

Nephroquiz 8: Perioperative Management of Paraganglioma

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CASE

A 32-year-old woman was admitted because of severe uncontrolled hypertension associated with intermittent headache, diaphoresis, and blurred vision. She had a 3-year history of hypertension. Her symptoms were worsened by urination. Physical examination revealed a blood pressure of 155/120 mm Hg and bilateral papilledema. The tilt test was negative. Bruit over the renal artery was not audible. Laboratory examinations are shown in the Table. Abdominopelvic computed tomography showed lymphadenopathy in the celiac region and a 23-mm enhancing lesion in the bladder floor. No mass lesions were seen in the adrenal glands. Abdominopelvic magnetic resonance imaging confirmed computed tomography findings (Figure 1). Metaiodobenzylguanidine scan was negative. A 2.5 × 2.5 × 1-cm mass was completely removed laparoscopically. Pathologic report concluded urothelial mucosa with submucosal neoplasm composed of monomorphic polygonal cells with central round nuclei. Fine speckled chromatin and marked nucleoli as well as granular eosinophilic cytoplasm arranged as nest formation. No obvious mitotic figures were seen. Diagnosis of paraganglioma was confirmed with chromogranin and synaptophysin immunohistochemical staining (Figure 2).

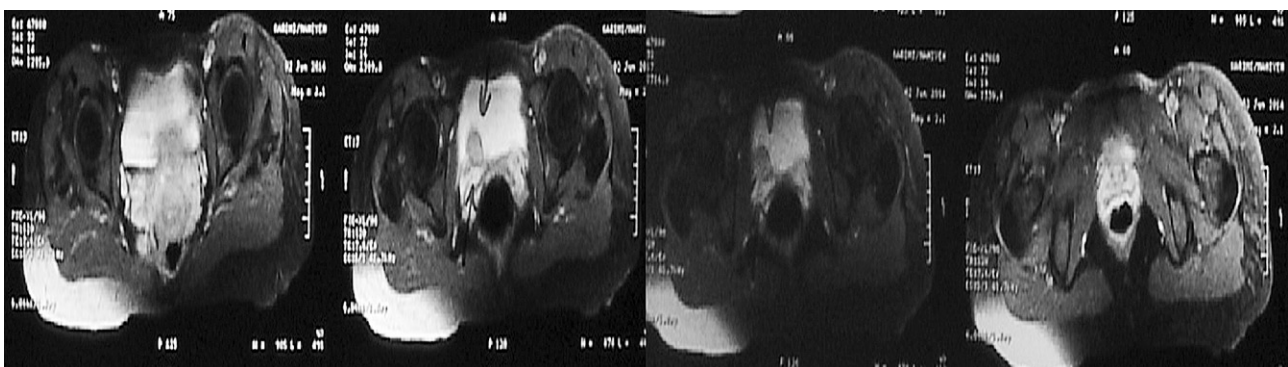


Figure 1. Pelvic magnetic resonance imaging showed a mass-like lesion on the bladder floor.

Patient's Laboratory Data

Parameter	Result	Reference Range
Leukocyte count, $\times 10^9/L$	4.6	4 to 10
Hemoglobin, g/dL	15	12 to 18
Blood chemistry		
Blood Urea Nitrogen, mg/dL	11	8 to 23
Creatinine, mg/dL	0.98	0.5 to 1.5
Sodium, mEq/L	140	135 to 145
Potassium, mEq/L	3.9	3.5 to 5.5
Calcium, mg/dL	9.8	8.1 to 10.4
Phosphorus, mg/dL	3.6	2.5 to 5
Albumin, g/dL	4.6	3.5 to 5.1
Total protein, mg/dL	7.7	6.4 to 7.4
Parathyroid hormone, pg/mL	33	15 to 65
Thyroid-stimulating hormone, $\mu g/dL$	2.4	0.27 to 4.2
Thyroxine, $\mu g/dL$	7.6	4.0 to 12.8
24-hour urine		
Vanillylmandelic acid, mg	11.4	0 to 13.6
Metanephrine, μg	43	0 to 350
Normetanephrine, μg	1095	0 to 600

QUIZ

How Should These Patients be Managed Before and During Surgery?

