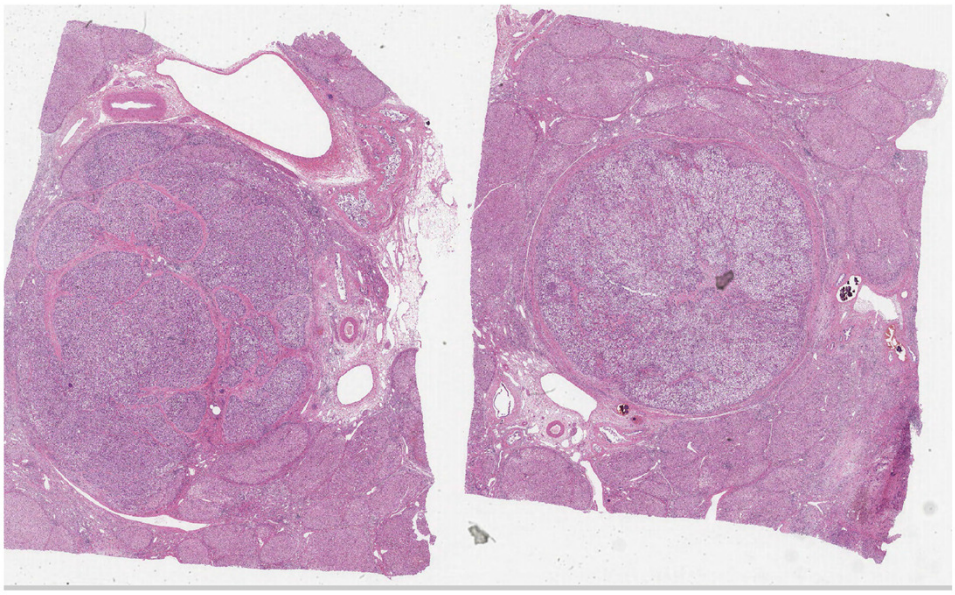
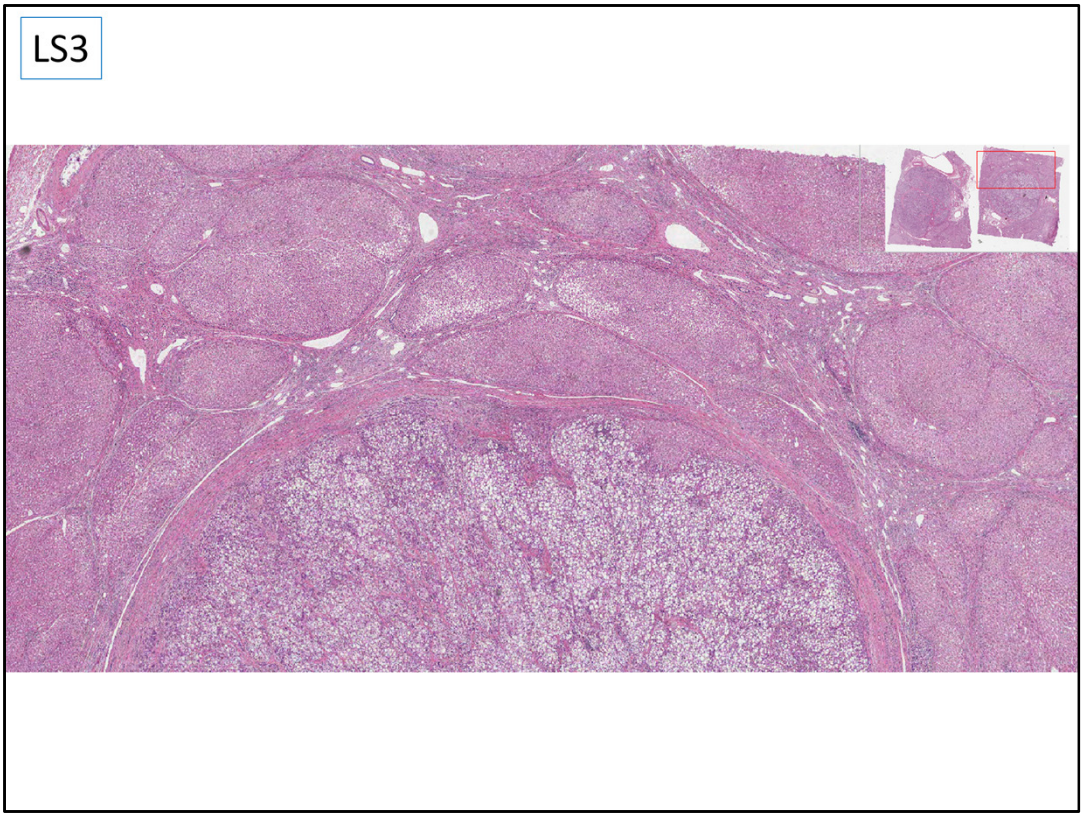
Case LS3 53M

