16- SS - 5

Male, 38 ys.old

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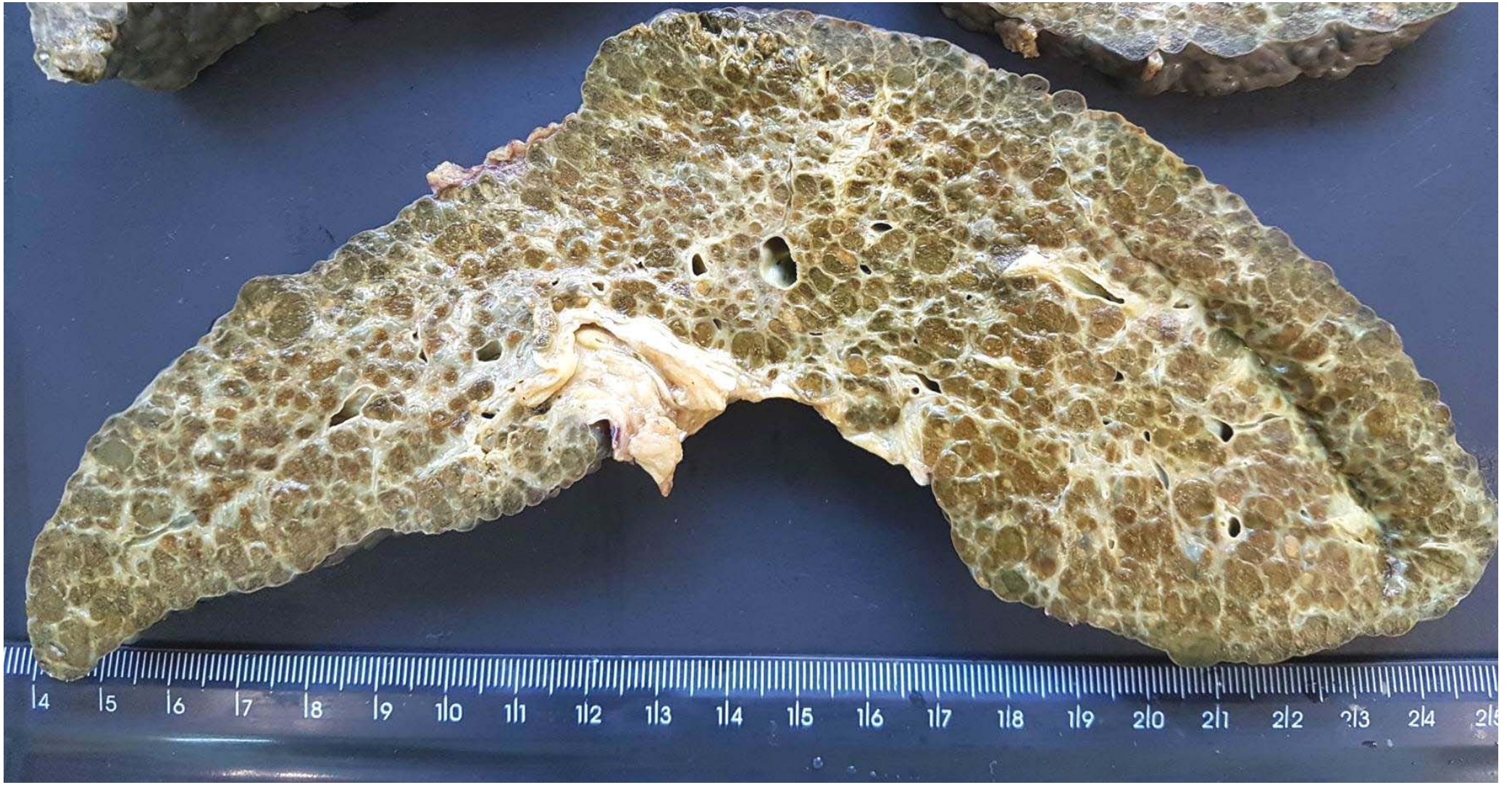
- **July 08 – LIVER TRANSPLANTATION :**
  sp1A = random area
  sp1B= macronodule, 1.0 cm, green, at segment IV

- **July 09 = Died due to shock**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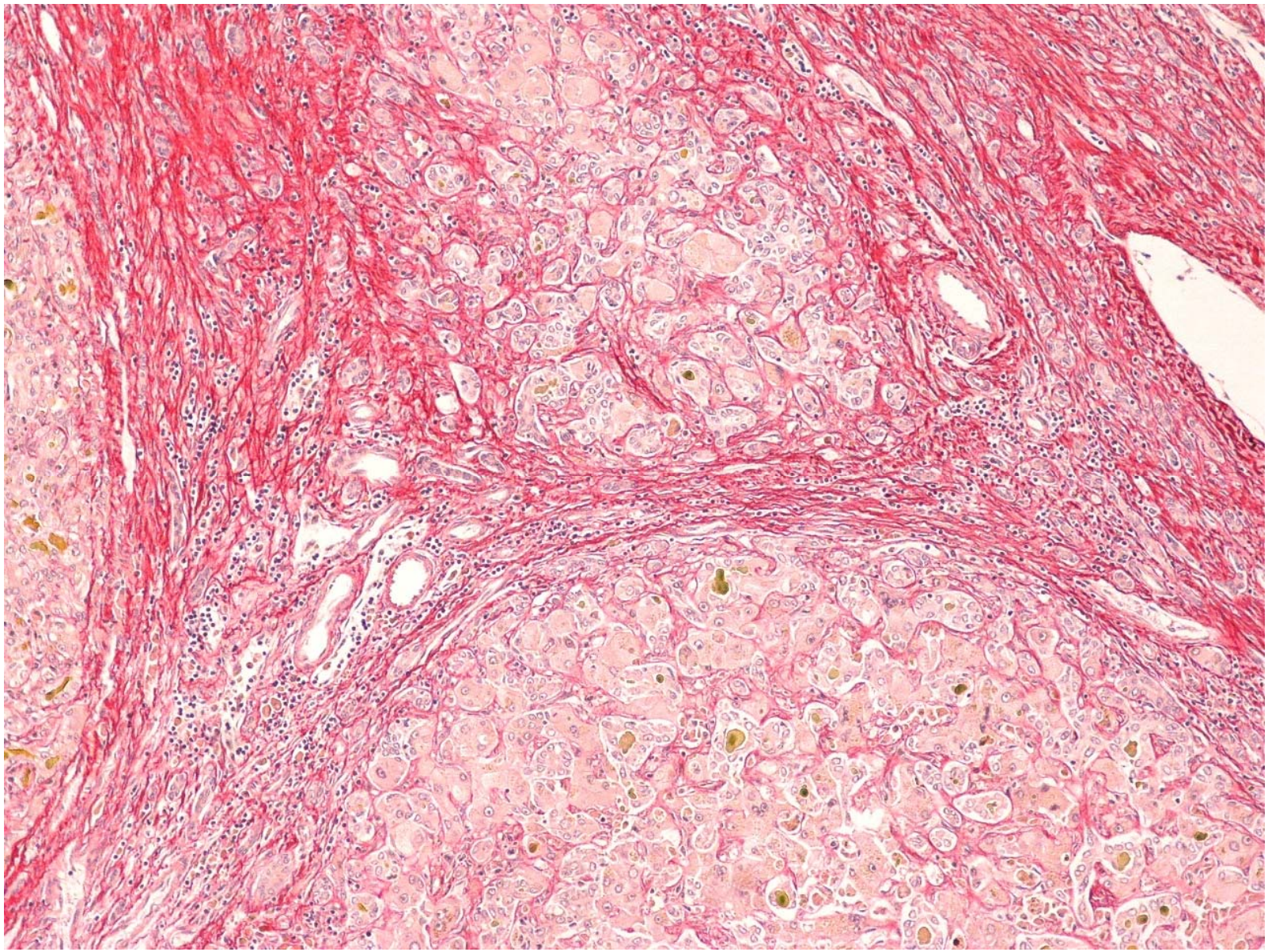
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT



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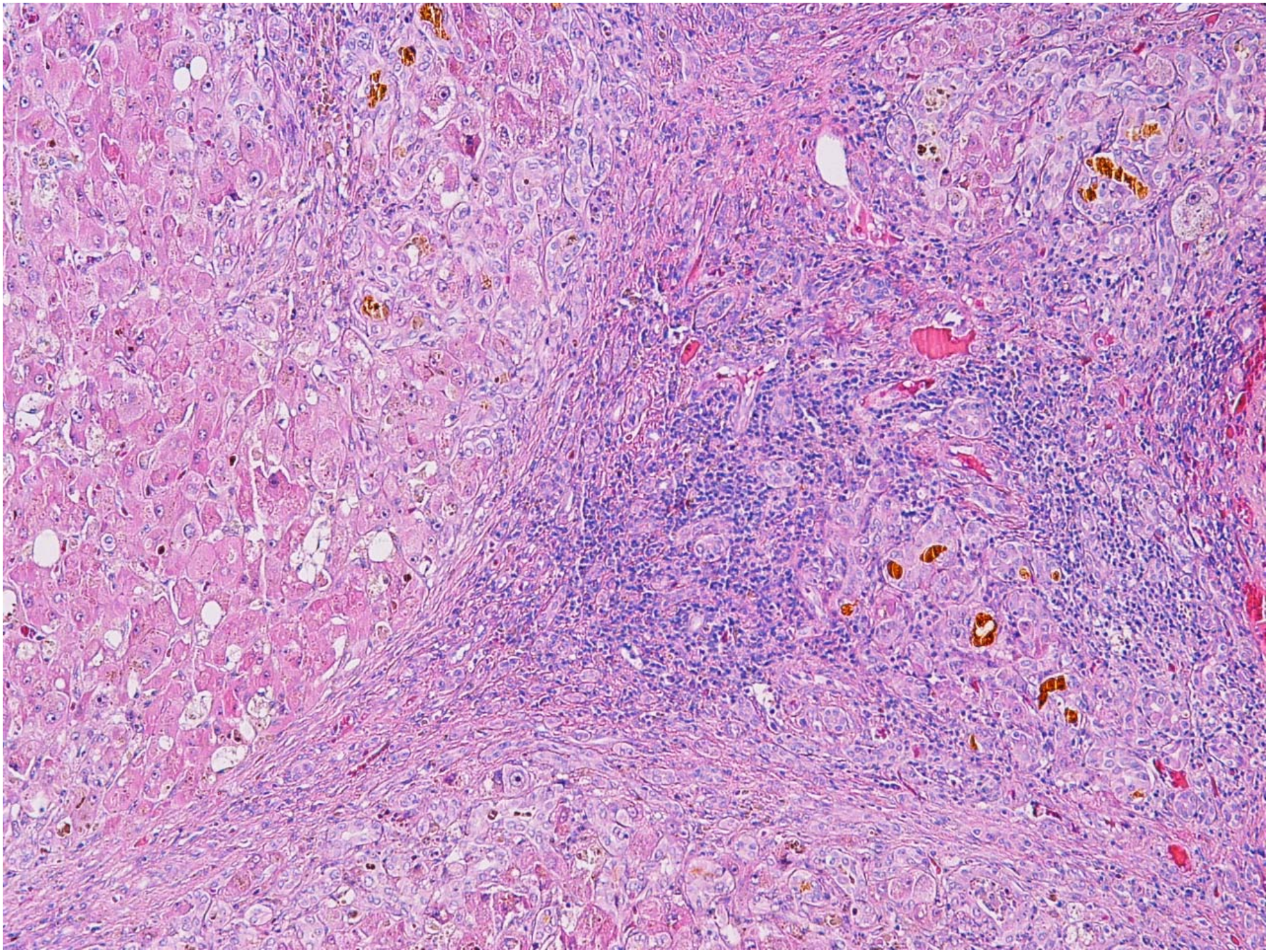

