The ‘slow loris’ of liver lesions

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Disclosure of Relevant Financial Relationships

Sponsored by Leica to research and present a talk on Albumin in situ hybridization at the Diagnostic IHC Conference, Gold Coast May 2022. Not relevant to this presentation.

Case presentation

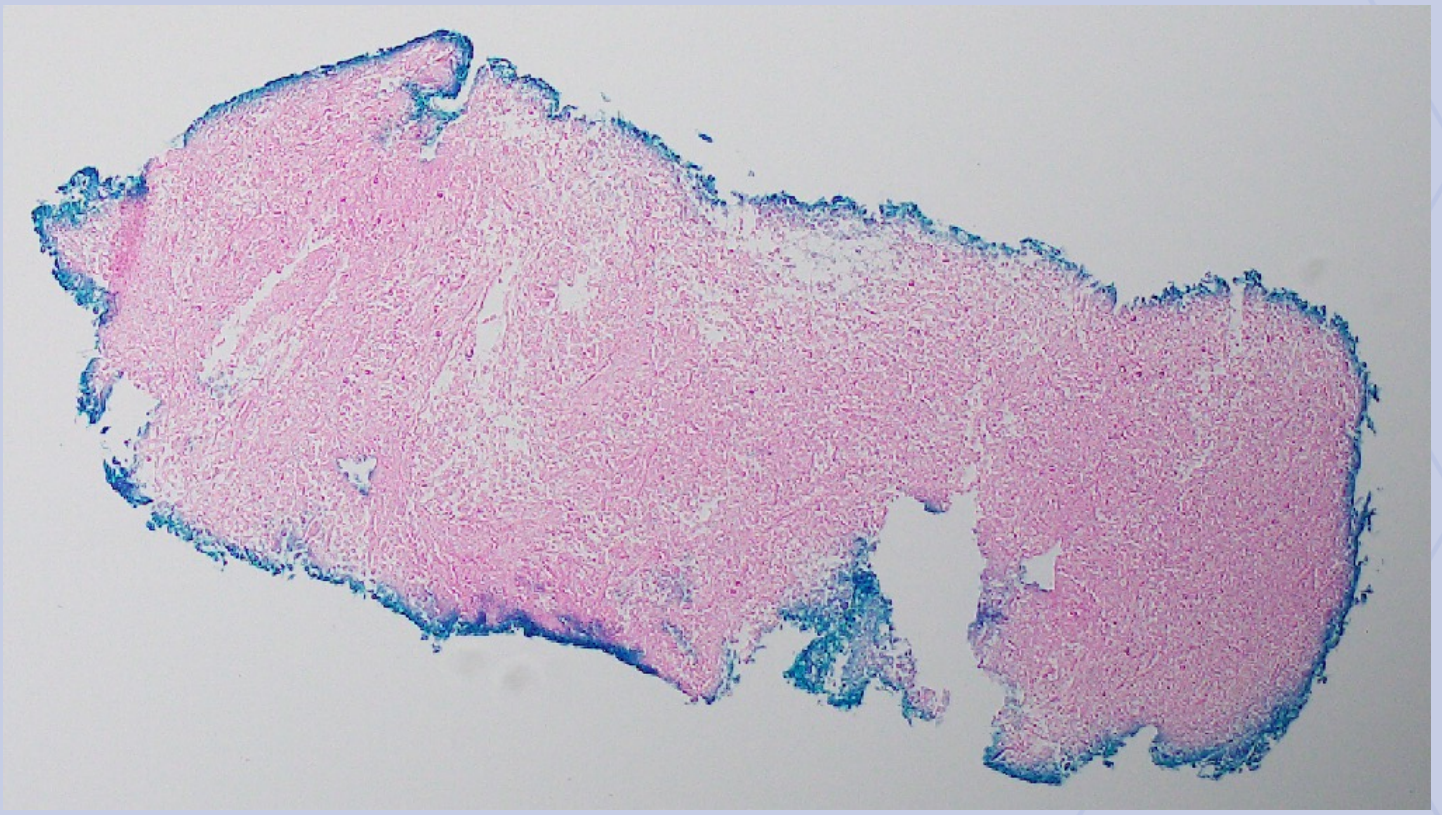
- 38y male presents with palpable and painful middle upper quadrant abdominal mass of rapid onset (not felt two weeks prior).
- Recent migration to NZ with no previous medical history and normal full medical work up.

Imaging

CT Chest, Abdomen, pelvis

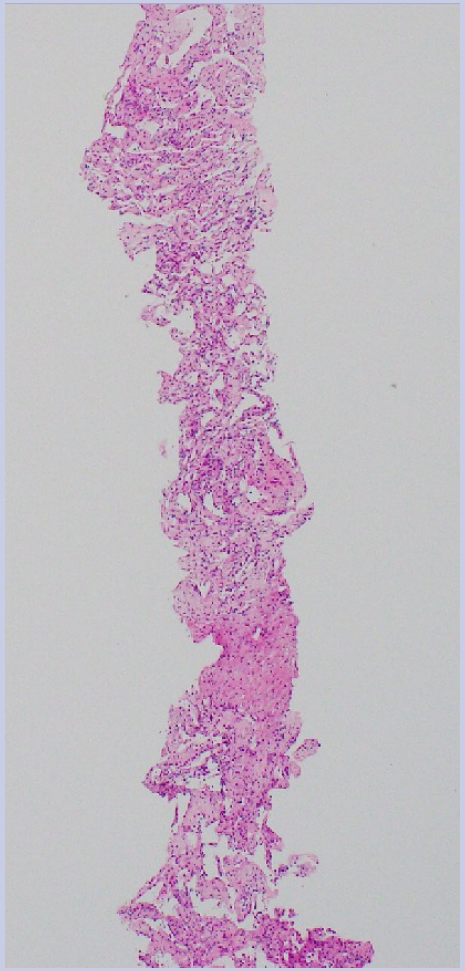
- 3 large malignant appearing masses in liver + innumerable other small hypodense lesions
- No lymphadenopathy
- Likely extensive metastatic disease
- No primary lesions demonstrated

