

Focal nodular hyperplasia

A benign, nonneoplastic hepatic mass

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

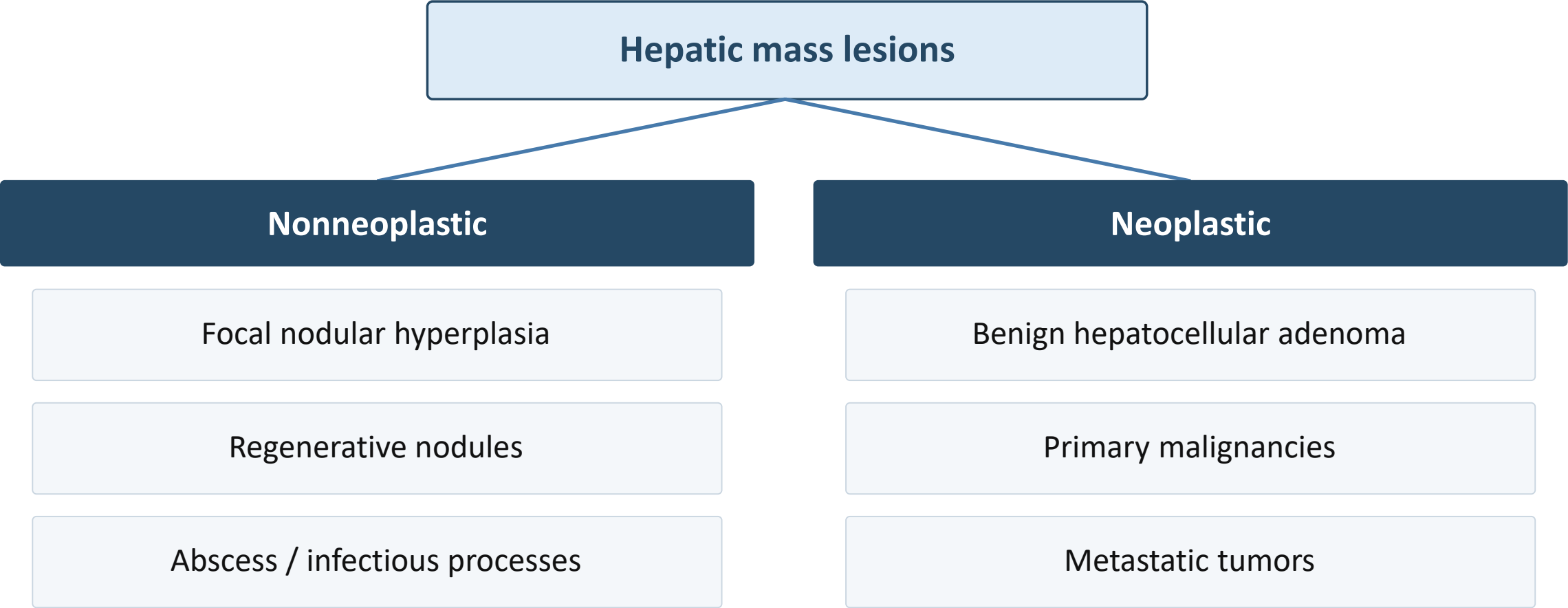
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Learning outcomes

- Explain why altered hepatic blood flow is implicated in FNH.
- Recognize the gross and microscopic findings that define FNH.
- Interpret the diagnostic map-like glutamine synthetase pattern.
- Distinguish FNH from hepatocellular adenoma and other hepatic masses.

The hepatic-mass framework

Hepatic mass lesions



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graph TD; A[Hepatic mass lesions] --> B[Nonneoplastic]; A --> C[Neoplastic]; B --> B1[Focal nodular hyperplasia]; B --> B2[Regenerative nodules]; B --> B3[Abscess / infectious processes]; C --> C1[Benign hepatocellular adenoma]; C --> C2[Primary malignancies]; C --> C3[Metastatic tumors];
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The diagram is a hierarchical flowchart. At the top is a light blue box labeled 'Hepatic mass lesions'. Two lines branch from this box to two dark blue boxes: 'Nonneoplastic' on the left and 'Neoplastic' on the right. Below 'Nonneoplastic' are three light blue boxes: 'Focal nodular hyperplasia', 'Regenerative nodules', and 'Abscess / infectious processes'. Below 'Neoplastic' are three light blue boxes: 'Benign hepatocellular adenoma', 'Primary malignancies', and 'Metastatic tumors'.

Nonneoplastic

Focal nodular hyperplasia

Regenerative nodules

Abscess / infectious processes

Neoplastic

Benign hepatocellular adenoma

Primary malignancies

Metastatic tumors

FNH belongs among nonneoplastic lesions

- FNH in the nonneoplastic mass-lesion category.
- A localized, nodular collection of hepatocytes can form a discrete hepatic mass without being a true neoplasm.
- This classification has direct implications for prognosis and the need for intervention.

Defining the entity

FNH is a benign, nonneoplastic hepatocellular lesion.

- It is a well-circumscribed hepatic mass.
- Its architecture reflects a localized hyperplastic response.
- Absence of cytologic and architectural atypia supports its benign nature.

Who most commonly develops FNH?

- FNH is most common in adult females.
- The demographic association is descriptive: It does not by itself establish the diagnosis.
- Morphology and characteristic imaging findings remain central to recognizing the lesion.

FNH often comes to attention incidentally

- Most lesions are asymptomatic.
- Detection commonly occurs during imaging undertaken for another reason.
- Some lesions are recognized during surgery or in resection specimens.
- An incidental liver mass requires correct classification before treatment decisions.