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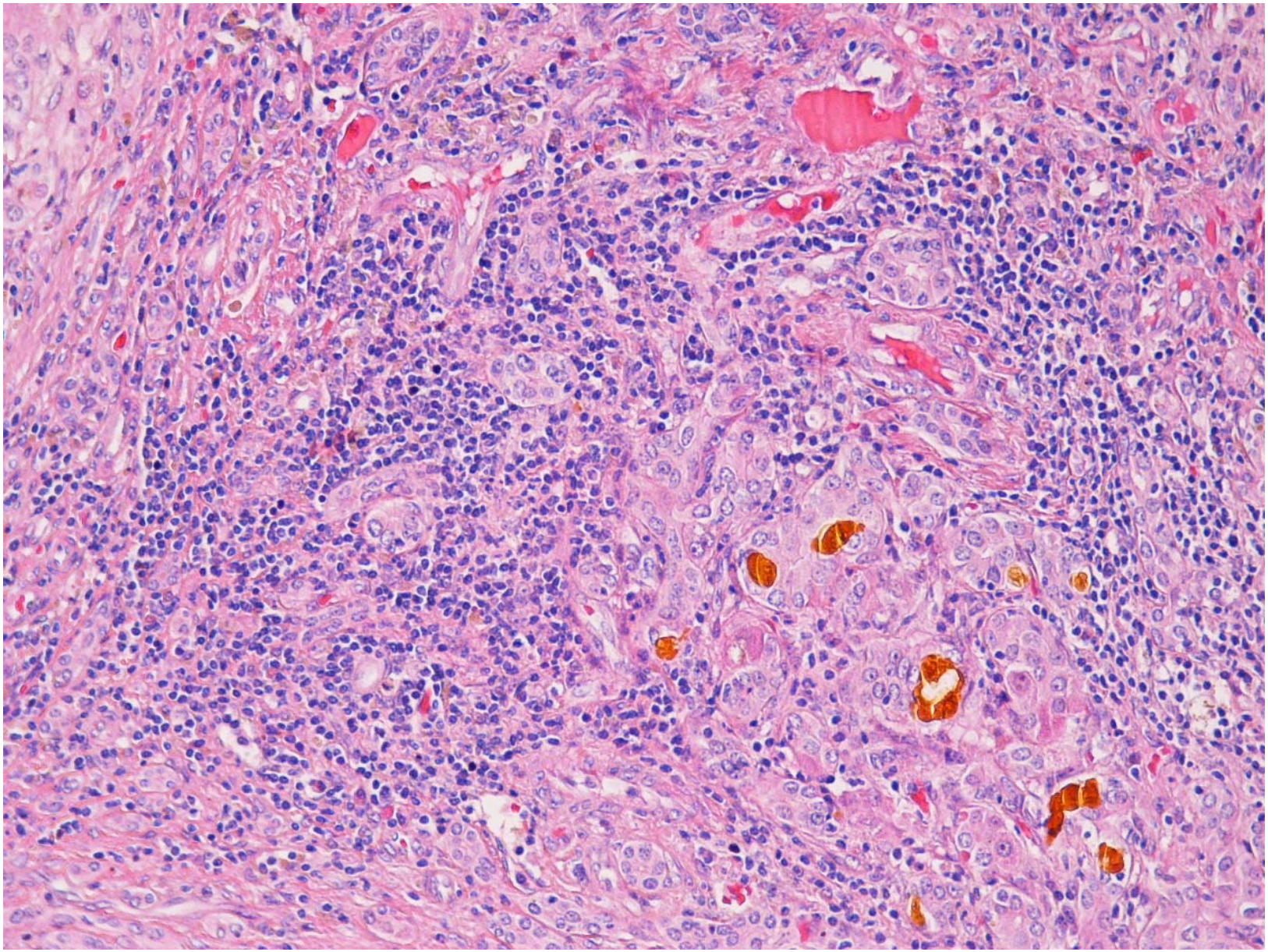
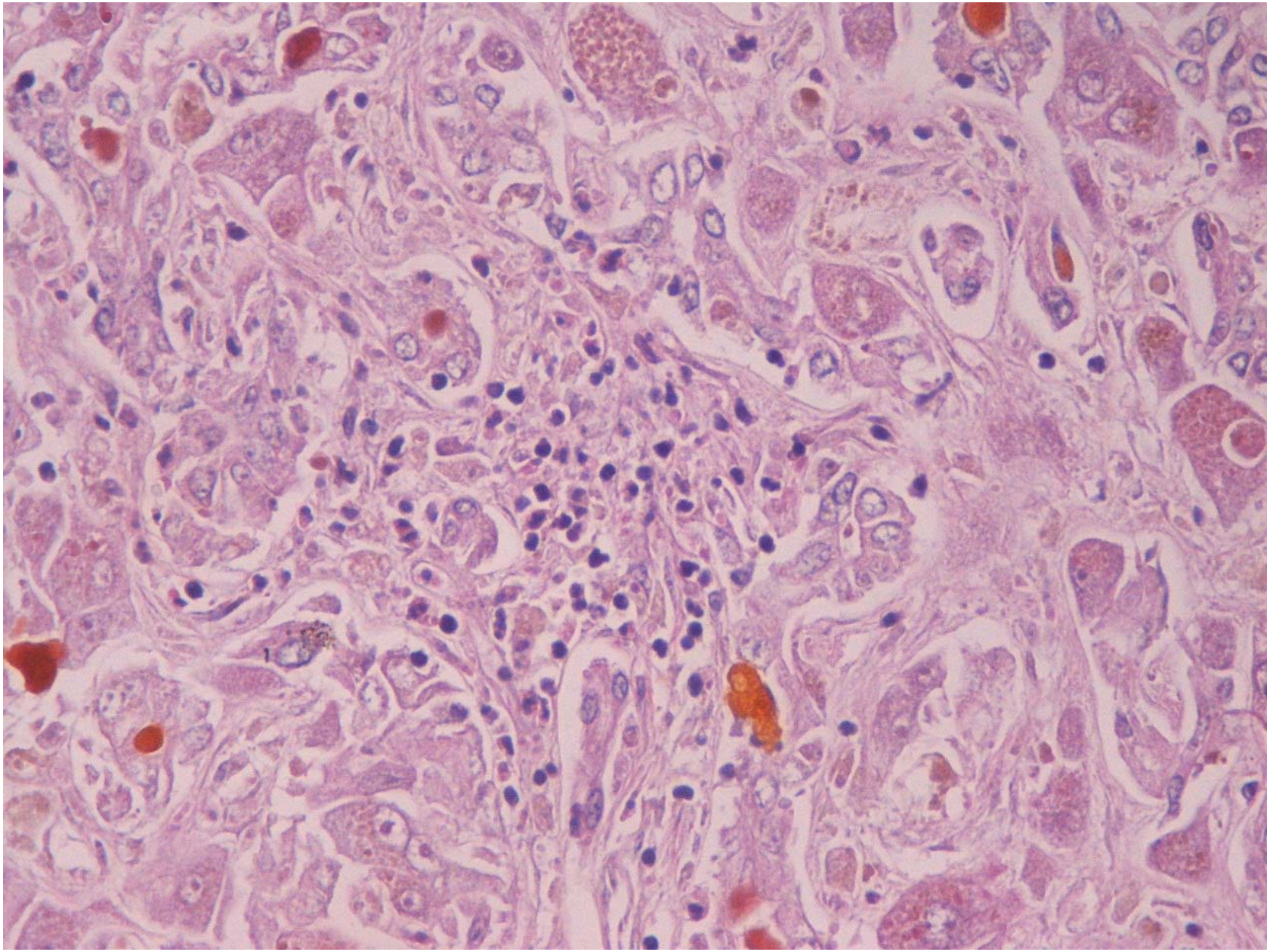
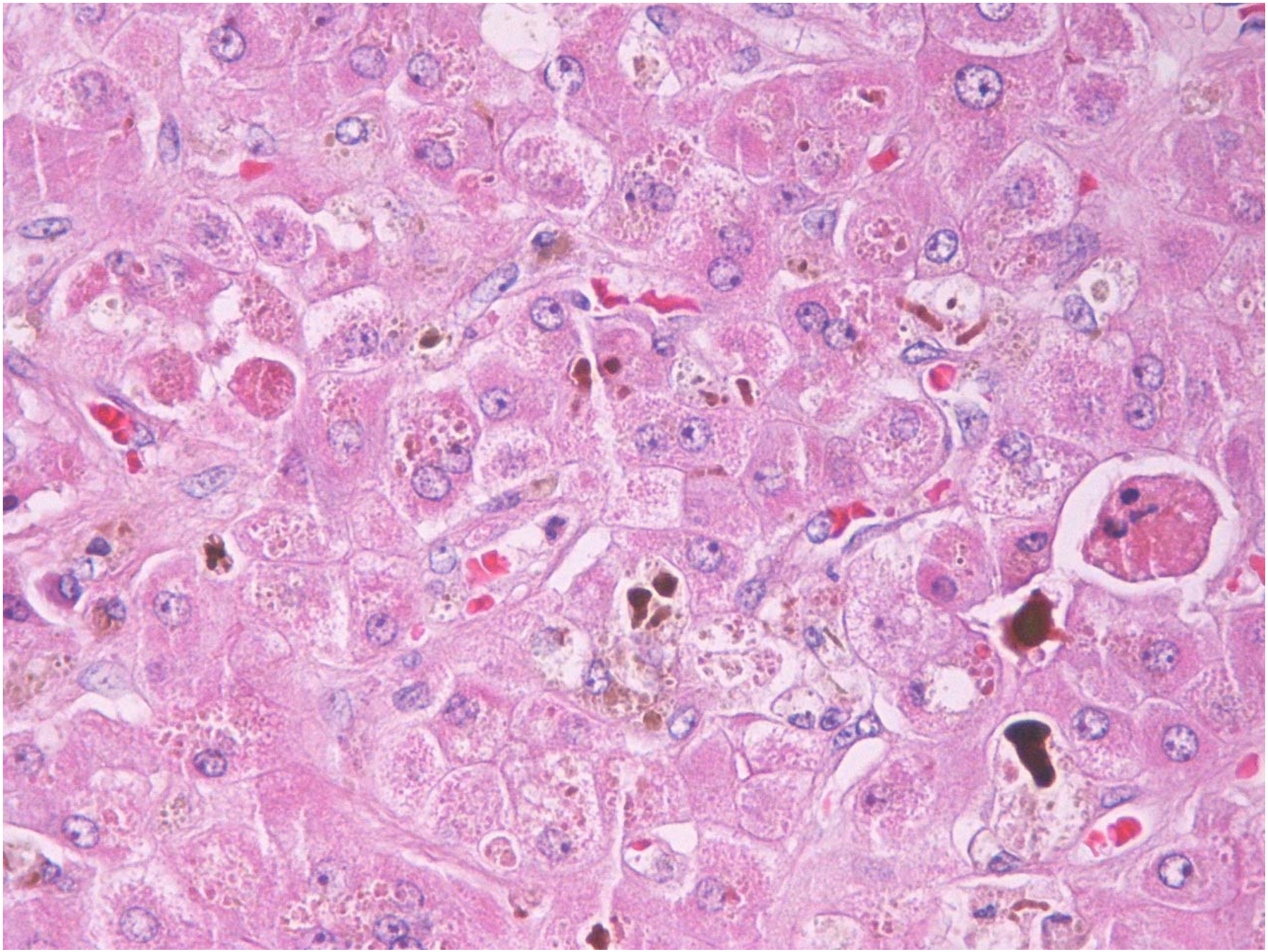


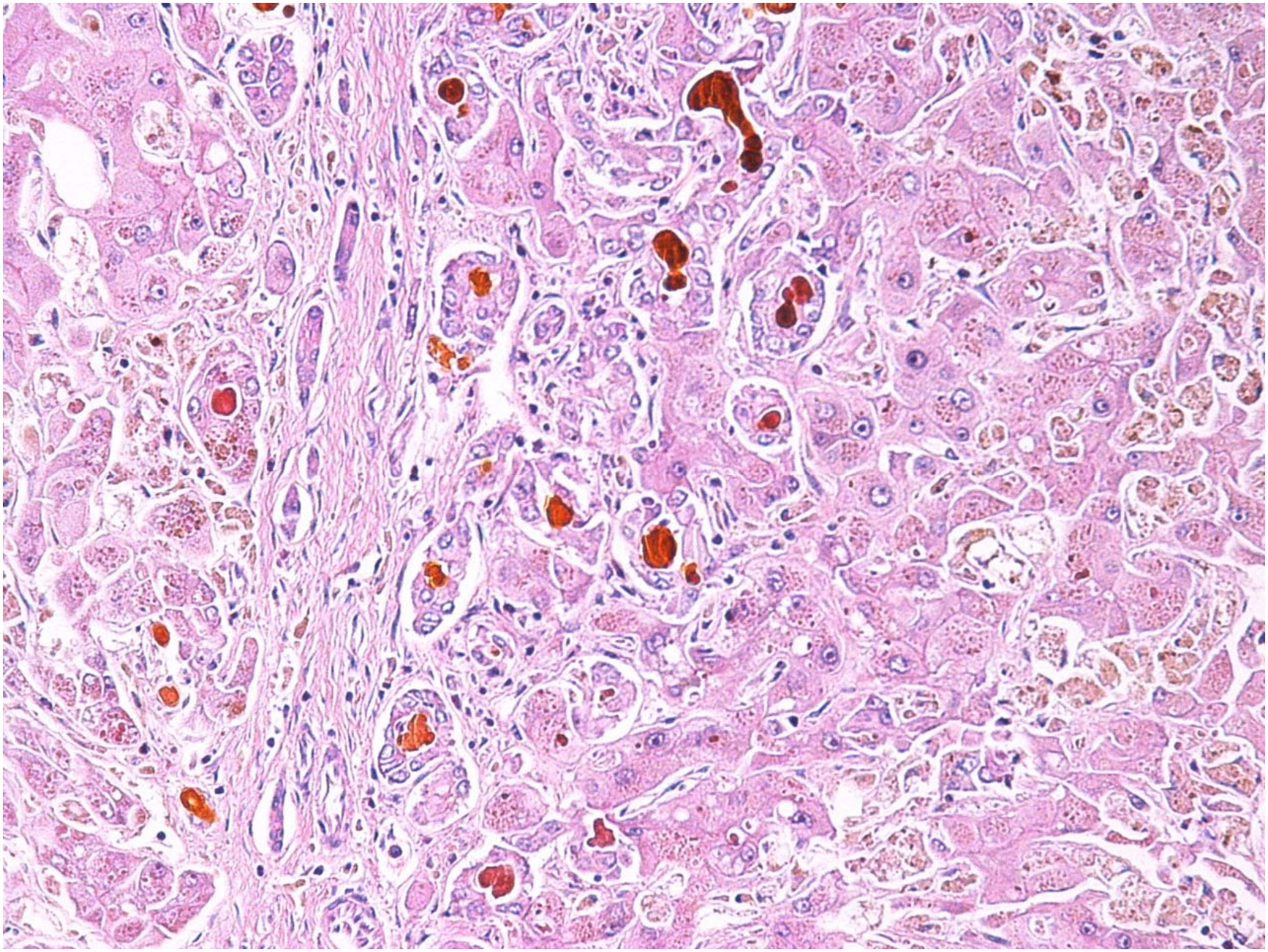
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT



