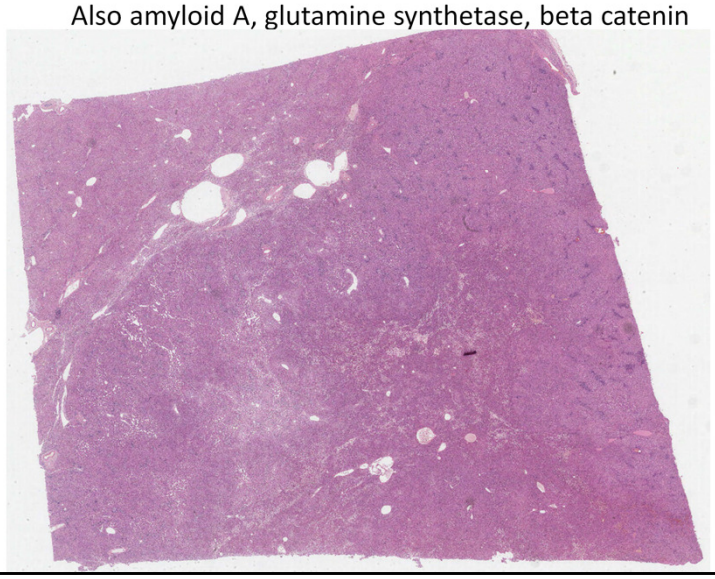
Case LS6 36 F

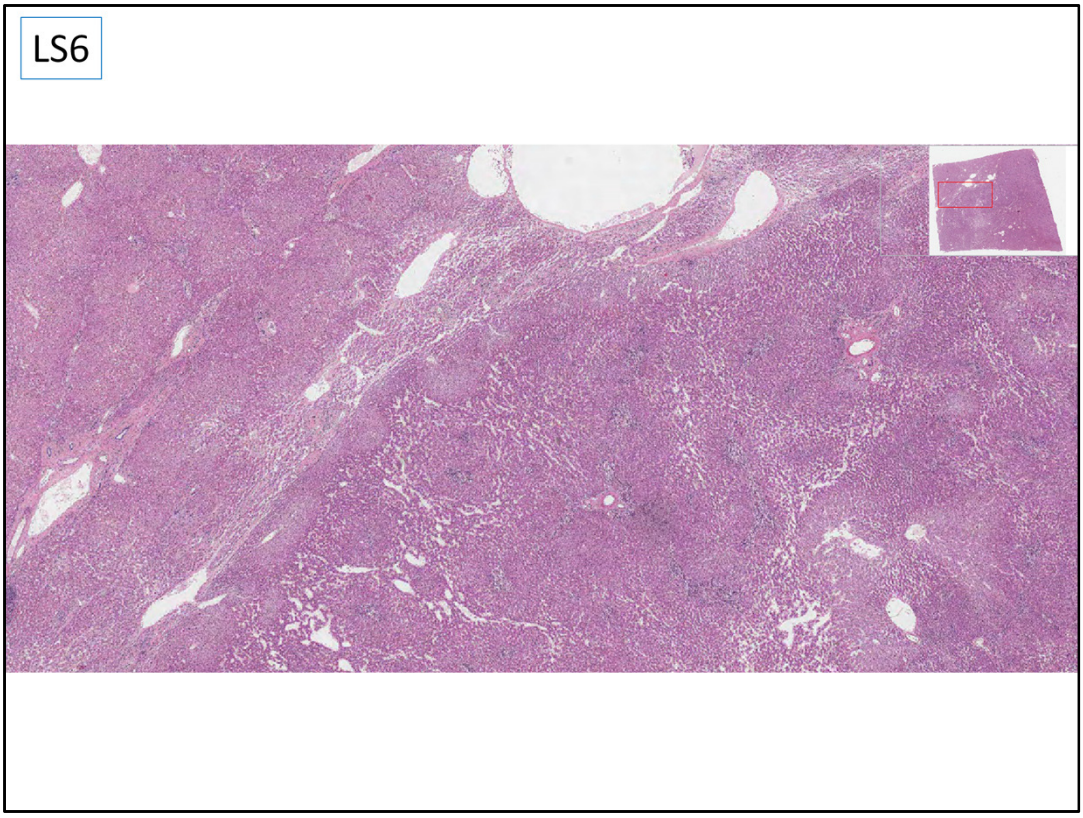
Turner syndrome. Focal liver lesion, ? Adenoma

Liver segments 6&7, contains a 50mm round tumour, slightly paler than surrounding liver.

