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Pheochromocytoma and Paraganglioma

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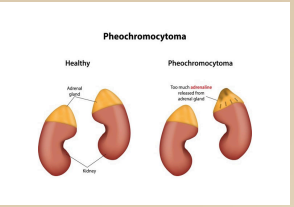
Introduction

What is the topic?

Pheochromocytoma and Paraganglioma (PPGL)



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Why choose PPGL?

- Possible malignant catecholamine secreting tumor
- Incidence in general population: 0.005-0.1%
- Incidence in adult hypertensive population: 0.1-0.2% (Farrugia et al., 2017)
- Direct relation to my past nursing practice in a surgical-oncology progressive care unit
- Close monitoring of vital signs and assessments preoperatively and postoperatively
- Potential to cause fatal complications if left untreated (Hekimian et al., 2016)
- No official guidelines for treatment (Jimenez, Tatsui, Jessop, Thosani, & Jimenez, 2017)
- Field of genetics and pheo's undergoing significant changes in understanding (Farrugia et al., 2017; Kantorovich & Pacak, 2018)
- Pheochromocytomas and paragangliomas are the highest hereditary-driven endocrine condition (Kantorovich & Pacak, 2018)
  - 40% related to mutations in well established 15 driver-genes. Numbers are expected to grow

Pathophysiological Processes

Underlying Pathophysiology

- Exact cause is unknown (Hines & Marschall, 2018)
  - 90% are an isolated finding
  - 10% inherited as autosomal dominant
- Chromaffin cell tumors originating from neural crest cells from the adrenal medulla and extra-adrenal sites (Manimaran, Khan, Bharathi, Thulasi, & Anuradha, 2016)
  - 80-85% from adrenal medulla
  - 15-20% extra-adrenal: organ of Zuckerkandl, neck, thorax, bladder, and prostate
- Most pheochromocytomas secrete norepinephrine and epinephrine at a 85:15 ratio (Nagelhout & Elisha, 2018, Hines & Marschall, 2018)
  - 15% secrete epinephrine predominantly
  - Can also secrete dopamine, though less common
- Neural stimulation does not cause hormone release due to lack of innervation
- "Rule of ten": Both adrenal glands involved in 10% of adults with tumor, 10-15% extraadrenal, and at least 10% are malignant
- Malignant spread typically through venous and lymphatic channels to liver (Nagelhout & Elisha, 2018)

Genetic Significance in Pathophysiology

- Anatomic classifications fall short of providing sufficient insight into pathogenesis, clinical presentation, and prognostic value with respect to malignant potential
- Functional, pathogenesis-based classification may offer better understanding of actual tumorigenesis, expected biochemical profiles, tumor location, and malignant potential
- Functional classification of current established susceptibility genes:
  - Pseudohypoxia group
  - Kinase signaling group
  - Wnt signaling group
  - Disease-modifying gene group
- Pathogenesis-based knowledge help design new therapeutic approaches that target specific gene pathways
  - Example: Hypoxia-inducible factor 2α antagonist (HIF-2α) which promote HIF hydroxylation and degradation of substances that promote tumorigenesis at a specific pathogenetic point
- Additional clinical presentations and genetic mutations will create opportunities to further understand the pathophysiology of pheochromocytoma and paraganglioma (Kantorovich & Pacak, 2019)

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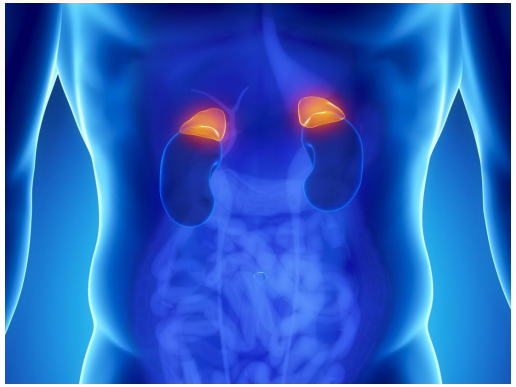
Signs & Symptoms

- Main signs and symptoms (catecholamine excess)
  - Hypertension
  - Palpitations
  - Headache
  - Perspiration
  - Pallor
  - Tremors
  - Anxiety
- Less common signs and symptoms (Farrugia et al., 2017; Hekimian et al., 2016)
  - Fatigue
  - Abdominal pain
  - Nausea
  - Vomiting
  - Myalgia
  - Weight loss
  - Constipation
  - Flushing
  - Fever
- Potential manifestations if untreated (Hekimian et al., 2016)
  - Myocardial infarction
  - Cardiogenic shock
  - Takotsubo-like cardiomyopathy
  - Hypertensive crisis
  - Pulmonary edema
  - Cerebral vascular accident
  - Dysrhythmias



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Implications for Nursing Care

- Close monitoring of BP, HR, pulse oximetry
  - Signs can occur once a month or multiple times per day ranging minutes to hours
- 24-hour urine collection of metanephrines and catecholamines or measurement of plasma free metanephrines
- Telemetry monitoring for abnormalities:
  - Elevation or depression of ST segment
  - Flattening or inversion of T wave
  - Prolongation of QT interval
  - High or peaked P waves
- Emphasis on BP mgmt. (Hines & Marschall, 2018)
  - Alpha blockade before beta blockade
  - Blocking vasodilatory β2-receptors results in unopposed α-agonism → vasoconstriction and hypertensive crisis
- Preoperative goals (Hines & Marschall, 2018; Tsegay, Anyango, Van Sell, & Miller-Anderson, 2008)
  - Euvolemia
  - Normotensive: Below 160/90 mmHg for at least 24 hours before surgery

Removal

- Surgical resection is the primary treatment strategy
- High risk for morbidity and mortality in the perioperative period (Bai et al., 2018)
  - Can be as high as 50%
  - Improvements in preoperative medical preparation, anesthesia, and surgical techniques have reduced risk to 0-2.9%
- Cardiovascular related complications occurred in 24% of patients who underwent removal in a study by Bai et al. 2018, which compared similarly to previous research.
  - Postoperative hypotension
  - Arrhythmia
  - Myocardial infarction
- Peripheral vasoconstriction induced by catecholamines preoperatively leads to possible use of vasoactive agents (norepinephrine) and volume expansion with crystalloid or colloid products
- Prolonged exposure of catecholamines to the myocardium and coronary arteries could presumably lead to collagen deposition and fibrosis in the myocardium
- Acute left cardiac dysfunction due to chronically elevated epinephrine was a root cause of hypotension and circulatory failure after pheochromocytoma removal
- Possible independent risk factors for severe morbidity (Bai et al., 2018)
  - Female sex
  - Coronary heart disease
  - BMI of 22 ± 2.9
  - Intraoperative hemodynamic instability
  - Longer duration of surgery: 171.1 ± 73 minutes
  - 4 of the 262 patients that died in this study all had coronary heart disease and died of circulatory collapse

Conclusion

- Pheochromocytoma and paraganglioma are rare neuroendocrine tumors associated with catecholamine production
- Surgical resection is the primary treatment
- Genetic research has provided additional information regarding pathogenesis and targeted treatment
- The classic triad of diaphoresis, palpitations, and headache has a reported sensitivity of 89% and specificity of 67% for pheochromocytoma specifically. In the presence of hypertension, it raises to 91% and 94%, respectively
- Rarity and variability of these tumors make them difficult to manage and many are discovered incidentally during radiologic examinations or at autopsy
- The key to diagnosing is to first think of it! (Bai et al., 2018; Farrugia et al., 2017)

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