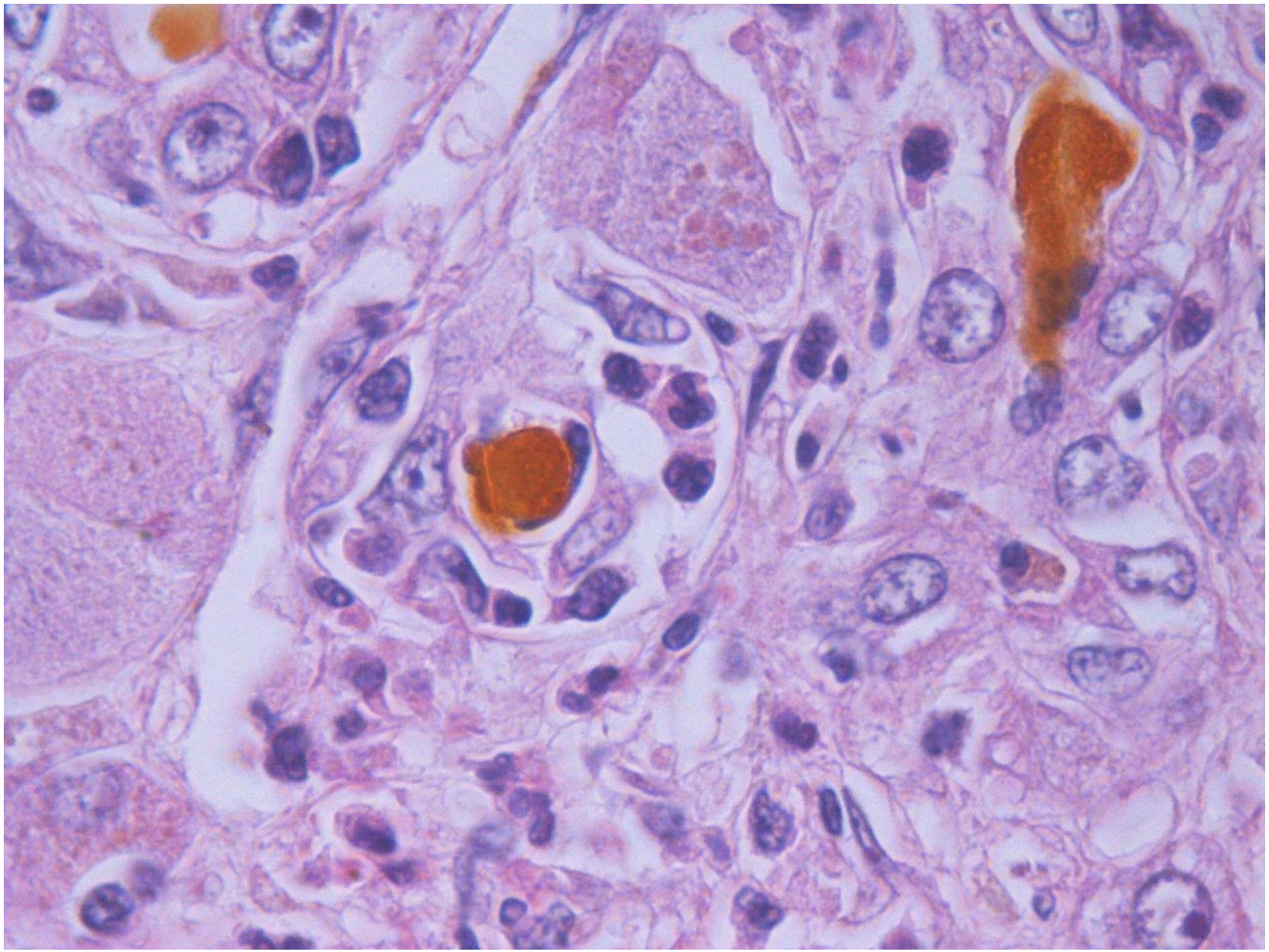
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT



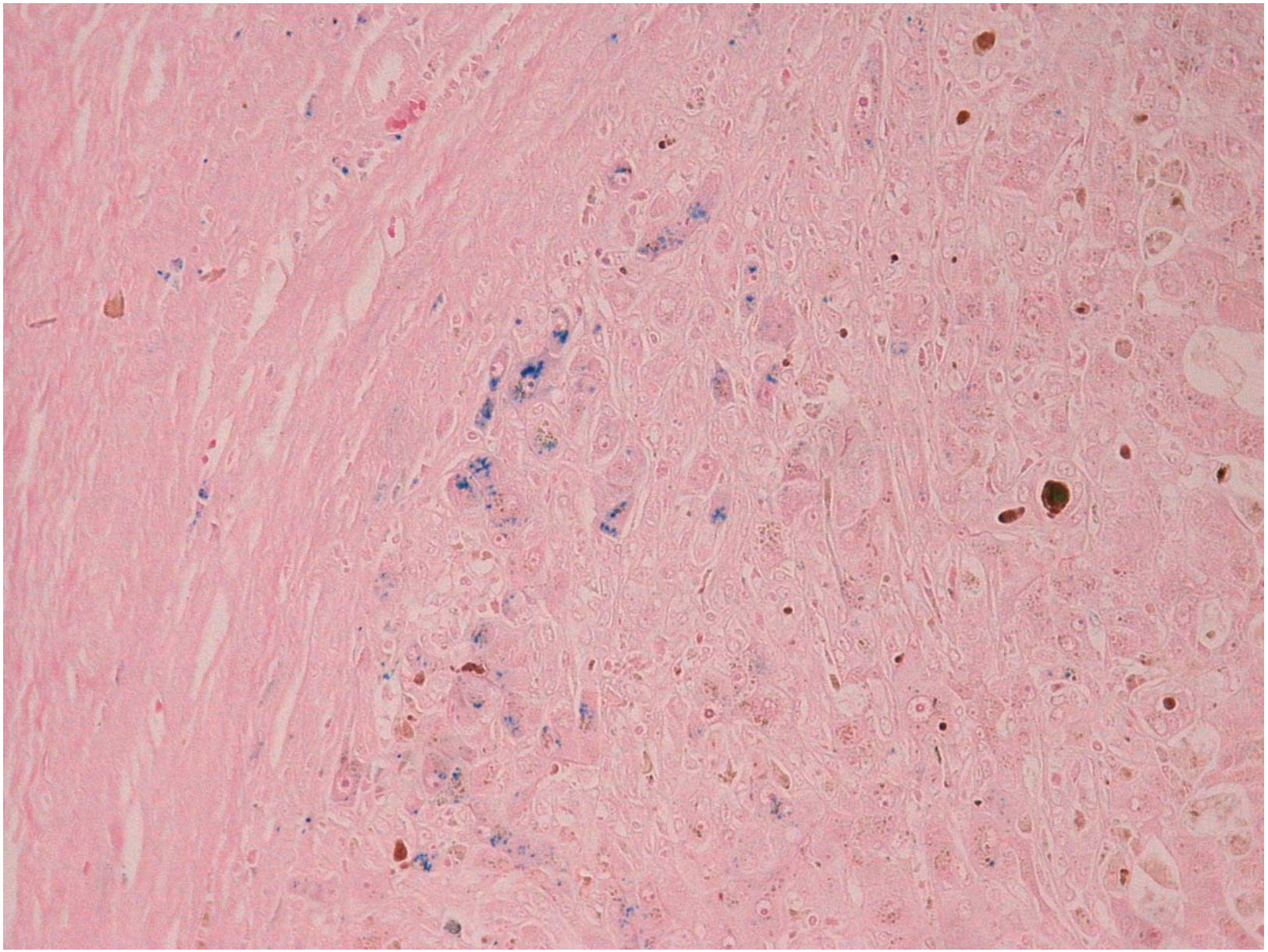
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT



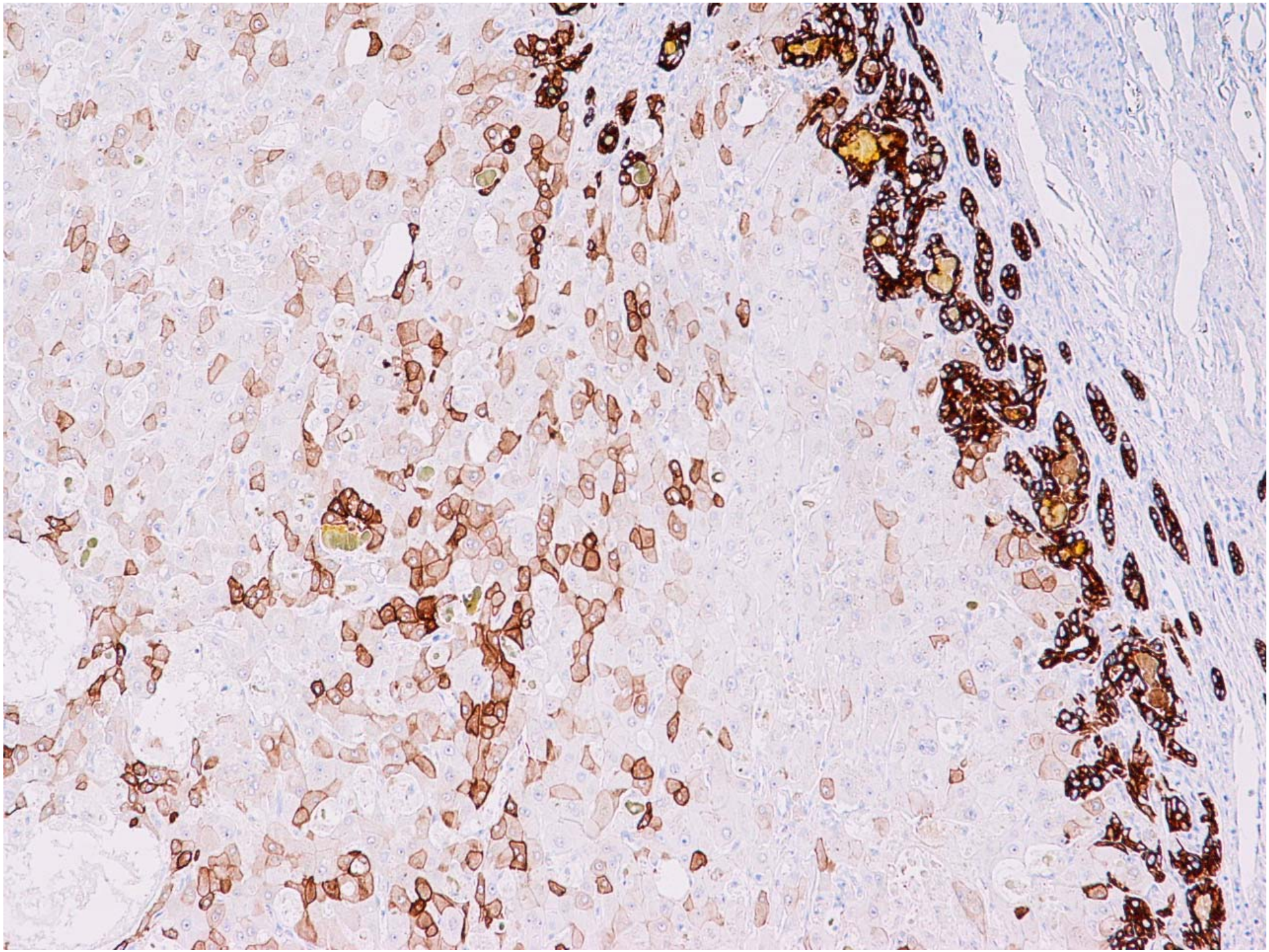
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT



Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

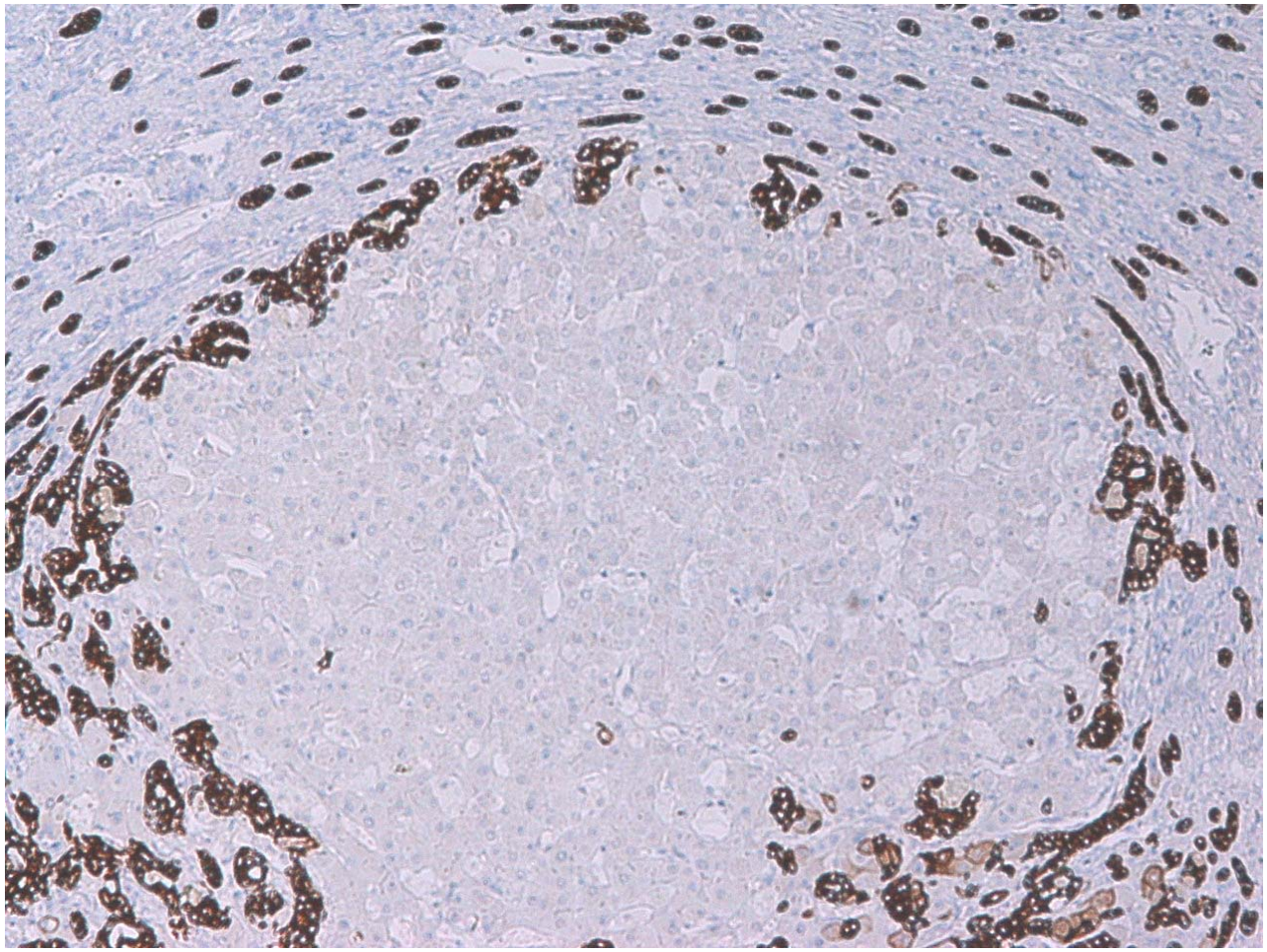


Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT **K7**



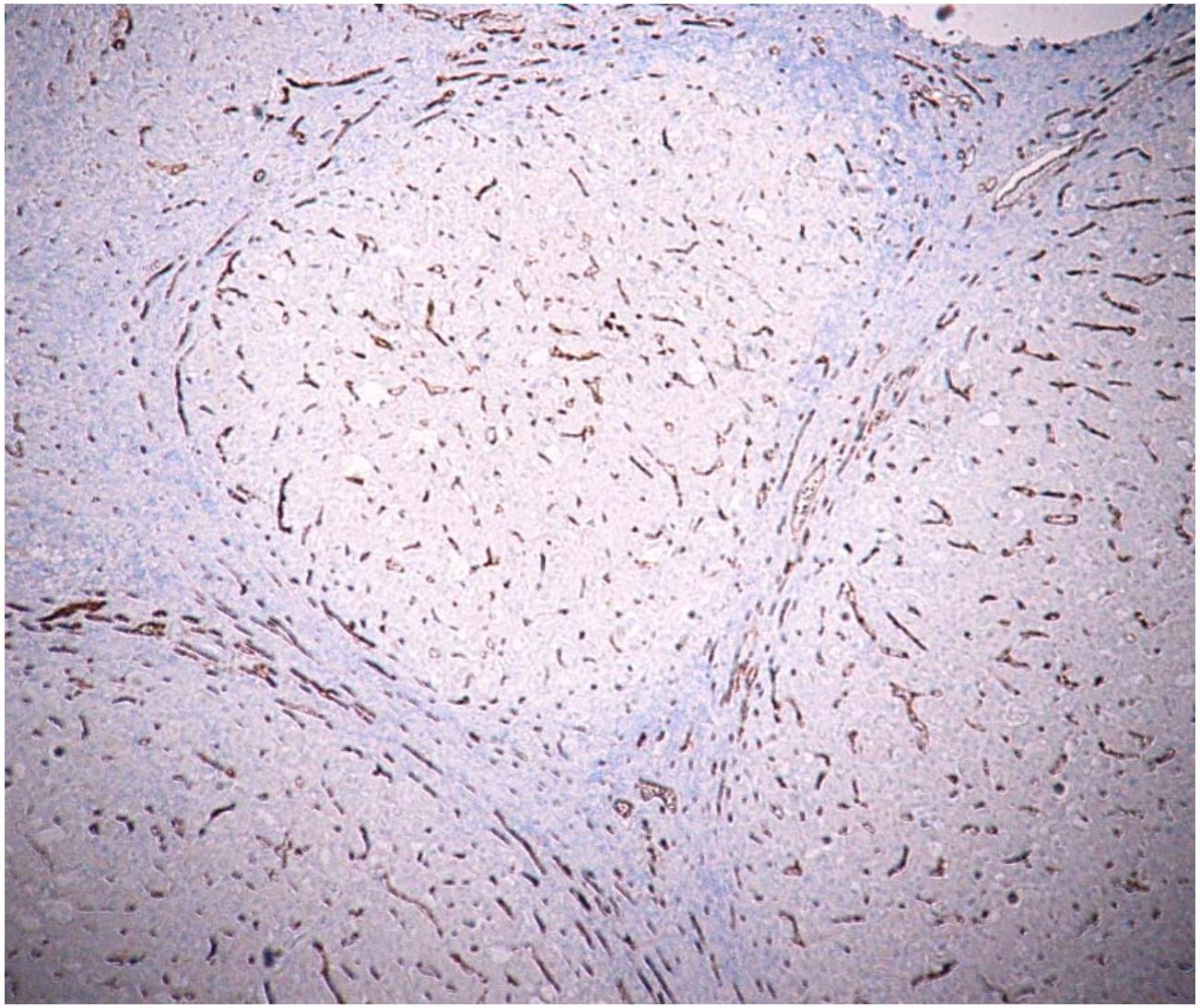
Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

