Pheochromocytoma
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Objectives

- Introduce the patient case significant for pheochromocytoma
- Review pathophysiology and clinical guidelines for treatment
- Discuss literature evaluating the different treatment options
- Discuss the outcomes of the patient case
Patient Overview

- 67 YOF admitted to Scott Memorial Hospital complaining of N/V, severe migraine, and chest pressure. Was transferred to Norton where she had tachycardia, blurred vision, dizziness and a severely elevated BP on admission.

- PMH: Hypertropic cardiomyopathy, hyperlipidemia, benign essential HTN, diabetes mellitus, orthostasis, migraine with aura, PAF, hypothryoidism

- Allergies: NKDA
Home Medications

- Lisinopril 20mg PO daily
- Metoprolol 50mg PO BID
- ASA 81mg PO daily
- Lantus 100units/ml. inject 22 units SQ nightly
- Crestor 40mg PO daily
- Levothyroxine 25 mcg PO daily
Timeline

- **7/1**
  - BP: 177/92
  - HR: 190–200 BPM
  - EKG: Afib
  - Increased metoprolol to 100mg BID, continue lisinopril home dose

- **7/2**
  - Neuro consult: migraine with aura
  - BP stable

- **7/3–7/4**
  - BP stable

- **7/5**
  - Headache, tachycardia and HTN
  - BP: 210/90
  - HR: 117
  - Hydralazine 10mg IV bolus and Q6H prn
  - 1 dose oral amlodipine 2.5mg

- **7/6**
  - CT of abdomen/pelvis
  - Plasma and urine metanephrine and normetanephrine levels
  - DC lisinopril – Scr 1.9
  - DC metoprolol, gave 1 dose Carvedilol 6.25mg
  - HR: 85–97

- **7/7**
  - Begin Carvedilol 3.125mg PO BID
CT Abdomen/pelvis

- 6.6 cm right adrenal mass

- Differential diagnoses: hemorrhagic adrenal renal mass and/or pheochromocytoma that has undergone adrenal hemorrhage
What is a Pheochromocytoma?

- Rare neuroendocrine tumor
- Arises from adrenomedullary chromaffin cells and intermittently secretes catecholamines
- May cause serious and lethal cardiovascular complications
- Classic triad:
  - Headache, sweating, and tachycardia associated with hypertension

Diagnosis

- Only investigate if clinical suspicion
- Urine and plasma metanephrine and normetanephrine
- CT scan of the abdomen
- MIBG scan

Medical preparation for surgery:

- **Purpose:**
  - Prevent hypertensive crisis and tachycardia during surgery
  - Promote volume expansion

- **Avoid agents that provoke an exacerbation:**
  - Glucagon, histamine, metoclopramide

- **Continuously measure hemodynamics**

- **Possible agents:**
  - Combined alpha and beta adrenergic blockade, CCB, or metyrosine

Alpha blocker given 7–14 days preoperatively to normalize BP and expand the contracted blood volume

- Phenoxybenzamine
  - Initial dose: 10mg once or twice daily
  - Final dose: 20–100mg daily
  - Cost: $129.44 per 10mg capsule

- When long term treatment is indicated:
  - Selective alpha 1 blockers preferred
    - Prazosin, terazosin, doxazosin
    - Lower cost and more favorable side effect profile
    - Cost: $1.34 per 1 mg tablet

After adequate alpha blockade is achieved, beta blockade is initiated

- 2–3 days pre-operatively
- NEVER start beta blockade first
- Administer cautiously and at a low dose:
  - 1st day: propanolol 10mg every 6 hours
  - 2nd day (if tolerated): convert to a single long acting dose
  - Titrate as necessary to control tachycardia (goal HR: 60–80BPM)

On day 2–3 of alpha blockade, patients are encouraged to start a diet high in sodium content
  ◦ >5000mg daily
  ◦ Prevent orthostatic hypotension before surgery and reduce risk of severe hypotension after surgery
  ◦ CI: CHF or renal insufficiency
Comparison of Two Preoperative Medical Management Strategies for Laparoscopic Resection of Pheochromocytoma

