IMAGING MANIFESTATIONS OF TUMORS IN VON HIPPEL-LINDAU

Aashish Patel, M.D.
Department of Radiology and Imaging Sciences
Indiana University School of Medicine
Indiana University Health
NO FINANCIAL DISCLOSURES
VHL RELATED TUMOR SITES AND TYPES

- Retinal hemangioblastoma
- Central nervous system hemangioblastoma – of cerebellum and spinal cord
- Endolymphatic sac tumors
- Pancreatic cysts
- Pancreatic serous cystadenomas
- Pancreatic neuroendocrine tumors
- Renal cysts
- Renal clear cell renal cell carcinomas
- Pheochromocytoma of adrenal gland
- Epididymal cystadenoma
- Papillary cystadenoma of epididymis
- Broad ligament cystadenoma
RETINAL CAPILLARY HEMANGIOBLASTOMA

- Aka retinal angiomomas or capillary hemangiomas
- May develop in up to 70% of VHL patients
- Multifocal/bilateral involvement in ~50% of cases
- Diagnosis by ophthalmic examination

- MRI of brain/orbit may reveal a tiny enhancing retinal nodule, with or without retinal detachment
- Typically found in the peripheral retina (85%) or juxtapapillary region (15%)
- Visual loss results from fluid exudation from tumor resulting retinal edema or traction effects causing retinal distortion
- Retinal detachment and vision loss can occur secondary to hemorrhage
CENTRAL NERVOUS SYSTEM
HEMANGIOBLASTOMA

- Prototypical tumor of VHL, frequency ~60-84%
- Sites and frequency
  - Cerebellum – 38%
  - Brainstem – 10%
  - Spinal cord – 51%
  - Supratentorial – 2%
- Quite often multifocal (up to 79% in one series)
- MRI typically reveals a hyperenhancing nodule, possibly with associated cystic component
- Well-circumscribed, capillary vessel-rich benign neoplasms
- Do not invade locally or metastasize
- Mass effect upon adjacent structures causes symptoms, either due to tumor itself or cyst formation around lesion
- Cerebellar HB - gait ataxia, dysmetria, headaches, diplopia, vertigo, and emesis
- Spinal cord HB – numbness/tingling; weakness in arms/legs; gait difficulty; bowel/bladder dysfunction
CENTRAL NERVOUS SYSTEM
HEMANGIOBLASTOMA

- Can remain dormant for unpredictable periods of time or can present with accelerated growth
- One review series (225 patients, 1921 lesions)
  - 51% - no growth
  - 49% - growth
    - 72% - stepwise growth
    - 6% - linear growth
    - 22% - exponential growth
- Because of this variable biologic activity and difficulty predicting evolution, ongoing surveillance is needed of brain and spine with MRI
- No specific imaging findings to predict growth pattern
- Symptoms and intervention often dependent upon cystic component and peritumoral edema
Intraaxial right inferior cerebellar mass with cystic component as well as an avidly enhancing nodule
ENDOLYMPHATIC SAC TUMOR - PAPILLARY CYSTADENOMA

- Develops in 10-15% of VHL patients
- Bilateral in 30%
- Benign tumors which occur in the endolymphatic duct as it extends through the vestibular aqueduct, which connects the inner ear with the extraosseous portion of the endolymphatic sac (dural fold at posterior surface of the petrous portion of temporal bone)
- Locally invasive, can erode into semicircular canals and cochlea
- Hearing loss, tinnitus, disequilibrium/vertigo, and facial paresis
- Symptoms may relate to:
  - Invasion of otic capsule with disruption of endolymphatic flow
  - Intralabyrinthine hemorrhage (sudden hearing loss)
  - Obstruction of endolymphatic sac resorption of fluid (gradual hearing loss/tinnitus/vertigo)
- Require dedicated imaging of temporal bones – CT or MRI
CT - Intratumoral calcification
MRI – Heterogeneous T2 signal
PANCREATIC LESIONS IN VHL