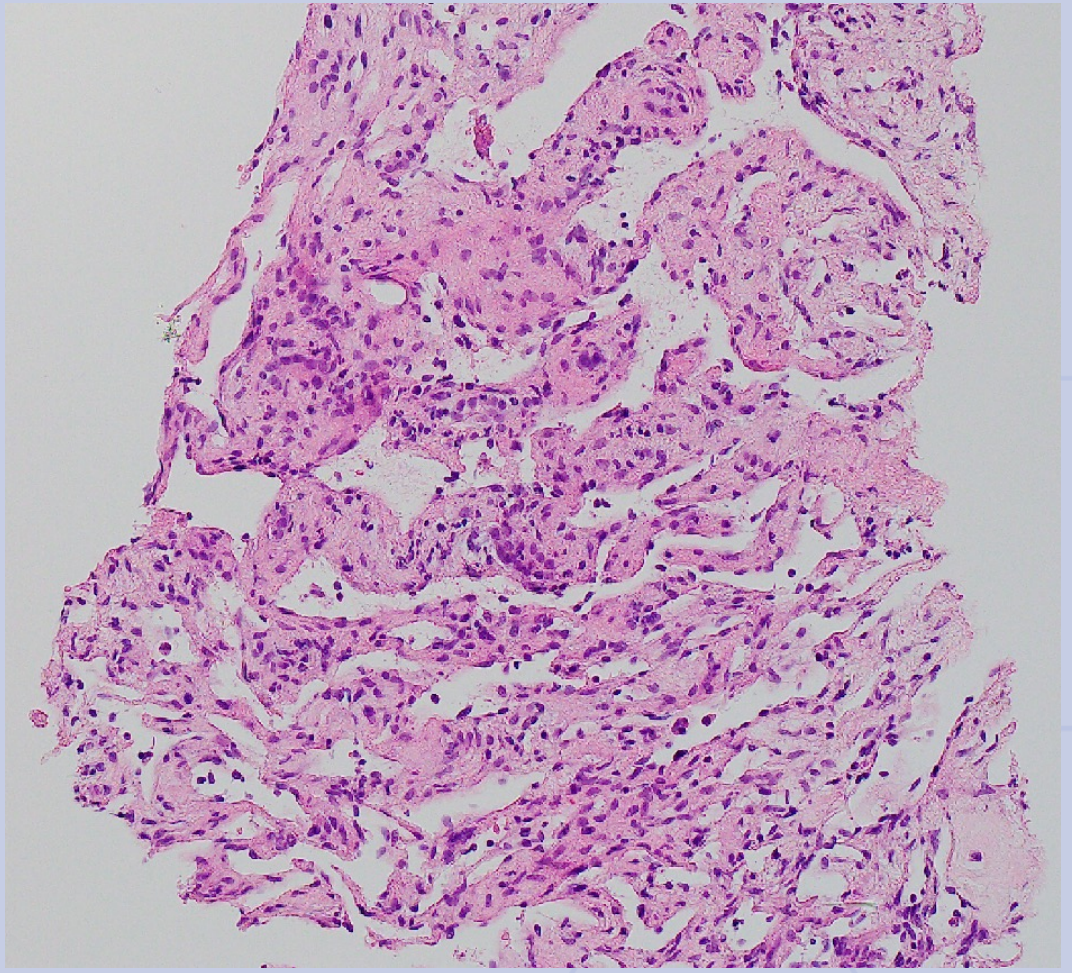
Ultrasound guided liver biopsy



Histology – necrosis only

Repeat biopsy





Repeat Biopsy

- Features in keeping with benign cavernous hemangioma
- Unusual to have necrosis
- Unsampled malignancy cannot not be excluded

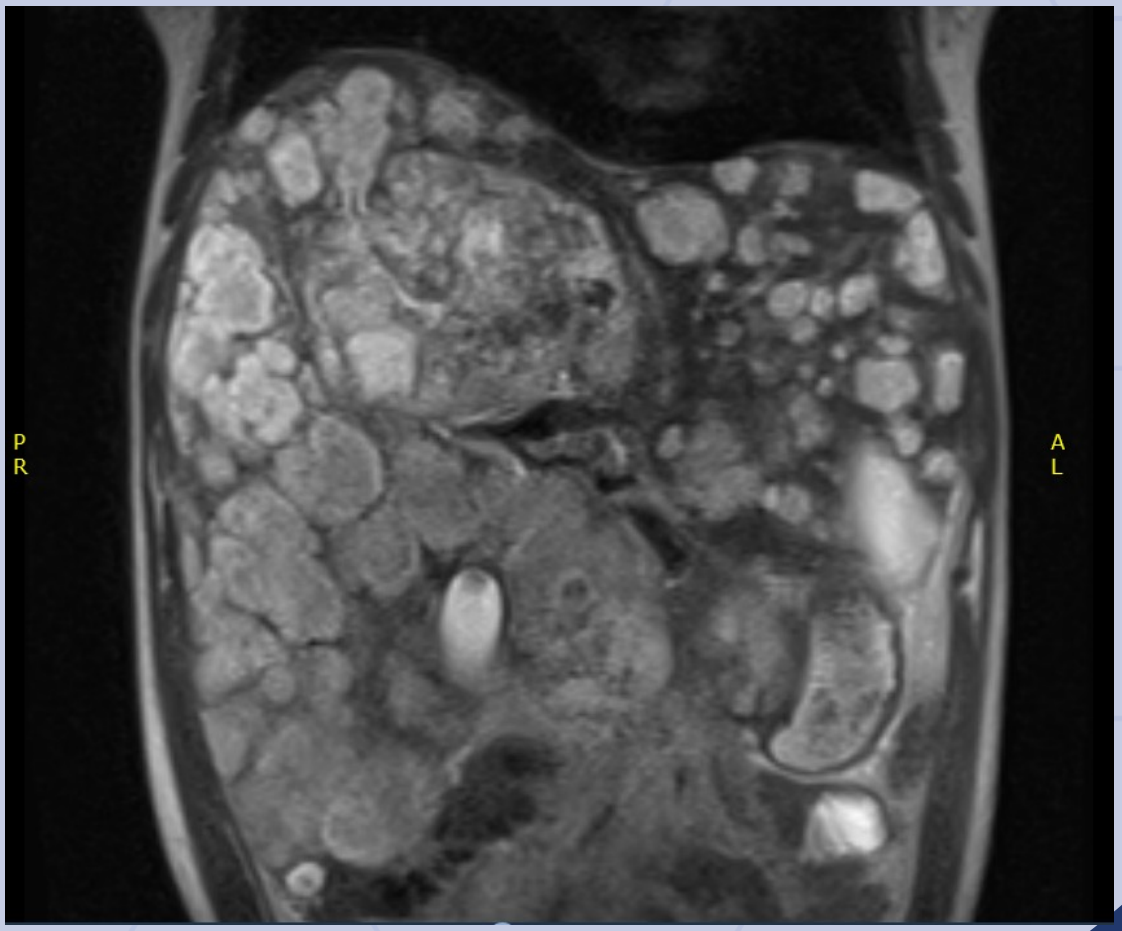
Further clinical progression

- Mass increasing in size
- Abdominal bleeding
- Worsening cholestasis and liver failure

Additional Imaging

MRI Liver Vascular – 2 weeks after CT

- Interval enlargement of several of the larger hepatic lesions with features suggestive of interval internal bleeding.
- Lesions show peripheral enhancement, with gradual infilling closely approximating blood pool, raising the possibility of diffuse hemangiomatosis given the biopsy result.
- The lesions remain markedly unusual, extent of hepatic replacement, increasing internal haemorrhage and peripheral enhancement within several of the larger lesions are atypical features. Underlying vascular neoplasm (angiosarcoma) remains a differential consideration.



Next steps...

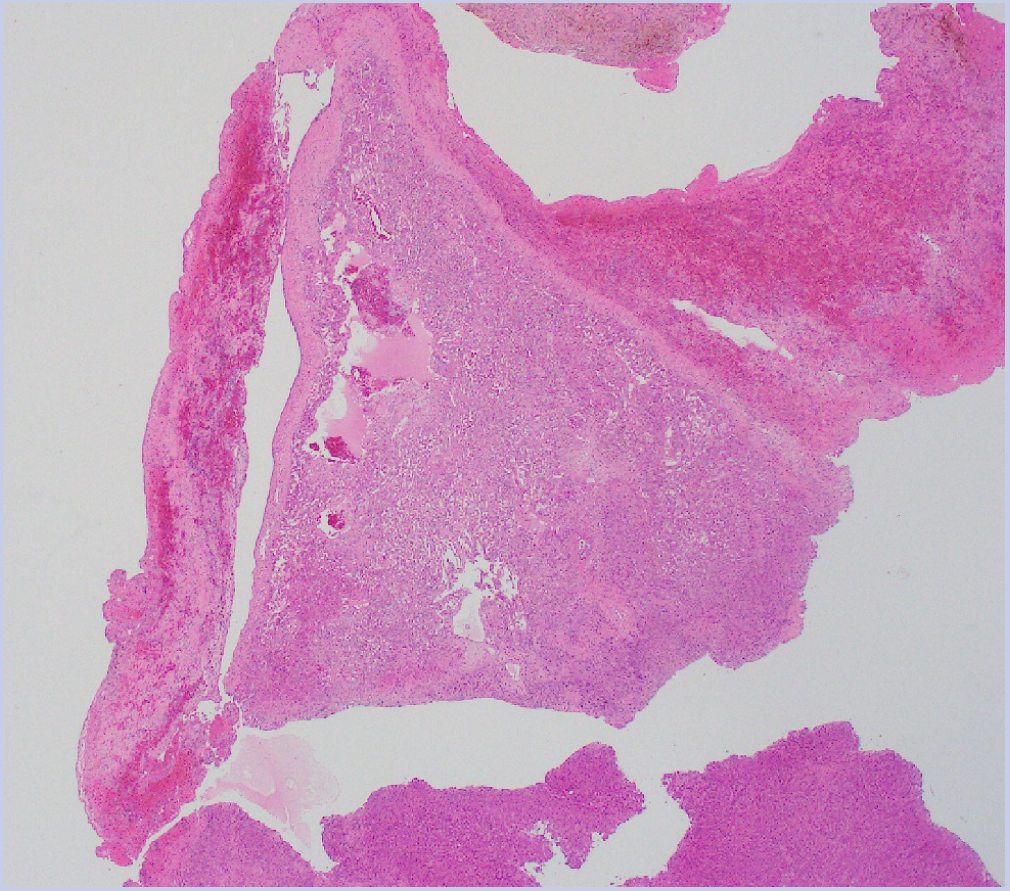
- Growing concern by the clinical team
- Treatment options
  - Benign diagnosis – urgently list for transplant
  - Malignant diagnosis – not a transplant candidate
- Surgeons perform laparoscopic liver biopsy for more definitive diagnosis.

