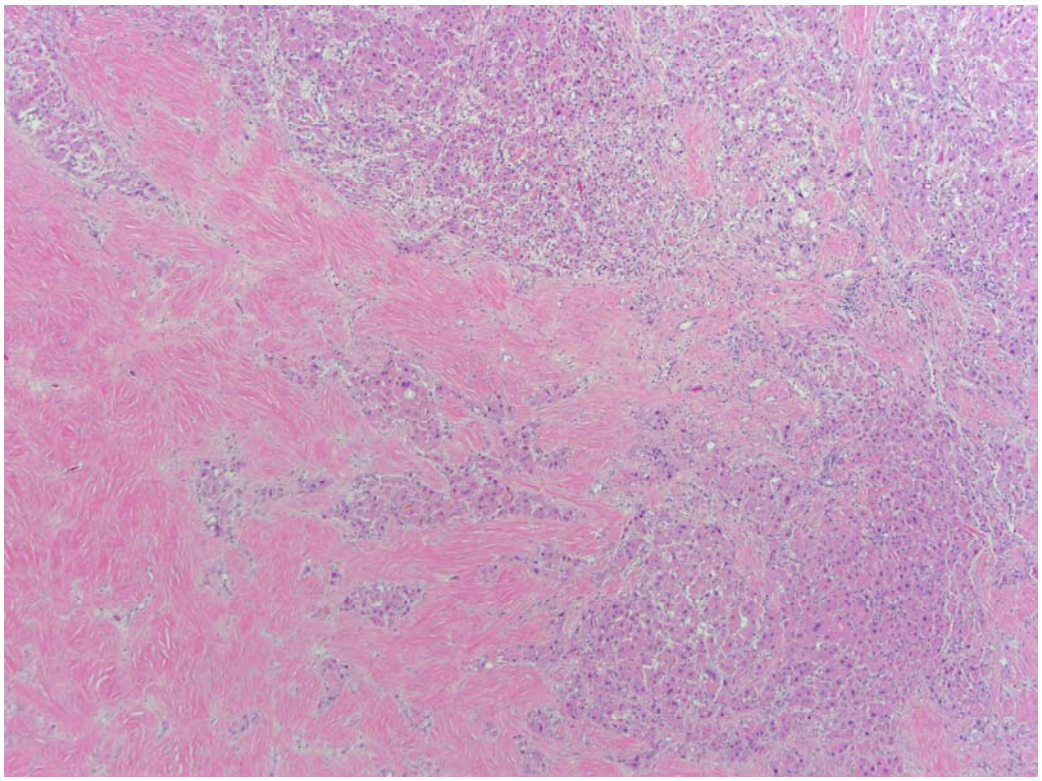
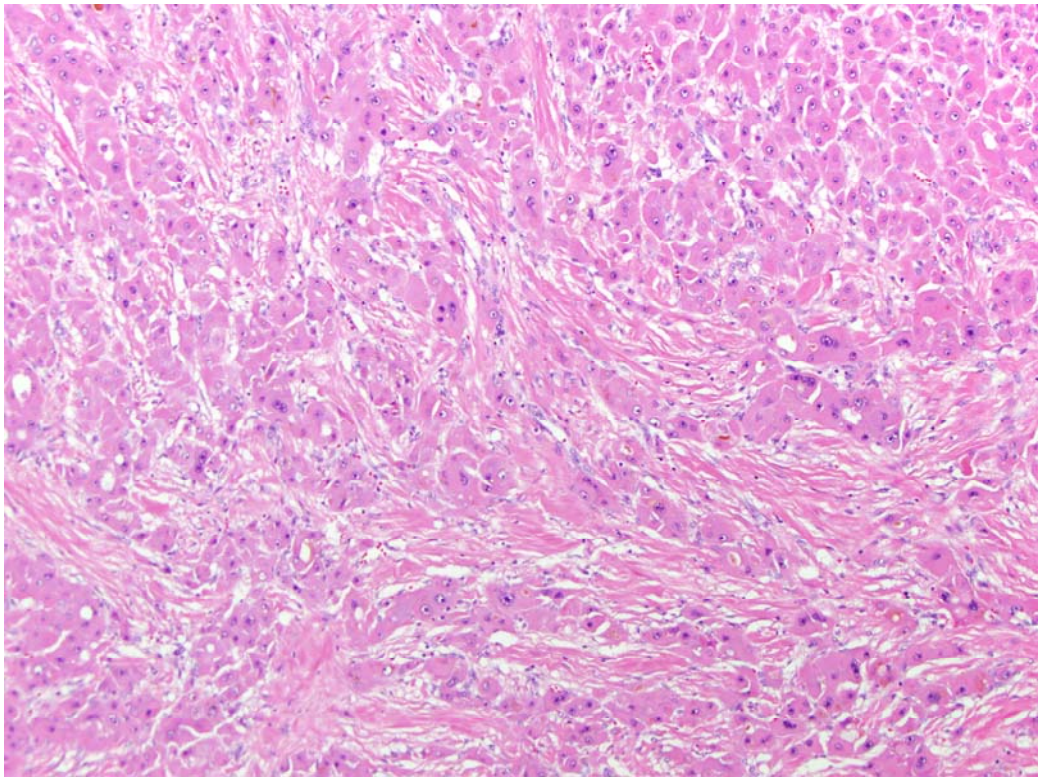
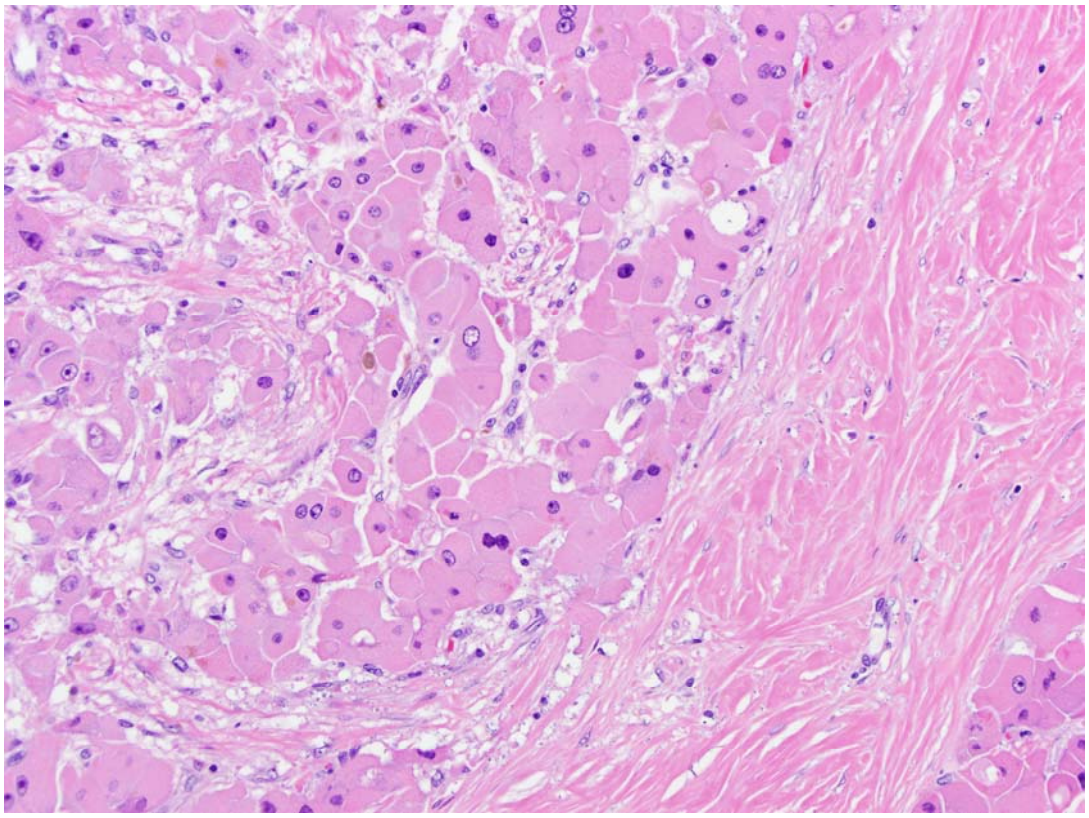
A 20 year old male with no history of previous liver disease undergoes resection for a 10 cm liver mass with a central scar, as depicted in the gross photo below. The hematoxylin and eosin stained sections are representative of the histology of the mass.