- Cysts (~70%)
- Serous cystadenomas (9%)
- Neuroendocrine tumors (9-17%)
PANCREATIC CYSTS

- Common in VHL population – may be seen in up to 70% of cases
- Typically multiple
- Often asymptomatic; may cause epigastric pain/discomfort
- Benign, without malignant transformation

- Imaging features
  - Fluid density –
    - US – anechoic
    - CT homogeneous low attenuation
    - MRI – T2 hyperintense; T1 hypointense
  - Imperceptible/thin wall
  - No solid elements, septations, or associated enhancement
  - No calcifications
  - No hemorrhage
  - Do not communicate to the pancreatic ductal system
PANCREATIC SEROUS CYSTADENOMA

- Benign
- Composed of multiple small cysts in honey-comb configuration
- Cysts lined by glycogen-rich cuboidal epithelium, separated by fibrous septae, extending radially from a central scar
- Does not communicate with the main pancreatic duct
- Central stellate scar with calcification and cluster of cysts, external lobulation; arterial phase enhancement of septae on CT/MRI
PANCREATIC NEUROENDOCRINE TUMORS

• Occur in ~15% of VHL patients
• Multifocal in ~50%
• Vast majority are nonfunctional
• Tend to be asymptomatic
• Symptoms can include abdominal pain, jaundice, pancreatitis, and gastrointestinal bleeding
• Imaging technique should include multiphase post-contrast imaging (including arterial phase)

• Imaging Findings
• Small tumors typically homogeneous, hyperenhancing during the arterial phase
• Larger tumors may demonstrate heterogeneity
• MRI – T1 hypointense, T2 hyperintense, with avid arterial enhancement with washout
• CT – hypoattenuating/isoattenuating on noncontrast CT, followed by avid arterial enhancement with washout
PHEOCHROMOCYTOMA

• Tend to be seen in younger patients
• Often multiple
• Can be extra-adrenal (paraganglioma)
• Less likely to be associated with symptoms or biochemical evidence of catecholamine production

• CT – noncontrast, intermediate attenuation; post contrast arterial phase hyperenhancement with slower washout (compared with adrenal adenoma)
• MRI – T2 fluid signal intensity “light-bulb” bright; T1 post-contrast avid enhancement
• MIBG – metaiodobenzylguanidine nuclear medicine scan – low sensitivity; high specificity
• DOTATATE PET/CT – somatostatin receptor expressing cells – high sensitivity and specificity
RENAL CELL CARCINOMA AND RENAL CYSTS

- VHL patients at risk for developing multiple renal cysts and renal cell carcinomas (~2/3 patients)
- Clear cell RCC, often multicentric and bilateral
- Clear cell RCC – heterogeneous hyperenhancing mass on US/CT/MRI, with necrosis, hemorrhage, and calcification possible
- Renal cysts in VHL patients may develop thickened wall or septations and associated nodularity, representing a manifestation of RCC
Epididymal papillary cystadenoma

- Commonly identified in vHL patients (~35% of patients, range 10-60% in series)
- Typically asymptomatic
- May manifest as a cystic lesion with thick wall and peripheral solid nodules, completely cystic, completely solid, or mixed cystic-solid

Broad Ligament papillary cystadenoma
RECENT TOPICS IN IMAGING

• Ultrasound – contrast enhanced ultrasound (CEUS)
• MRI – risk for nephrogenic systemic fibrosis with use of gadolinium contrast agents in the setting of renal dysfunction
• CT – advances in techniques including the use of iterative model-based reconstruction to lower x-ray dose, as well as dual-energy techniques that can utilized to pursue lower iodine contrast volumes
LUMASON

• Bracco Diagnostics, Monroe Township, New Jersey

• Chemical nomenclature – sulfur hexafluoride lipid-type A microspheres (for injectable suspension, for intravenous use)
CONTRAST ENHANCED ULTRASOUND - BENEFITS/INDICATIONS

