Context

- Working RAZ
- Time seen: 1552 (shift finishes at 1630)
- Last two patients both female, worried well
"headache with nausea since 1300, pt was very teary eyed and anxious initially however has settled down now"
Vitals

- 160/90
- 36.6
- 76
- 18
- 100%
- 6/10
- GCS 15
33 y/o ♀

CC: “spells” over the past two years

Severe headache, vice like, pulsating

10-15 minutes

q4-6 months

Feels well between episodes

6 episodes in the past 3 hours

No photo or phonophobia
Begins in abdomen, rises up through chest and to the top of her head.

Headache feels like a volcano coming out of the crown of her head.

Accompanied by CP, heart racing, difficult to get breath.

Finds herself on the floor moaning without knowing how she got there.

“out of body experience”

Pain radiates to pinky finger L hand.
Past Medical History

- Migraines x 4 years
- Adenoidectomy
- G3P3, SVDs, no complications
- Non smoker
- Rare etoh
- Denies all illicit drug use
- Had these episodes worked up by GP before - nil
Family History

- Cousin had a stroke in her 20s
- Mother hyperthyroid
- Brother Crohn’s
- Aunt breast ca in 40s
Thoughts?
Physical examination

- Teary, over the garbage can
- Improves over course of history taking
- PEARL
- EOM normal, no nystagmus
- CN normal
- Finger to nose normal
- Strength 4/5 throughout
- Gait normal, but slow
Next steps?

- Maxeran
- Wait
- EKG

- Returned to her room
  - Looked well
  - Fatigued, dry mouth, otherwise felt OK
Next steps!

- Pt transferred to acute
- Interventional cardiology called
- Bloods drawn
Interventional’s ddx:
- ACS
- Coronary artery dissection*
- Coronary artery spasm
- Focal myocarditis

“Haven’t seen anything like this in 30 years”

EKG does not fit any coronary distribution
I want a second opinion.
Blood work

- WBC 17.1
- Trop 372
- CK 119
- Glu 11.2
- Lytes N
- Cr 77
- HgB 134
Thoughts?
CT Cardiac

- Large calibre normal right dominant coronaries
- Large segment of mid anterior and septal akinesis with borderline EF of 48%
- R heart and R atrium are normal in size
CT Cardiac Continued

- 8.1cm LUQ mass anterior and inferior to pancreatic tail, abutting the spleen
- ?pancreatic mass vs adrenal lesion vs renal neoplasm
- Recommend MIBG scan for pheo
- DDx: myocardial dysfunction related to intermittent coronary spams vs. unopposed effects of long term catecholamine secretion
- Treat HTN and follow LV function with ECHOs
Repeat Investigations

CK now elevated: 237

Medicine called cardiology:
Stop doing bloodwork
Admitted to 4CN

- Aggressive control of her hypertension (as per radiology)
  - Labetatol 200mg PO q8h
  - Labetalol 10mg IV PRN HTN
  - Prazosin 1.25mg PO q6h
  - Metoprolol 150mg PO q12h
- Pheochromocytoma workup
  - ACTH
  - Catecholamines
  - Metanephrines
  - MIBG NM
- Consult
  - Anesthesiology
  - Urology
  - Cardiology
So... what is a pheo?
Pheo-chromo-cyt-oma

- From Greek:
  - phaios "dark"
  - chroma "color"
  - kytos "cell"
  - oma "tumor"
Pheochromocytoma

- Neuroendocrine tumour
- From chromaffin cells of adrenal medulla
- Secretes large amounts of catecholamines
  - Epinephrine > norepinephrine
- Potentially fatal “pheo crisis”
  - Stoke, MI, organ failure
“Classic” Triad

headache

tachycardia

diaphoresis

40%
Epidemiology

- 2–8 in 1,000,000
- 30s-50s
  - earlier in familial cases
- \( \text{♂} = \text{♀} \)
Cause

- 25% familial
- Associated with
  - Neurofibromatosis 1
  - Multiple endocrine neoplasia (MEN) syndromes
  - Von Hippel–Lindau disease

Bilateral pheochromocytoma in MEN2.
Characteristics

- 80% unilateral (R>L)
- 10% bilateral (MEN)
- 10% extra-adrenal
  - organ of Zuckerkandl
- Usually <10cm
- Highly vascular
Malignant vs. Benign

- 90% benign*
- Histologically and biochemically identical
- Think malignant if:
  - local invasion into surrounding tissues
  - distant metastases
- Mets may occur 20 years after resection (surveillance)
Diagnosis

- **Urine**
  - 24 hour collection for catecholamines and total metanephrines

- **Blood**
  - Fractionated metanephrines

- **NM Scan**
  - 123-I-metaiodobenzylguanidine (MIBG) scintigraphy
  - MIBG resembles norepinephrine, is taken up by adrenergic tissue
Evaluation and treatment of catecholamine-producing tumors

1. Discontinue interfering medications

2. Case detection testing with either:
   - 24-hour urine fractionated metanephrines and catecholamines, or
   - Plasma fractionated metanephrines drawn from indwelling cannula following 30 minutes of supine rest

   - Normal
     - Recheck during a spell
     - Normal: Investigate other causes of spells
     - Twofold elevation above upper limit of normal in urine catecholamines or urine metanephrines (Nmet >900 mcg per 24 hours or Met >400 mcg per 24 hours) or "significant increase" in fractionated plasma metanephrines

3. Localization:
   - Adrenal/abdominal MRI or CT scan
     - Typical adrenal or para-aortic mass
       - 123I-MIBG scan if:
         - >10 cm adrenal mass
         - Paragangioma
     - Negative abdominal imaging
       - Reassess the diagnosis
         - Consider:
           - 123I-MIBG scan
           - In-III pentetrotide scan
           - Whole body MRI scan
           - PET scan
         - Tumor found