The pathogenesis is hemodynamic

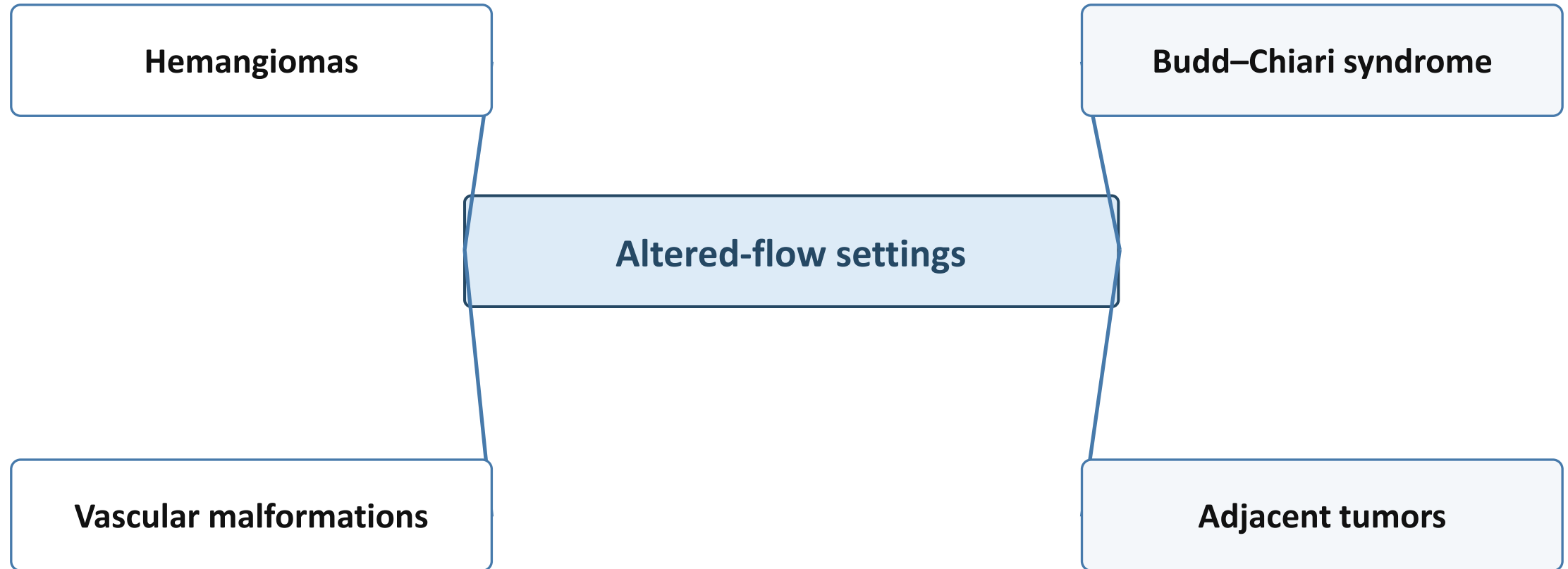


- This is the proposed mechanism.
- The model is an association-based pathogenesis, not proof of one initiating event.

Why the vascular hypothesis matters

- FNH-like nodules can arise in conditions with disturbed hepatic circulation.
- Vascular alterations and hyperplasia occur together in its characteristic structure.
- This helps interpret the thick-walled arteries and nodular parenchyma as linked findings.

Vascular settings associated with FNH-like nodules



FNH-like nodules can occur beside other tumors

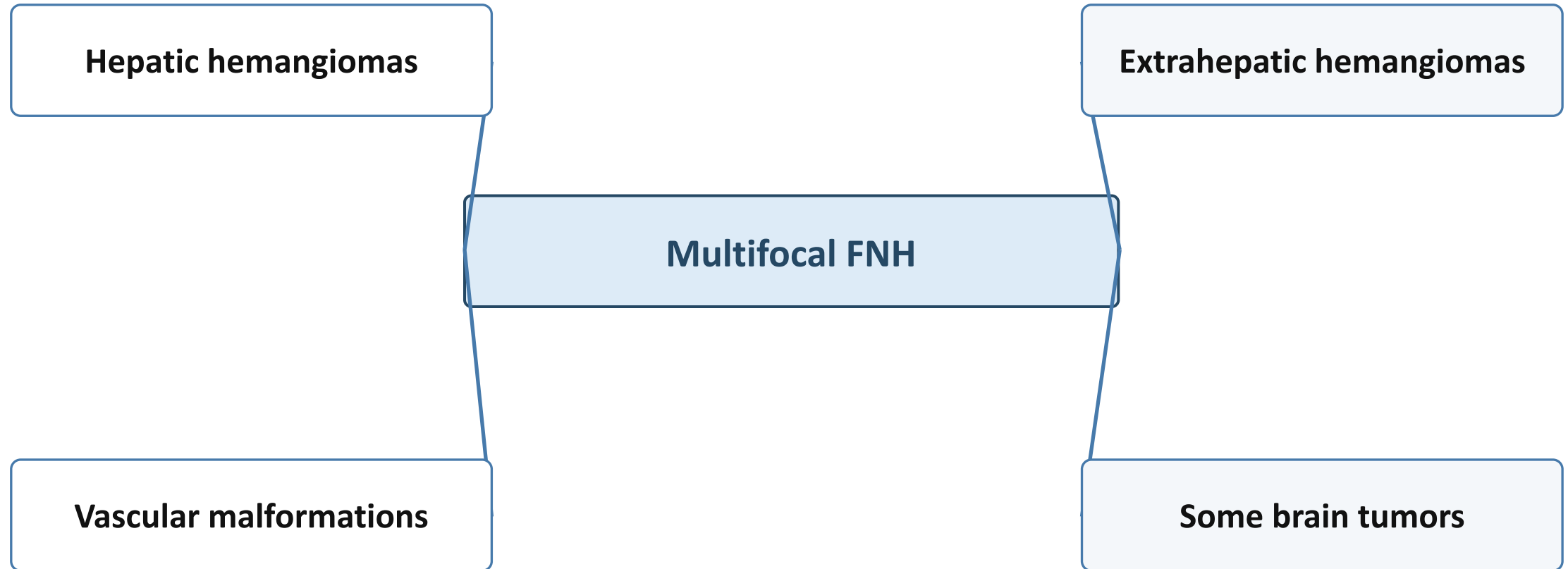
- FNH-like nodules adjacent to other tumors.
- The accompanying lesion and altered local circulation are useful diagnostic context.
- The term “FNH-like” should not be mistaken for a claim that the neighboring tumor is FNH.

Budd–Chiari syndrome provides a vascular context



- Budd–Chiari syndrome to both FNH-like and large regenerative nodules.
- This is a clinicopathologic association, not a universal sequence.

Multifocal FNH has characteristic associations



Brain tumors mentioned in the multifocal setting

- Meningioma and astrocytoma are among the associated brain tumors named.
- The source describes an association; It does not establish causality.
- Clinical history should be interpreted with the hepatic findings rather than replacing them.

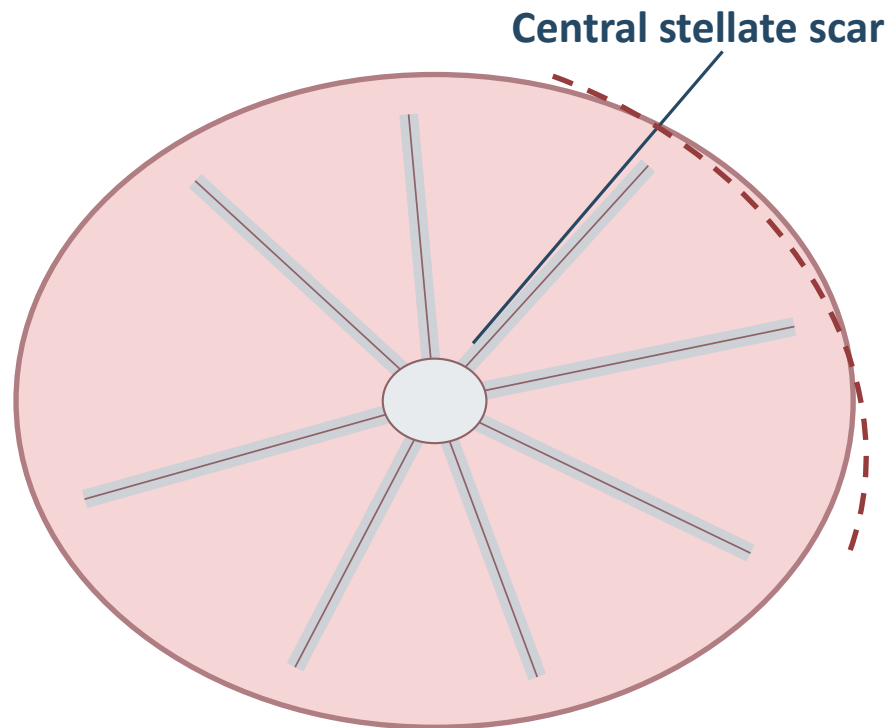
Single versus multifocal disease

Solitary FNH	Multifocal FNH
One identifiable hepatic mass	Several FNH-type nodules
Characteristic architecture still matters	Consider associated vascular disorders
No neoplastic implication from the label	Multiplicity alone does not establish malignancy

Gross recognition begins with circumscription

- FNH is well circumscribed within surrounding liver.
- Its interface is usually visible despite lacking a true capsule.
- A well-defined border and absence of a capsule are compatible observations.

