



# AMSER Rad Path Case of the Month:



22-year-old woman with  
Li-Fraumeni syndrome

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# Patient Presentation

## Clinical history

- Asymptomatic 22F presents for genetic counselling

## Family history:

- Known family history of germline TP53 mutation R213Q (Li-Fraumeni syndrome)
- Mother: cancer-free; TP53+
- Maternal aunt: bilateral breast cancer in 40s; TP53+
- Maternal grandmother: breast cancer in old age; TP53 unknown
- Maternal grandfather: cancer-free; TP53 unknown

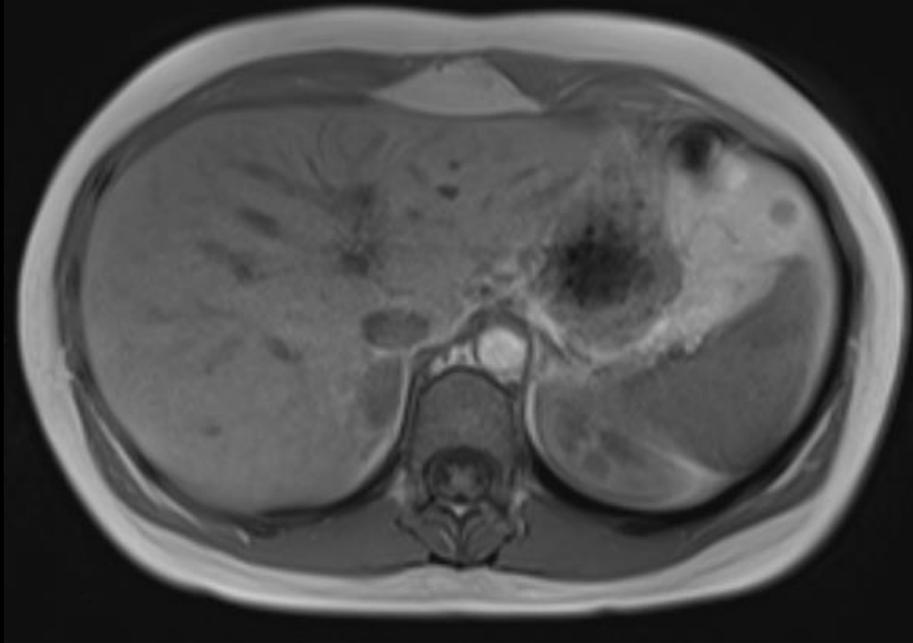
## Physical exam

- unremarkable

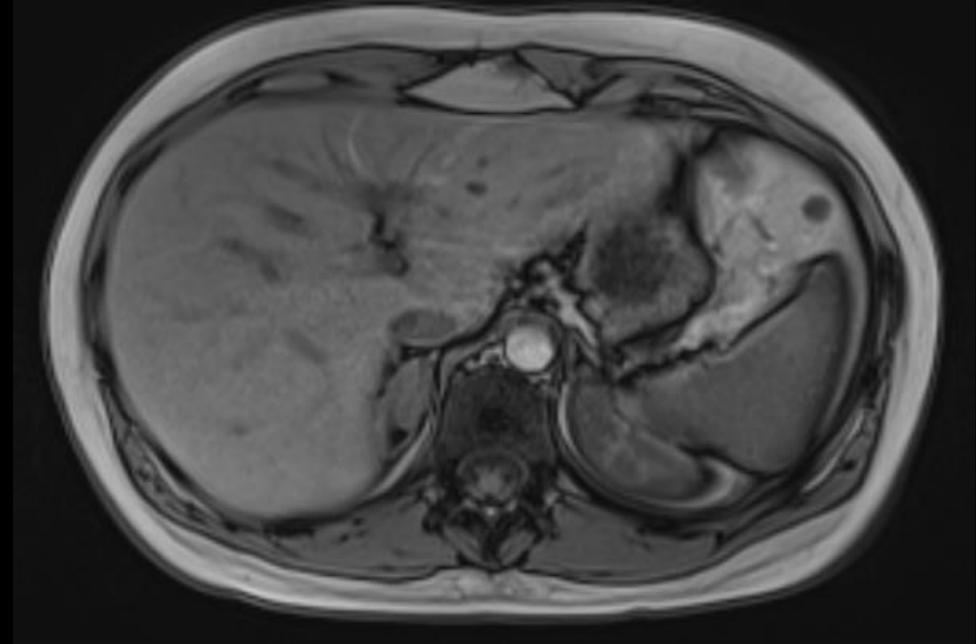
# Pertinent Labs

- Urine metanephrines = negative
- Genetic testing for TP53 mutation R213Q = positive