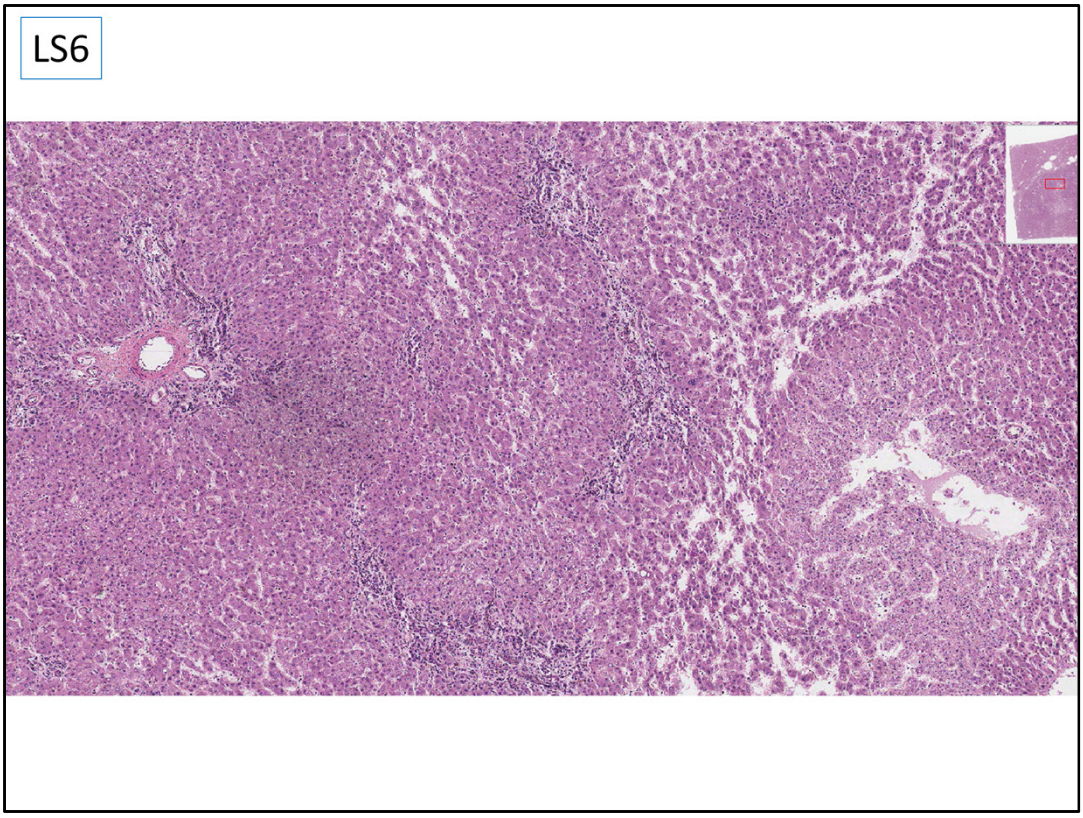
Also amyloid A, glutamine synthetase, beta catenin



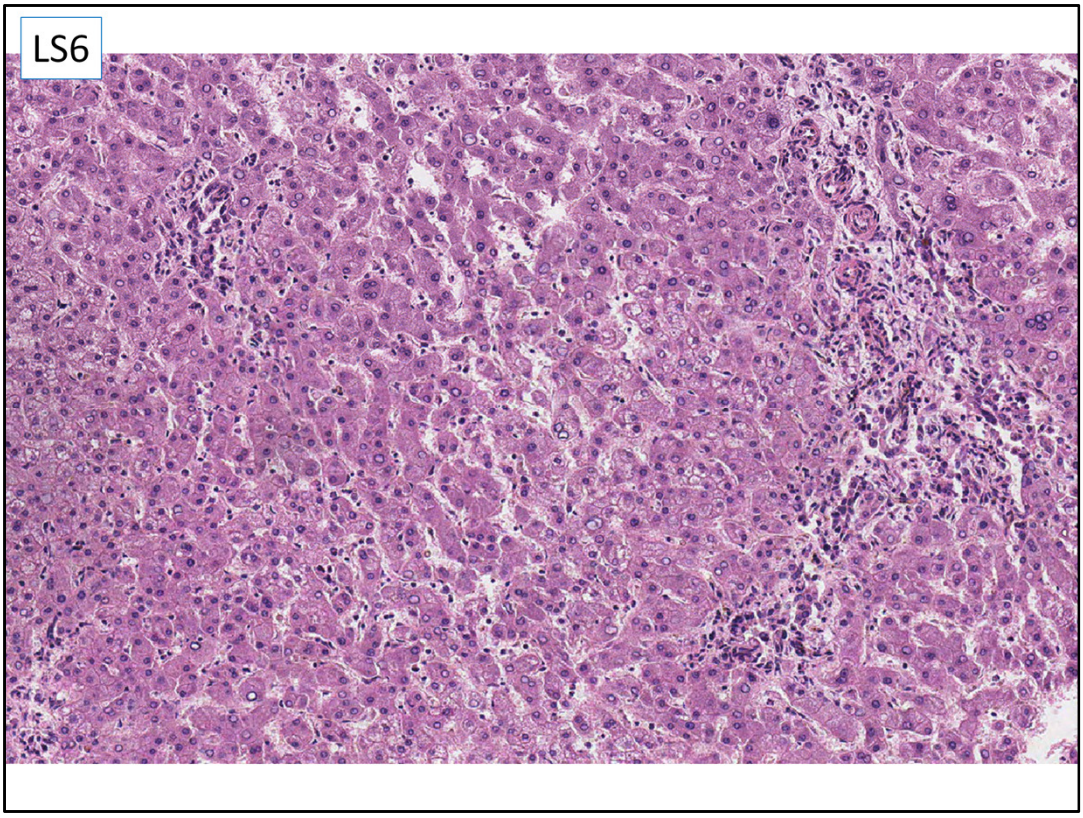
Low magnification – the lesion is expansile without a surrounding capsule. It is composed of near-normal hepatocytes.