A capsule is typically absent



No complete capsule

Schematic cut surface. Not a gross specimen

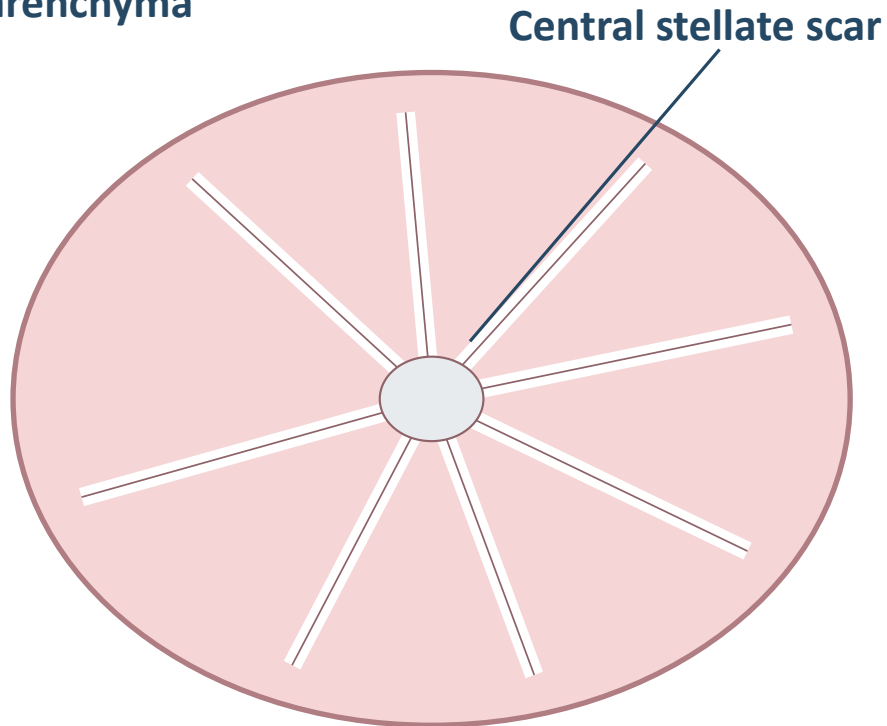
- The lesion typically lacks a capsule.
- The liver–lesion boundary is distinct without a continuous fibrous shell.
- Do not equate circumscription with encapsulation.

Most FNH lesions are relatively small

- Most lesions measure 5 cm or less in diameter.
- This is a descriptive distribution, not a stand-alone diagnostic cutoff.
- Robbins reserves resection mainly for large symptomatic lesions.

The central stellate scar is a key gross finding

Nodular parenchyma



Schematic cut surface: Not a gross specimen

- A central fibrous scar has a stellate configuration.
- It provides a core from which septa radiate.
- This configuration is highly characteristic, but not universal.

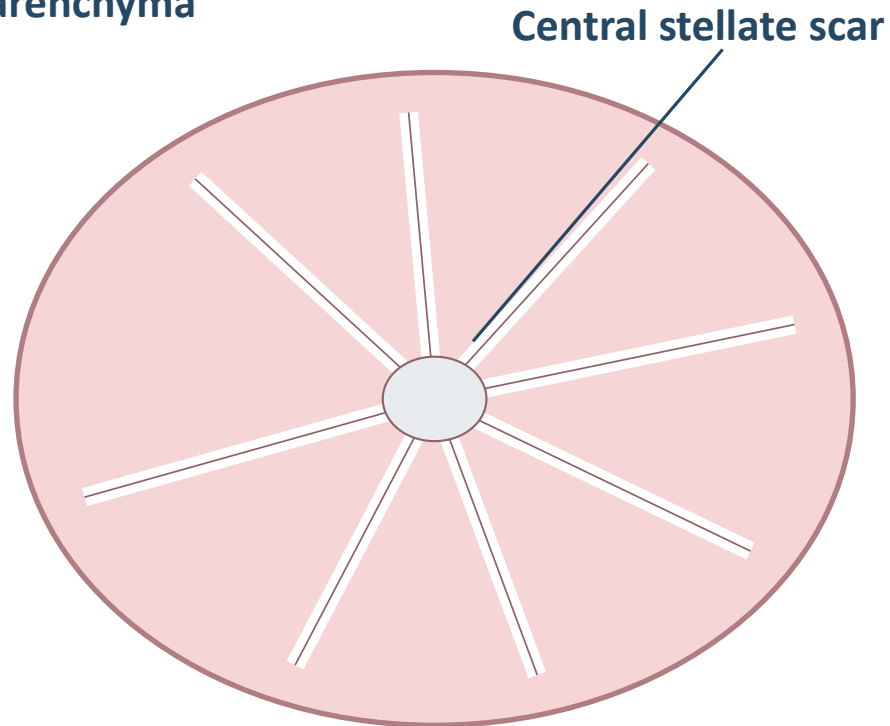
The central scar is not present in every case

A central stellate scar is present in up to 80% of FNH cases.

- Its presence is a strong diagnostic clue.
- Its absence does not by itself exclude FNH.
- Architecture and immunohistochemistry provide additional evidence.

Lobulated architecture at the cut surface

Nodular parenchyma

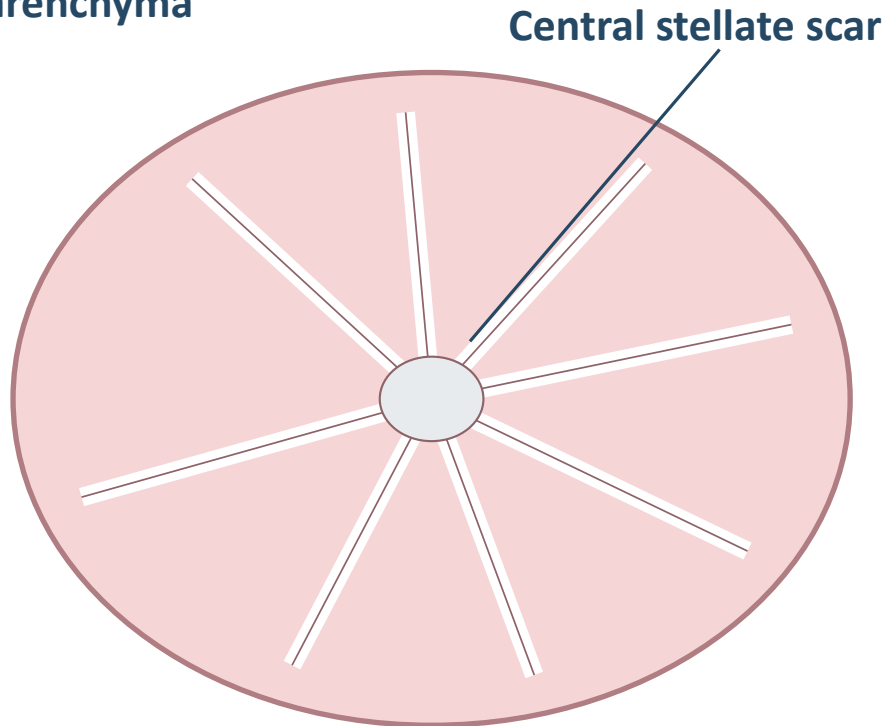


Schematic cut surface: Not a gross specimen

- Radiating septa partition the lesion into nodules.
- The resection specimen may show a lobulated contour.
- The lobular pattern reflects architectural organization, not infiltrative growth.