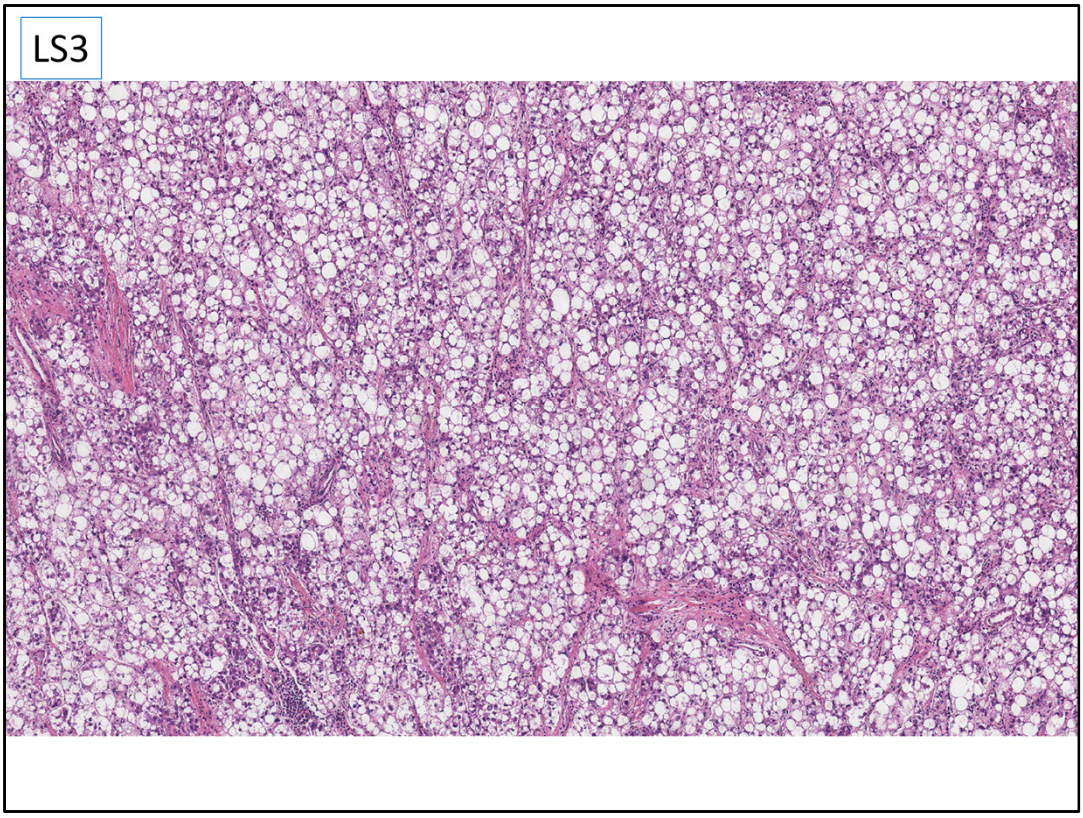
HCC on background of treated HCV. No additional stains