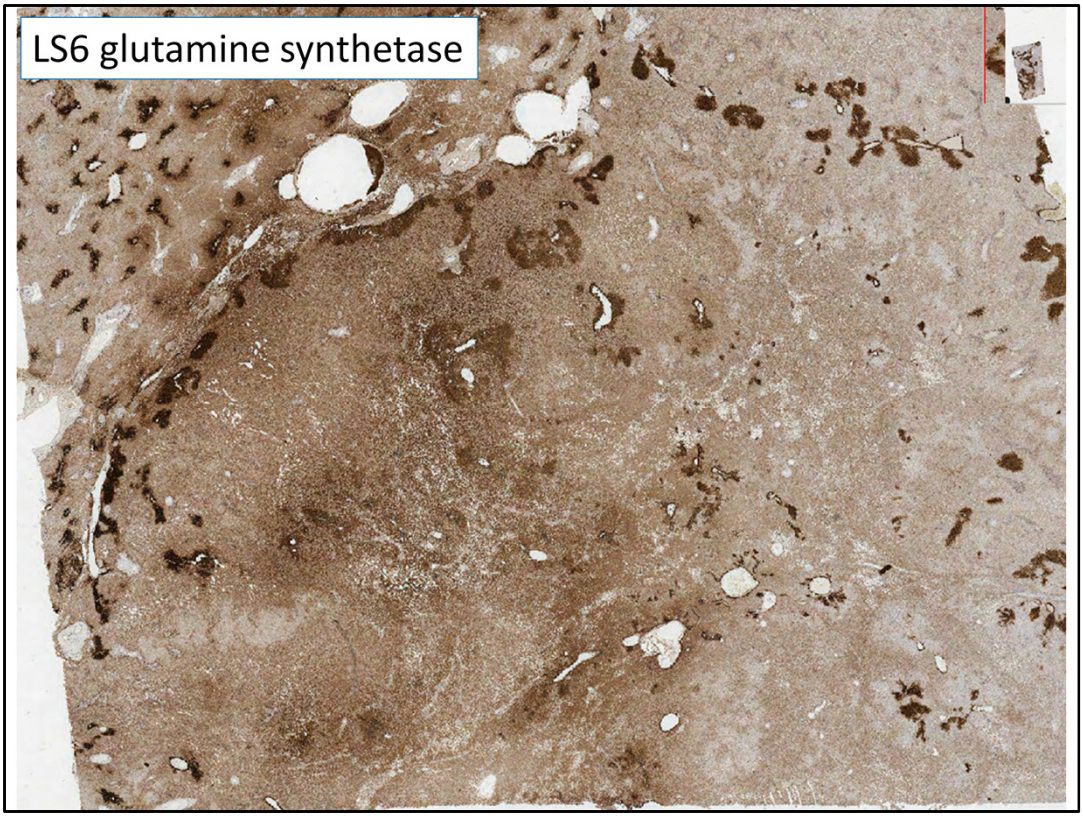
The edge of the lesion which is in the lower right of the field. There is some telangiectasia in the lesion.