K 19

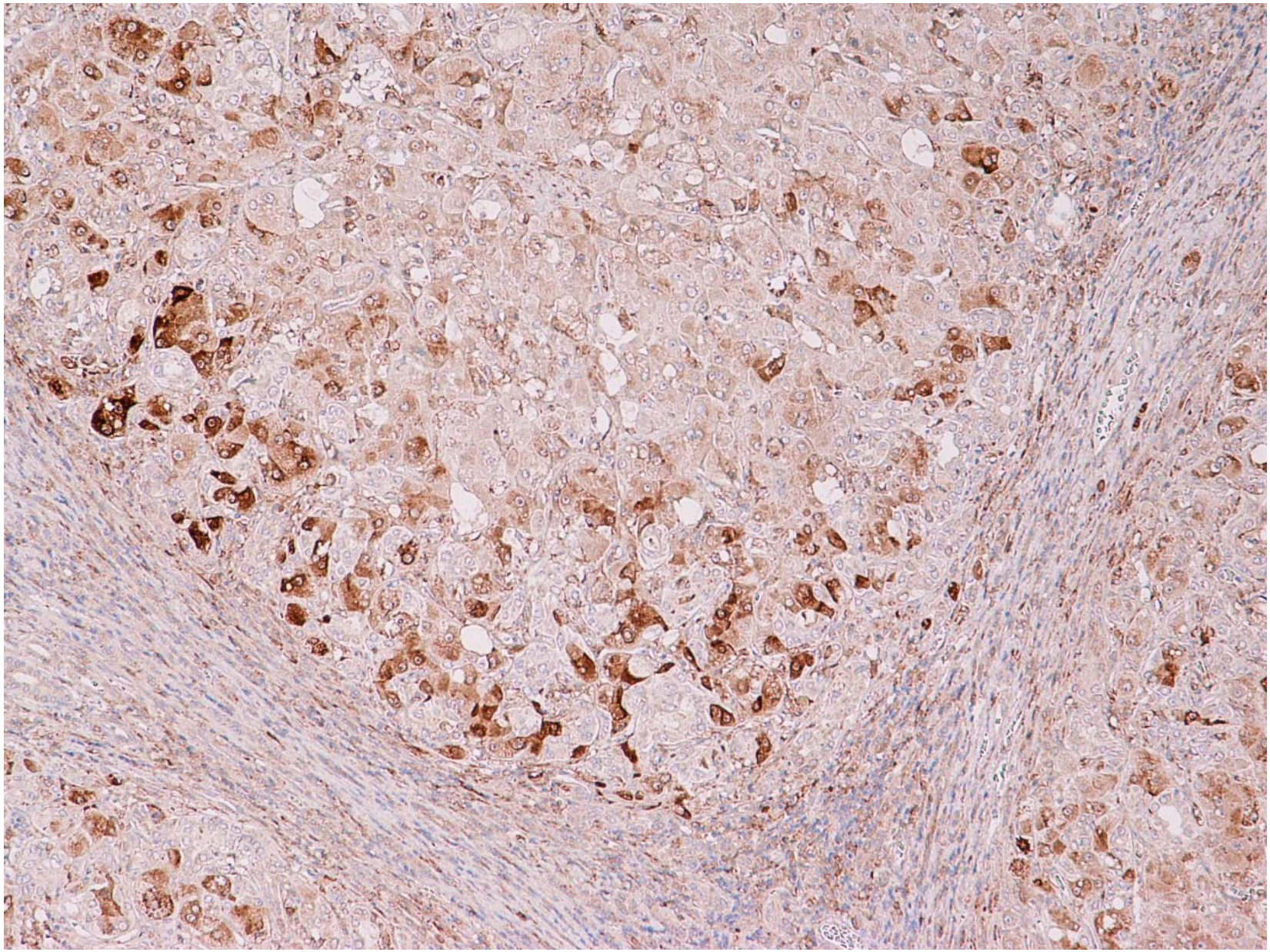


Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

CD34

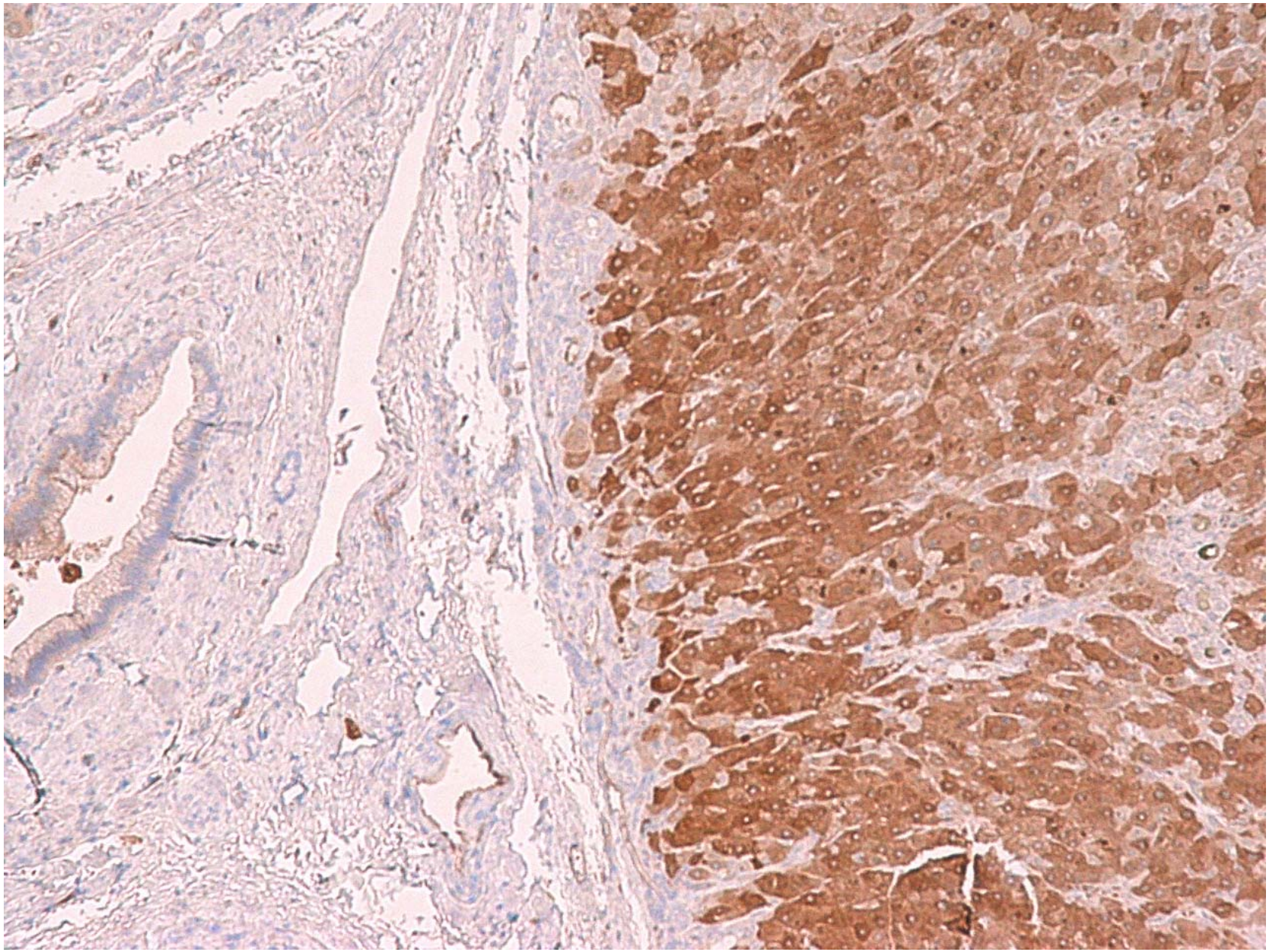


Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT
Glutamine-synthase



Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

Arginin-Succinate-Synthase -ASS-1



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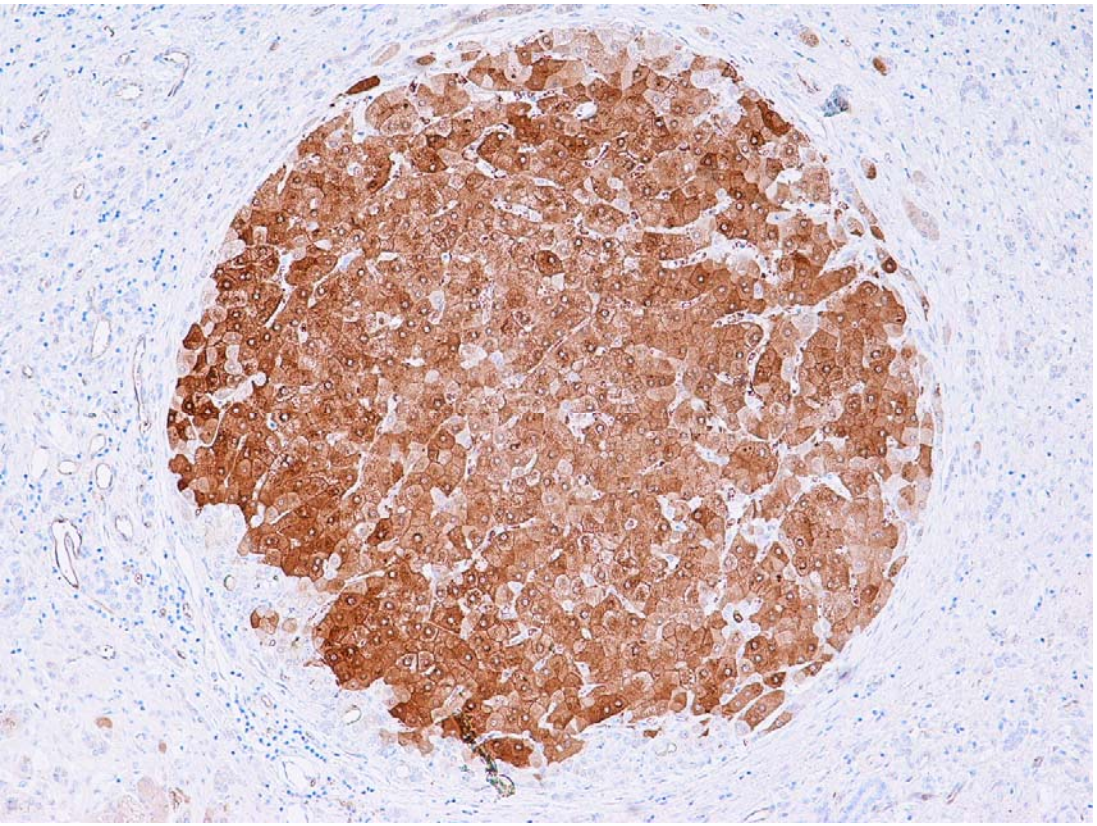
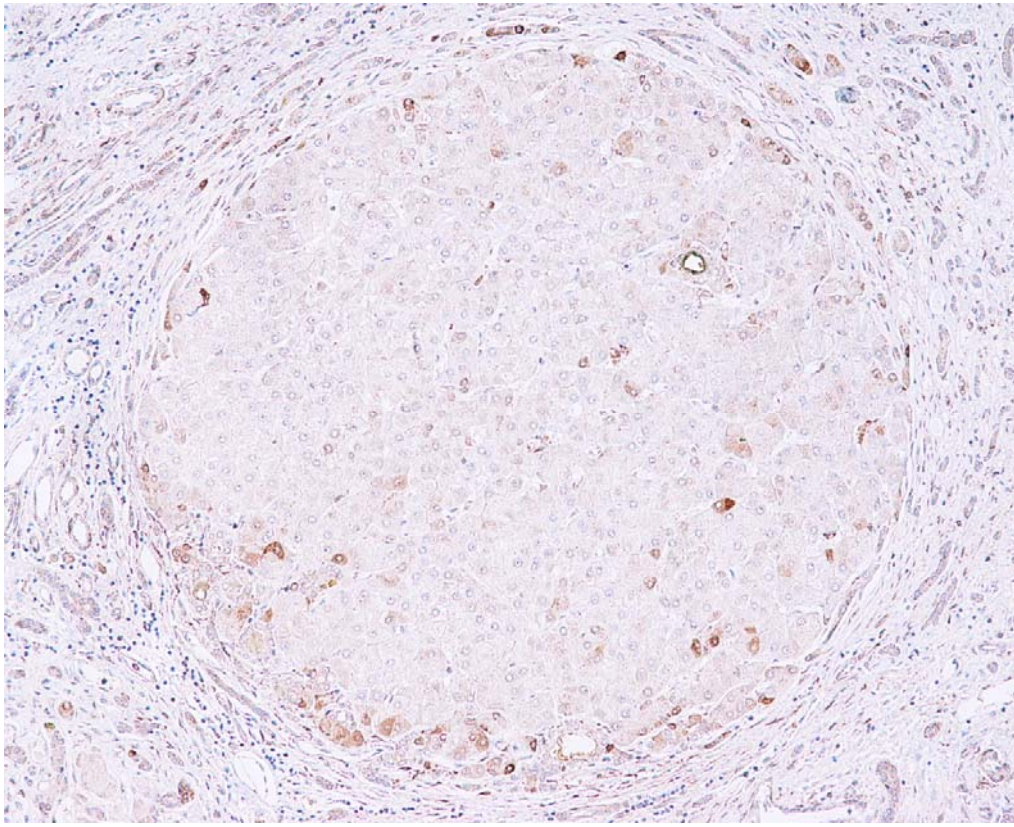
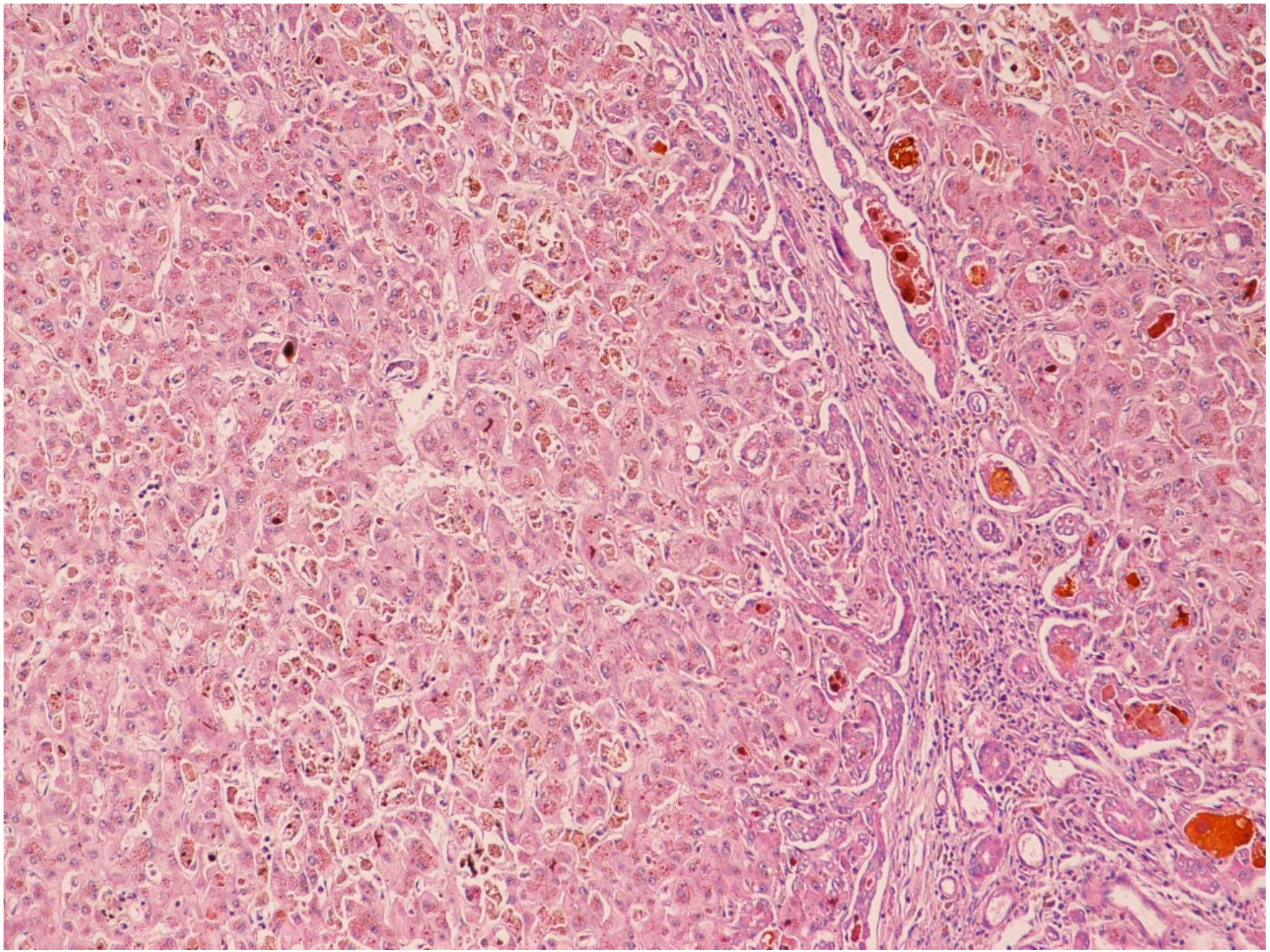
ASS-1



