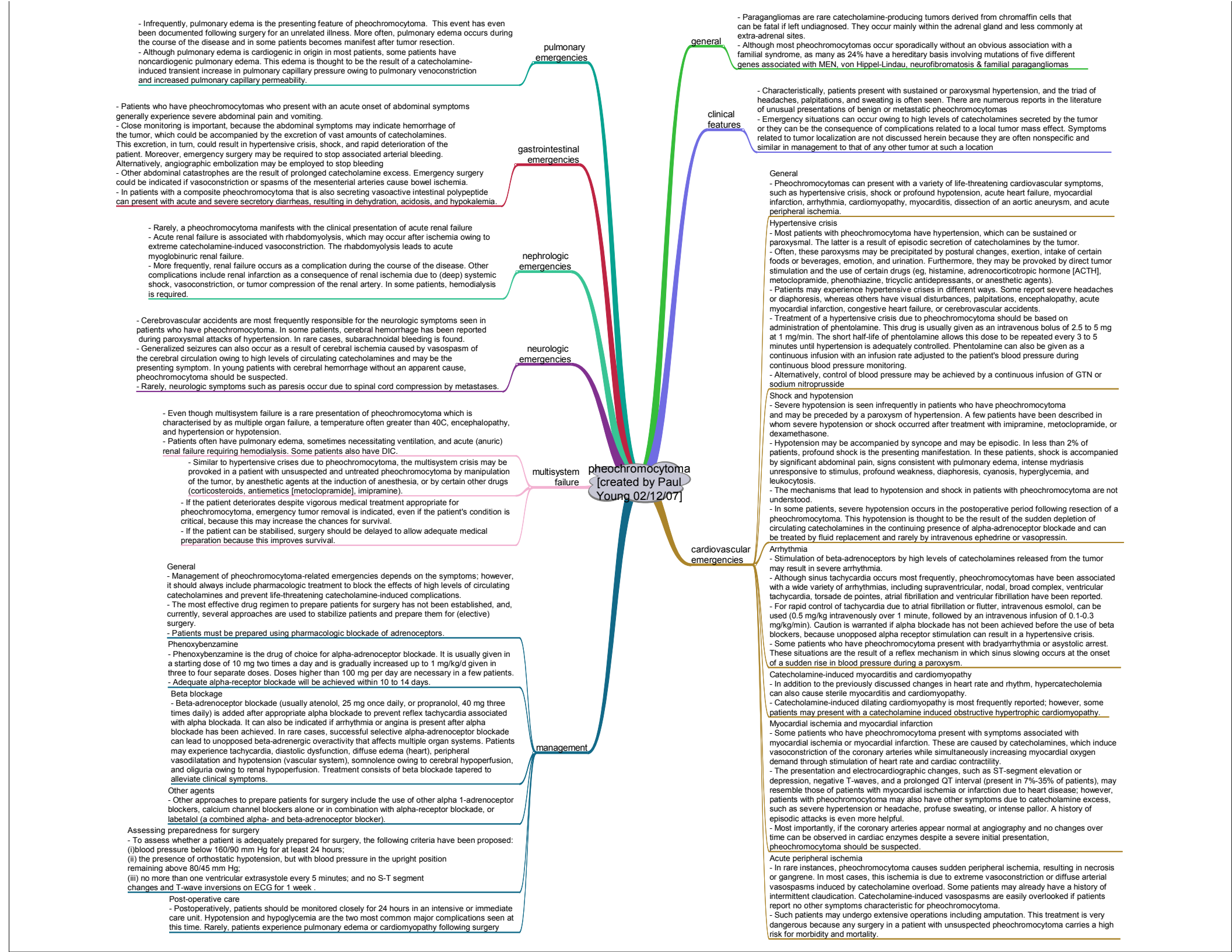
pheochromocytoma [created by Paul Young 02/12/07]
general
- Paragangliomas are rare catecholamine-producing tumors derived from chromaffin cells that can be fatal if left undiagnosed. They occur mainly within the adrenal gland and less commonly at extra-adrenal sites.
- Although most pheochromocytomas 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 MEN, von Hippel-Lindau, neurofibromatosis & familial paragangliomas
clinical features
- 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
- Emergency situations can occur owing to high levels of catecholamines secreted by the tumor 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
cardiovascular emergencies
General
- Pheochromocytomas can present with a variety of life-threatening cardiovascular symptoms, such as hypertensive crisis, shock or profound 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.
