenting as reversible acute cardiomyopathy. Int J Cardiol 2006;108:395–6.
[204] Baratella MC, Menti L, Angelini A, et al. An unusual case of myocarditis. Int J Cardiol 1998;65:305–10.
[205] Magalhaes LC, Darze ES, Ximenes A, et al. Acute myocarditis secondary to pheochromocytoma. Arq Bras Cardiol 2004;83:346–8, 343–5.
[206] Stevenson S, Ramani V, Nasim A. Extra-adrenal pheochromocytoma: an unusual cause of deep vein thrombosis. J Vasc Surg 2005;42:570–2.
[207] Munk Z, Tolis G, Jones W, et al. Pheochromocytoma presenting with pulmonary edema and hyperamylasemia. Can Med Assoc J 1977;116:357–9.
[208] Joshi R, Manni A. Pheochromocytoma manifested as noncardiogenic pulmonary edema. South Med J 1993;86:826–8.
[209] Okada Y, Suchi M, Takeyama H, et al. Noncardiogenic pulmonary edema as the chief manifestation of a pheochromocytoma: a case report of MEN 2A with pedigree analysis of the RET proto-oncogene. Tohoku J Exp Med 1999;188:177–87.

[210] Bos JC, Toorians AW, van Mourik JC, et al. Emergency resection of an extra-adrenal phaeochromocytoma: wrong or right? A case report and a review of literature. Neth J Med 2003;61:258–65.
[211] Baguet JP, Hammer L, Mazzuco TL, et al. Circumstances of discovery of phaeochromocytoma: a retrospective study of 41 consecutive patients. Eur J Endocrinol 2004;150:681–6.
[212] Grinda JM, Bricourt MO, Salvi S, et al. Unusual cardiogenic shock due to pheochromocytoma: recovery after bridge-to-bridge (extracorporeal life support and DeBakey ventricular assist device) and right surrenalectomy. J Thorac Cardiovasc Surg 2006;131:913–4.
[213] O'Hickey S, Hilton AM, Whittaker JS. Phaeochromocytoma associated with adult respiratory distress syndrome. Thorax 1987;42:157–8.
[214] Chan MK, Tse HW, Mok FP. Ruptured phaeochromocytoma—a lesson in acute abdomen. Hong Kong Med J 2003;9:221–3.
[215] Orikasa K, Namima T, Ohnuma T, et al. Spontaneous rupture of adrenal pheochromocytoma with capsular invasion. Int J Urol 2004;11:1013–5.
[216] Cruz SR, Colwell JA. Pheochromocytoma and ileus. JAMA 1972;219:1050–1.
[217] Blecha M, Galanopolous C, Dharkar D, et al. Massive organ of Zuckerkandl inducing small bowel obstruction. J Am Coll Surg 2005;201:480–1.
[218] Carr ND, Hulme A, Sheron N, et al. Intestinal ischaemia associated with phaeochromocytoma. Postgrad Med J 1989;65:594–6.
[219] Hashimoto Y, Motoyoshi S, Maruyama H, et al. The treatment of pheochromocytoma associated with pseudo-obstruction and perforation of the colon, hepatic failure, and DIC. Jpn J Med 1990;29:341–6.
[220] Karri V, Khan SL, Wilson Y. Bowel perforation as a presenting feature of pheochromocytoma: case report and literature review. Endocr Pract 2005;11:385–8.
[221] Salehi A, Legome EL, Eichhorn K, et al. Pheochromocytoma and bowel ischemia. J Emerg Med 1997;15:35–8.
[222] Sohn CI, Kim JJ, Lim YH, et al. A case of ischemic colitis associated with pheochromocytoma. Am J Gastroenterol 1998;93:124–6.
[223] Morris K, McDevitt B. Phaeochromocytoma presenting as a case of mesenteric vascular occlusion. Ir Med J 1985;78:356–7.
[224] Greaves DJ, Barrow PM. Emergency resection of phaeochromocytoma presenting with hyperamylasaemia and pulmonary oedema after abdominal trauma. Anaesthesia 1989;44: 841–2.
[225] Sweeney AT, Malabanan AO, Blake MA, et al. Megacolon as the presenting feature in pheochromocytoma. J Clin Endocrinol Metab 2000;85:3968–72.
[226] Onozawa M, Fukuhara T, Minoguchi M, et al. Hypokalemic rhabdomyolysis due to WDHA syndrome caused by VIP-producing composite pheochromocytoma: a case in neurofibromatosis type 1. Jpn J Clin Oncol 2005;35:559–63.
[227] Smith JC, Meehan C, Lyons P, et al. A man presenting with limb weakness and electrolyte imbalance. Postgrad Med J 1999;75:691–3.
[228] Dewan M, Rasshid M, Elmalik EM, et al. Lessons to be learned: a case study approach. Paraganglioma of the urinary bladder. J R Soc Health 2001;121:193–8.
[229] Ishii C, lnoue K, Negishi K, et al. Diabetic ketoacidosis in a case of pheochromocytoma. Diabetes Res Clin Pract 2001;54:137–42.
[230] Bornemann M, Hill SC, Kidd GS 2nd. Lactic acidosis in pheochromocytoma. Ann Intern Med 1986;105:880–2.