# Screening Whole-Body MRI, dual gradient echo, in-phase and out-of-phase

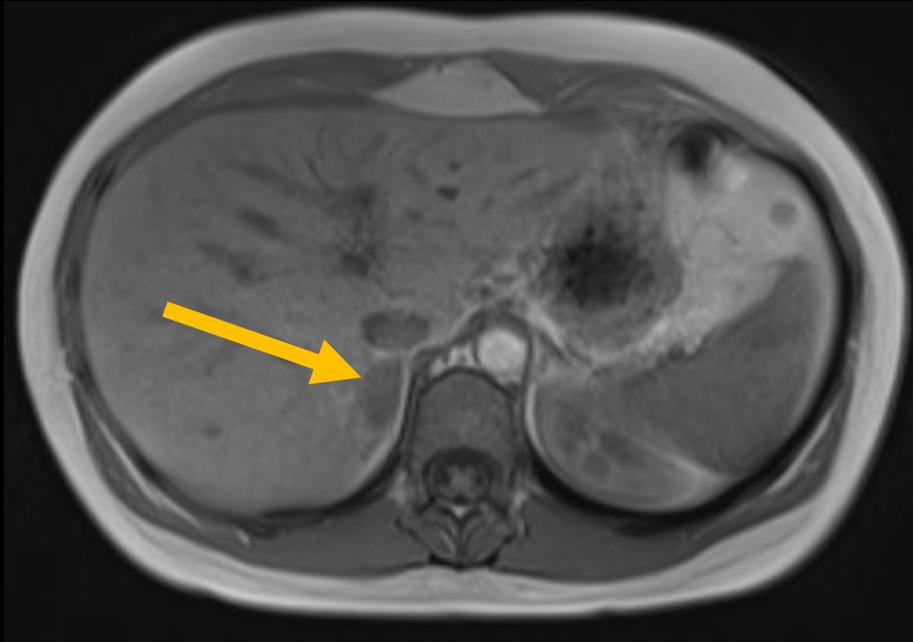


Axial in-phase

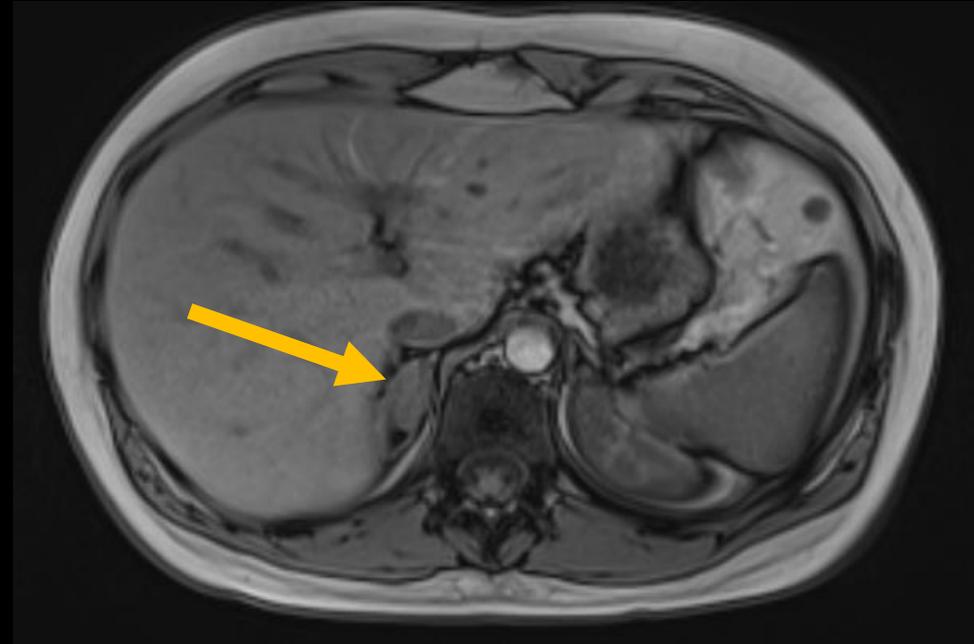


Axial out-of-phase

# Screening Whole-Body MRI, dual gradient echo in-phase and out-of-phase (labeled)



Axial in-phase



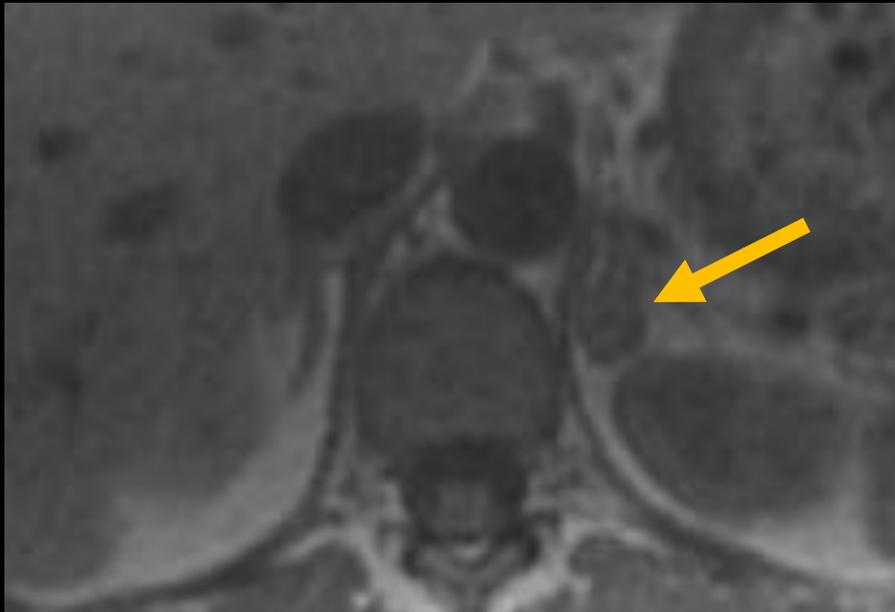
Axial out-of-phase

In- and out-of-phase imaging demonstrates a right adrenal gland nodule (arrow). Signal intensity was similar on both sequences with no drop in signal on out-of-phase. Given no signal dropout on out-of-phase imaging, this does not fulfill diagnostic criteria for an adrenal adenoma.