Gross morphology: Integrated pattern

Nodular parenchyma



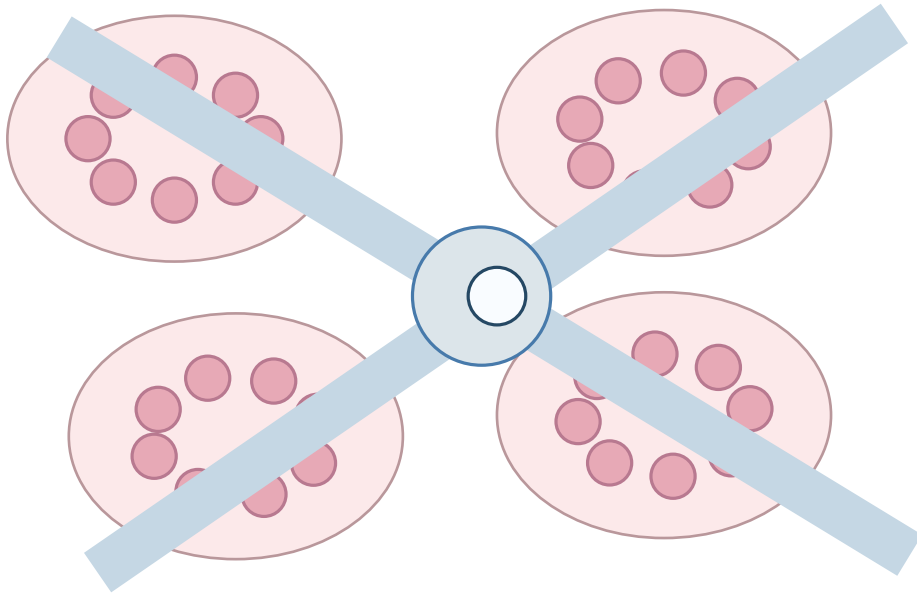
- Well-circumscribed, usually unencapsulated mass
- Often a central stellate fibrous scar
- Radiating septa subdividing nodules

Schematic cut surface: Not a gross specimen

Fibrous septa radiate from the central scar

Hepatocyte nodules

Fibrous septa



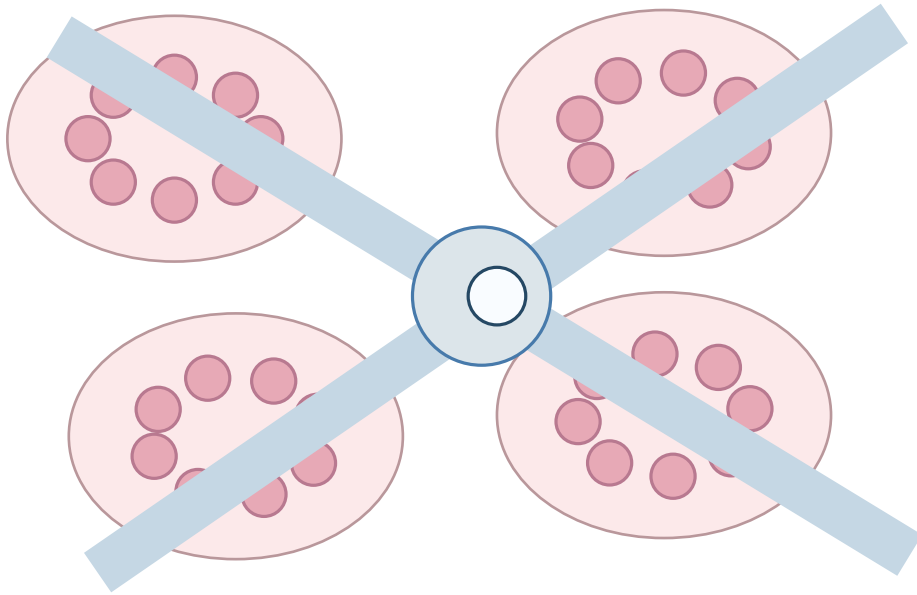
Schematic low-power architecture: Not histology

- Septa extend from central fibrous tissue into the lesion.
- They partition hepatic parenchyma into discrete nodules.
- The pattern can be appreciated at low magnification.

Hepatocyte nodules occupy the intervening spaces

Hepatocyte nodules

Fibrous septa

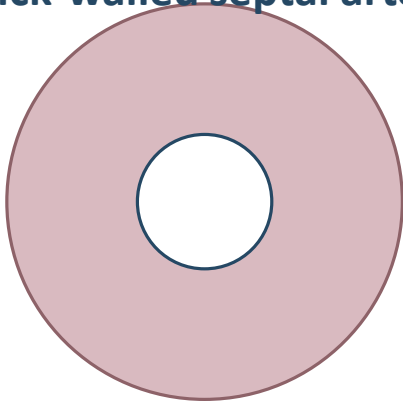


Schematic low-power architecture: Not histology

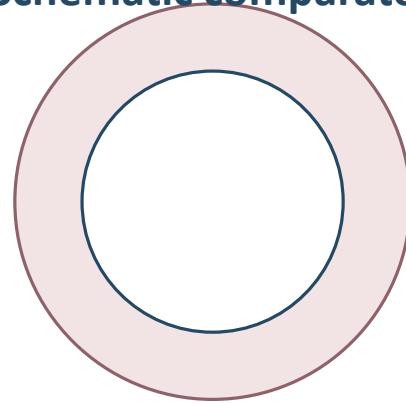
- The nodules consist of hepatocytes rather than atypical tumor cells.
- Fibrous bands, rather than invasive tumor borders, separate the nodules.
- Architecture must be interpreted at low and higher magnification.

Central scar and septa contain abnormal arteries

Thick-walled septal artery



Schematic comparator



Hyperplastic arterial wall

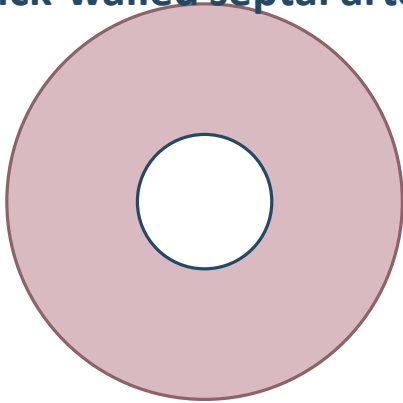
- Thick-walled arteries are a characteristic finding.
- The changes are particularly prominent in the central scar and septa.
- Vascular morphology supports the proposed altered-flow mechanism.

