Pheochromocytoma

Case presentation

50M with T1DM, chronic inflammatory demyelinating polyneuritis (monthly IVIG), CKD4, pheochromocytoma 2016 s/p resection, presenting for a second opinion for recently discovered metastatic disease.

- 2014-xx-xx ~50lb weight loss, recurrent diaphoresis and feeling of being hot, extreme fatigue
- 2014-06-xx presented to OSH
- 2014-06-15 10.2x9.0x6.8 cm mass on CTAP, taken to surgery. L adrenalectomy, L partial nephrectomy, splenectomy. Clean margins. 7 LN w/o cancer. Path: mostly necrotic tissue, low Ki-67 (specifics not available)

Case presentation

2021-08-xx plasma normetanephrine elevated

2021-09-xx PET dotatate: 1.8cm nodule in surgical bed, multiple b/l pulm nodules, LN: [paraaortic RP, mediastinal].

Told to get his affairs in order, consult to VUMC entered.

Case presentation

Labs

- Cr 2.75 (b/l)
- plasma normetanephrine 990
- plasma metanephrine <10
- otherwise bland

Exam

- SBP 140s, at baseline
- nothing else of note

Questions

How common is pheochromocytoma/paraganglioma?

- sites of disease?
- symptoms?

Is there a link between autoimmunity and pheo/para?

- Answer: not a robust one.

After initial management, what should surveillance look like?

- labs?
- imaging?

How should we think about prognosis?

Terminology

Pheochromocytoma

Neuroendocrine tumors arising from *chromaffin* cells of the *adrenal medulla* (usually, "pheochromocytoma" refers specifically to adrenal tumors).

Paraganglioma

Same idea, paraganglia NET, but not adrenal (chromaffin staining usually less robust).

PPGL

Catch-all term ("pheochromocytoma and paraganglioma") Different papers use different acronyms for the same thing.

Terminology

Malignant PPGL

Determined by:

- ~~imaging~~
- ~~pathology~~
- ~~mutations~~

"Malignancy can only be determined from the presence of metastatic lesions at sites where chromaffin cells are normally absent."[1] Proven by bx, functional imaging and catecholamines can also be helpful.

Terminology

Metastatic, Recurrent, Synchronous

Metastatic: wrong place (bone ~60%, distant LN ~40%, lung ~30%, liver ~25%)

Synchronous: multiple right places (sympathetic trunk, H&N)

Recurrent: right place, again

[1] Fassnacht 2020

Epidemiology

Detected incidence for PPGL: 0.6/100k, rising with time

~0.5% of all pts with HTN

~4% in adrenal incidentaloma

>35% of cases are associated w germline mutations

~2/3-3/4 p/w with hormone-related sx, ~2/3-3/4 p/w with tumor-related sx

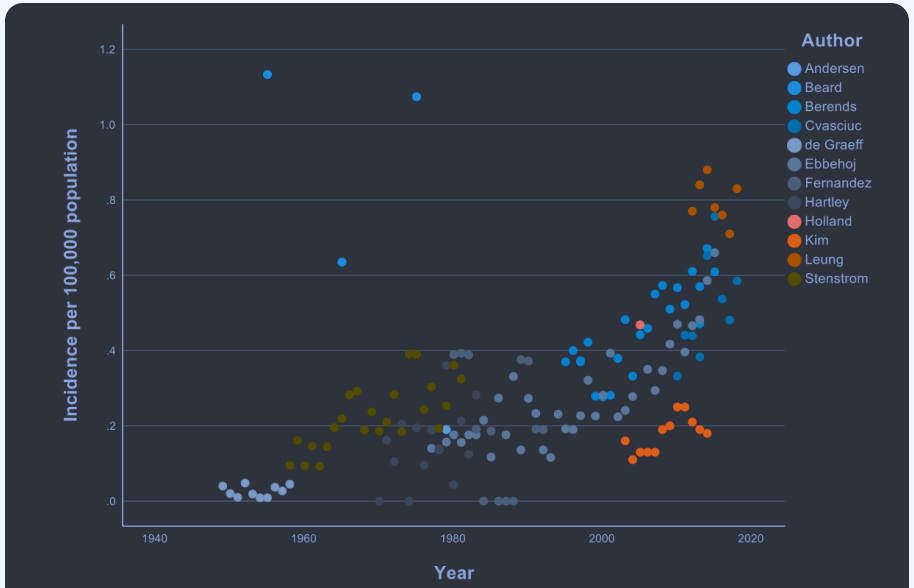


Figure 2. Annual incidence of PPGL 1949 to 2018.