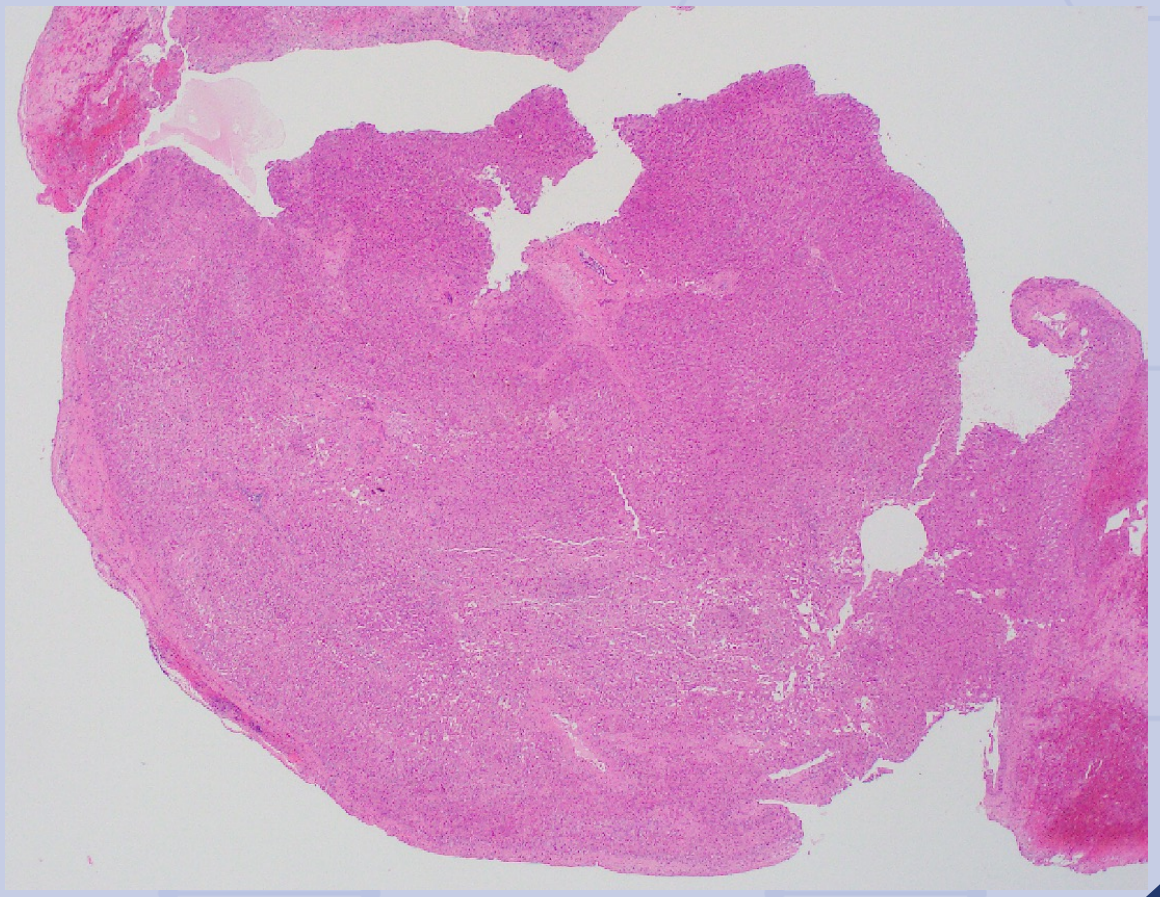
Operation Report

- Massive haemoperitoneum (3L of blood drained)
- Massive hepatomegaly – liver replaced by vascular lesions

- Wedge of tissue taken for frozen section
- Additional cores of tissue taken for processing