GLUT-SYNT



MACRONODULE AT EXPLANT



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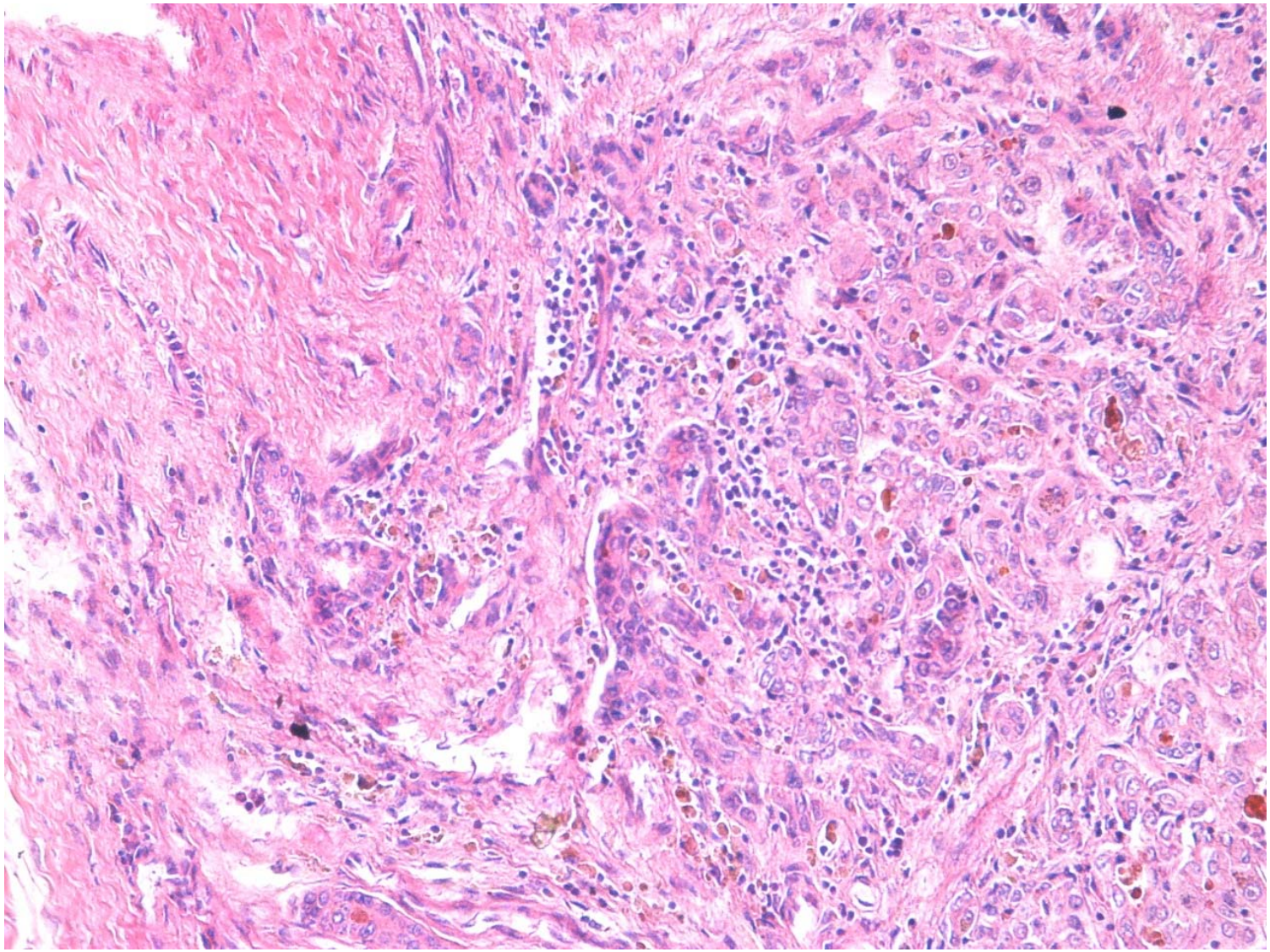

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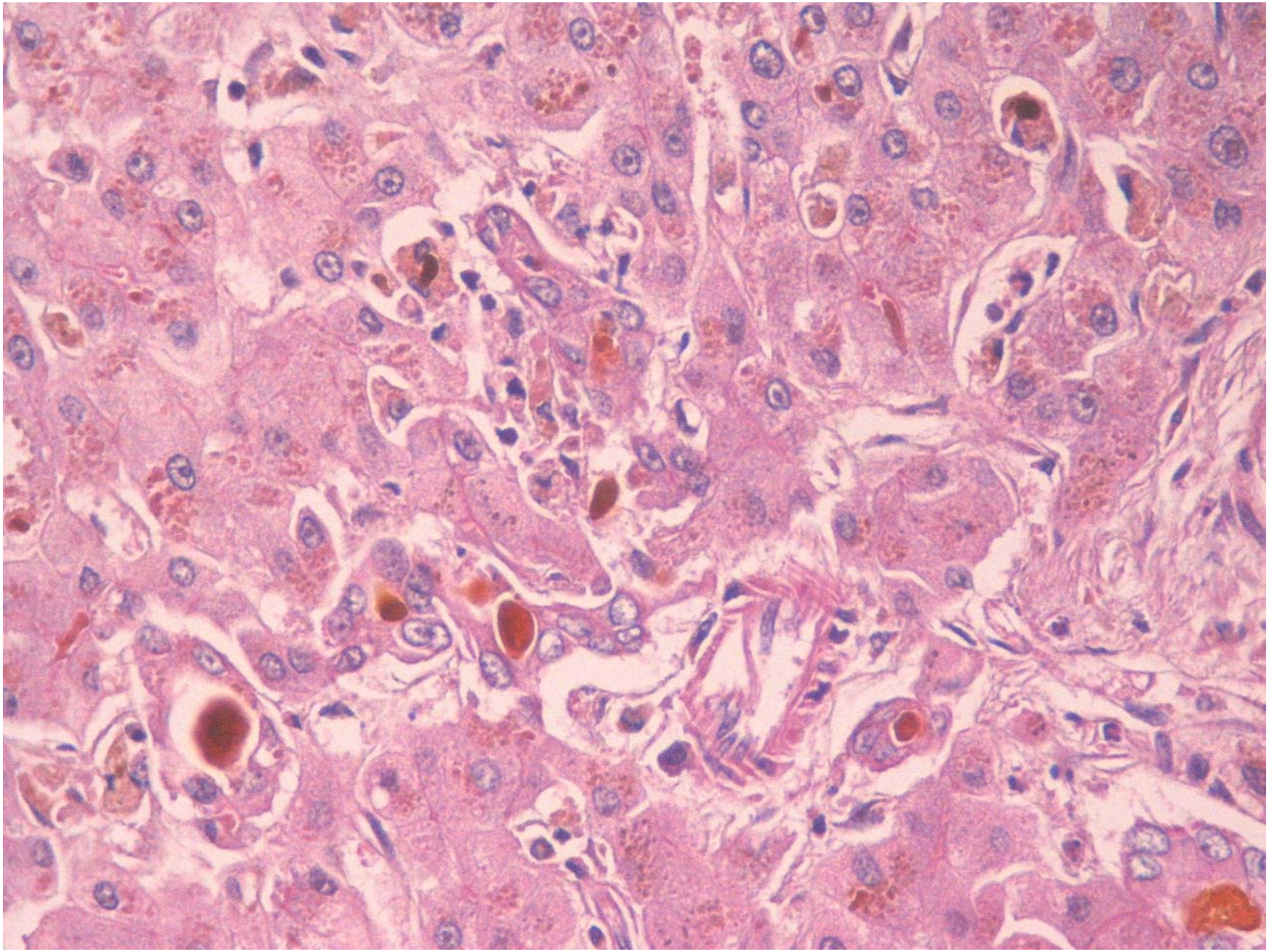
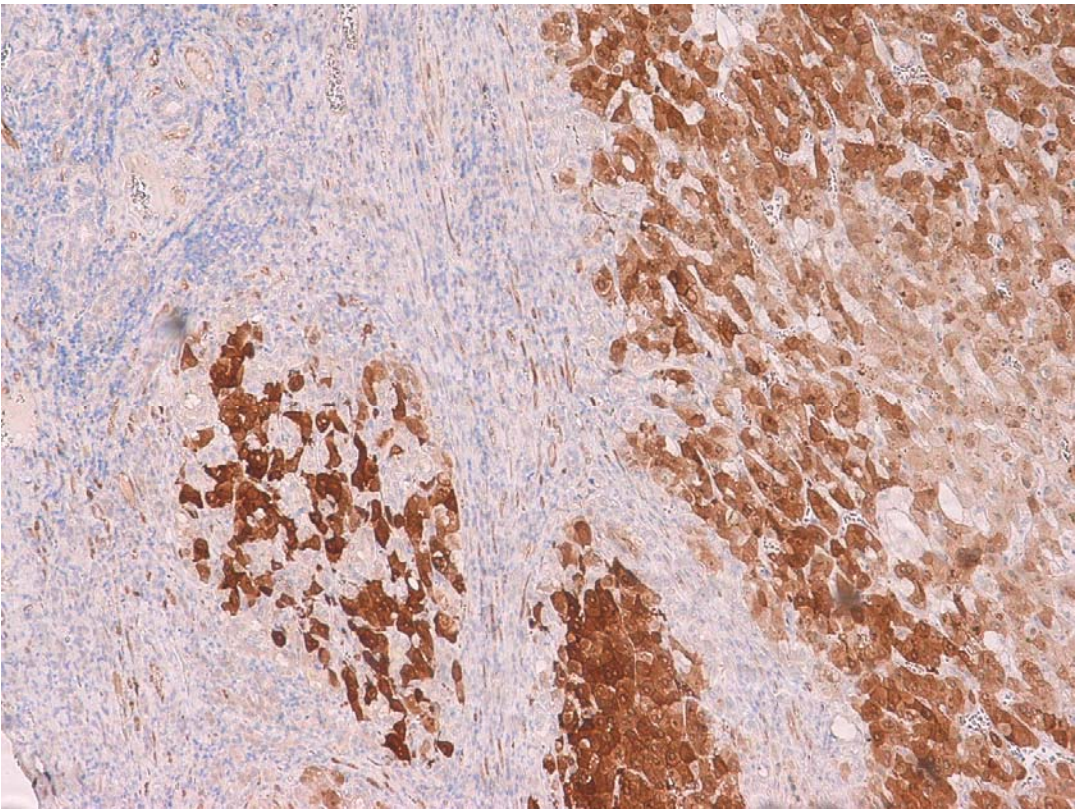
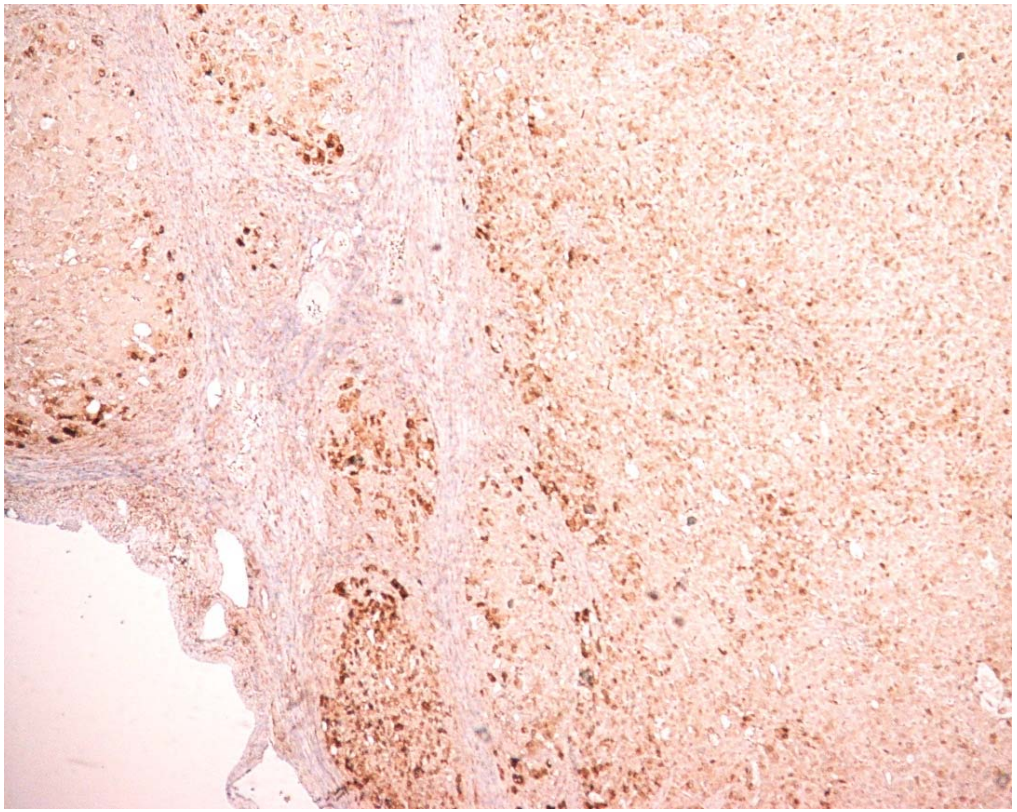


MACRONODULE AT EXPLANT

ASS-1



Glut-Synth



Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

CONCLUSION

Advanced cirrhosis (4C)(Hepatitis C pattern prevailed)
High septal angiogenesis and parenchymal vessel dilatation,
“moderate chronic hepatitic type activity”
High ACLF-Type activity” (High ductular reaction; High ductular cholestasis and inflammation ; confluent hepatic necrosis)
(Type 1- severe – Rastogi et al, 2011)

ACLF-related lesions especially intense in the Macro-Regenerative Nodule measuring 1.0 cm in segment IV.

