Hypertensive Emergencies
Case and discussion
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R1 Boot Camp
July 2015
Objectives

- Case discussion
- Identify accelerated target organ damage in hypertensive emergencies
- Correctly evaluate patient and work up secondary causes of hypertension where necessary
- Manage patient appropriately depending on hypertensive urgency or emergency
Case

- 55 yo male sent by GP to SPH ED for high BP, recent d/c from MSJ for hypertensive urgency sent home on amlodipine 10 od, labetalol 200 bid
  - No secondary work up undertaken or planned
- 40 pk/yr smoker, current ½ ppd, no other CRFs, no prior meds
- BP 250/120 both arms in ED, asymptomatic
- AV nicking, normal neuro exam, JVP 2cm, S4,+ periph edema
- Hb 106, plts 96 (N at MSJ), Cr 161 (125 - 150 at MSJ)
- LVH on ECG, CXR nil acute, CT head old lacunes
What is going on?

a) Hypertensive emergency - IV hypertensive therapy and ICU consult

b) Hypertensive urgency - oral antihypertensive then send home with good follow-up plan

c) Malignant hypertension - IV hypertensive therapy and ICU consult

d) Uncontrolled severe hypertension - d/c with follow up with GP
Definitions - JNC 7 JAMA 2003

- **Hypertensive urgency** → SBP >180 or DBP > 120 without accelerated target organ damage (TOD)

- **Hypertensive emergency** → SBP >180 or DBP >120 with ACCELERATED TOD
  - BP number not criterion for Dx but DBP usually >120

- **Malignant hypertension** → severe HTN + papilledema, retinal hemorrhages, or exudates (severe hypertensive retinopathy)
  - Acute hypertensive nephrosclerosis may be present - AKI, proteinuria, hematuria
  - MAHA may be present (anemia and schistocytes)
  - Often in chronic, poorly controlled hypertensives
Severe Hypertensive Retinopathy
Definitions

- Definitions are arbitrary - severity of BP rise really depends on baseline BP
- Not all symptoms equal emergency!
- Pt with hypertensive urgency may present with non-progressive h/a, SOB, epistaxis, anxiety
  - Some of these Sx are common in many pts in the ER
  - Context is important!!
Importance of Context

- When faced with any high BP - always recheck BP yourself
- Use proper BP technique
- Ensure patient is in quiet room, resting comfortably
- ALWAYS consider common reasons for high BP
  - Pain, volume overload, distended bladder...
Importance of Context

- Always ask yourself these questions when faced with pt with high BP....

  - IS THIS PATIENT AT RISK OF TARGET ORGAN DAMAGE RIGHT NOW OR IN THE NEXT FEW DAYS?
  - IS THERE SOMETHING ELSE I CAN TREAT THAT WILL HELP LOWER THE BP (ie. treating pain, diuresing for volume overload)
Etiology

- Acute and severe BP rise can arise from essential or secondary HTN
- Usually essential HTN with acute worsening
- Precipitants:
  - Non-adherence (in pts with treated HTN)
  - Beta blocker or clonidine w/d
  - OCP, MAOIs, NSAIDs, cocaine/other stimulants
  - Secondary causes of HTN - OSA, renal parenchymal disease/RAS, endocrine causes, post-op, eclampsia
Drugs to ask about...

Table 4. Drugs That May Precipitate A Hypertensive Emergency.

- Oral contraceptives
- Monoamine oxidase inhibitors
- Tricyclic antidepressants
- Steroids
- Nonsteroidal anti-inflammatory drugs
- Nasal decongestants
- Cold remedies
- Appetite suppressants
Pathophysiology

- Tissues normally protected by autoregulation:
  - Muscular arteries dilate or constrict depending on BP, ensuring relatively constant pressure to arterioles/capillaries that supply target organs
  - Flow = Pressure/Resistance

- In chronic HTN, autoregulation prevents high BP from damaging capillaries/target organs

- In HTN emergencies → factors leading to severe/rapid BP elevations not fully known in most cases...
  - Likely combination of inappropriate vasoconstrictor release (ie. Norepi) and RAS activation that leads to critical systemic BP level
Cerebral autoregulation in hypertension

Schematic representation of autoregulation of cerebral blood flow in normotensive and hypertensive subjects. In both groups, initial increases or decreases in mean arterial pressure are associated with maintenance of cerebral blood flow due to appropriate changes in arteriolar resistance. More marked changes in pressure are eventually associated with loss of autoregulation, leading to a reduction (with hypotension) or an elevation (with marked hypertension) in cerebral blood flow. These changes occur at higher pressures in patients with hypertension, presumably due to arteriolar thickening. Thus, aggressive antihypertensive therapy will produce cerebral ischemia at a higher mean arterial pressure in patients with underlying hypertension.