4. Consider genetic testing
   - Preoperative alpha- & beta-adrenergic blockade
     - Surgical resection
Treatment

- Surgery

- Requires aggressive pre and intra op alpha antagonists (prazosin)

- combined alpha/beta blocker (labetalol) – target HR 60-80

- Manipulation of the tumor is intraoperatively can cause severe hypertension

- A "pure" beta blocker such as atenolol contraindicated:
  - risk of unopposed alpha agonism → severe and refractory hypertension
PubMed

- ("Pheochromocytoma"[Mesh]) AND "Acute Coronary Syndrome"[Majr]

- 6 results
  - 1 spanish, 1 french
  - 1 assd with hyperthyroidism
  - 1 extra-adrenal
A case of unusual acute coronary syndrome

Abstract

Pheochromocytoma is a rare tumor that usually develops ahead of the neuroectodermal chromaffin cells of the adrenal medulla, but it may arise anywhere within plexus of sympathetic adrenergic nerves. Headache, palpitations, tremor, excessive sweating, abdominal pain, and hypertensive paroxysm are the common clinical presentations of the tumor, but it has also been reported several cardiac symptoms.

Takotsubo cardiomyopathy is a widely accepted syndrome generally characterized by transient systolic dysfunction of the apical or, more rarely, of the mid left ventricular segments (inverted takotsubo).

A case of pheochromocytoma presenting as inverted takotsubo is described in this article.

A 28-year-old man, 20 cigarettes/day smoker, without other cardiovascular risk factors, was admitted to our emergency department because of onset of dizziness, diaphoresis, stomachache, and vomiting at awakening and persisting during the day. Physical examination was unremarkable, and blood pressure was normal. The rest electrocardiogram (ECG) showed a sinus tachycardia of 105 beats per minute, tall upright T waves with ST-segment depression in V4 to V6 leads and increased troponin (Roche Troponin T, 0.07 ng/mL). In the coronary care unit, serial ECG showed a gradual resolution of ST-segment depression with persistent tall upright T waves. A transthoracic

Pheochromocytoma is a rare catecholamine-secreting tumor typically located in the adrenal medulla or along the sympathetic ganglia. It exerts distant effects by secretion of catecholamines and usually manifests with headache, sweating, tachycardia, pallor, hypertension, and abdominal pain but also with cardiac symptoms simulating an ACS like angina, dyspnea, syncope [1], ST-segments and T-waves abnormality, elevated cardiac biomarkers, and temporary impairment of the left ventricular function. Liao et al [1] reported cardiovascular manifestations in patients discharged with diagnosis of pheochromocytoma; of note, angina was a frequent initial presentation, often associated with abnormal ECG.

Approximately 15% of patients with non-ST-elevation ACS have normal coronary arteries. The pathophysiology is heterogeneous, and possible mechanisms include coronary artery spasm, embolism, acute thrombosis followed by recanalization, congenital abnormalities, and other causes such as myocarditis and takotsubo syndrome [2].

Takotsubo cardiomyopathy is a widely accepted syndrome generally characterized by transient systolic dysfunction of the apical (apical ballooning syndrome) or, more rarely, of the mid left ventricular segments (inverted takotsubo). Pheochromocytoma has been associated with inverted pattern [3].

In our case, an inverted takotsubo was suspected because of transient severe cardiac dysfunction with typical motion abnormalities.
Overview of cases

1. 48 y/o ♂ in Taiwan presented with chest pain radiating to back, fever and leukocytosis
   - ST elevation, +cardiac markers
   - Angio normal, discharged
   - Readmitted 4 months later, labile BP, Found on CT

2. 79 y/o ♀ in France presented with chest pain radiating to the back, hypertension (220/118) and diaphoresis
   - ST elevation, slight trop rise, BNP rise
   - Found on CT (to R/O dissection)
   - Normal angio
Overview of cases

3. 48 y/o ♂ in France, presented with recurrent abdominal pain, palpitations and hypertension (190/100)
  - EKG: left axis deviation, incomplete RBBB
  - ?pheo found on CT
  - Admitted 2 weeks later for surgical removal:
    - Hours after his admission, → sudden left thoracic pain → syncope
    - EKG: ST depression >5 mm in all leads, 35bpm
    - Angio: only moderate stenosis of the first marginal artery
    - 2nd episode of syncope with hypotension, bradycardia and cardiac arrest
    - Transvenous pacing
    - Surgery
Overview of cases

4. 42 y/o ♂ in the Netherlands presented with chest pain, dyspnea, and nausea
   - EKG: left-axis deviation, ST elevations V1 to V5, TWI in I, aVL and V2
   - Elevated trop, normal CK
   - Angio normal
   - Fluctuating HTN – urinary catecholamines to dx

5. 28 y/o ♂ in Italy presented with dizziness, diaphoresis, stomachache, and vomiting
   - EKG: Tall upright T waves, ST depression V4-V6, increased troponin
   - Angio normal
   - Abdo U/S revealed ?pheo, then CT and MRI
Theories

- “diagnostic criteria for takotsubo syndrome recommends to rule out the diagnosis of pheochromocytoma to confirm the diagnosis”

1. Oxidation of catecholamines → toxic metabolites and free radicals, which can cause intracellular calcium overload and myocardial damage

2. Alpha1-norepinephrine vasospasm of the coronary arteries

3. Direct epinephrine-mediated effects on cardiomyocytes
Follow up patient

- ICU post op
- High risk hypotension
- Volume loaded, with salt, monitor urine output
- Did well, transferred to floor
- Plan to discharge home today
- Heart failure improving with BP control