Characteristic arterial wall abnormalities

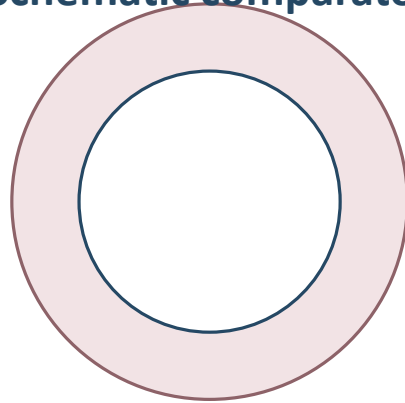
Wall abnormality	Key Pathologic Findings
Intimal changes	Intimal hyperplasia
Muscular changes	Fibromuscular hyperplasia
Elastic architecture	Poorly formed elastic lamina

Vessel wall versus lumen: Schematic anatomy

Thick-walled septal artery



Schematic comparator

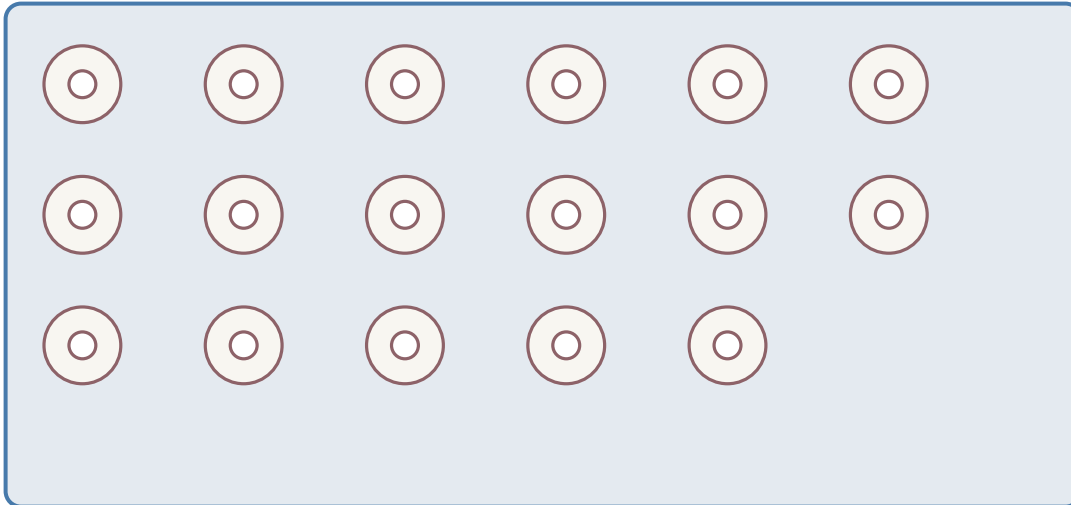


Hyperplastic arterial wall

- An enlarged muscular wall should not be mistaken for a typical portal tract artery.
- The altered arteries occur in scar and septa.
- Diagram is conceptual; Not a measurement or specimen image.

Ductular reaction is often prominent

Small ductular profiles in a fibrous band

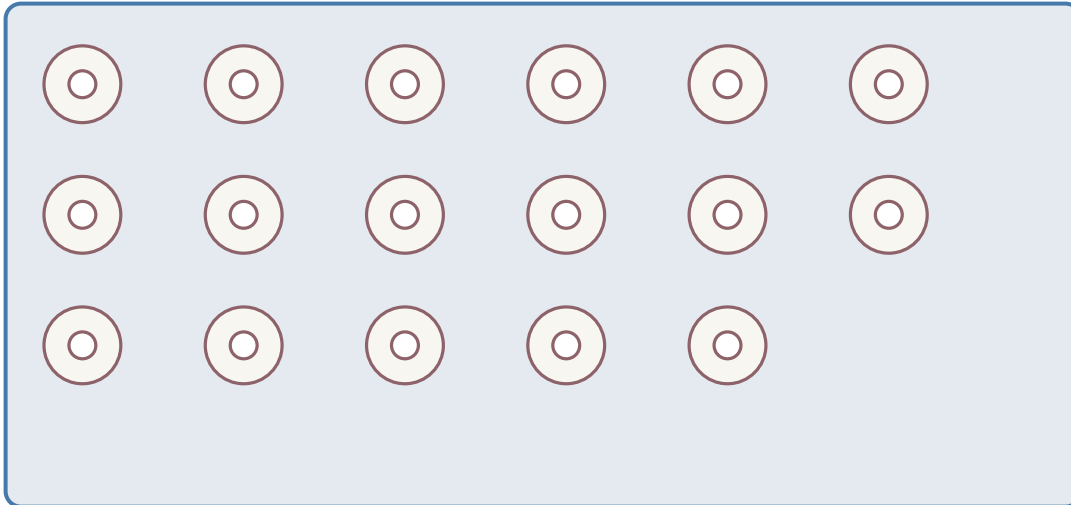


Schematic ductular reaction; No mature portal tract shown

- Ductular structures are often abundant along fibrous bands.
- Their prominence is part of the FNH morphologic pattern.
- A ductular reaction does not imply intact normal portal-tract architecture.

Interlobular bile ducts are absent

Small ductular profiles in a fibrous band



Schematic ductular reaction; No mature portal tract shown

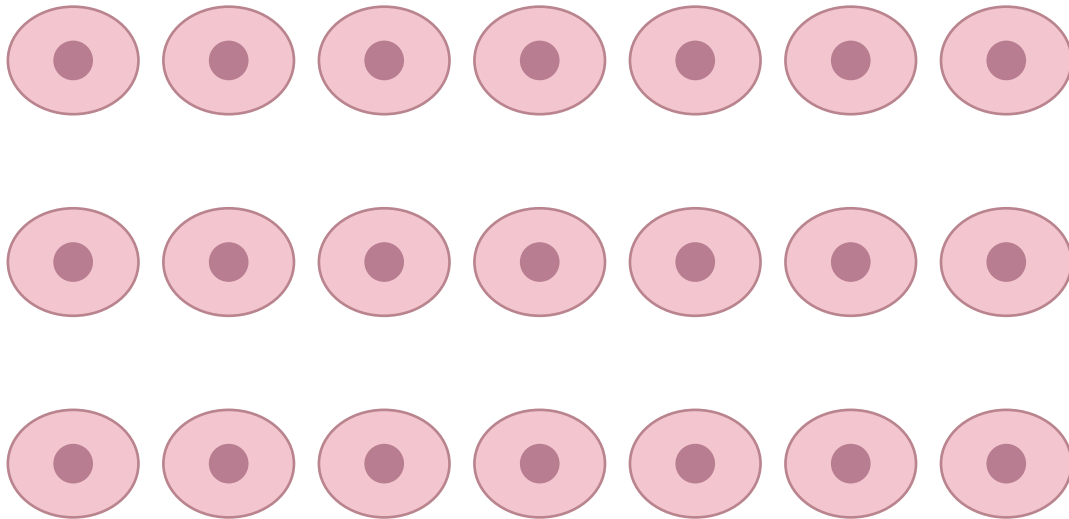
- Interlobular bile ducts are absent within the lesion.
- Ductular reaction and mature interlobular bile ducts are distinct findings.
- This distinction is important when assessing FNH histology.

Ductular reaction is not a normal portal tract

Ductular reaction	Interlobular bile duct
Proliferating ductular profiles in fibrous tissue	A mature component of a normal portal tract
Often conspicuous in FNH septa	Absent in FNH lesional architecture
Supports the characteristic reaction pattern	Would imply preserved portal-tract organization

Hepatocyte plates retain normal thickness

1–2-cell-thick plates



Spaces between cords represent sinusoids

Schematic hepatocyte plates; Not microscopy

- Hepatocytes form one- to two-cell-thick plates.
- This arrangement resembles nonneoplastic liver organization.
- Plate thickness should be assessed alongside cellular and architectural features.