Pathophysiology

- High BP reaches critical point → autoregulation fails and high pressure damages vessel walls
  - plasma contents enter damaged wall (fibrinoid necrosis), narrowing or obliterating lumen
  - damage to vessels leads to ischemia → further vasoconstrictor release, RAS activation → begets higher BP
- Pathologic findings in acute hypertensive nephrosclerosis
  - Ischemic/vascular injury to glomerulus from fibrinoid necrosis
Fibrinoid necrosis
Pathophysiology

- MAHA results from direct endothelial damage causing shearing of RBCs → anemia, schistocytes, thrombocytopenia
- Pressure natriuresis with higher BP leads to volume depletion → increased vasoconstrictor, RAS activity
- Rodriguez Cardio in Rev 2010
Clinical Evaluation
Evaluation

- FIRST - ABCs, then rule out emergency!
- Hypertensive emergencies:
  - Hypertensive encephalopathy - insidious symptoms/signs, non-localizing, altered LOC, seizures
  - Severe hypertensive retinopathy - papilledema, exudates, hemorrhages
  - Ischemic/hemorrhagic stroke - neuro signs
  - CHF - SOB, pulmonary edema
  - MI - CP, ECG changes, troponin rise
  - Aortic dissection - chest or back pain, asymmetric pulses/BP
  - Acute hypertensive nephrosclerosis - AKI + proteinuria/hematuria
  - Eclampsia
Clinical presentation and evaluation

- ABCs!

- History - HTN onset, duration, baseline BP, known TOD, recent drug/EtOH use, meds, adherence, timing/dose of last Rx

- How does current BP compare with their usual?

- Ask about Sx - headache, visual changes, neuro Sx, CP, back pain, SOB

- H/A, CP, SOB, anxiety, epistaxis, vertigo may not indicate emergency (often present in HTN urgency)
  - Bender J Clin Hypertens 2006
Evaluation

- Physical - AxOx3, BP both arms, PPP x 4, **fundoscopy**, carotid and abdo bruits, volume assessment, CVS, resp, abdo (palpate kidneys), **neuro exam**

- CBC, lytes, Cr, PBS, INR, LDH, bili, troponin, urinalysis (proteinuria, RBCs, cellular casts)

- ECG, CXR

- CT head if altered MS or abnormal neuro exam
Evaluation

- Consider secondary causes of HTN, in appropriate context (!)
    - 161 pts presenting to ED, 37% met criteria for resistant HTN, 29% had prior ED visits for HTN crisis
    - Sleep apnea 71%
    - Hyeraldosteronism 14%
    - RAS 8%
    - At least one secondary cause 77%
PRES

- Posterior Reversible Encephalopathy Syndrome
- Clinical/radiographic diagnosis characterized by h/a, altered LOC, visual disturbances, seizures and symmetric white matter edema in posterior hemispheres
  - Confluent areas of increased signal on T-2 weighted MRI imaging
- Arises usually from sudden increases in BP, not necessarily high levels (depends on baseline!) and loss of autoregulation/endothelial dysfunction
- Reversible with BP treatment
Treatment

- Determine whether URGENCY or EMERGENCY first!
- URGENCY not life-threatening but may increase risk of accelerated TOD if BP not improved over several days
- EMERGENCY is potentially life-threatening and BP must be reduced immediately
Hypertensive urgency can be managed with oral Rx and plan to lower BP over 48 hrs (< 160/100 - guideline)

Treatment depends on whether previously treated or untreated

- Previously treated - increase dose or add another agent; restart meds in non-adherent pt; add diuretic
- Untreated - short acting oral Rx (ie. captopril, labetalol) with transition to longer acting Rx
Avoid parenteral Rx and high loading doses of oral Rx → BP may fall below range wherein autoregulation maintains tissue perfusion (ie. sublingual nifedipine)

Even “normal” blood pressures can cause hypoperfusion in severely hypertensive patient → predispose to AKI etc.
Treatment - Hypertensive Urgency

- Monitor for BP decrease over several hours before decision to d/c...
  - However... NO evidence that failure to lower BP in ER associated with worse short term outcomes in HTN urgencies
- Plan for outpatient f/u within 2 days
- Consider inpatient observation if high risk → DM, Hx stroke, CAD, social situation
Remember...

- Even if the BP is really high, in the absence of accelerated TOD, there is no evidence that IV medication is a better bet!!!

- There may be evidence that IV therapy WORSENS outcomes....