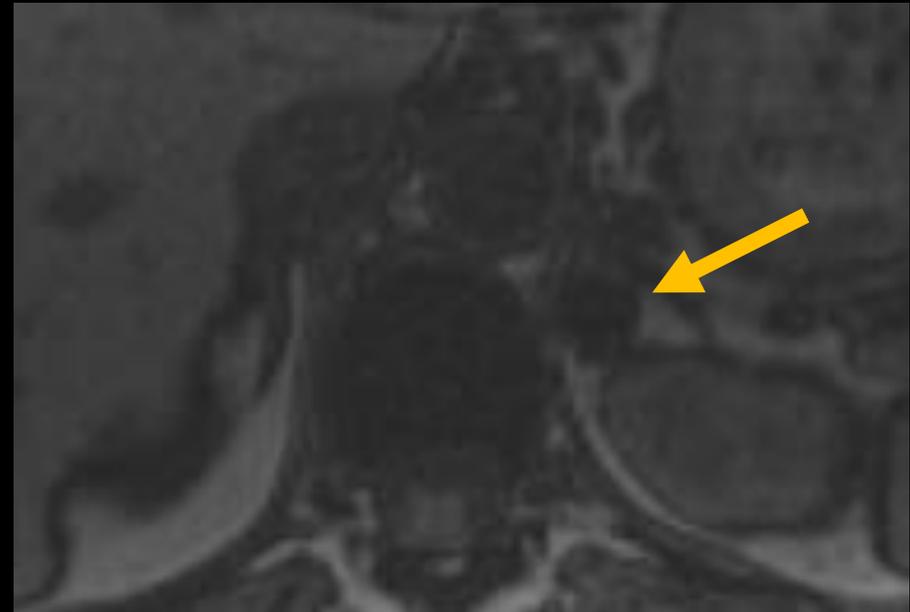
# Out-of-phase imaging

- Most adrenal adenomas have sufficient intracytoplasmic lipid (lipid-rich) and can be diagnosed on non enhanced CT with Hounsfield unit of 10 or less
- Lipid-poor adrenal adenomas can be difficult to differentiate from other entities, including neoplastic entities
- Lipid-poor adrenal adenomas can be diagnosed using out-of-phase imaging if they contain enough intravoxel fat to cause signal intensity drop relative to in-phase image<sup>[1]</sup>
- Signal drop occurs due to chemical shift artifact

# Out-of-phase imaging: example



In-phase



Out-of-phase

Axial MRI, T1 displaying left adrenal mass (arrow). Diffuse visual signal drop on out-of-phase imaging consistent with an adenoma. Images courtesy of Dr. Cheryl Sadow.

# Adrenal Washout CT

(A)



(B)



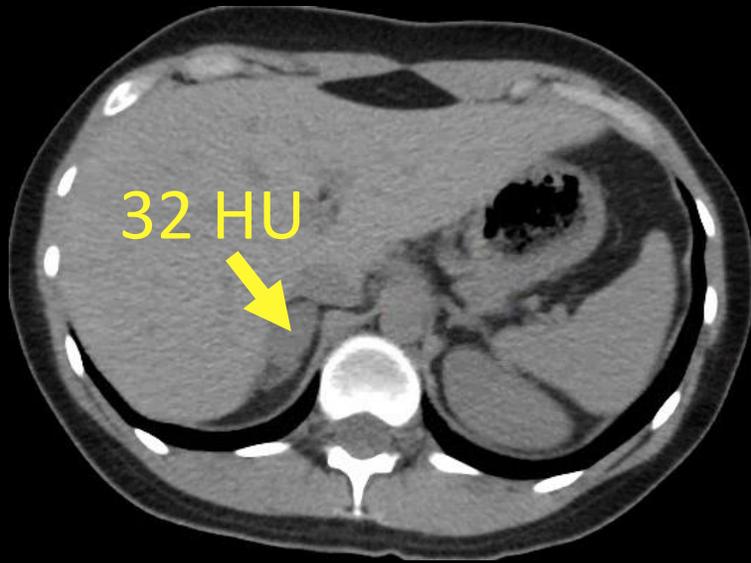
(C)



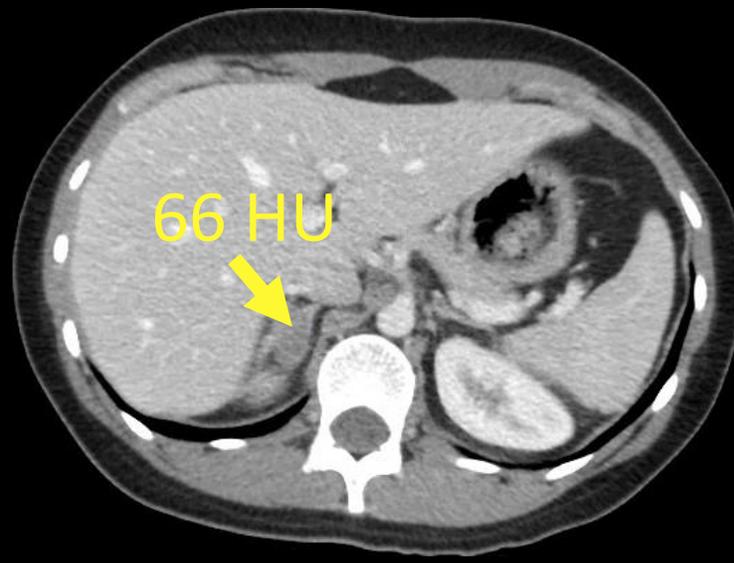
Axial images through the right adrenal gland, (A): pre contrast administration , (B): 60 seconds post IV contrast administration, and (C): 15 minutes post IV contrast administration.