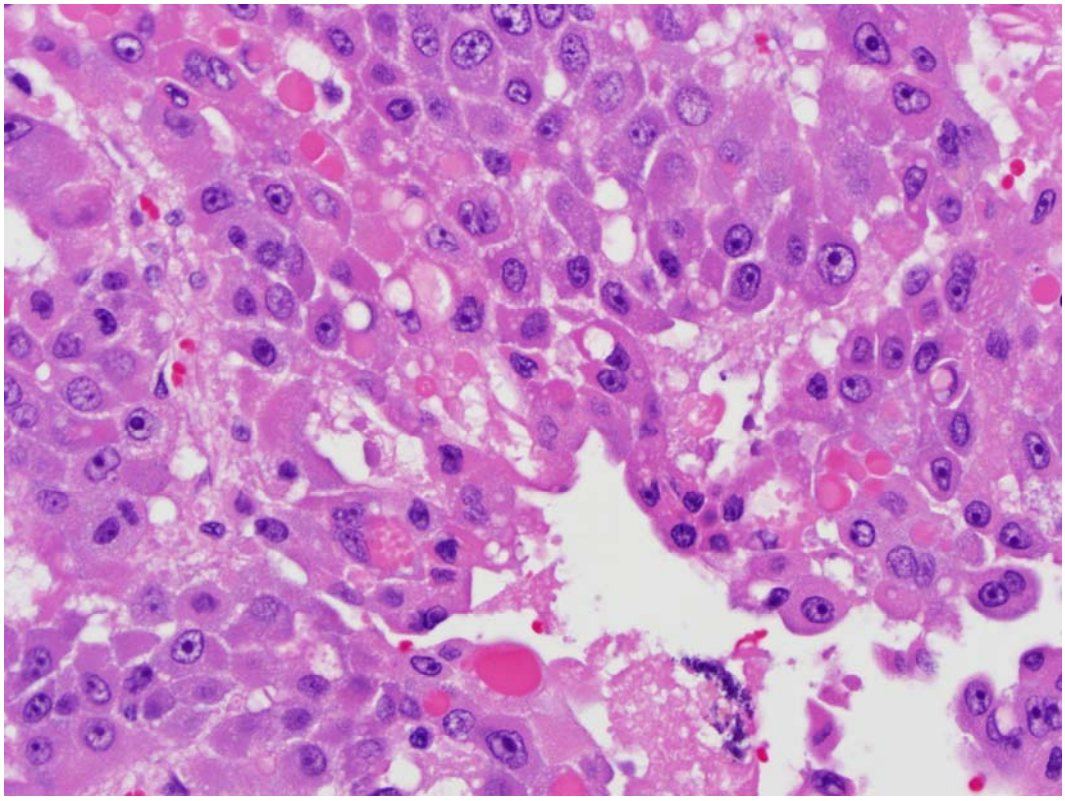
4x



10x

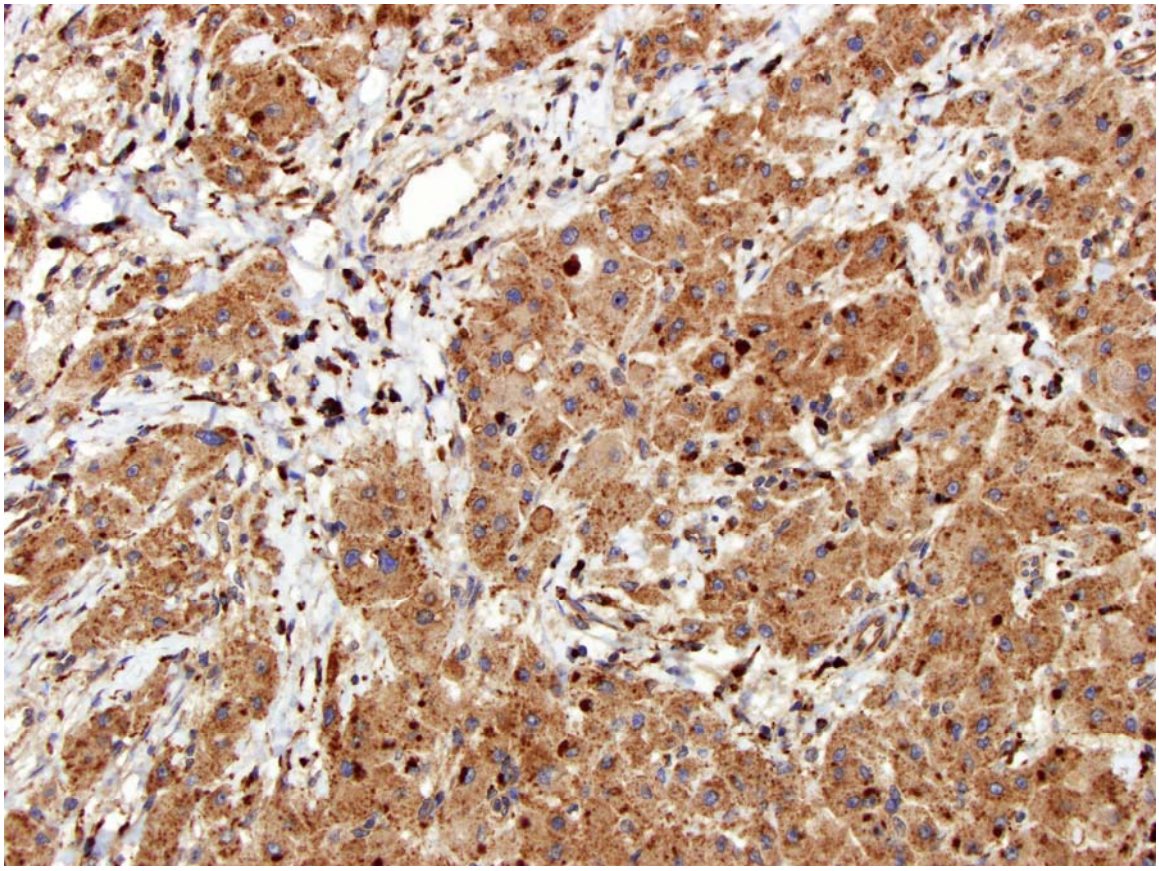


20 x



40 x

An immunostain is also provided for your review.



Which of the following represents this immunostain?

A. CD10
B. CD68
C. CD34
D. PAX-8
E. PSA

Answer:
B. CD68

Discussion:
The case describes fibrolamellar carcinoma (FLC). These are uncommon hepatic neoplasms that occur in young patients without underlying liver disease. Although the patients are often diagnosed with advanced disease, almost 70% can be resected and up to 70% of patients are alive after 5-10 years. Compared to typical HCC, FLC are usually larger and are more likely to metastasize to lymph nodes.

The provided gross photograph demonstrates the classic appearance of fibrolamellar carcinomas: a heterogeneous, tan, well-circumscribed mass with a central scar arising in a non-cirrhotic liver. The hematoxylin and eosin stained sections show the typical morphology of FLC: large polygonal neoplastic cells with abundant eosinophilic cytoplasm, large nuclei with prominent macronucleoli, and bands of fibrosis around cords of tumor cells. In many cases (approximately 70% as quoted in some papers) the dense fibrous bands coalesce to form the large central scar. Globular cytoplasmic inclusions and 'pale bodies' can be present (seen in the 5th photo labeled "40x"), which can represent alpha-1 antitrypsin globules or fibrinogen, respectively, but these are not exclusive to fibrolamellar carcinomas, and can also be seen in conventional hepatocellular carcinomas (HCC).

