Incidental bilateral adrenal masses with pheochromocytoma and MAX mutation of unknown significance in a hypertensive young man

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- Disclosures
- Thank you
Learning objective

- Discuss the clinical implications of novel germ-line mutations in non-syndromic pheomchromocytoma
Clinical context & relevance

- Rare catecholamine secreting neoplasms
  - “Rule of 10’s”
- Causative germline mutations identified in 30-50%
  - 2002 Neumann et al [NEJM]
- Rapid expansion in number of identified genes
  - Advances in testing
Clinical context & relevance

- Contributory gene clusters
Chief concern

- 41 yo M complains of eight weeks watery diarrhea and weight loss
History

- HTN from age 20, treated with Diltiazem + Olmesartan
- Dyslipidemia, Obesity
- Father passed “in his sleep” at age 34
Initial investigation

- Gastroenterology consultation and endoscopy unrevealing
- Diarrhea and weight loss resolved with change in class of anti-HTN medications
Incidental imaging findings

- Bilateral solid enhancing adrenal masses
  - Left: 2.4 cm, Right 1.1 cm
- Pancreas uncinate process 7 mm enhancing lesion
  - Endoscopic U/S most consistent with non-functioning islet cell tumor, biopsy not obtained
- Octreoscan without somatostatin receptor uptake
Laboratory results

- Strongly suggestive of pheochromocytoma
  - Free normetanephrine 402 pg/mL (RR < 148)
  - Free metanephrine < 25 pg/mL (RR < 57)
  - Neuroendocrine studies

*RR = Reference Range
Clinical course

● Genetic testing?
  ○ Indications

● Characteristics suspicious for hereditary etiology
  ○ Multifocal
  ○ Extra-adrenal
  ○ Young age at presentation
Clinical course

- Unilateral vs bilateral adrenalectomy
  - Likelihood of bilateral disease?
  - Malignant potential?
  - Adverse implications of bilateral procedure
Clinical course

- Left-sided adrenalectomy performed
- Pathology confirmed pheo
Clinical course

- Heterozygous variant in last intron of the MAX gene
  - c.296-1G>A
  - Not previously reported, uncertain significance
MAX mutation

- 1-2%
- Increased normetanephrine : metanephrine ratio
- Almost exclusively adrenal
- Often bilateral
- Paternal transmission pattern?
Follow-up

● Will right-sided adrenal lesion become unmasked?
  ○ MAX case reports requiring a second surgery
    ■ Bilateral with recurrence after 5 months
    ■ Metachronous contralateral after four years
7 Months follow-up

- Normotensive
  - “Pins & needles feeling in face and left arm, intermittent but progressive, almost a flushed feeling”

- Labs
  - Normetanephrine 301 pg/mL (RR < 148)
  - Metanephrine 44 pg/mL (RR < 57)
  - Total metanephrine 345 pg/mL (RR < 205)
9 Months follow-up

- BP remains <140/90
- "this is the first time in 20 years that I haven't taken meds for hypertension"
Discussion

- Limited data exists to guide decision-making
  - Surveillance?
  - Testing of family members?
  - Counseling re malignant potential?
  - True nature of pancreatic lesion?
Discussion

- Be suspicious, especially when:
  - multifocal, extra-adrenal, or young age
- Need for characterization of clinical phenomena as they relate to genetic findings
- Need for development of evaluation, surveillance, management protocols
References

Thank you