- BP 200/90 + no accelerated TOD → what do you do?
- BP 220/120 + no accelerated TOD → what do you do?
- BP 240/130 + no accelerated TOD → what do you do?
Treatment - Hypertensive Emergency

- Hypertensive emergency requires admission to ICU/CCU with close monitoring - parenteral antihypertensives, art line, urine output, neuro vitals
- Strictly speaking, not CTU candidates, but often taken to CTU (consider mild AKI, mild CHF)
- Need close monitoring - if not critical care then at least step-down bed
Treatment - Hypertensive Emergency

- Decrease MAP by 25% in the first hour, then to 160/100-110 over next 6 hours (JNC 7 clinical practice guideline)
- Gradual reduction to preserve autoregulation of BP to brain, kidneys
- Major exceptions to this guideline are:
  - Ischemic stroke - can let BP ride up to 220/120 (unless thrombolytics used)
  - Aortic dissection - reduce SBP to 100-120, as tolerated, with BB

- Which agent/drug class to use?
  - Best agent has rapid onset, predictable dose-response, limited duration to allow titratability...
  - Will also depend on systems/organs affected
Treatment

- Optimal treatment unknown! Cochrane review of treatment in HTN EMERGENCIES, J Hum Hypertens 2008
- 15 RCTs found, 2 trials placebo controlled, only 1 trial double-blinded, others were open label
- Most trials reported data over 2-6 hrs
- NO trial had enough power to detect diffs in clinical outcomes
- NO RCT evidence to demonstrate reduced mortality with antihypertensive use in hypertensive emergencies!
- Reduced subjective severity of pulmonary edema with captopril compared to placebo in one trial but no diff in need for mechanical ventilation
- Overall recommendation - “use nitrates/nitroprusside because most studied”
<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Onset and duration</th>
<th>Specific uses</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>α/β blocker</td>
<td>5 mins/4-8 hrs</td>
<td>Most emergencies except CHF</td>
<td>Bronchoconstr’n, heart block, N/V</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Venous &gt; arterial dilator</td>
<td>2-5 mins/5-10 mins</td>
<td>ACS, pulmonary edema</td>
<td>h/a, vomiting, met-hemoglobinemia, tolerance</td>
</tr>
<tr>
<td>Nitroprusside</td>
<td>Arterial and venous dilator</td>
<td>30 secs/2 mins</td>
<td>Most emergencies</td>
<td>Increased ICP, coronary steal, cyanide toxicity (esp. in AKI)</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Arteriolar dilator</td>
<td>20 mins/1-4 hrs</td>
<td>Eclampsia</td>
<td>Tachycardia, worsening angina, h/a, unpredictable</td>
</tr>
</tbody>
</table>
Treatment - other considerations

- High BP may lead to pressure natriuresis/diuresis and therefore volume depletion
- Use IV NS to correct volume depletion
  - may help suppress renin secretion and further BP elevation via activation of RAAS
  - May prevent hypotension with onset of action of antihypertensives
Case

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Not an easy answer...

- Treated initially as hypertensive urgency with plan to discharge with close follow up...
  - Very high BP but asymptomatic and no acute eye findings (on non-dilated eye exam in ED)
  - Some BW abnormalities but nothing drastic

- No improvement in BP with labetalol 20 mg IV x 2 doses (given by ED) or captopril 25 mg po and several hours of observation
- Repeat BW: Hb decreased 10 points, plts also 10 points and now schistocytes seen on PBS, LDH 340
- Creatinine still elevated
- Urinalysis - blood, protein
Not an easy answer...

- Could this be malignant HTN?
  - Mild hypertensive changes on fundoscopy but non-dilated exam - may have missed more severe changes
  - Worsening kidney function although not dramatic - could this indicate development of fibrinoid necrosis and ischemic injury to glomeruli?
- Blood, protein on urinalysis
- Anemia, schistocytes, thrombocytopenia on PBS consistent with MAHA
Case

- Admitted to CTU for treatment
- BP, Hb, and plts improved
- TSH N, Ca N, lipids N, A1c 5.0
- ARR on labetalol and amlodipine not elevated (renin not suppressed, PAC 213 pmol/L)
- 24-hour urine fractionated metanephrines/catecholamines in normal range
- Abdo U/S - medical renal disease L kidney (11.4 cm vs 10.6 cm R side), “vascular flow to both kidneys visually symmetric bilaterally”
- MR angiogram - non-diagnostic (recommend CTA)
Case

- D/C’ed on hydralazine 25 mg qid, NTG 0.4 mg/hr, amlodipine 10 mg od, labetalol 200 mg bid

- Awaiting f/u in HTN clinic - ensure good volume control on hydralazine!!

- Will need careful work-up for secondary causes
  - RAS or renal parenchymal disease - may choose not to test further if GFR stable and BP well controlled
  - OSA
  - What is his FHx?

- Quit smoking!
- Needs ACEI or ARB regimen (LVH, proteinuria)
Questions?

- Thank you!