Choice B is correct. CD68 is a sensitive marker for FLC. In one study it showed a granular, dot-like, or stippled pattern of cytoplasmic staining in FLC (KP1 clone antibody of CD68 was used). It was positive in 96% (31 of 32) cases of fibrolamellar carcinomas, 25% of conventional HCC from non-cirrhotic livers, and 11% of HCC from cirrhotic livers. Hence, the study concluded that not only should special attention be placed on the distinctive morphology of fibrolamellar carcinomas, but the absence of CD68 immunoreactivity should cause one to reconsider the diagnosis of fibrolamellar carcinoma. Other immununoreactive markers for fibrolamellar carcinomas include cytokeratin 7, HepPar-1, and epithelial membrane antigen.

Choice A is incorrect. CD10 immunostaining usually highlights a membranous pattern in HCC, not cytoplasmic as seen in the provided photo.

Choice C is incorrect. CD34 can highlight the sinusoid-like vasculature around tumor cells in HCC, not cytoplasmic tumor cell staining.

Choices D and E are incorrect. PAX-8 and PSA do not stain HCC.

References:
Ross HM, et al. Fibrolamellar carcinomas are positive for CD68. Mod Pathol. 2011 Mar;24(3): 390-395.

Ang CS, et al. Clinicopathologic characteristics and survival outcomes of patients with fibrolamellar carcinoma: data from the fibrolamellar carcinoma consortium. Gastrointest Cancer Res. 2013 Jan;6(1):3-9.

Liu S, et al. Fibrolamellar hepatocellular carcinoma. Am J Gastroenterol. 2009; 104:2617-2624.

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