16- SS - 5

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Rastogi A... Liver histology as predictor of outcome in patients with acute-on-chronic liver failure (ACLF) Virchows Arch (2011) 459:121–127

Univariate analysis of correlation of liver histology with outcome in patients of ACLF

Liver histology variable	Good outcome (n=25)	Poor outcome (n=25)	P value
HAI (index≥6)	17 (68%)	19 (76%)	0.754
Fibrosis (stage≥3)	14 (56%)	25 (100%)	<0.001
Ballooning (score, 2–3)	22 (88%)	6 (24%)	<0.001
Eosinophilic degeneration (score, 2–3)	0 (0%)	15 (60%)	<0.001
Rosettes (score, 2–3)	10 (40%)	8 (32%)	0.769
Ductular proliferation (score, 2–3)	4 (16%)	22 (88%)	<0.001
Pericellular fibrosis (score, 2–3)	0 (0%)	18 (72%)	<0.001
Cholangiolitis (score, 2–3)	4 (16%)	9 (36%)	0.196
Mallory's hyaline (score, 2–3)	0 (0%)	6 (24%)	0.022
Foci of CN/BN (score, 2–3)	0 (0%)	9 (36%)	0.002
Cholestasis (types, 2–3)	13 (52%)	24 (96%)	0.001
Apoptosis (present)	17 (68%)	24 (96%)	0.023
Parenchyma left (≥50%)	24 (96%)	12 (48%)	<0.001
Fatty change (≥30%)	0 (0%)	2 (8%)	0.490

Lefkowitch J - **CHOLANGITIS LENTA in SEPSIS**

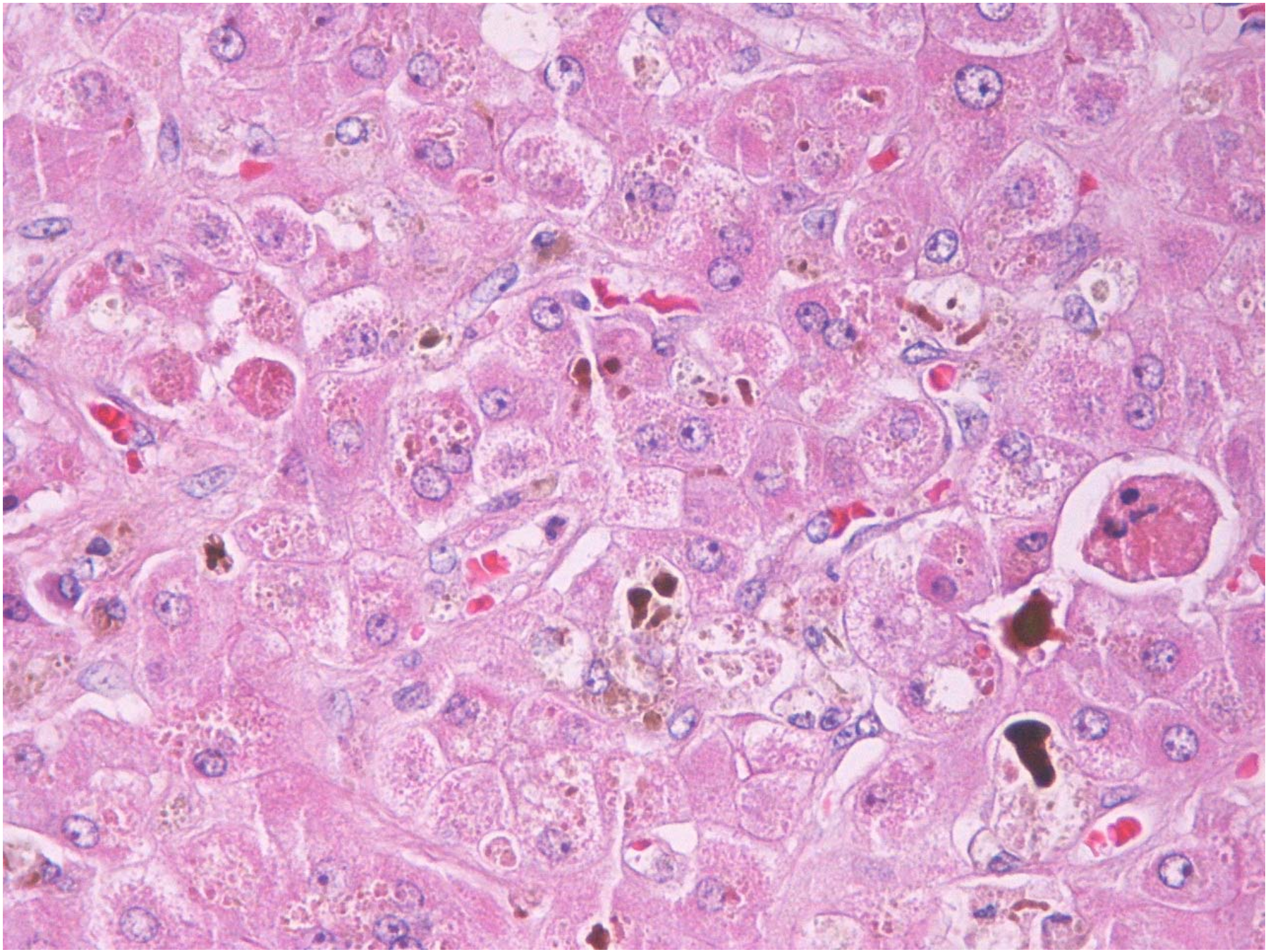
Scheuer´s Liver Biopsy Interpretation, 2010,pg 57:

"Septicaemia uncommonly is associated with a particular form of histological cholangitis **principally affecting the canals of Hering . Affected ductules are dilated and filled with inspissated bile.**
Neutrophils acccumulate around and sometimes within them. Larger ducts may be affected, as may the periportal parenchyma in which bile is seen
in dilated bile canaliculi**.** Theses changes are easily confused with those of large bile-duct obstruction, **but in obstruction the inspissated bile in the canals of Hering is not a feature, unless there is concomitant sepsis. Sepsis more often gives rise to widesperad canalicular cholestasis...**

Lefkowitch JH. **Bile ductular cholestasis: an ominous histopathologic sign related to sepsis and "cholangitis lenta".** Hum Pathol. 1982;13:19-24.

An unusual form of intrahepatic cholestasis manifested by **inspissated bile within dilated and proliferated portal and periportal bile ductules** was seen in liver biopsy and autopsy specimens from three patients. **Features of sepsis and severe systemic illness with jaundice** dominated their clinical presentations, and no autopsy evidence of large bile duct obstruction could be found. This lesion may be related to the old entity, "cholangitis lenta," a form of chronic sepsis associated with biliary tract inflammation in the absence of demonstrable extrinsic obstruction.
Identification of this pattern of cholestasis in liver biopsy specimens is useful in certain patients who may be a great risk of mortality and who require serious clinical attention directed toward elucidating a source for sepsis as well as aggressive management of other systemic disease.

Male, 38 ys.old. Obese , Diabetic,HCV + NASH = EXPLANT

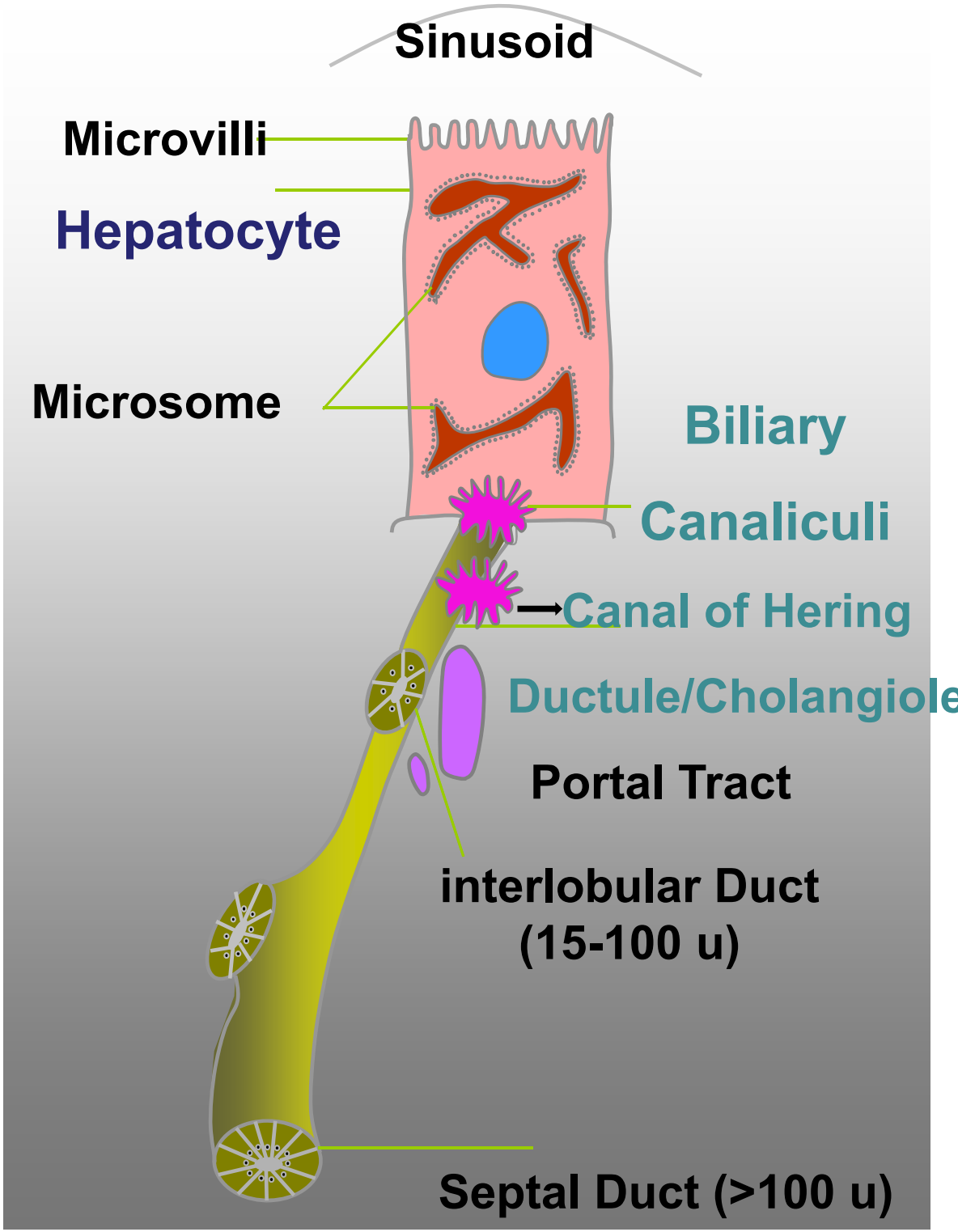


INTRA-HEPATIC

BILIARY SYSTEM

Biliary Canaliculi
Canals of Hering (CoH)
Biliary Ductules (Cholangioles)
Biliary Ducts :
Interlobular:
Small: 15-40μm
Intermediate: 40-100μm
Septal: > 100μm

Large biliary ducts:
3rd generation : 300-400μm
2nd generation : 400-800μm
1st generation : > 800μm
(hepatic right and left)



LIM 14-LIVER PATHOLOGY
HC-FMUSP, 2018

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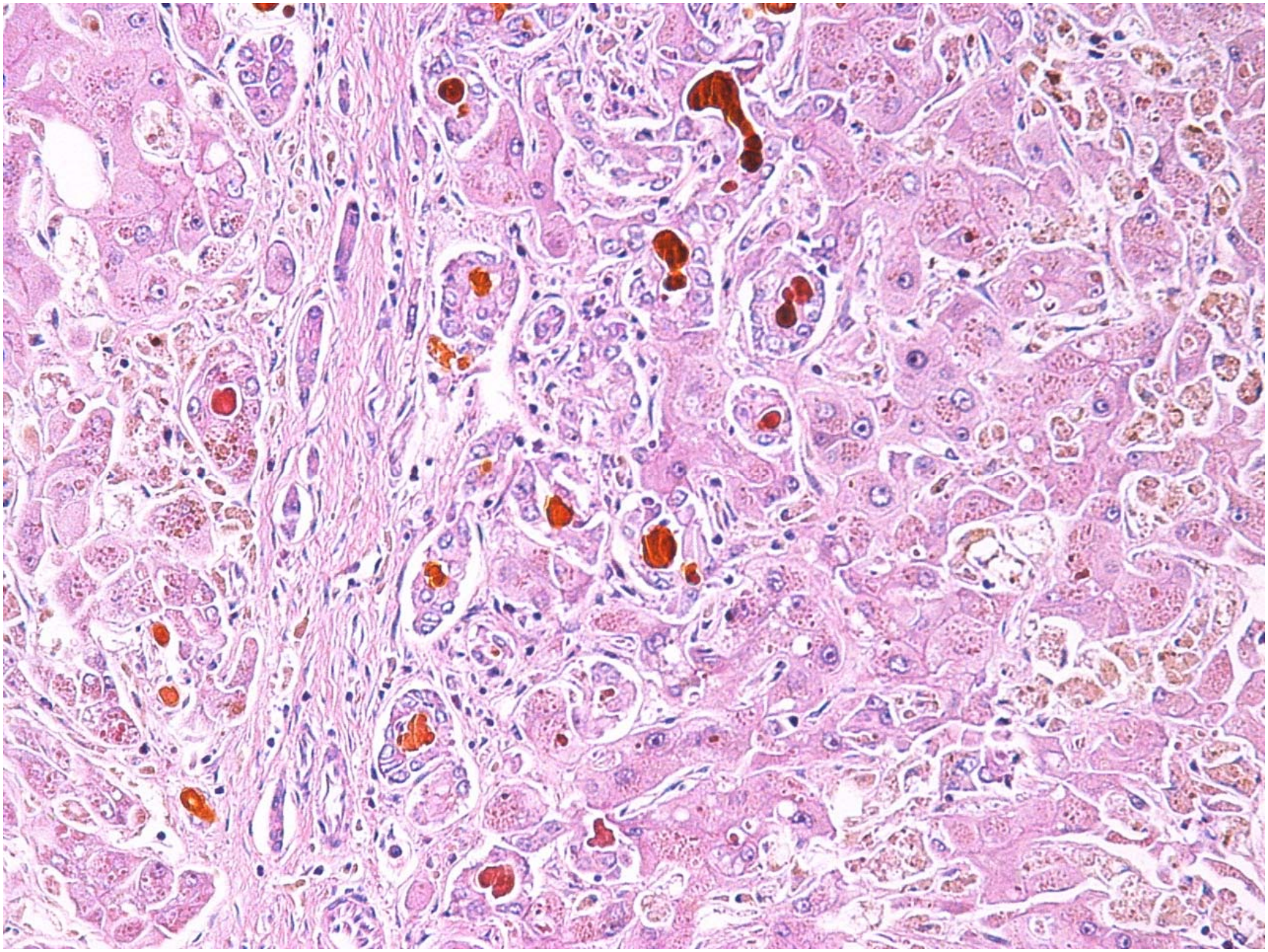