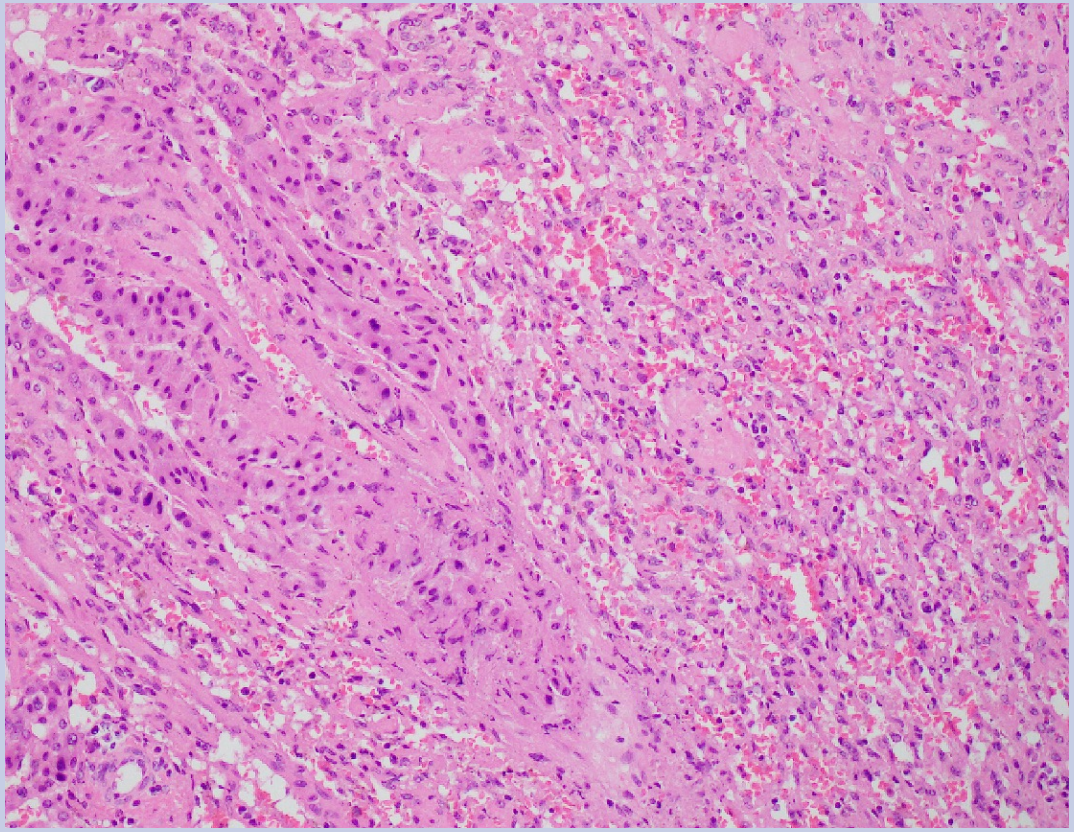
Frozen section – wedge biopsy

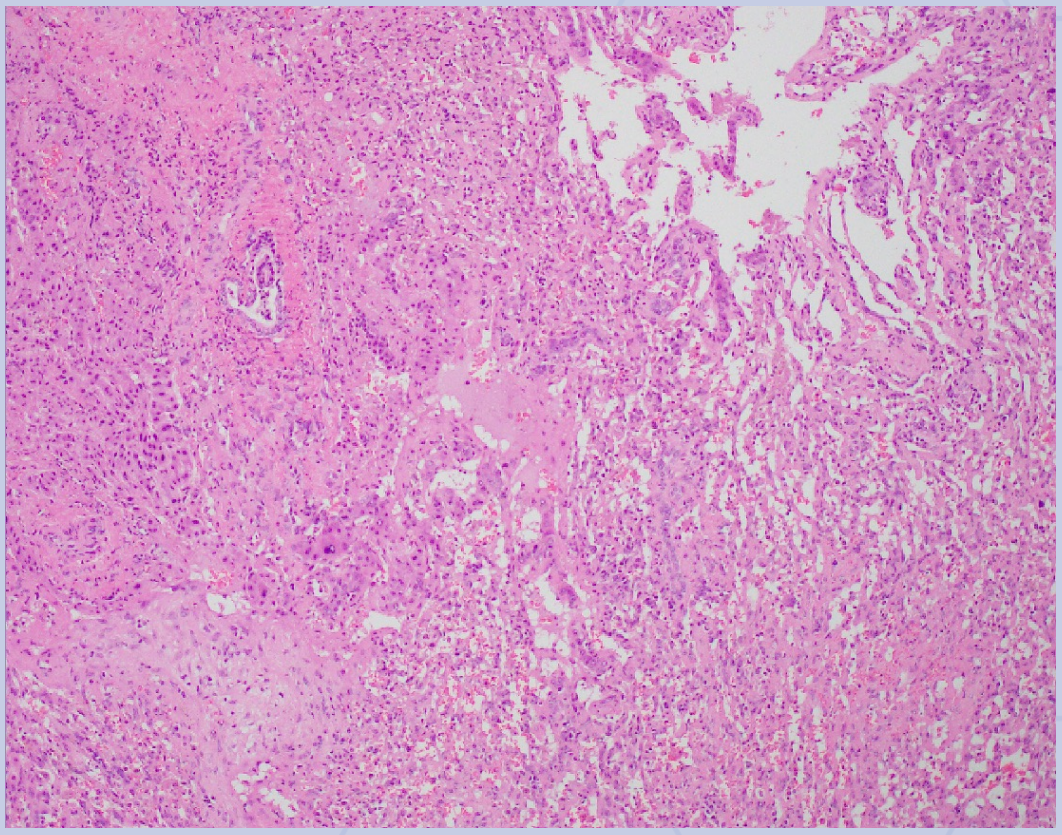




- No well defined lesion – some blood-filled spaces

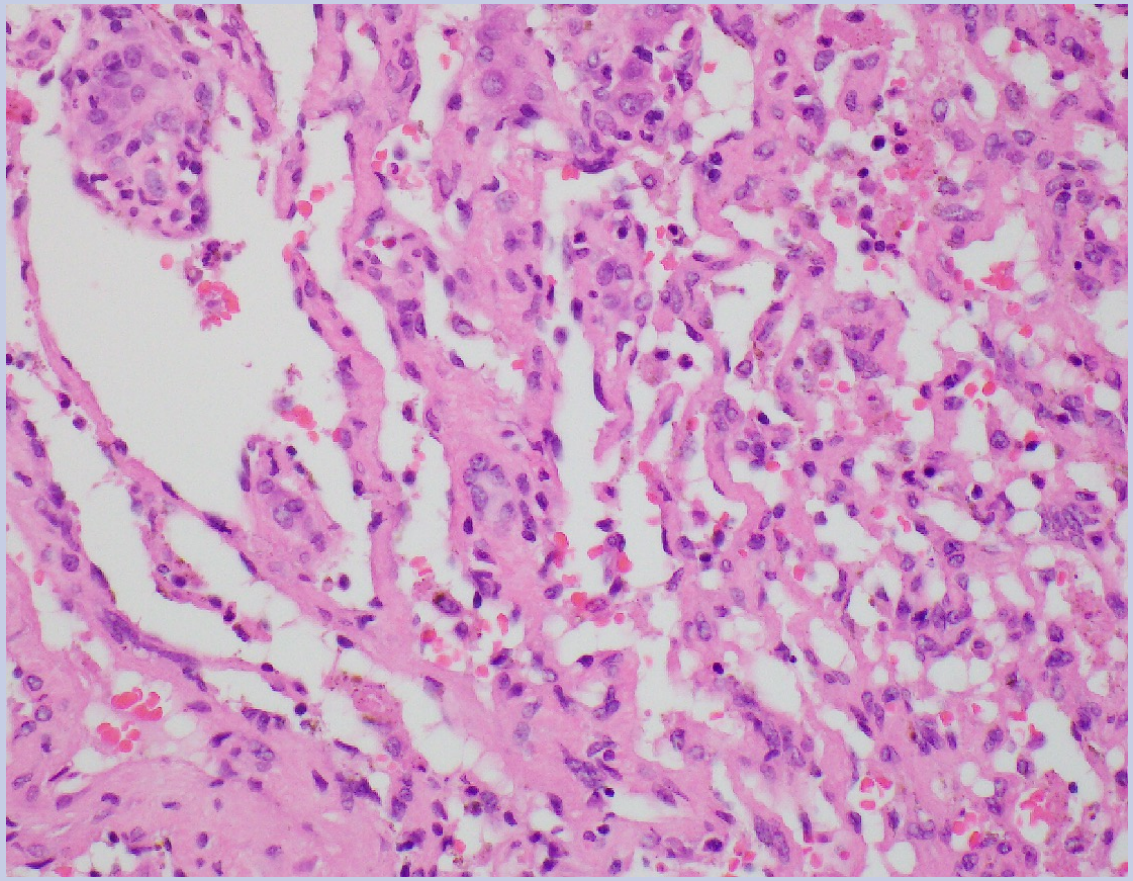
Frozen section – wedge biopsy

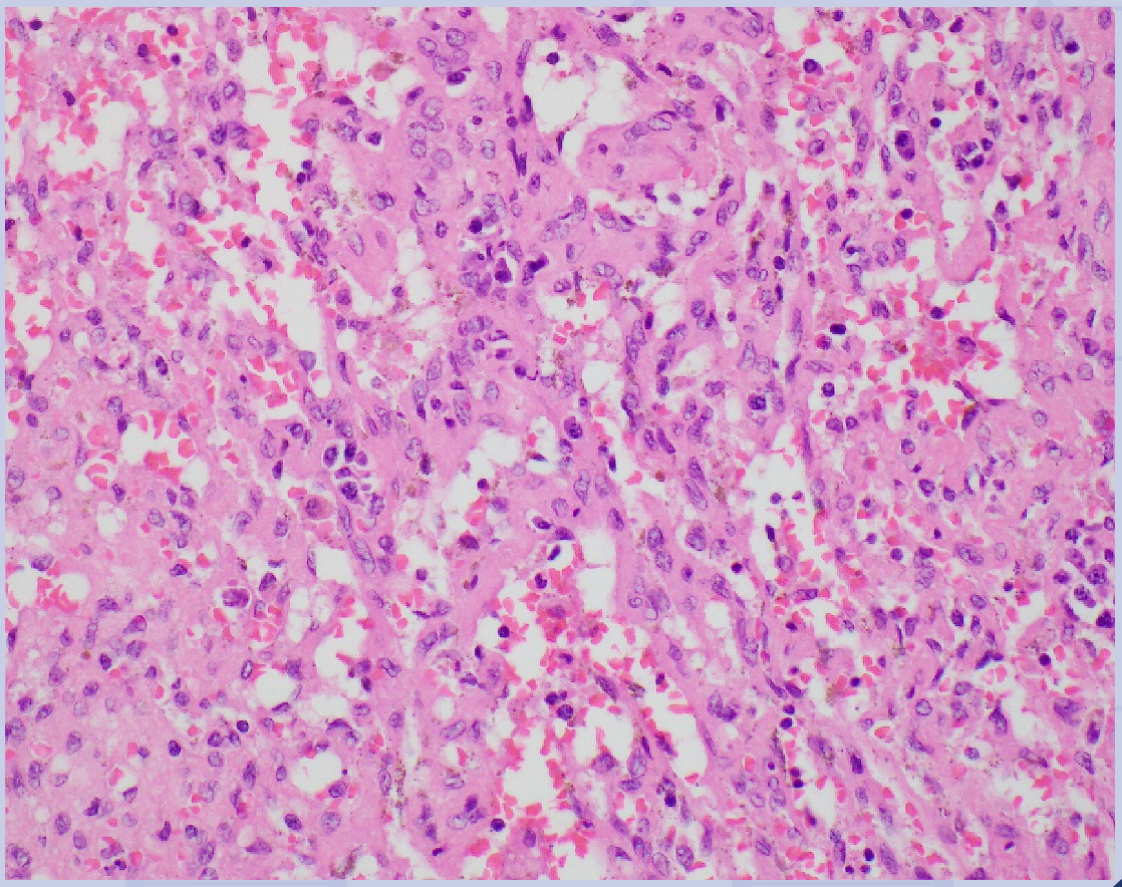




- Lesional areas intermingled with normal liver and bile ducts

Frozen section – wedge biopsy





Thin walled vessels lined by bland endothelial cells

Vascular lesions of the liver

Benign