# Adrenal Washout CT (labeled)

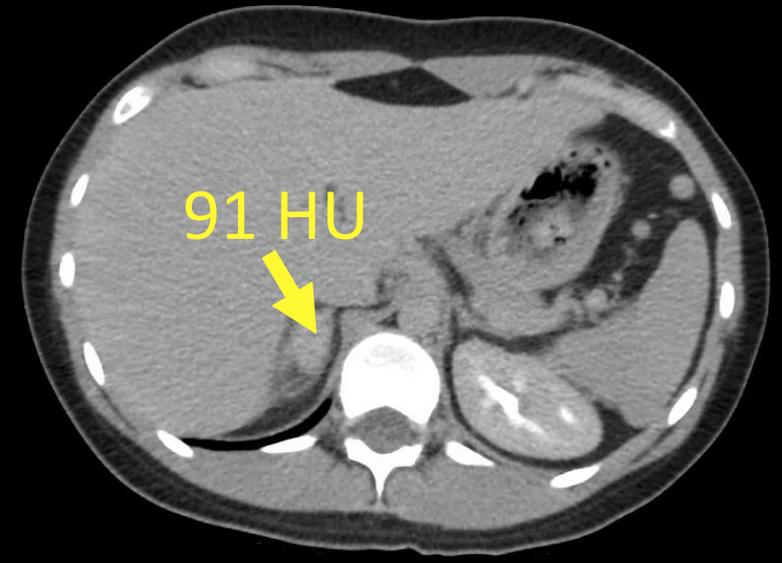
Precontrast



60 seconds



15 minutes



2.7 cm right adrenal gland nodule (arrow) displaying progressive enhancement on delayed imaging, i.e. no washout.

# Adrenal washout CT

- Hounsfield unit calculation:

$$\frac{HU_{portal\ venous\ phase} - HU_{delayed}}{HU_{portal\ venous\ phase} - HU_{non-enhanced}} \times 100$$

- >60% absolute washout, suggestive of adrenal adenoma [2]
- 98% sensitivity, 92% specificity [n=166] [3]

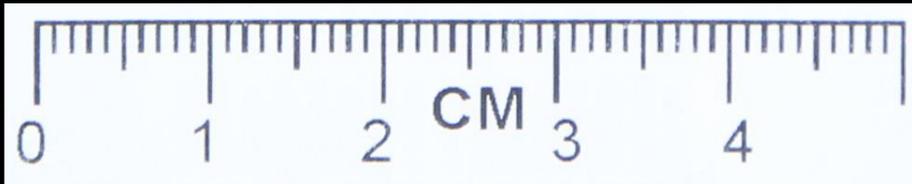
# DDx (based on imaging)

- Adenoma
- Adrenal cortical carcinoma
- Pheochromocytoma
- Metastasis
- Other

## Next step

- Because the nodule was indeterminate by imaging and given the patient's clinical history, the patient underwent laparoscopic resection of the right adrenal gland.