- 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).
- 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.
- 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 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 GTN or sodium nitroprusside
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, metoclopramide, or dexamethasone.
- Hypotension may be accompanied by syncope and may be episodic. In less than 2% of patients, profound shock is the presenting manifestation. 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.
- The mechanisms that lead to hypotension and shock in patients with pheochromocytoma are not understood.
- 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.
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, nodal, broad complex, ventricular tachycardia, torsade de pointes, atrial fibrillation and ventricular fibrillation have been reported.
- For rapid control of tachycardia due to atrial fibrillation or flutter, intravenous esmolol, can be used (0.5 mg/kg intravenously over 1 minute, followed by an intravenous infusion of 0.1-0.3 mg/kg/min). 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.
- Some patients who have pheochromocytoma present with bradyarrhythmia or asystolic arrest. 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.
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; however, some patients may present with a catecholamine induced obstructive hypertrophic cardiomyopathy.
Myocardial ischemia and myocardial infarction
- Some patients who have pheochromocytoma present with symptoms associated with myocardial ischemia or myocardial infarction. These 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, negative T-waves, and a prolonged QT interval (present in 7%-35% of patients), 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.
Acute peripheral ischemia
- In rare instances, pheochromocytoma causes sudden peripheral ischemia, resulting in necrosis or gangrene. 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. Catecholamine-induced vasospasms are easily overlooked if patients report no other symptoms characteristic for pheochromocytoma.
- Such patients may undergo extensive operations including amputation. This treatment is very dangerous because any surgery in a patient with unsuspected pheochromocytoma carries a high risk for morbidity and mortality.
pulmonary emergencies
- Infrequently, pulmonary edema is the presenting feature of pheochromocytoma. This event has even been documented following surgery for an unrelated illness. More often, pulmonary edema occurs during the course of the disease and in some patients becomes manifest after tumor resection.
- Although pulmonary edema is cardiogenic in origin in most patients, some patients have noncardiogenic pulmonary edema. 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.
gastrointestinal emergencies
- Patients who have pheochromocytomas who present with an acute onset of abdominal symptoms generally 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, 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
- 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 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.
nephrologic emergencies
- Rarely, a pheochromocytoma manifests with the clinical presentation of acute renal failure
- 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.
- More frequently, renal failure occurs as a complication during the course of the disease. Other complications include renal infarction as a consequence of renal ischemia due to (deep) systemic shock, vasoconstriction, or tumor compression of the renal artery. In some patients, hemodialysis is required.
neurologic emergencies
- Cerebrovascular accidents are most frequently responsible for the neurologic symptoms seen in patients who have pheochromocytoma. In some patients, cerebral hemorrhage has been reported during paroxysmal attacks of hypertension. In rare cases, subarachnoidal bleeding is found.
- 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. 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.
multisystem failure
- Even though multisystem failure is a rare presentation of pheochromocytoma which is characterised by as multiple organ failure, a temperature often greater than 40C, encephalopathy, and hypertension or hypotension.
- Patients often have pulmonary edema, sometimes necessitating ventilation, and acute (anuric) renal failure requiring hemodialysis. Some patients also have DIC.
- 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).
- 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 stabilised, surgery should be delayed to allow adequate medical preparation because this improves survival.
management
General
- 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.
- Patients must be prepared using pharmacologic blockade of adrenoceptors.
Phenoxybenzamine
- 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. 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 blockage
- 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 blockada. 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. Treatment consists of beta blockade tapered to alleviate clinical symptoms.
Other agents
- 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, or labetalol (a combined alpha- and beta-adrenoceptor blocker).
Assessing preparedness for surgery
- To assess whether a patient is adequately prepared for surgery, the following criteria have been proposed:
(i)blood pressure below 160/90 mm Hg for at least 24 hours;
(ii) the presence of orthostatic hypotension, but with blood pressure in the upright position remaining above 80/45 mm Hg;
(iii) no more than one ventricular extrasystole every 5 minutes; and no S-T segment changes and T-wave inversions on ECG for 1 week .
Post-operative care
- 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. Rarely, patients experience pulmonary edema or cardiomyopathy following surgery