- Cavernous haemangioma

Intermediate

- Hepatic small-vessel neoplasm

Malignant

- Angiosarcoma
- Epithelioid haemangioendothelioma
- Kaposi sarcoma

Malformations

- Telangiectasias (HHT)
- Arteriovenous malformation
- Hereditary lymphodema

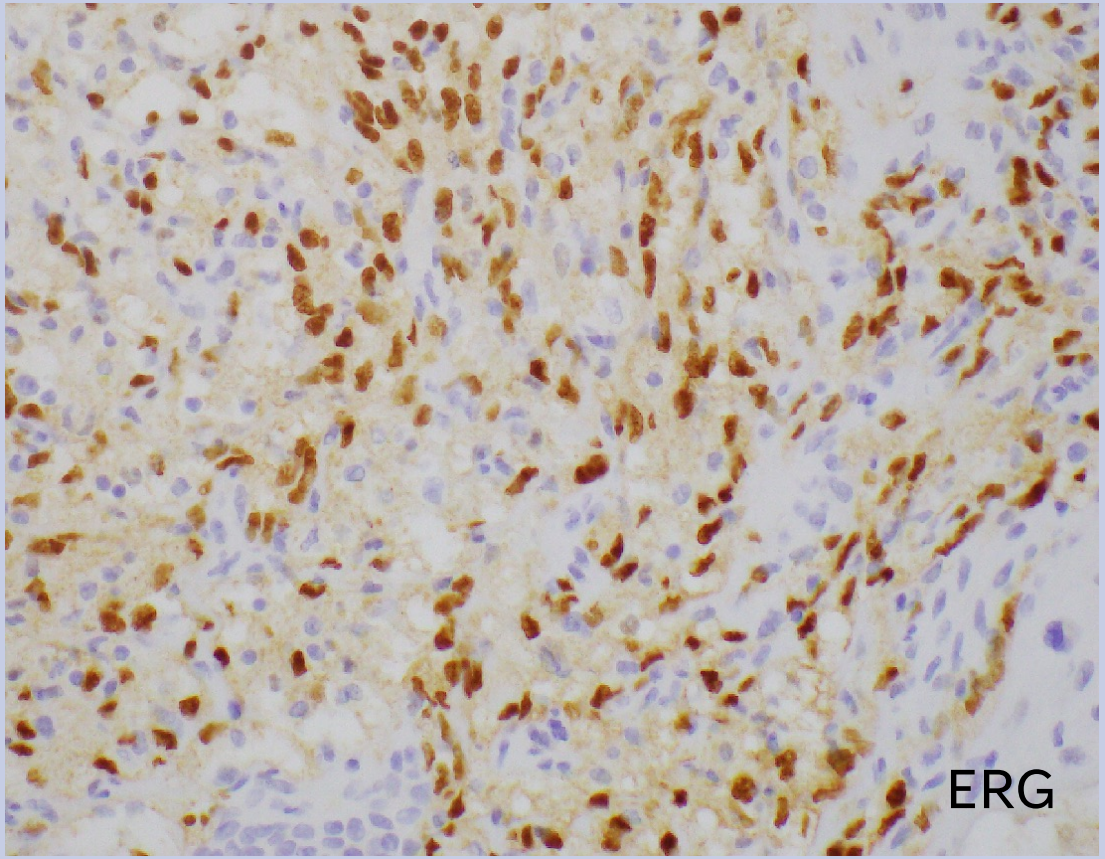
Frozen section result

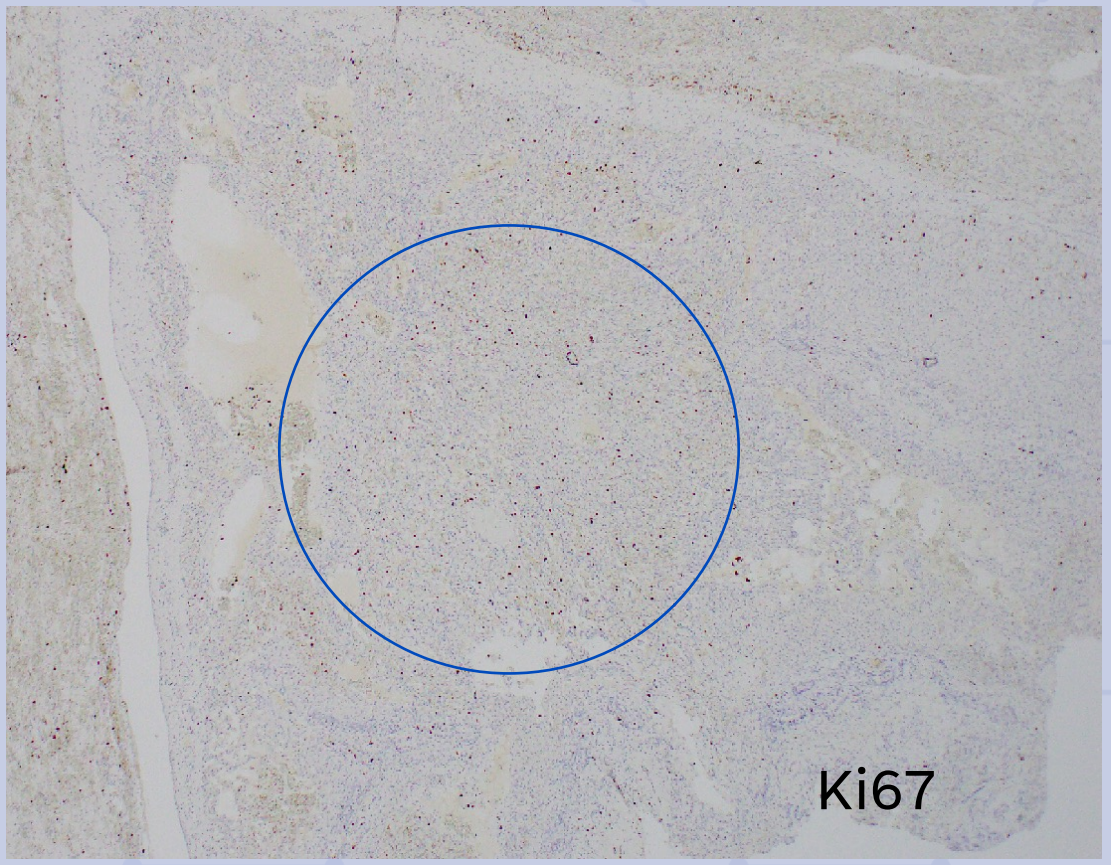
- Telangiectatic appearance
- No overtly malignant cells
- No mitoses
- No necrosis in this biopsy (but present previously)