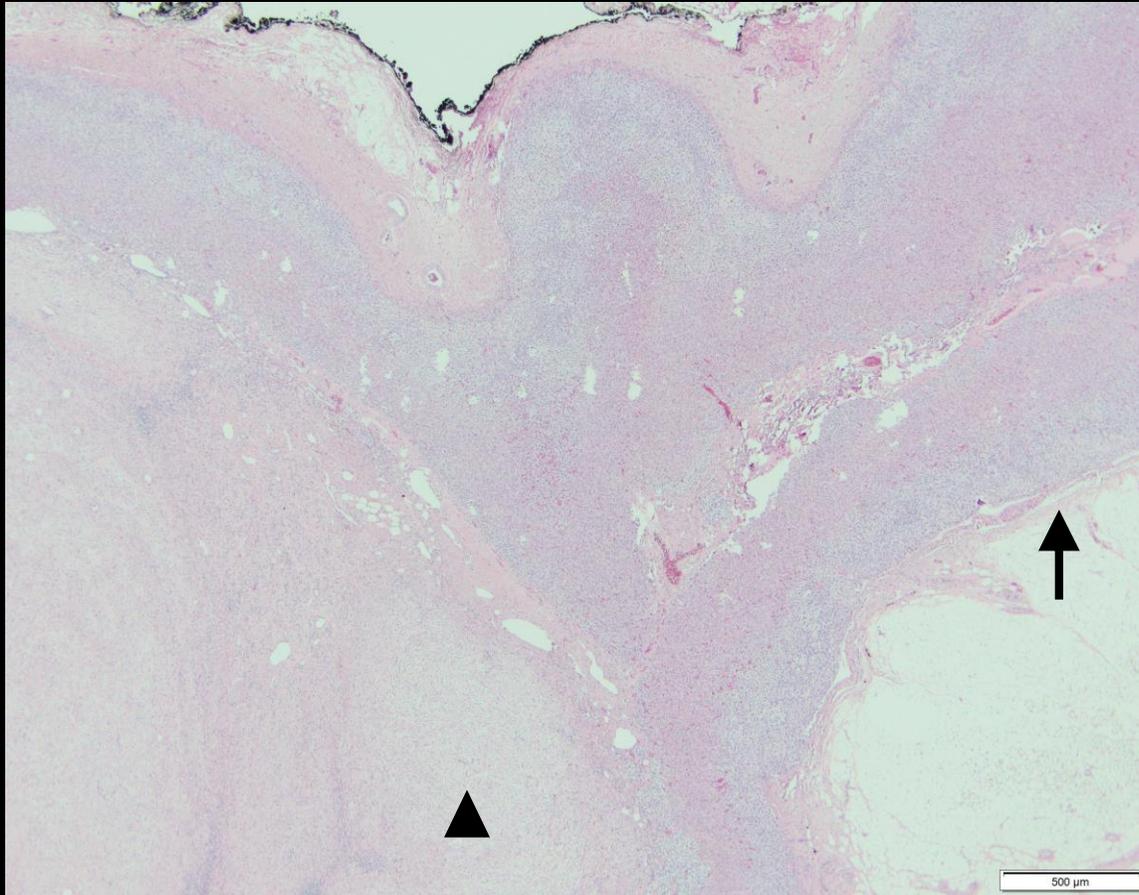
# Gross Path



Mass: 19.0 grams.

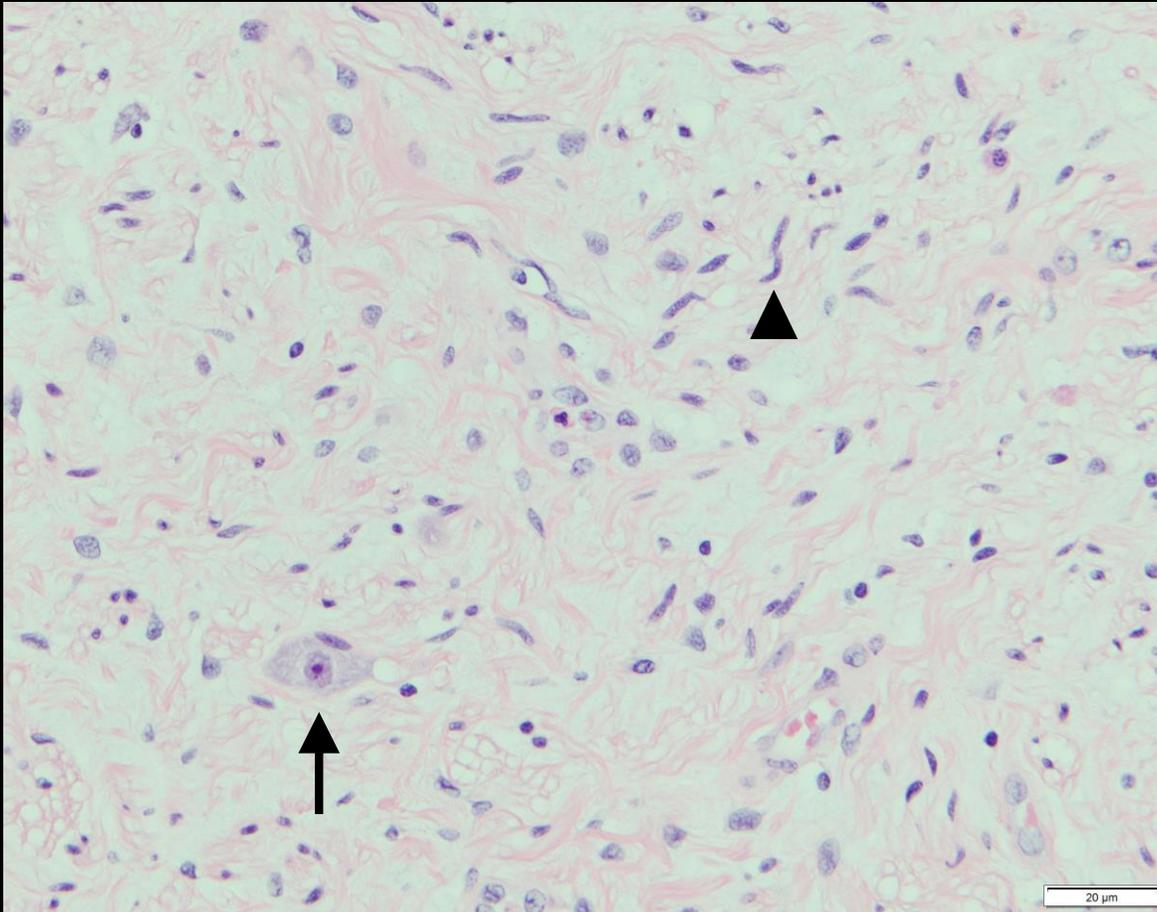
Well-circumscribed and homogeneous mass within the medulla of the adrenal gland, without cystic, hemorrhagic or necrotic areas.