Purpose: Compare intra and postoperative course of patients at Mayo Clinic vs Cleveland clinic

Method: Retrospective chart review of 50 Mayo Clinic patients and 37 Cleveland Clinic patients
- Mayo Clinic: almost all patients received phenoxybenzamine (98%)
- Cleveland Clinic: predominantly use doxasosin, terazosin, or prazosin (63%)
- All patients at both centers were evaluated and treated by an endocrinologist.
- Both centers encouraged liberal dietary salt intake to restore the intravascular volume

Results:

- **Significant**
  - Mayo clinic:
    - More episodes of BP $\leq 30\%$ of baseline
    - Lower Max SBP

- **Non-significant**
- Both groups:
  - Satisfactory preoperative BP control
  - Length of stay and proportion admitted to ICU

- Mayo clinic:
  - The duration of severe hypertension tended to be less

# Intraoperative Hemodynamic Data

<table>
<thead>
<tr>
<th>Intraoperative Hemodynamics</th>
<th>Mayo Clinic (n = 50)</th>
<th>Cleveland Clinic (n = 37)</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Greatest intraoperative BP (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>187 ± 30</td>
<td>209 ± 44</td>
<td>.011</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>109 ± 18</td>
<td>114 ± 26</td>
<td>.294</td>
</tr>
<tr>
<td>Systolic BP ≥30% baseline (min)</td>
<td>2 (0–11)</td>
<td>5 (0–22)</td>
<td>.119</td>
</tr>
<tr>
<td>Systolic BP ≥200 mm Hg (min)</td>
<td>0 (0–2)</td>
<td>0 (0–7)</td>
<td>.071</td>
</tr>
<tr>
<td><strong>Lowest intraoperative BP (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>73 ± 14</td>
<td>78 ± 15</td>
<td>.159</td>
</tr>
<tr>
<td>Mean BP</td>
<td>55 ± 11</td>
<td>56 ± 10</td>
<td>.870</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>46 ± 9</td>
<td>43 ± 9</td>
<td>.191</td>
</tr>
<tr>
<td>Systolic BP ≤ 30% baseline, min</td>
<td>28 (6–62)</td>
<td>13 (3–49)</td>
<td>.114</td>
</tr>
<tr>
<td><strong>Systolic BP ≤30% baseline (% anesthesia time)</strong></td>
<td>15.7 (3.3–24.9)</td>
<td>5.1 (0.9–16.0)</td>
<td>.026</td>
</tr>
</tbody>
</table>

Conclusion

- Phenoxybenzamine produced better attenuation of intraoperative hypertension, but at the cost of longer lasting intraoperative hypotension that required a greater use of vasopressors.

- These 2 different approaches were associated with differences in intraoperative hemodynamics, but no difference in clinically significant outcomes.
Calcium Channel Blockade

- Monotherapy is not recommended
- The most often used add–on drug class
- Some studies suggest this class can be used as the first choice
Alpha Blockade vs. Calcium Channel Blockade

Article: Both preoperative alpha and calcium channel blockade impact intraoperative hemodynamic stability similarly in the management of pheochromocytoma

Purpose: Determine the difference between alpha blockers and CCB in minimizing intraoperative hemodynamic instability (IHD)

Method: Retrospective analysis of tri-institutional database
  - IHD defined as at least one SBP measurement >160mmHg and at least one episode of MAP 60mmHg

Results:

- 155 patients included
  - 110 receiving CCB, 41 receiving alpha blockers, 4 receiving no medication
  - Goal BP: ≤130/85 mmHg
  - MAP cutoff: 100mmHg

- Significant difference
  - Max SBP and max DBP
  - SBP ≥160 mm Hg duration
  - SBP ≥200 mm Hg duration
  - Severe intraoperative hypotensive episodes
  - SBP ≤30% baseline duration
## Intraoperative hemodynamic data