- Favour a benign process, possible telangiectatic process such as HHT

- Discussed with surgical team
- No family history, no history of nose bleeds etc
- Lesions clinically and radiologically increasing in size rapidly
- Unusual behaviour for a benign process

Immunostains on wedge biopsy





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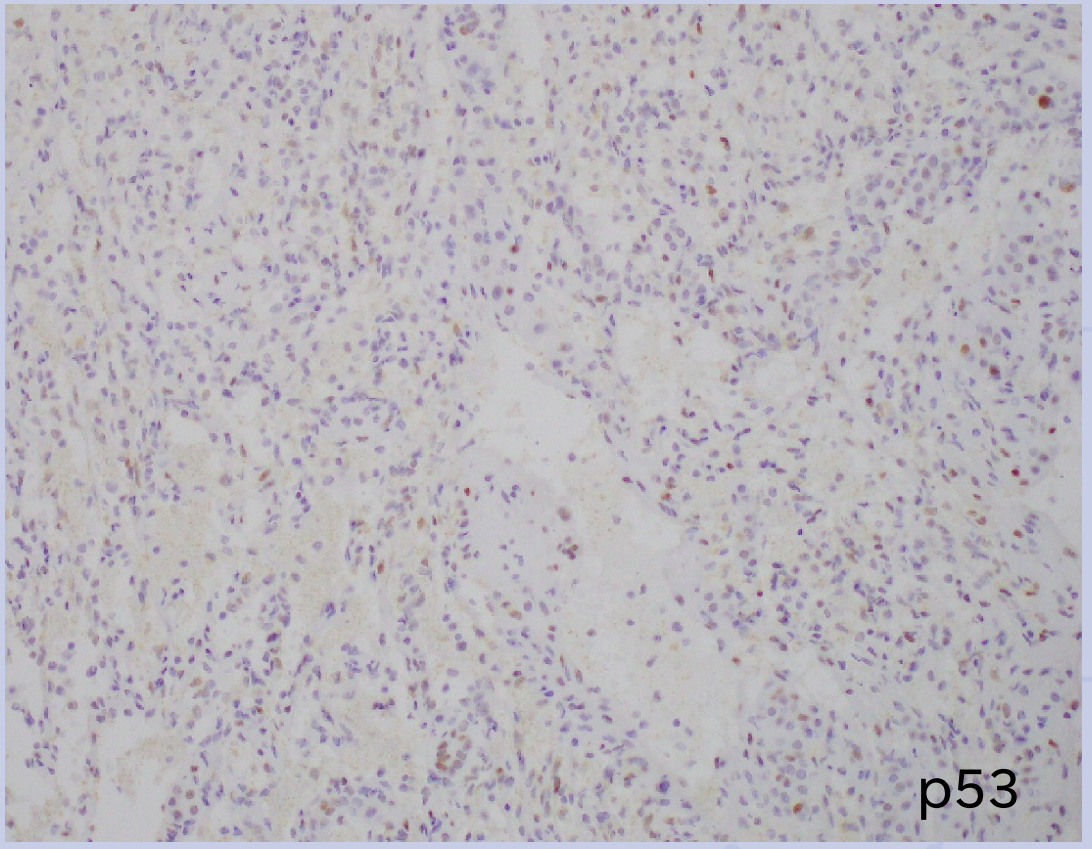
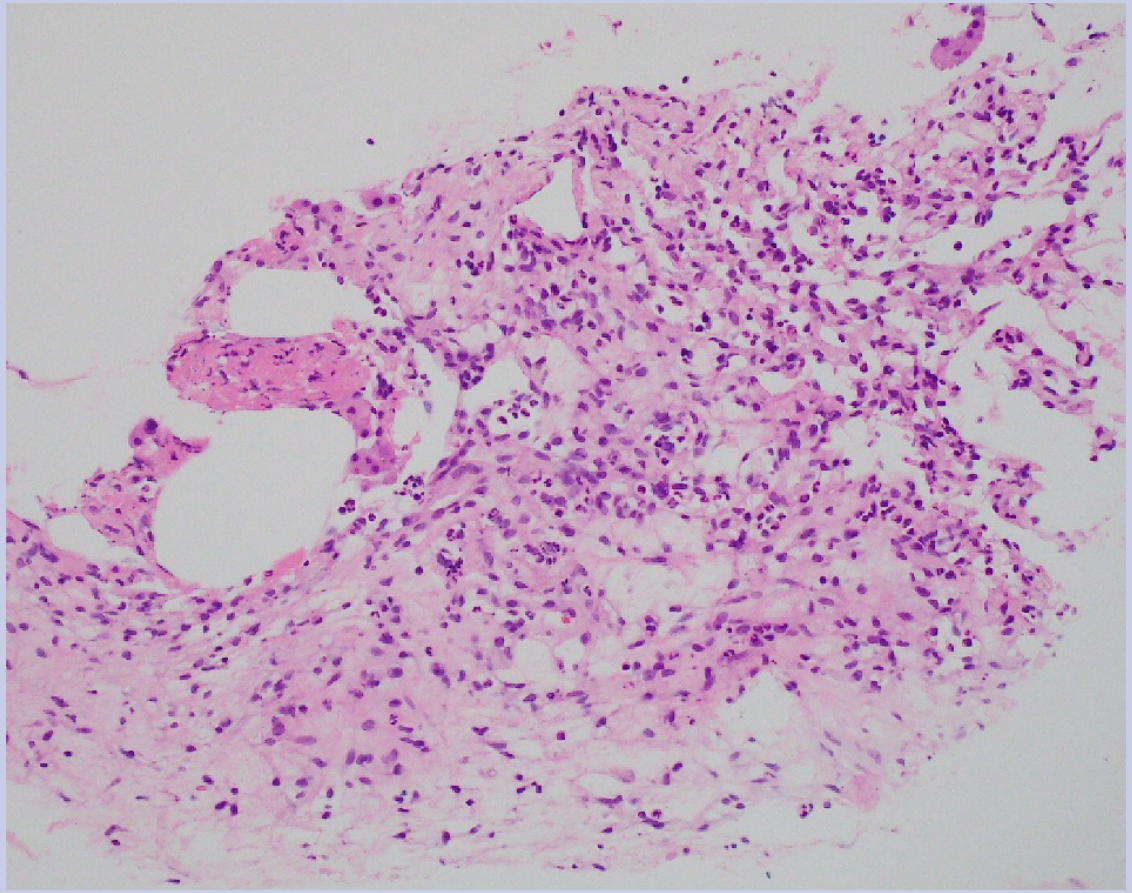
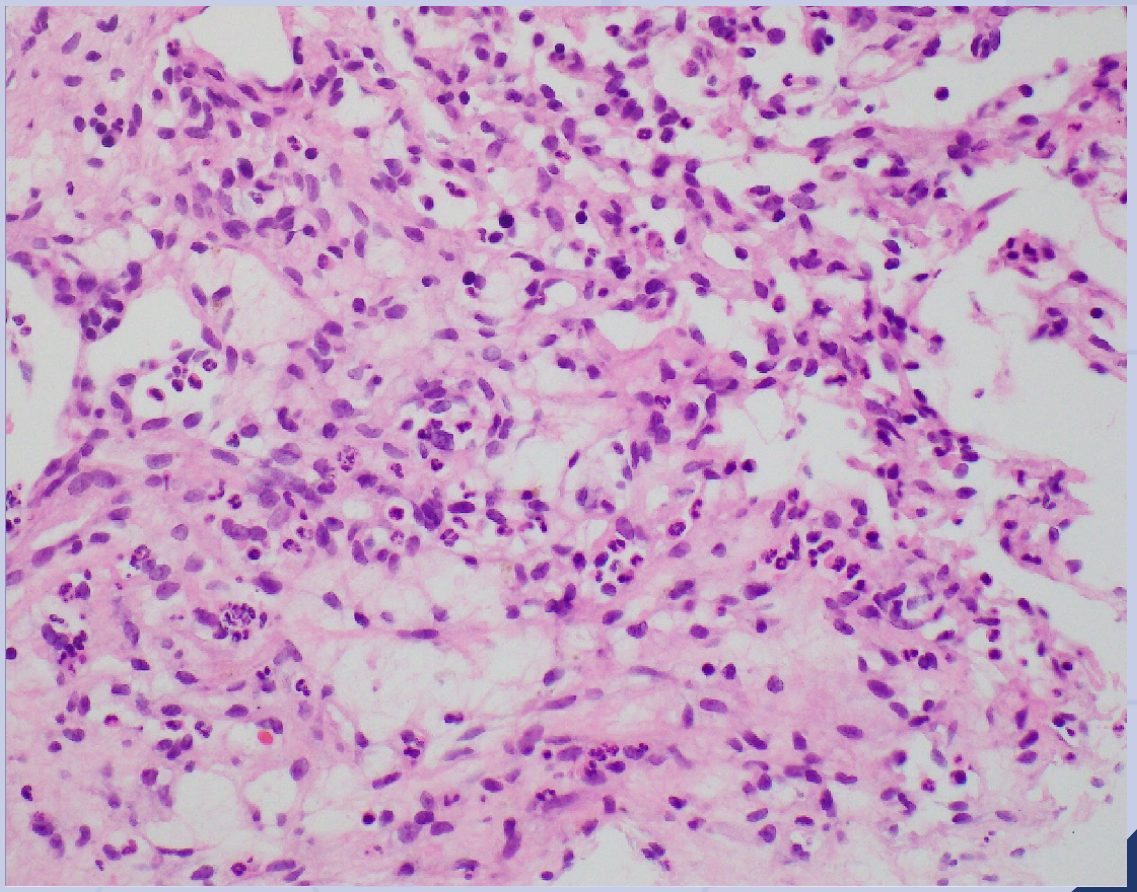