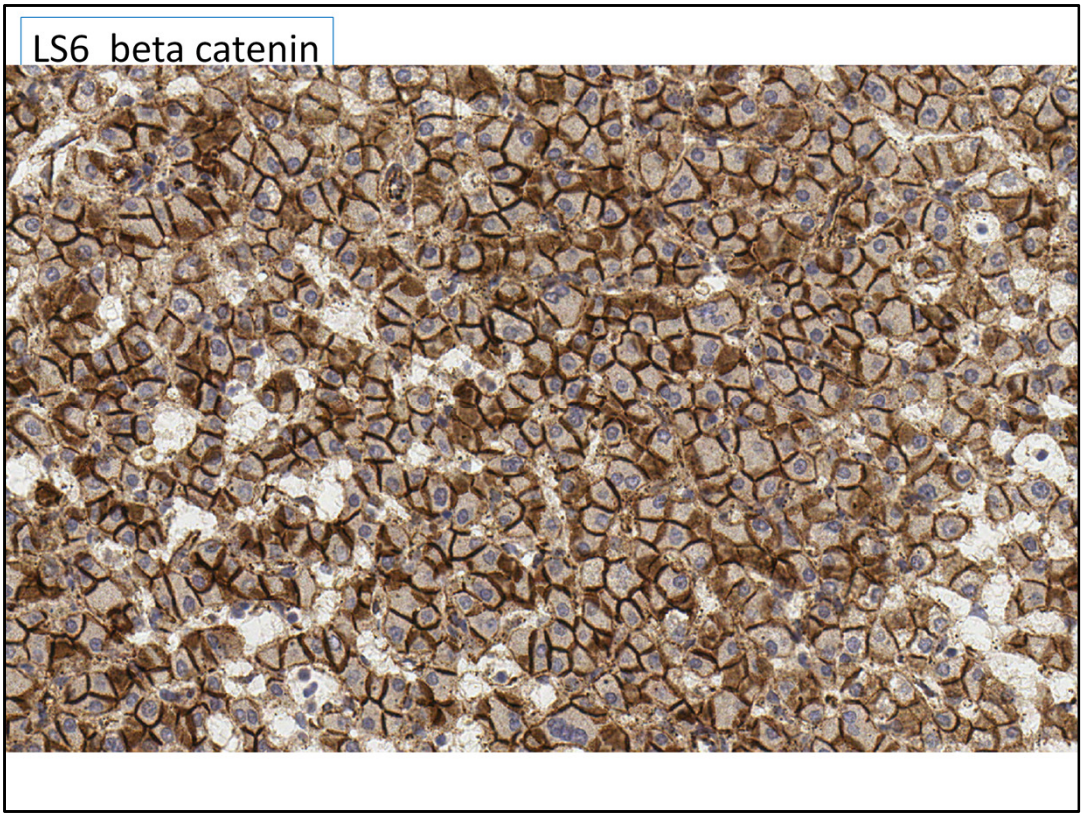
Within the lesion – there are unaccompanied arteries associated with a little ductular reaction but no bile duct or portal vein. The