# Micro Path



Interface between unremarkable adrenal cortex and medulla (arrow) with adjacent mass (arrow head) replacing the medullary components of the adrenal gland.

# Micro Path

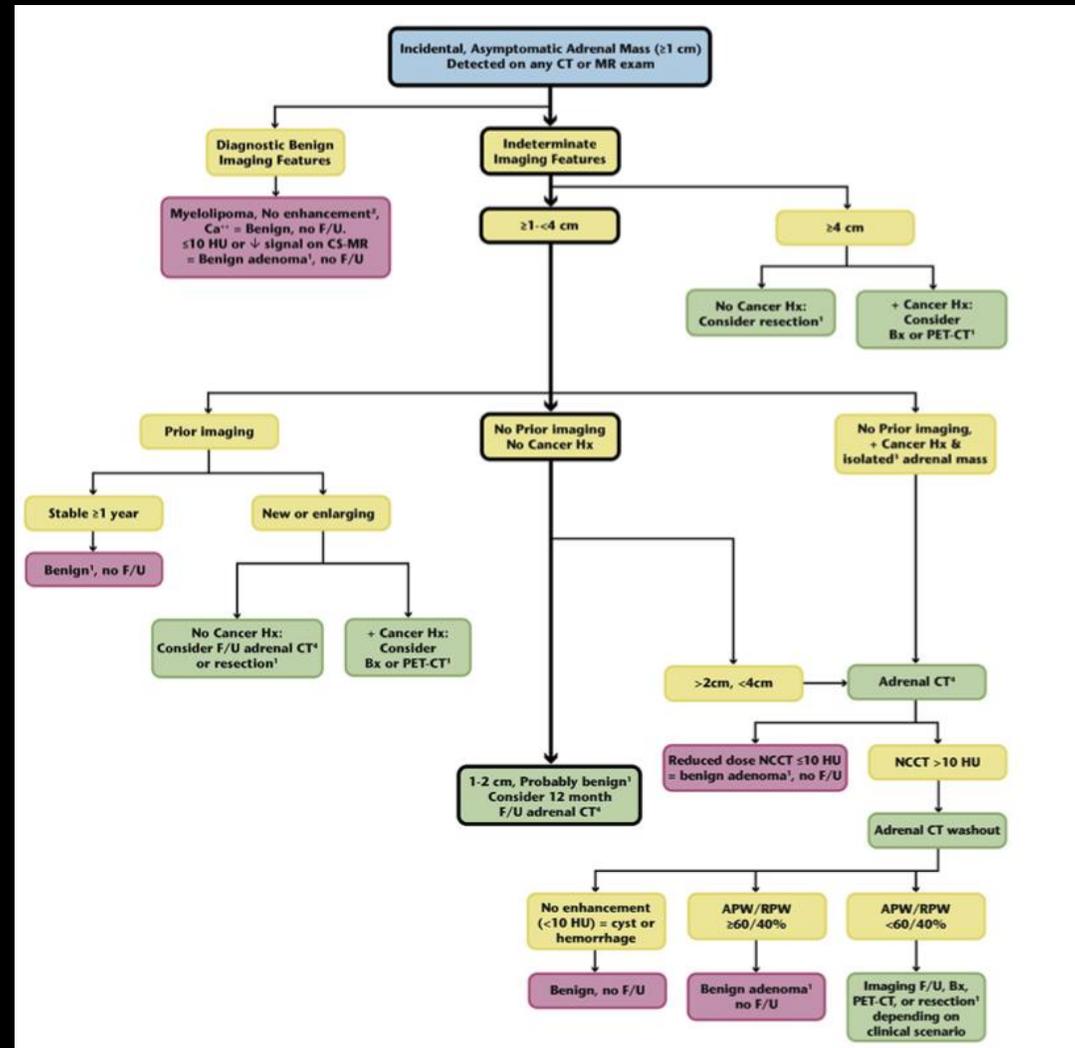


Ganglion cells (arrow) are widely interspersed within the Schwannian cells and stroma (arrow head). The ganglion cells are variable in size and neuroblasts, a component for the differential diagnosis of neuroblastoma, are absent. Areas of calcification, cystic change and hemorrhage are also absent in mass.

Final Dx:

Adrenal ganglioneuroma: a rare, benign mass of autonomic fibers arising from the neural crest

# Case Discussion: ACR Guidelines for Workup of Incidental Adrenal Masses<sup>[2]</sup>



# Case Discussion

- Li Fraumeni syndrome<sup>[4]</sup>
  - Rare, autosomal dominant syndrome of early-onset malignancy risk
  - Germline knockout of tumor suppressor gene TP53
  - Common tumors:
    - Sarcomas, including bone tumors and soft-tissue sarcomas
    - Breast, including premenopausal breast cancer
    - Hematologic malignancies
    - Adrenal cortical carcinoma
- Age and sex-dependent lifelong screening strategies advised

# Case Discussion

- Imaging recommendations for confirmed Li-Fraumeni
  - Published by American Association for Cancer Research<sup>[5]</sup>
  - Annual breast MRI screening (ages 20 to 75)