Paraganglioma. Paragangliomas are rare neuroendocrine tumors which consist of extra-adrenal sympathetic or parasympathetic paraganglia cells.¹ Having the same clinical presentation of paraganglioma with pheochromocytoma, it is hard to find the exact incidence of paraganglioma. Together with pheochromocytoma, their yearly incidence is approximately 0.8 per 100 000 person-years.² Among paragangliomas, those which are derived from parasympathetic nervous system are mostly located in the skull base, upper mediastinum, or neck. Only 5% of them hypersecrete catecholamines. Sympathetic paragangliomas are typically located in the lower mediastinum, abdomen, or pelvis, most of which are symptomatic.^{3,4}

Patients mostly experience paroxysmal

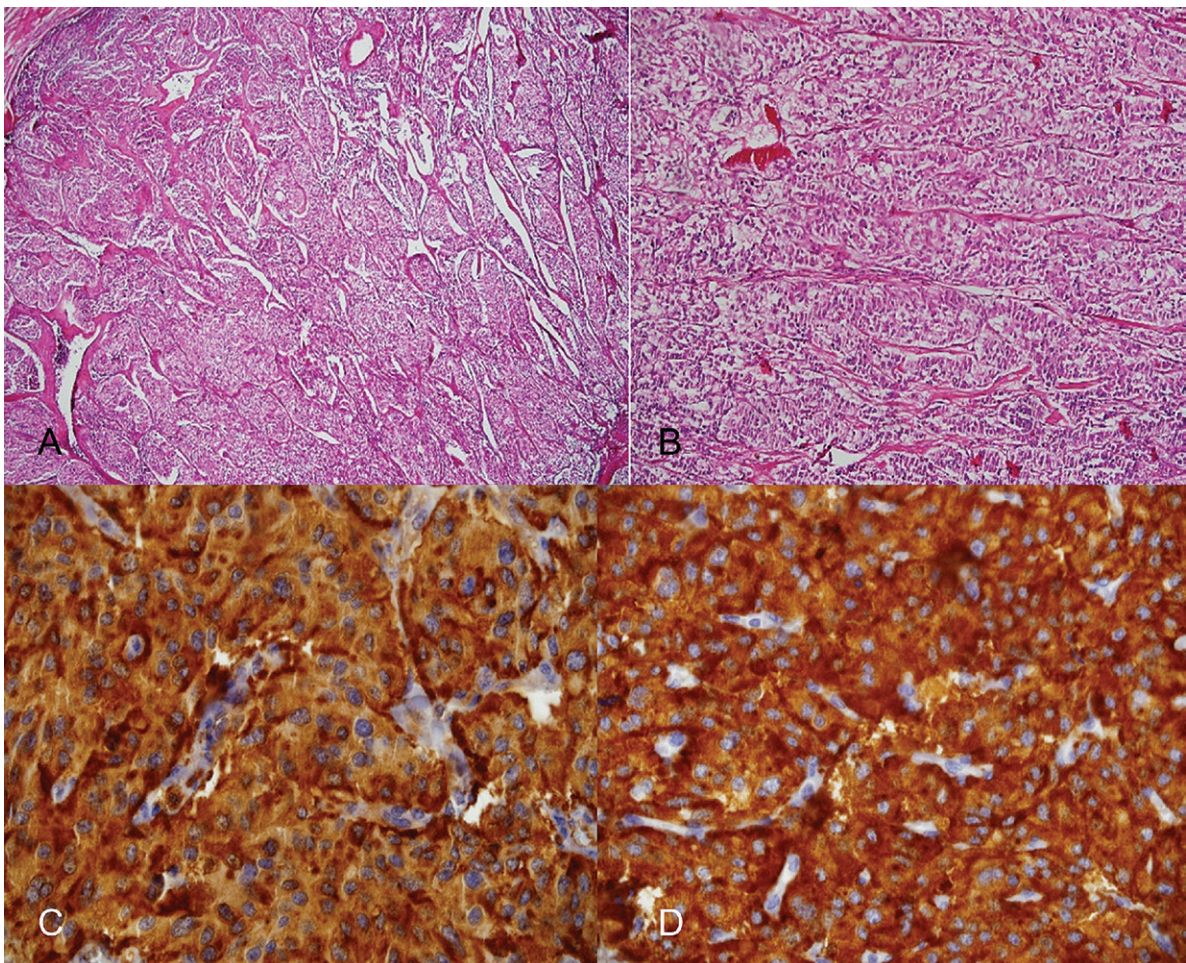


Figure 2. A, Zellballen growth pattern (hematoxylin-eosin, $\times 40$). B, The tumor is composed of large polygonal cells with eosinophilic granular cytoplasm and central vesicular nuclei (hematoxylin-eosin, $\times 100$). C, The neoplastic cells are positive for chromogranin. D, The neoplastic cells are positive for synaptophysin.