<table>
<thead>
<tr>
<th></th>
<th>All, n = 155</th>
<th>Alpha-B, n=41</th>
<th>CC-B , n=110</th>
<th>No PMP, n=4</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Greatest systolic BP</strong></td>
<td>190 ± 42</td>
<td>169 ± 24</td>
<td>198 ± 45</td>
<td>163 ± 25</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Greatest diastolic BP</strong></td>
<td>105 ± 26</td>
<td>95 ± 15</td>
<td>109 ± 29</td>
<td>87 ± 16</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>SBP &gt;200 mm Hg, min</strong></td>
<td>4.8 ± 12</td>
<td>0.6 ± 1.9</td>
<td>6.3 ± 14</td>
<td>2.5 ± 5</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>SBP &gt;160 mm Hg, min</strong></td>
<td>17 ± 19</td>
<td>11 ± 14</td>
<td>19 ± 21</td>
<td>25 ± 50</td>
<td>0.026</td>
</tr>
<tr>
<td><strong>Lowest systolic BP</strong></td>
<td>82 ± 16</td>
<td>82 ± 10</td>
<td>82 ± 18</td>
<td>94 ± 13</td>
<td>0.916</td>
</tr>
<tr>
<td><strong>Lowest diastolic BP</strong></td>
<td>48 ± 12</td>
<td>45 ± 7</td>
<td>49 ± 13</td>
<td>46 ± 7</td>
<td>0.087</td>
</tr>
<tr>
<td><strong>SBP ≤30% baseline, min</strong></td>
<td>23 ± 31</td>
<td>35 ± 46</td>
<td>18 ± 22</td>
<td>12 ± 16</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*Surgery 156.6 (2014): 1410–7; discussion 17–8.*
Metyrosine

- Inhibits catecholamine synthesis

- May be used in combination with adrenergic receptor blockers for a short period before surgery

- Further stabilizes blood pressure to reduce blood loss and volume depletion during surgery
Adrenalectomy

- Laparoscopic approach is procedure of choice if less than 8 cm diameter and no malignant features
  - If in the adrenal gland, the entire gland should be removed
  - After tumor removal, catecholamine secretion should fall to normal in approximately 1 week

Laparoscopic vs Open Adrenalectomy

Article: Anesthetic aspects of laparoscopic and open adrenalectomy for pheochromocytoma

Purpose: Compare intraoperative hemodynamics and postop outcomes in laparoscopic vs. open adrenalectomy

Methods: Retrospective review of 14 patients that underwent laparoscopic removal vs. 20 that underwent open removal

Results:
- Postop pathologic examination confirmed pheochromocytoma in all patients
- No significant difference:
  - Highest intraoperative BP
  - Number of severe hypertensive episodes
  - Tachycardic and bradycardic episodes
  - Amount of fluid administered or duration of surgery
- Significant difference:
  - Laparoscopic group:
    - Intraoperative hypotension less severe
    - Number of hypotensive episodes was less frequent
    - Less patients required treatment for intraoperative hypotension
    - Less blood loss
    - Recovery was faster
    - Median hospital stay was 3 days vs. 7.5 days in open group
<table>
<thead>
<tr>
<th>Perioperative hemodynamic variables</th>
<th>Open (n = 20)</th>
<th>Laparoscopic (n = 14)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean preoperative blood pressure *(mm Hg)</td>
<td>140 ± 18/78 ± 10</td>
<td>144 ± 13/74 ± 14</td>
<td>0.5</td>
</tr>
<tr>
<td>Highest blood pressure *(mm Hg)</td>
<td>191 ± 33/98 ± 25</td>
<td>194 ± 19/106 ± 19</td>
<td>0.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.5 (0–5)</td>
<td>1 (0–3)</td>
<td>0.41</td>
</tr>
<tr>
<td>SBP ≥200 mm Hg</td>
<td>0 (0–4)</td>
<td>0 (0–2)</td>
<td>0.7</td>
</tr>
<tr>
<td>Lowest blood pressure *(mm Hg)</td>
<td>88 ± 14/50 ± 13</td>
<td>98 ± 19/57 ± 8</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2 (0–6)</td>
<td>0 (0–2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Highest heart rate (bpm)</td>
<td>104 ± 15</td>
<td>101 ± 24</td>
<td>0.78</td>
</tr>
<tr>
<td>Heart rate ≥110 bpm</td>
<td>0 (0–3)</td>
<td>0 (0–3)</td>
<td>0.36</td>
</tr>
<tr>
<td>Lowest heart rate (bpm)</td>
<td>61 ± 11</td>
<td>60 ± 9</td>
<td>0.81</td>
</tr>
<tr>
<td>Heart rate ≤50 bpm</td>
<td>0 (0–1)</td>
<td>0 (0–5)</td>
<td>0.81</td>
</tr>
<tr>
<td>Patients requiring treatment for hypertension (n)</td>
<td>17</td>
<td>13</td>
<td>0.63</td>
</tr>
<tr>
<td>Patients requiring treatment for hypotension (n)</td>
<td>9</td>
<td>1</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Patient Case