  - Annual brain MRI (first MRI with contrast; thereafter without contrast if previous MRI normal)
  - Annual Whole Body MRI
  - Ultrasound of abdomen and pelvis every 12 months
  - Upper endoscopy and colonoscopy every 2 to 5 years

# References:

1. Shetty, A. S., Sipe, A. L., Zulfiqar, M., Tsai, R., Raptis, D. A., Raptis, C. A., & Bhalla, S. (2019). In-Phase and Opposed-Phase Imaging: Applications of Chemical Shift and Magnetic Susceptibility in the Chest and Abdomen. *RadioGraphics*, 39(1), 115-135.
2. Mayo-Smith, W. W., Song, J. H., Boland, G. L., Francis, I. R., Israel, G. M., Mazzaglia, P. J., ... & Pandharipande, P. V. (2017). Management of incidental adrenal masses: a white paper of the ACR Incidental Findings Committee. *Journal of the American College of Radiology*, 14(8), 1038-1044.
3. Caoili, E. M., Korobkin, M., Francis, I. R., Cohan, R. H., Platt, J. F., Dunnick, N. R., & Raghupathi, K. I. (2002). Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology*, 222(3), 629-633.
4. Villani A, Shore A, Wasserman JD, et al. Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study. *Lancet Oncol* 2016; 17:1295.
5. Kratz, C. P., Achatz, M. I., Brugieres, L., Frebourg, T., Garber, J. E., Greer, M. L. C., ... & Mullighan, C. G. (2017). Cancer screening recommendations for individuals with Li-Fraumeni syndrome. *Clinical Cancer Research*, 23(11), e38-e45.