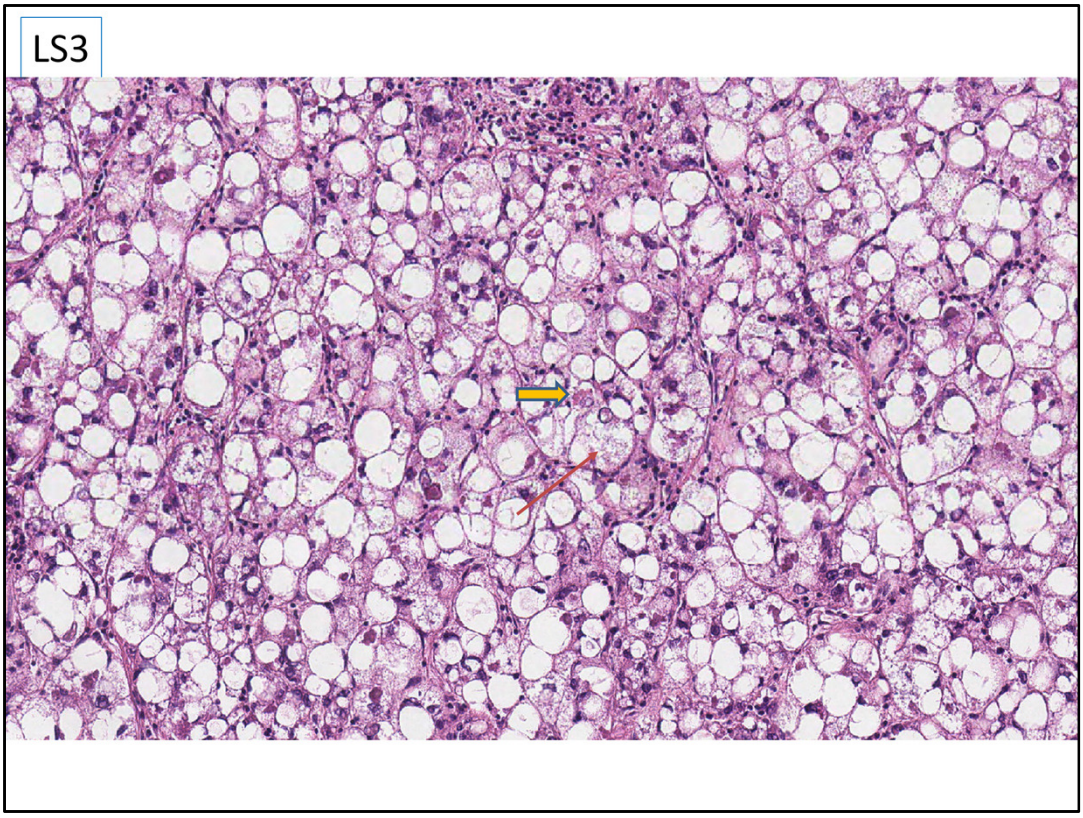
There is clearly a nodular hepatocellular lesion with a background of cirrhotic liver. This is presumably an explant liver.



Both the cirrhosis and part of the lesion are seen here. The cirrhotic background has broad and narrow fibrous septa surrounding nodules of hepatocytes – there is minimal inflammation in keeping with previously treated hepatitis C. Most patients now have cleared hepatitis C virus by the time of liver transplant, due to previous antiviral treatment.