- Diagnosis:
  - Clinical presentation: Severe hypertensive episodes, tachycardia, severe headache
  - CT scan: 6.6cm mass on right adrenal gland
  - MIBG: increased activity on the right adrenal mass
  - 24 hour urine and plasma metanephrines and catecholamines: elevated
## Vitals

<table>
<thead>
<tr>
<th>Date</th>
<th>BP (range)</th>
<th>Pulse (range)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/5</td>
<td>7/5</td>
<td>90–210/60</td>
<td>90–117</td>
</tr>
<tr>
<td>7/6</td>
<td>7/6</td>
<td>79–233/56</td>
<td>DC lisinopril and metoprolol. Begin carvedilol</td>
</tr>
<tr>
<td>7/8</td>
<td>7/8</td>
<td>78–236/41</td>
<td>Begin Doxazosin</td>
</tr>
<tr>
<td>7/9</td>
<td>7/9</td>
<td>77–174/43–70</td>
<td>48–87</td>
</tr>
<tr>
<td>7/10</td>
<td>7/10</td>
<td>83–168/49–69</td>
<td>74–88</td>
</tr>
<tr>
<td>7/11</td>
<td>7/11</td>
<td>102–143/52–73</td>
<td>71–87</td>
</tr>
<tr>
<td>7/12–7/13</td>
<td>7/12–7/13</td>
<td>112–170/54–68</td>
<td>75–98</td>
</tr>
<tr>
<td>7/14</td>
<td>7/14</td>
<td>112–149/68–84</td>
<td>67–88</td>
</tr>
<tr>
<td>7/16–7/17</td>
<td>7/16–7/17</td>
<td></td>
<td>1 dose Levophed</td>
</tr>
</tbody>
</table>
Patient Treatment

- **Initial treatment:**
  - 7/1: Increased metoprolol to 100mg BID, continue lisinopril home dose
  - 7/5: Hydralazine 10mg IV bolus and Q6H prn. 1 dose amlodipine 2.5mg
  - 7/6: DC home BP meds and amlodipine, Continue hydralazine, 1 dose of carvedilol 6.25mg
  - 7/7: Started carvedilol 3.125mg BID

- 7/8
  - Doxazosin 1mg Q12H

- 7/15: Laparoscopic right adrenectomy
  - Nicardipine 5mg/hr continuous infusion prn
  - NaCl 0.9% continuous infusion
  - Phenylephrine continuous infusion prn
Blood pressure and volume stable postop

No discharge needs
- Carvedilol 6.25mg PO BID

Patient is to follow up in 4 weeks
- Plasma and/or urine levels of metanephrines will be measured to diagnose persistent disease
- Patient should have lifelong annual testing to check for recurrent or metastatic disease
The preoperative preparation of patients with pheochromocytoma is believed to be important to improve intraoperative hemodynamic stability and reduce morbidity during resection.

Several therapeutic regimens have been recommended, but there are few direct comparisons between regimens.
References