[1] Al Subhi 2022

Surveillance

Type and frequency depends on low- vs high-risk status.

High-risk features

- tumor size >=5cm
- any paragangliomata (extra-adrenal)
- SDHx mutation
- plasma methoxytyramine >=3x ULN

If low-risk

- metanephrines 2-6wk s/p surgery, then dealer's choice (usu yearly)
- image if metanephrines get out of whack

Prognosis

If malignant[1]

5y OS ~60-80%

PPGL-attributable death 85%
Modes of death?

Poor prognostic factors: sporadic disease, hypersecretion

Favorable prognostic factors: H&N disease, SDHx mutation (availability of drugs, usu younger, more often H&N locale, less likely to be hypersecretors)

If benign[2]

5y OS >95%

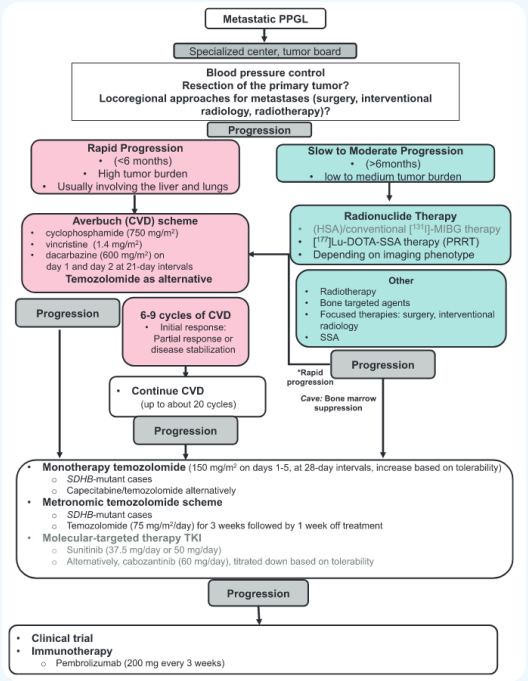
Management

Observation

- most of the time, surveil closely after initial resection (if it was done)

Active

- next slide


Metastatic PPGL
Specialized center, tumor board
Blood pressure control
Resection of the primary tumor?
Locoregional approaches for metastases (surgery, interventional radiology, radiotherapy)?
Progression
Rapid Progression
(<6 months)
High tumor burden
Usually involving the liver and lungs
Slow to Moderate Progression
(>6months)
low to medium tumor burden
Averbuch (CVD) scheme
cyclophosphamide (750 mg/m²)
vincristine (1.4 mg/m²)
dacarbazine (600 mg/m²) on day 1 and day 2 at 21-day intervals
Temozolomide as alternative
Radionuclide Therapy
(HSA)/conventional [131I]-MIBG therapy
[177]Lu-DOTA-SSA therapy (PRRT)
Depending on imaging phenotype
Other
Radiotherapy
Bone targeted agents
Focused therapies: surgery, interventional radiology
SSA
Progression
6-9 cycles of CVD
Initial response: Partial response or disease stabilization
*Rapid progression
Cave: Bone marrow suppression
Continue CVD
(up to about 20 cycles)
Progression
Monotherapy temozolomide (150 mg/m² on days 1-5, at 28-day intervals, increase based on tolerability)
SDHB-mutant cases
Capecitabine/temozolomide alternatively
Metronomic temozolomide scheme
SDHB-mutant cases
Temozolomide (75 mg/m²/day) for 3 weeks followed by 1 week off treatment
Molecular-targeted therapy TKI
Sunitinib (37.5 mg/day or 50 mg/day)
Alternatively, cabozantinib (60 mg/day), titrated down based on tolerability
Progression
Clinical trial
Immunotherapy
Pembrolizumab (200 mg every 3 weeks)

Resources

HemOnc.org entry

ESMO-EURACAN Guidelines 2020

NANETS Guidelines 2021

NCCN Guidelines

PathologyOutline Features to Report

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