Core biopsies





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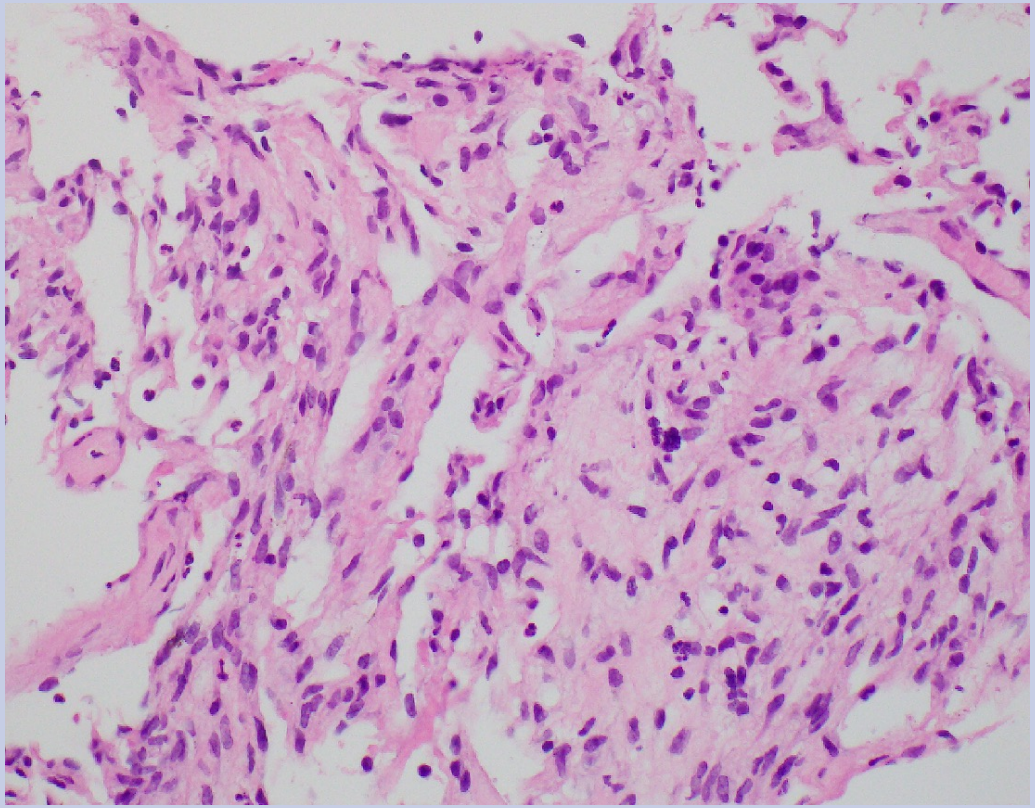
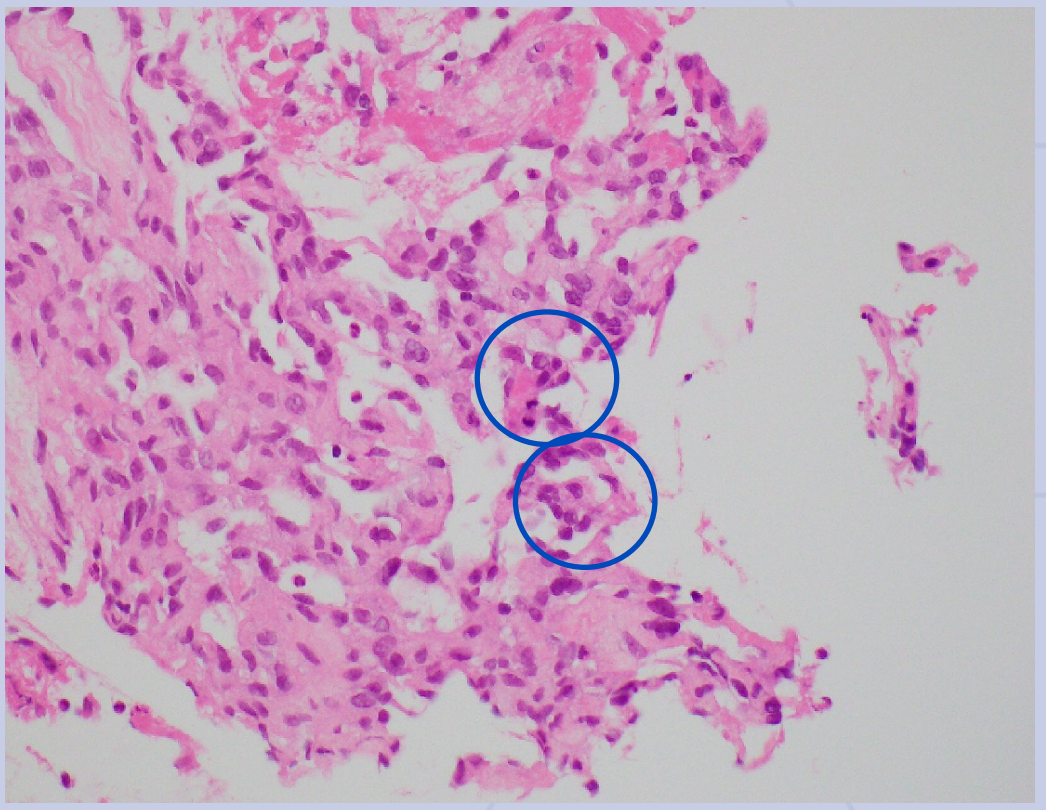