hypertension together with palpitations, headache, and sweating.⁵ Diagnosis relies on biochemical evidence of catecholamine hypersecretion. Because of catecholamine metabolization within chromaffin cells, measurement of its metabolites in urine or plasma (ie, metanephrine or normetanephrine) has a higher diagnostic sensitivity.⁶ The most sensitive diagnostic test is plasma metanephrine (96%), which is better to obtain in the supine position, after 15 to 20 minutes of intravenous line insertion.^{6,7} The patient should be instructed to avoid food, smoking, caffeine, or vigorous activity for about 8 to 12 hours before the test.⁸ The specificity of plasma metanephrine is low (85%). The most specific test is measurement of catecholamines and metanephrine in 24-hour urine collection (99.7%), but with a sensitivity of 87.5%.⁹ The diagnostic utility of these tests may be affected by tricyclic antidepressants and some other antipsychotic drugs; therefore, they should be discontinued at least 2 weeks before any test.¹⁰

The tumor can be localized either by computed tomography or magnetic resonance imaging with excellent sensitivity.¹¹ Unlike the earlier belief that intravenous contrast may cause hypertension crisis, studies showed no increased risk with the use of nonionic contrast materials.¹² For equivocal masses, metaiodobenzylguanidine scan, with 83% to 100% specificity, can localize the adrenergic tumor^{13,14}; however, it has a high false negativity of 29% to 44%.¹⁵

Pre-operation management. The best treatment option is surgery.¹⁶ Due to excessive catecholamine release, they are at increased risk of intra-operative hemodynamic instability. Therefore, preoperative medical therapy and close monitoring of cardiovascular and hemodynamic variables is necessary during surgery.

The main purpose of preoperative medical therapy is controlling blood pressure and replenishing preexisting volume depletion. Administration of combined α - and β -blockades and high-sodium diet are recommended. Despite no consensus, most medical centers start medical therapy at least 7 to 14 days before surgery.¹⁷ The preferred α -adrenergic blocker is phenoxybenzamine because of irreversible binding and long acting effect. The usual initial dose is 10 mg, twice daily, which can be increased every 2 to 3 days until the patient becomes normotensive, maximum dose is achieved,

or side effects appear.¹⁸ Prazosin, trazosin, and doxazosin all are alternatives to phenoxybenzamine with α_1 -specific competitive short-acting effect. Because of their shorter half-lives, some institutions replace phenoxybenzamine with one of them before surgery, to reduce the risk of postoperative hypotension.¹⁹ With use of α -adrenergic blockers, β -receptors will be left unopposed, so the patient may become prone to reflex tachycardia. Therefore, after the optimal dose of α -blockers is achieved, β -adrenergic blockers should be started. There are different options but β_1 -selective adrenoceptor blockers are preferred.¹⁸

Since the action of norepinephrine on vessel wall is mediated by calcium influx into vascular smooth muscle cells, calcium channel blockers are another option specifically for those who experience side effects with α -adrenoceptor blockers or inadequate blood pressure control despite high doses of α -blocker.²⁰ Metyrosine, a tyrosine hydroxylase inhibitor, which restrains catecholamine synthesis, has also been used with better hemodynamic control. It can be used either as a single agent or in combination with α -blockers.¹⁸ Finally, in order to reduce the risk of postoperative hypotension, pre-operative volume expansion with increased water intake or isotonic saline infusion should be kept in mind.²¹

For malignant cases, the goal is resection of all metastatic sites; otherwise, radionuclide therapy and chemotherapy followed by debulking should be considered.²²

Intra-operative management. Since the operation is extremely high risk, close monitoring of the patient is essential. Drugs that are used for induction of anesthesia should be selected carefully and those which may increase catecholamine release, such as ketamine and morphine, should be avoided.²³ It seems that thiopental, etomidate, and propofol are appropriate for induction and isoflurane for maintenance of anesthesia.¹⁴

Any manipulation, like intubation and tumor resection, can lead to catecholamine release and hemodynamic instability; hence, cardiac monitoring, close monitoring of blood pressure with an arterial line, and monitoring of intravascular volume with use of central venous catheter is necessary.²⁴ For intra-operation hypertensive crisis, sodium nitroprusside with rapid onset and short duration of action is preferred. For management of arrhythmias,

esmolol and lidocaine seems to be the best.

Postoperation. Immediately after the operation, patients are prone to hypotension and hypoglycemia. Hypotension is managed by intravenous crystalloid, and in refractory cases vasopressors could be used.²⁵

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