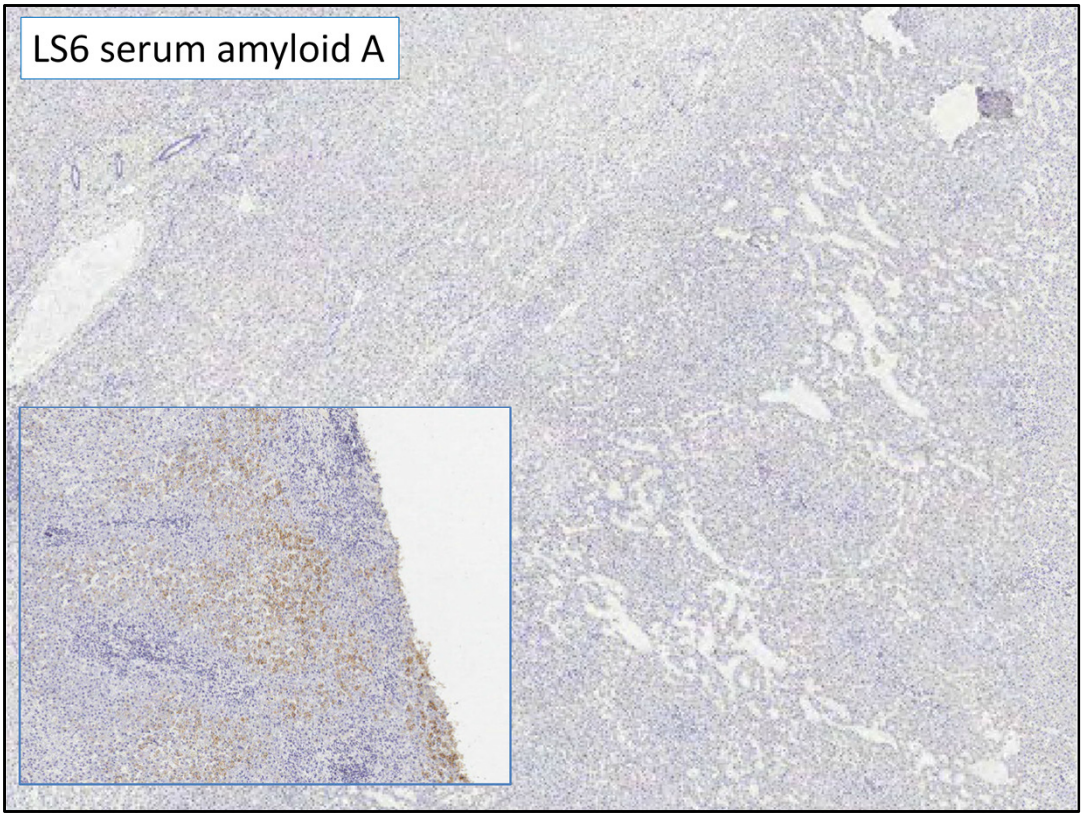
A higher power view of a typical unaccompanied artery with some adjacent ductules and lymphocytes, and mild telangiectasia elsewhere.



Glutamine synthetase the background liver shows characteristic strong positive staining in perivenular zone 3 hepatocytes. Within the lesion – there is focal strong positivity mainly at the periphery, but no map like pattern (the pattern seen in focal nodular hyperplasia). There is also no diffuse positivity – the pattern of beta catenin activated adenoma.



Beta catenin showing the normal membranous pattern of staining. In beta catenin activated adneomas (and in hepatocellular carcinoma) there is nuclear positivity for beta catenin, although only very infrequent neoplastic hepatocytes show nuclear positivity, which may need a lot searching to find.



Amyloid A positivity would be characteristic of inflammatory adenoma. In this slide it is patchy, but present in places. The morphological features in this case are characteristic of the inflammatory type of adenoma, supported by the positivity for amyloid A. Some inflammatory adenomas are also beta catenin activated – with diffuse positivity for glutamine synthetase - not in this case.

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B	Hamartoma
C	Focal nodular hyperplasia
D	Hepatocellular adenoma
E	Haemangioma

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Correct answer: D
This is a focal lesion in a young female patient, composed of well differentiated hepatocytes, in background liver without chronic liver disease. There is no central scar or map-like positivity as would be expected for focal nodular hyperplasia. There is no atypia. Histology is of a hepatocellular adenoma.

These are now sub-classified, into types based on molecular changes, which usually have morphological counterparts. In this case, the unaccompanied arteries with a little ductular reaction and inflammation, and with telangiectasia in the intervening parts of the lesion, are characteristic of the inflammatory type of adenoma. Previously before genetic studies were available, these were classified as 'telangiectatic focal nodular hyperplasia'.

<u>Comments on other options:</u>
A The distinction from well differentiated hepatocellular carcinoma can be very difficult, sometimes impossible to make. Any morphological atypia is suspicious of HCC, as are pseudoglandular structures and 'nodule in nodule' appearance. The presence of focal reticulin deficiency favours hepatocellular carcinoma. Diffuse endothelial positivity for CD34 in the lesion ('capillarisation of sinusoids') shows that it has an arterial blood supply, but may also be present in adenomas.

B Hamartoma – in the liver, hamartomas are bile duct lesions, either von Meyenberg complexes or peribiliary gland hamartomas – they do not have a hepatocyte morphology.

C focal nodular hyperplasia – the main differential, also composed of near-normal hepatocytes. They contain arteries without bile ducts, often within broader fibrovascular scars with abnormal thick walled vessels. Often there are patchy areas of ductular reaction and/or inflammation at the edge of the fibrous septa, so that there is a resemblance to biliary disease. Immunohistochemistry for glutamine synthetase (which in normal liver is strongly positive in perivenular, zone 3 hepatocytes) shows a characteristic 'map like' staining pattern at low power in FNH.

E Haemangioma – a lesion of vascular structures with varying amounts of fibrous tissue, which may at most have some entrapped hepatocytes at the edge.