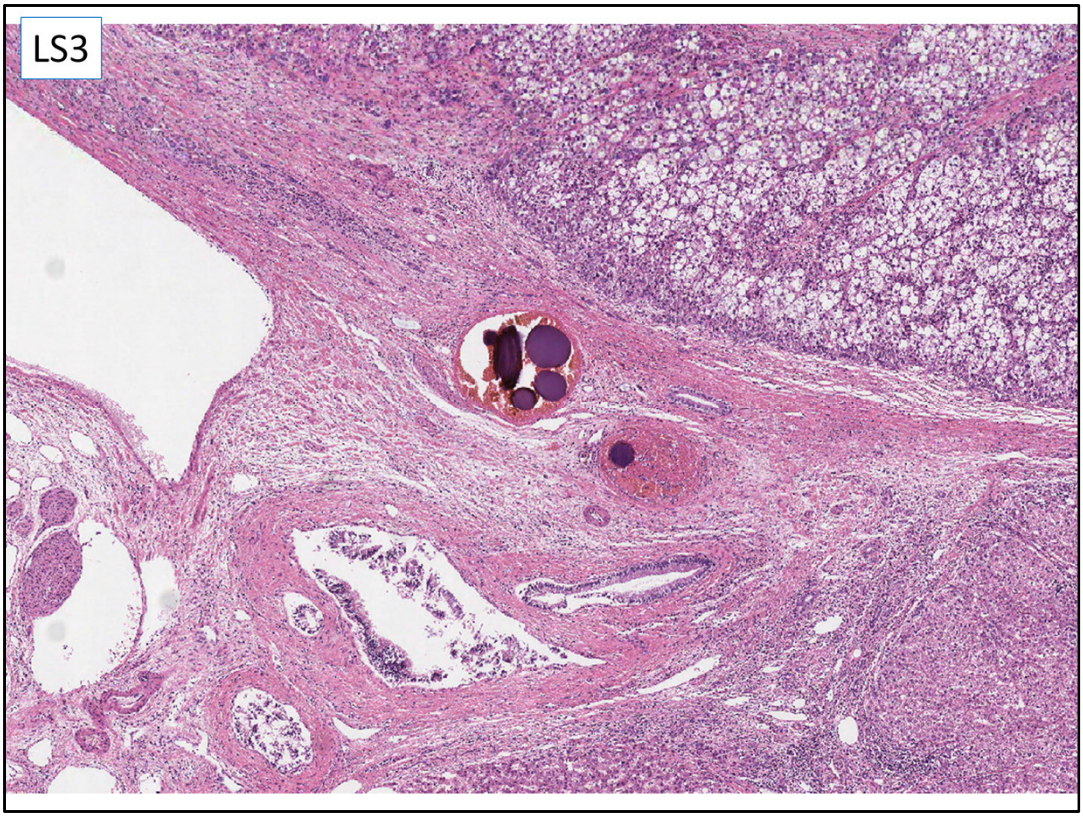


Parts of the lesion show a marked degree of steatosis.

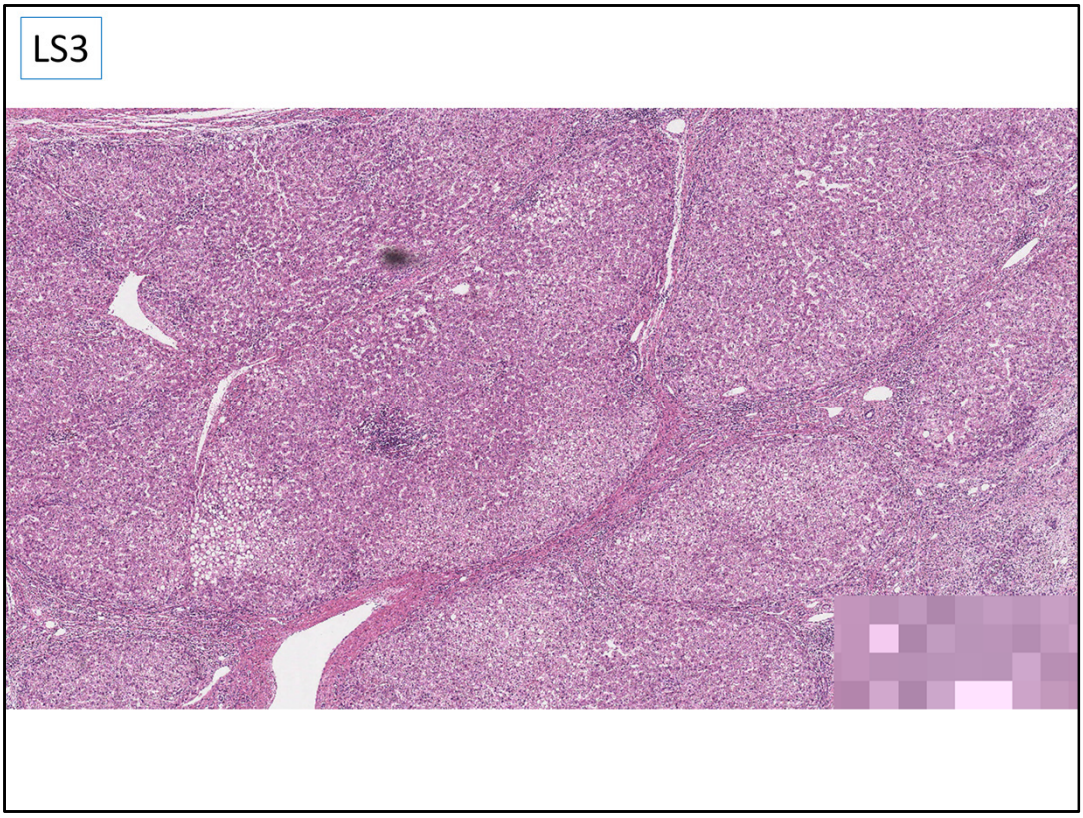


In addition to steatosis, there are frequent hepatocytes showing ballooning (long arrow) and also Mallory Denk bodies (short block arrow).