- Increased atypia
- 1 mitosis
- Suggestion of multilayering

Final diagnosis

- Based on these features combined with the clinical and radiological appearance the diagnosis of **primary hepatic angiosarcoma** was made

Hepatic Angiosarcoma – Clinical features

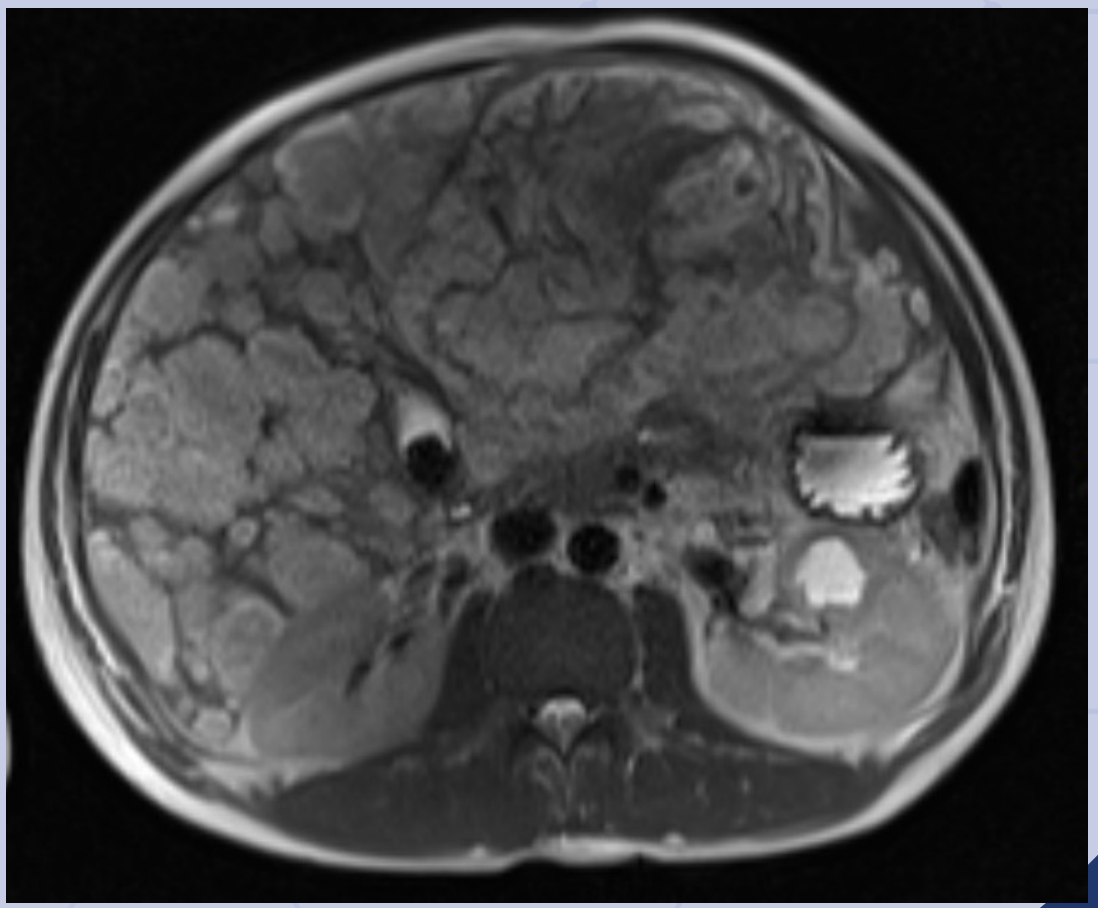
- Account for 2% of all primary hepatic neoplasms
- Presentation with non-specific abdominal symptoms
- Palpable abdominal mass/hepatomegaly
- May present with spontaneous rupture and haemoperitoneum

Etiology

- May be associated with environmental exposure to thorotrast, arsenic, ionizing radiation, or vinyl chloride – such exposure now rare
- Most are sporadic

Radiologic appearance

- Variable
- May present as a single lesion or multiple/innumerable masses
- CT – hypoattenuating masses, nodular enhancement is common
- MRI – heterogenous areas of high signal on T1/T2 reflecting mixed tumour and haemorrhage
- FDG PET-CT - avid



Morphological patterns of hepatic angiosarcoma

Mass forming

- Vasoformative morphology
- Solid
  - epithelioid
  - spindle morphology

Non-mass forming

- Sinusoidal growth
- Peliotic
- Other

Mass-like growth patterns - vasoformative

- Architecturally complex interconnecting vascular channels
- Lining endothelial cells show tufting, hobnailing, striking cytologic atypia
- Frequent mitotic figures

Mass-like growth patterns: solid and non-vasoformative

Spindle pattern

- High grade malignant neoplasm
- Red cell extravasation
- Mimics high grade undifferentitated sarcoma

Mass-like growth patterns: solid and non-vasoformative – Epithelioid pattern

- Solid sheets and clusters of neoplastic cells infiltrating surrounding liver parenchyma
- Eosinophilic cytoplasm, round/oval vesicular nuclei with prominent nucleoli
- Can have tumour giant cells

Non-mass forming: Sinusoidal pattern

- Sinusoidal dilation and congestion
- Low power – resembles venous outflow impairment
- Sinusoids lined by atypical cell with hyperchromatic nuclei

Non mass-forming: Peliotic Pattern

- Peliotic-like areas with pooled blood, fibrin an clotted material surrounded by benign hepatocytes
- Clustered atypical cells present at periphery of peliotic areas, admixed with inflammatory cells

Other patterns

- Whorling
- Infantile hamangioma-like pattern
- Haemangioma-like areas

Ancillary tests - IHC

- All neoplastic cells show positive staining with vascular markers – ERG, CD31, CD34 etc
- CK can be positive, especially in epithelioid angiosarcoma

Molecular aberrations

- Complex karyotypes without recurrent chromosomal changes
- TP53 mutations – rare in angiosarcomas (4%) compared to other sarcomas (LMS, UPS - 60-80%)
- TP53 mutations may be seen in vinyl chloride-related cases
- Frequently ATRX-deficient
- No MYC amplification (compared to secondary angiosarcomas in which 50% harbour a MYC amplification)

- Ancillary testing not useful aside from confirming endothelial nature

Treatment & Prognosis

- Rapidly progressive with frequent metastases
- Partial liver resection may be an option for disease confined to one lobe
- Resistant to chemoradiotherapy
- Median survival <6 months
- Survival beyond one year is rare

- Our patient died 4 months after presentation

Lessons learnt

- Many patterns of angiosarcoma – non-mass forming types
- May lack frankly malignant cytology, appearing to be a harmless lesion, but beware
- Clinical and radiologic correlation

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Hepatic Angiosarcoma