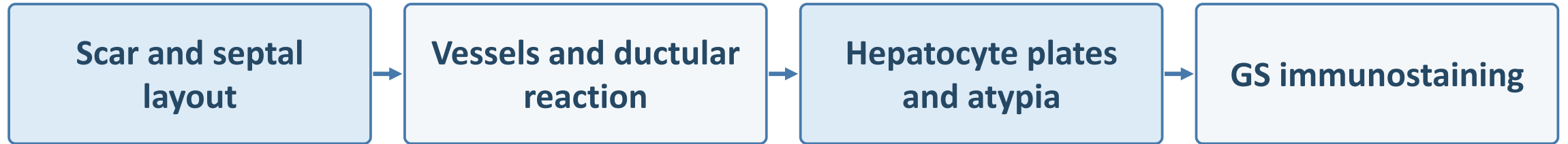
Cytologic atypia is not a feature of typical FNH

- No cytologic atypia in the lesional hepatocytes.
- Absence of conspicuous nuclear abnormalities supports benign hyperplasia.
- This finding should be integrated with architecture rather than used in isolation.

Architectural atypia is also absent

- FNH lacks the architectural atypia expected in an aggressive hepatocellular lesion.
- Preserved thin hepatocyte plates are one expression of orderly architecture.
- Fibrous nodules and abnormal arteries are organized alterations, not malignant invasion.

A low-power-to-high-power review sequence



- An organized examination avoids overinterpreting a single microscopic detail.

The morphologic constellation is more informative

FNH morphologic diagnosis

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graph TD; A[FNH morphologic diagnosis] --> B[Gross / low power]; A --> C[Microscopic]; B --> B1[Well circumscribed]; B --> B2[Stellate scar ± radiating septa]; B --> B3[Hepatocyte nodules]; C --> C1[Thick-walled arteries]; C --> C2[Ductular reaction; No interlobular ducts]; C --> C3[Thin plates; No atypia];
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Gross / low power

Well circumscribed

Stellate scar ± radiating septa

Hepatocyte nodules

Microscopic

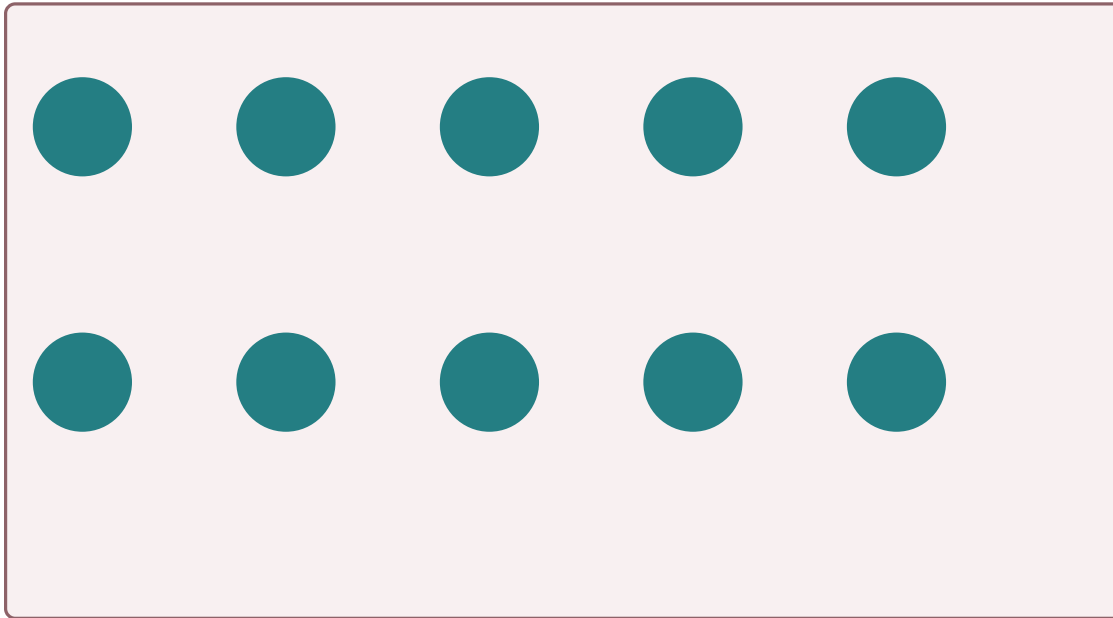
Thick-walled arteries

Ductular reaction; No interlobular ducts

Thin plates; No atypia

Glutamine synthetase normally has zonal expression

Centrizonal hepatocytes

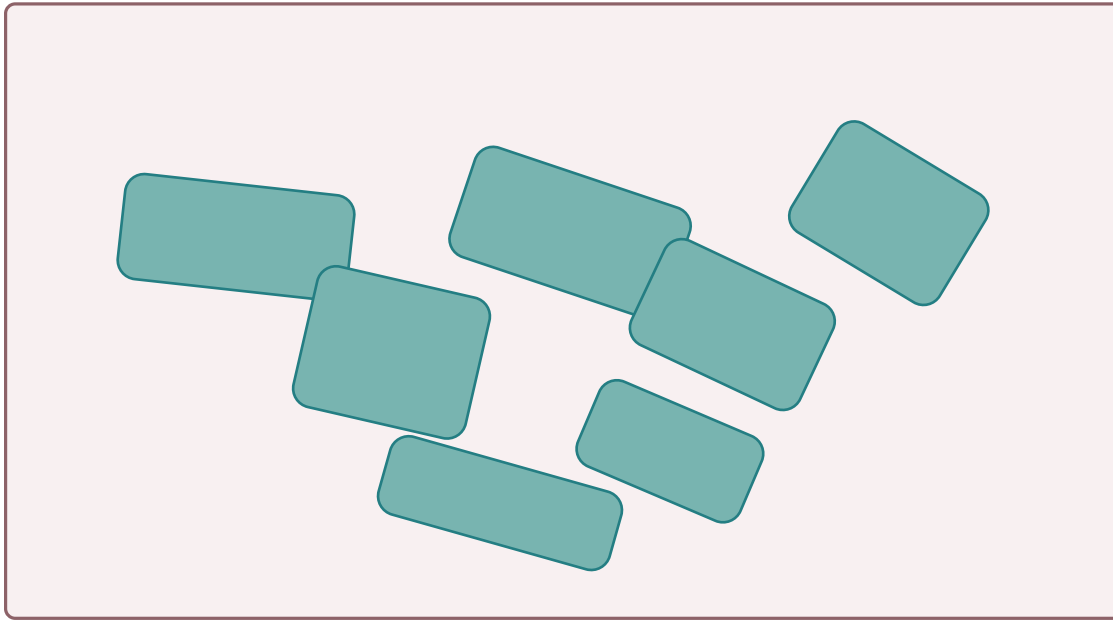


Schematic GS distribution; Not an immunohistochemical image

- GS is an enzyme normally expressed in centrizonal hepatocytes.
- Normal zonation provides the comparator for lesional expression.
- A staining pattern is evaluated spatially, not only as positive or negative.