The diagnosis of hepatocellular carcinoma, as distinct from macro-regenerative nodules – can be difficult. It is based on morphological features supported by additional stains where necessary (see discussion at end of LS3).



At the edge of the lesion, there are vessels containing acellular spheres. These are the beads from previous chemo-embolization (TACE – trans-arterial chemo-embolization). This is used to limit progression of hepatocellular carcinoma while the patient is on the waiting list. Also, for treating HCC in patients who are not candidates for transplant.



Background liver cirrhosis.

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A	Hepatocellular carcinoma arising in cirrhosis
B	Dysplastic nodule in cirrhosis
C	Hepatocellular carcinoma arising in normal liver
D	Focal nodular hyperplasia in cirrhosis
E	Metastatic deposit in a cirrhotic liver

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Correct answer: A. There is a focal nodule quite different to the background cirrhotic nodules. The hepatocytes in the nodule show abnormal architecture, widened cell plates, as well as some atypia. In this particular example, there is also steatosis, ballooning and Mallory Denk bodies in the lesion – features of steatohepatitic variant of hepatocellular carcinoma, which has an association with cirrhosis due to non-alcoholic fatty liver disease, although this example is in a patient with treated hepatitis C.

Comments on other options:

Dysplastic nodule – is a distinct nodule usually apparent macroscopically and >10mm diameter, which has some alteration of hepatocytes, but not fulfilling criteria for hepatocellular carcinoma. Criteria for HCC would include – degrees of cellular atypia, clearly amounting to malignancy, usually together with deficiency of reticulin (at least focally), and diffuse positivity of the sinusoidal endothelium for CD34. Invasion of the fibrous capsule or vascular invasion, if present, are clear indicators of HCC. I difficult lesions, positivity for at least two of the immunohistochemical markers glypican 3, glutamine synthetase, heat shock protein 70, support the diagnosis of HCC. However, diagnosing early, well differentiated HCC v dysplastic nodule is subjective and an area of some inter-observer variation.

Hepatocellular carcinoma arising in normal liver – clearly the background liver is cirrhotic in this case. The background liver is important in focal liver lesions – cirrhosis is a major risk factor for HCC, such that metastatic carcinoma is rare in cirrhotic liver. Conversely with a normal background – HCC is rare, and usually larger at the time of diagnosis. The differential diagnosis for well differentiated hepatocellular lesions in non-

cirrhotic liver is with hepatocellular adenoma or focal nodular hyperplasia – the term ‘dysplastic nodule’ is only used in the context of cirrhosis.

Focal nodular hyperplasia (FNH) – is a focal lesion in non-cirrhotic liver, due to local hepatocyte hyperplasia associated with an aberrant arterial supply. It can also show ‘capillarisation of sinusoids’ where arterial flow directly into sinusoids results in a change in their structure with loss of fenestration and acquisition of CD34 positivity of the endothelium. FNH does not occur in cirrhotic liver – although ‘FNH-like’ non-neoplastic arterialised nodules can occasionally develop and cause difficulty on imaging.

Metastatic deposit in a cirrhotic liver – not suggested in this case where the lesion is clearly hepatocellular. Sometimes HCC is so poorly differentiated that it lacks any resemblance to hepatocytes. These often produce alpha fetoprotein – which may be raised in blood pre-operatively, or be demonstrable on immunohistochemistry – even an occasional positive cell is diagnostically useful. Alternatives are glypican 3, another oncofetal antigen, or arginase 1. If metastatic malignancy is a clinical possibility, then comparison with previous histology fo the primary is useful, together with a wider panel of immunos. In general, malignancy in cirrhosis is much more likely to be primary (hepatocellular or cholangiocarcinoma) than metastatic.