- Improve characterization of renal lesions (initially identified by grayscale ultrasound) by observation of dynamic contrast appearance during arterial, portal venous, delayed venous timings (improve specificity)

- Can be used to further characterize solid renal lesions; can also be used for complex cystic lesions

- Excretion is via pulmonary exhalation
  - No hepatic or renal excretion
  - No hepatic/renal toxicity
  - Can be used in patients with hepatic/renal dysfunction
CONTRAST ENHANCED ULTRASOUND – IMAGING TECHNIQUE

• Perform routine protocol diagnostic examination of the kidneys with grayscale technique (color flow and spectral Doppler as appropriate)

• Once identifying renal lesion(s), identify best anatomic imaging window and administer Lumason intravenous contrast bolus (2.4 mL suspension for adult; 0.03 mL/kg for pediatric)

• Perform imaging for 3-5 minutes to allow characterization –
  • Arterial phase
  • Portal venous phase
  • Delayed phase
NEPHROGENIC SYSTEMIC FIBROSIS

- Fibrosing disorder that occurs exclusively in patients with kidney failure
- Thickening of the skin of trunk/extremities
- Some experience fibrosis of deeper structures, including muscle, fascia, lungs, and heart
- Occurs in patients –
  - On hemodialysis
  - On peritoneal dialysis
  - Renal transplant patients with reduced function
  - Advanced chronic kidney disease
  - Acute renal failure

- Etiology – exposure of patients with renal failure to new medication, infectious agent, or toxin; increasing evidence that gadolinium contrast agent exposure
- Because Gadolinium+3 ions are close in size to Calcium+2 ions, Gd is an effective calcium channel blocker
- Patients with eGFR <30 mL/min/1.73m²
DUAL ENERGY CT / SPECTRAL CT

- CT technique that uses two separate x-ray photon energy spectra
- This dual energy data can be used to reconstruct numerous image types
  - Virtual mono-energetic images
  - Material decomposition maps (for iodine or calcium)
- Benefits for clinical imaging
- ****Potential to decrease iodinated contrast dose, as lower energy mono-energetic images
- ****Potential to decrease x-ray dose by creating virtual non-contrast images
DOTATATE PET/CT

- Somatostatin receptor-based functional imaging using Gallium-68 labeled DOTATATE positron emission tomography (PET) combined with CT
- Pheochromocytoma and pancreatic neuroendocrine tumors demonstrate avidity for somatostatin analogs
- Hemangioblastoma, renal cell carcinoma, endolymphatic sac tumor, and epididymal cystadenoma also can demonstrate avidity
- Higher detection of extra-pancreatic lesions
- Comparable to CT/MRI for pancreatic lesions
- Potential role in the surveillance of VHL-associated lesions

The Utility of 68Gallium-DOTATATE PET/CT in the Detection of von Hippel-Lindau Disease Associated Tumors
Eur J Radiol 2019 Mar 01;112(112)130-135, J Shell, A Tirosh, C Millo, SM Sadowski, Y Assadipour, P Green, D Patel, N Nilubol, E Kebebew
ENDOSCOPIC ULTRASOUND

- Small subject number, prospective study
- EUS shown as superior to standard CT/MRI for detection of small solid pancreatic lesions in VHL patients
- EUS performed well in early detection of small solid lesions and multifocal cystic disease
- Overall role in surveillance, however, is unclear

Potential Value of EUS in Pancreatic Surveillance of VHL Patients

# IMAGING MODALITIES

## Pros

- **US** – no ionizing radiation; widely available; real-time imaging; lower cost
- **CT** – short examination time; high spatial resolution; large volume anatomic coverage
- **MRI** – high tissue contrast; no ionizing radiation; large volume anatomic coverage

## Cons

- **US** - Limited anatomic coverage secondary to osseous structures; dependent upon operator
- **CT** – radiation exposure; iodinated contrast in renal dysfunction; higher cost
- **MRI** – Duration of examination; gadolinium contrast in renal dysfunction; higher cost
REFERENCES


THANK YOU