FNH has a characteristic map-like GS pattern

Irregular interconnected GS-positive zones

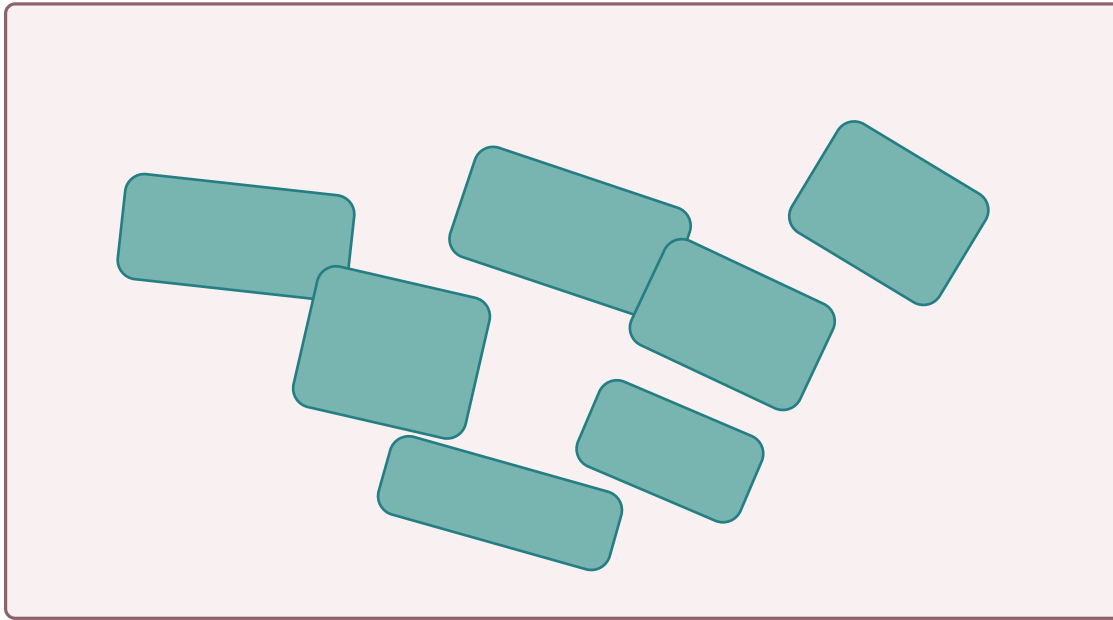


Schematic GS distribution; Not an immunohistochemical image

- Strong cytoplasmic GS expression involves anastomosing hepatocyte groups.
- The network-like distribution is described as map-like.
- This pattern is particularly useful diagnostically.

“Map-like” refers to spatial distribution

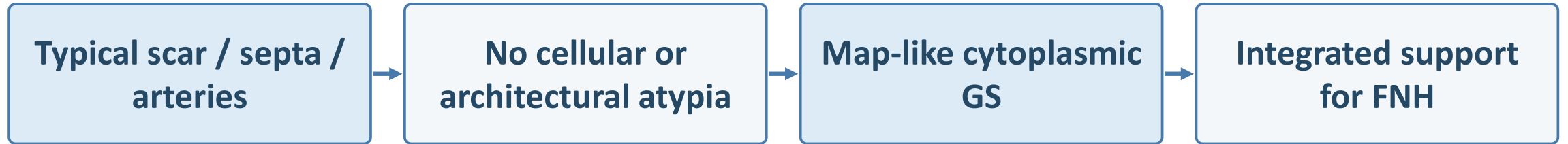
Irregular interconnected GS-positive zones



Schematic GS distribution; Not an immunohistochemical image

- Broad, irregularly interconnected zones stain strongly.
- The pattern is not simply uniform positivity across all hepatocytes.
- Interpret the topology of positive groups rather than the color intensity alone.

GS staining must be read with morphology



- GS is very useful; It does not replace histologic correlation.

An integrated FNH recognition checklist

- Well-circumscribed, usually nonencapsulated mass
- Central stellate scar when present
- Radiating septa and thick-walled arteries
- Ductular reaction without interlobular bile ducts
- One- to two-cell-thick bland hepatocyte plates
- Map-like glutamine synthetase staining

Clinical presentation is usually silent

- Most FNH cases are asymptomatic.
- The diagnosis often follows imaging or an unrelated operation.
- An asymptomatic lesion with convincing FNH features generally does not require treatment.

The central scar helps establish an imaging diagnosis

- The central scar as a highly characteristic imaging finding.
- The scar is supportive, not compulsory, because some FNH lesions lack one.
- Imaging findings and clinical context should be concordant.

Imaging and pathology answer different questions

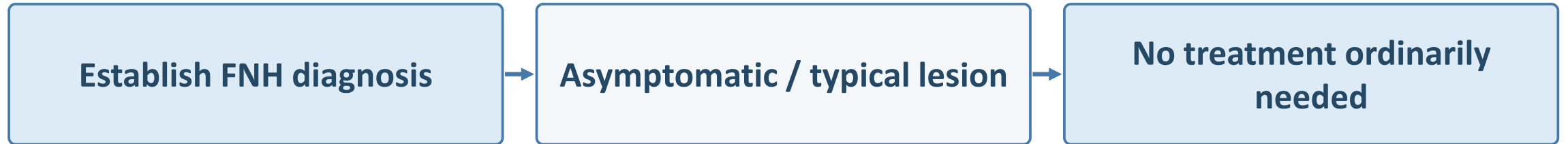
Imaging assessment	Tissue assessment
Mass, contours, central scar	Scar, septa, vessel and hepatocyte morphology
Can suggest a characteristic FNH pattern	Can evaluate GS spatial distribution
May establish the diagnosis in context	Useful when diagnostic uncertainty warrants tissue review

Benign natural history drives management

FNH is benign and generally needs no treatment.

- Classification as nonneoplastic is central to risk assessment.
- Correct recognition avoids management based solely on the presence of a mass.
- Treatment decisions depend on clinical circumstances, not FNH morphology alone.

Resection is reserved for selected cases



- Resection for large symptomatic lesions.
- This is a pathology-oriented summary, not a substitute for an individual multidisciplinary decision.

A symptomatic large lesion changes the decision

- Large FNH lesions may become symptomatic.
- Large symptomatic lesions as the principal resection setting.
- The reason for surgery is symptoms and lesion-specific context—not malignant transformation of typical FNH.

The major differential is hepatocellular adenoma

Focal nodular hyperplasia	Hepatocellular adenoma
Benign, nonneoplastic hyperplasia	Benign hepatocellular neoplasm
Linked to altered blood flow	Distinct molecular subtypes described
No treatment for typical lesions	Hemorrhage and transformation risks affect management

FNH and adenoma overlap demographically

- FNH is most common in adult females.
- Hepatocellular adenoma also commonly occurs in young females.
- Female sex is not sufficient to discriminate these two lesions.
- Exposure history, morphology, immunohistochemistry and clinical course become more useful.

Hormonal associations distinguish adenoma

FNH	Hepatocellular adenoma
Altered blood flow	Strong association with oral contraceptive use
No hormonal cause specified in FNH section	Association with anabolic steroids
A distinct nonneoplastic mechanism	Obesity / metabolic syndrome noted for rising adenoma incidence

FNH versus adenoma: Gross anatomy

FNH	Hepatocellular adenoma
Often central stellate scar	Discrete mass; Sometimes hemorrhage
Radiating fibrous septa	No characteristic FNH-type scar required
Typically lacks a capsule	Gross appearance assessed with clinical context

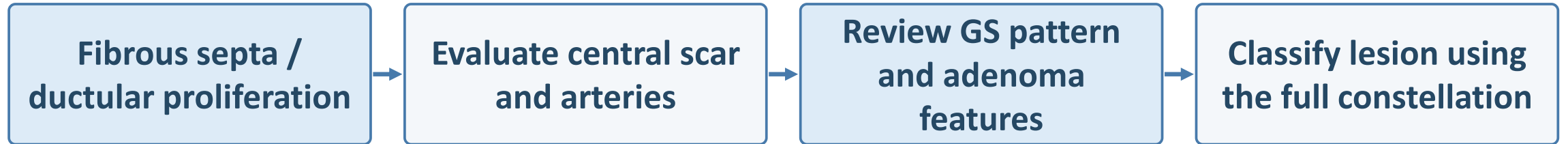
Both lesions may form thin hepatocyte plates

FNH	Hepatocellular adenoma
One- to two-cell-thick plates	One- to two-cell-thick plates
Thick-walled arteries in scar / septa	Arteries in scant fibrous stroma
Ductular reaction; No interlobular ducts	Normal portal tracts and interlobular ducts absent

Inflammatory adenoma may mimic FNH

- Inflammatory HCA may show fibrous septa and a ductular reaction.
- These features overlap with FNH and cannot be considered in isolation.
- Sinusoidal dilation and acute-phase protein expression in inflammatory HCA.

Histologic overlap demands pattern integration



- Do not assume septa alone establish FNH.

Adenoma has molecularly distinct subtypes

Hepatocellular adenoma

Molecular classes

HNF1A-inactivated

Inflammatory (JAK–STAT)

β -catenin–activated

Sonic hedgehog–activated

Why these matter

Diagnostic phenotype differs

Hemorrhage risk varies

Malignant potential varies

IHC findings may favor adenoma instead

Pattern / biomarker	Adenoma context
Loss of liver fatty acid–binding protein	HNF1A-inactivated adenoma
Nuclear β -catenin staining	β -catenin pathway activation
C-reactive protein / serum amyloid A	Inflammatory adenoma
Map-like GS distribution	Characteristic support for FNH

Management contrast emphasizes the diagnosis

Established FNH	Hepatocellular adenoma
No treatment in most cases	Some tumors require resection or follow-up
Large symptomatic FNH may be resected	Hemorrhage and malignancy risk inform decisions
No source-described malignant progression	Risk differs by subtype and lesion features

Cavernous hemangioma is a vascular tumor

FNH	Cavernous hemangioma
Hepatocyte nodules separated by fibrous septa	Dilated, thin-walled vascular channels
Stellate scar and thick-walled arteries	Red-blue soft vascular nodule
Nonneoplastic hyperplasia	Most common benign liver tumor

Regenerative nodules belong in the nonneoplastic differential

- Large regenerative nodules can arise in noncirrhotic liver.
- Budd–Chiari syndrome, hemangioma and vascular malformations as settings.
- The shared vascular background requires careful interpretation of nodule type.

Nodular regenerative hyperplasia is diffuse

Focal nodular hyperplasia	Nodular regenerative hyperplasia
Localized hepatic mass lesion	The entire liver may become nodular
Central scar and septa often present	Can occur without significant fibrosis
Usually incidental / benign	Can cause portal hypertension and mimic cirrhosis on imaging

Inflammatory mass lesions can mimic tumors

Other nonneoplastic mass lesions

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graph TD; A[Other nonneoplastic mass lesions] --> B[Inflammatory / infectious]; A --> C[Regenerative / biliary]; B --> D[Abscesses]; B --> E[Granulomas]; B --> F[Inflammatory pseudotumors]; C --> G[Large regenerative nodules]; C --> H[Nodular regenerative hyperplasia]; C --> I[Benign biliary proliferations];
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Inflammatory / infectious

Abscesses

Granulomas

Inflammatory pseudotumors

Regenerative / biliary

Large regenerative nodules

Nodular regenerative hyperplasia

Benign biliary proliferations

Case 1: Incidentally detected scarred liver lesion

An adult woman undergoes imaging for an unrelated indication. A circumscribed hepatic mass has a central scar and no symptoms.

Which diagnosis is strongly suggested, and why?

- FNH is strongly suggested.
- The incidental presentation and central scar match the characteristic pattern.
- The scar alone is supportive, not definitive.

Case 2: Scar, septa, and bland hepatocytes

Resection reveals a central stellate scar, thick-walled septal arteries, ductular reaction and one- to two-cell-thick hepatocyte plates without atypia.

Which combined findings establish the morphologic pattern?

- Fibrous/nodular architecture plus abnormal vessels
- Prominent ductular reaction without interlobular bile ducts
- Bland hepatocytes with preserved thin plates

Case 3: Interpret the GS stain

A hepatocellular lesion demonstrates strongly positive cytoplasmic GS staining in irregular anastomosing groups of hepatocytes.

What is the diagnostic significance of this pattern?

- It is the characteristic map-like GS distribution of FNH.
- Use it alongside the scar, arterial and ductular features.
- It is not a reason to ignore contradictory histology.

Case 4: A misleading ductular reaction

A hepatocellular mass shows fibrous septa and a prominent ductular reaction. Sinusoidal dilation and inflammatory phenotype are also described.

Which competing entity must remain in the differential?

- Inflammatory hepatocellular adenoma.
- It can mimic FNH through fibrous septa and ductular proliferation.
- Evaluate the broader morphology and IHC profile.

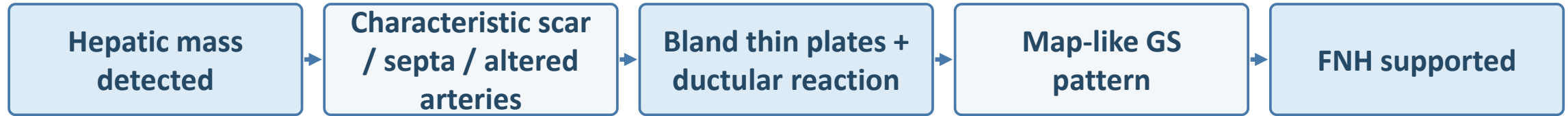
Case 5: Multiple nodules and vascular abnormalities

Multiple FNH-like nodules occur in a patient with a vascular malformation and hepatic vascular disturbance.

How does this context inform the pathogenesis?

- It supports the association with altered blood flow.
- Multiplicity alone does not establish a neoplastic process.
- Correlate the lesion architecture with the vascular disease.

A practical recognition pathway



- Consider hepatocellular adenoma and regenerative lesions when features are discordant.

Core pathologic discriminators

- Benign, nonneoplastic hepatocellular lesion
- Altered-flow hypothesis and vascular associations
- Well-circumscribed; Generally unencapsulated
- Central scar and septa; Abnormal thick-walled arteries
- Ductular reaction without mature interlobular ducts
- Bland thin hepatocyte plates; Map-like GS staining

Clinicopathologic synthesis

Recognizing FNH links hemodynamics, architecture, and benign clinical behavior.

- Altered blood flow is associated with hepatocyte hyperplasia.
- Scar–septum–artery organization and map-like GS are distinctive.
- Most patients need no treatment once the diagnosis is established.

Selected source and image provenance

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026. Chapter 18, pp. 787–790.

FNH definition, pathogenesis, morphology and clinical features: pp. 787–788.

Comparison context: hepatic nodules, hepatocellular adenoma, hemangioma and regenerative nodules: pp. 787–790.

All architectural illustrations in this lecture are original editable schematics—not clinical specimens or reproduced textbook figures.