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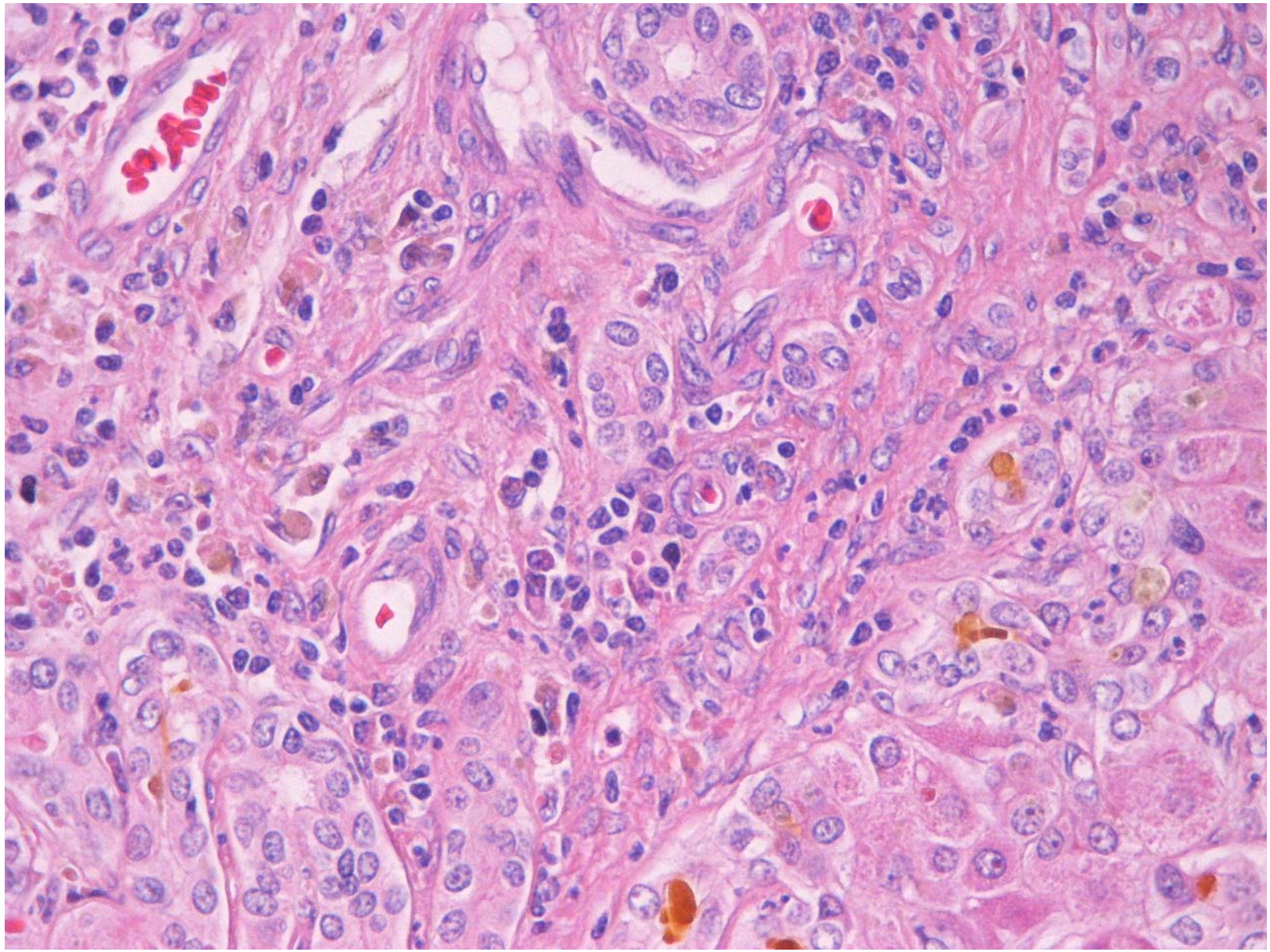

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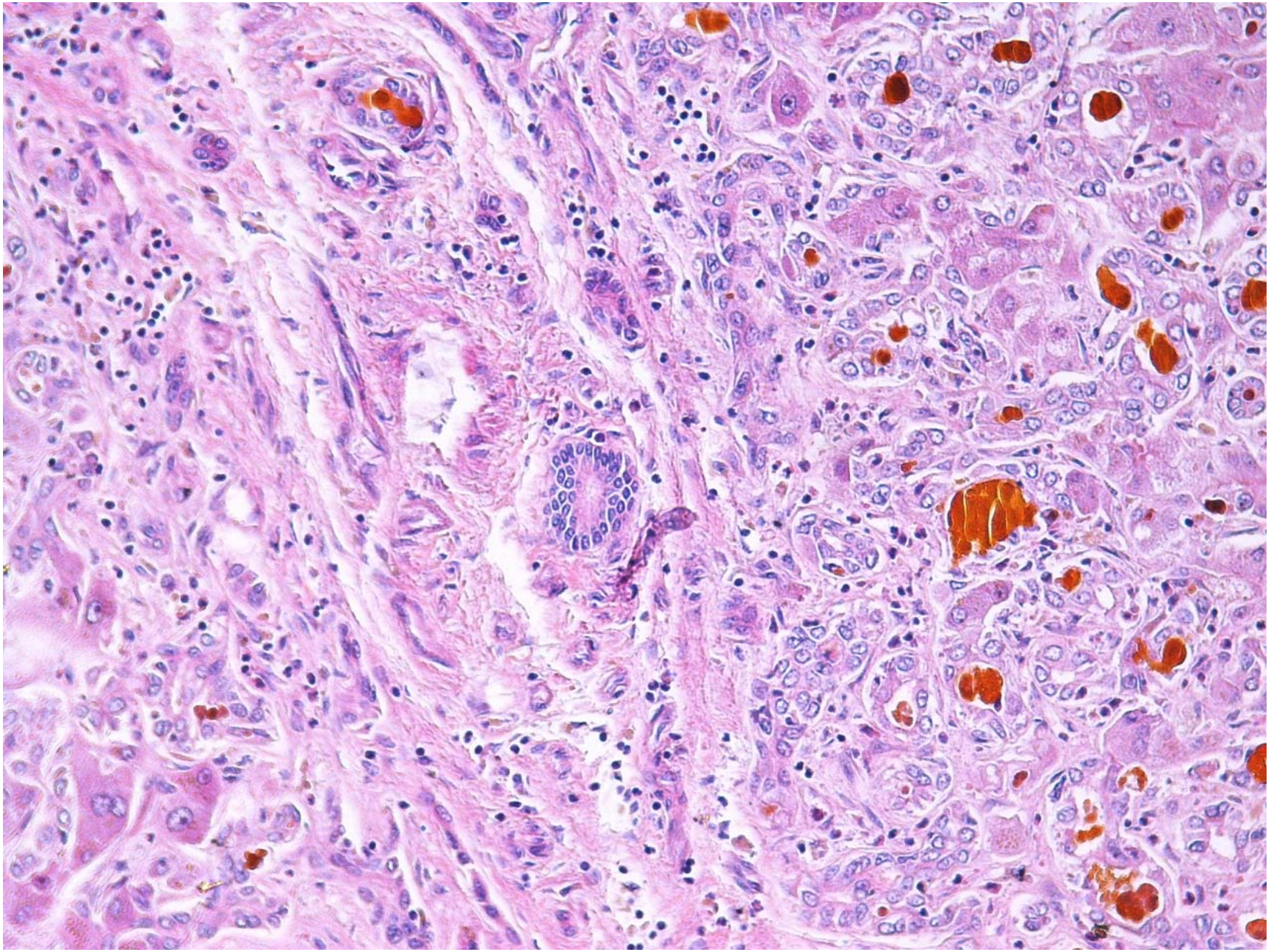
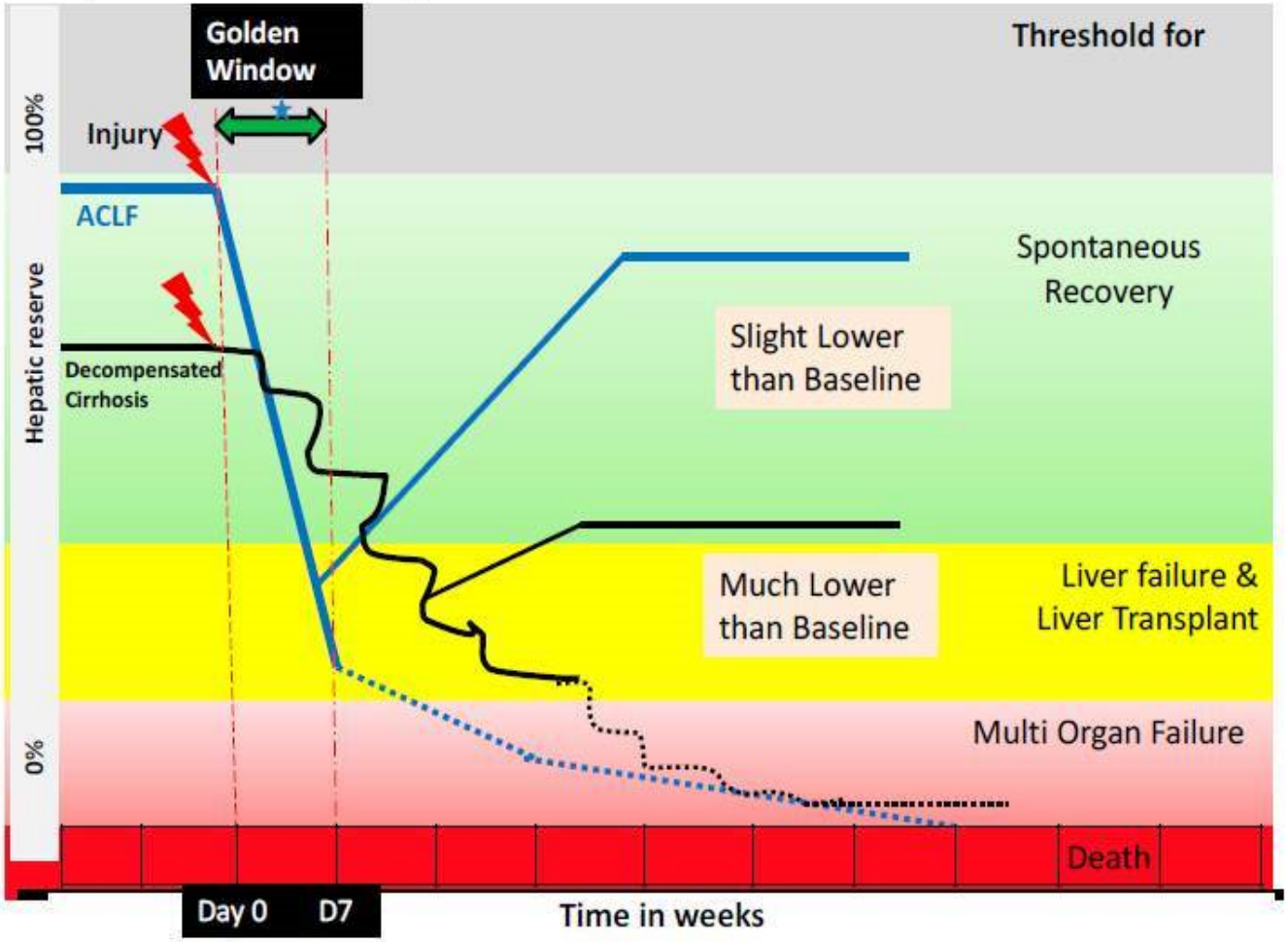


gure 2- Hepatic reserve concept: acute injury and the "Golden Window" (modified from
rin SK, Nature Reviews 2016)



If acute injury is controlled, recovery is more likely in ACLF

In the first 1–2 weeks after injury onset,the patient can develop sepsis.

This intervening period is a 'golden window' for treatment

Jindal A,Rastogi A, Sarin S:
Exp. Rev. Gastroenterol & Hepatology, 2016

Acute-on–chronic liver failure 2018: a need for (urgent) liver biopsy?

Expert Review of Gastroenterology & Hepatology 2018

The International Liver Pathology Study Group

Dirk J. van Leeuwen, Venancio Alves,Charles Balabaud
Prithi S. Bhathal, Paulette Bioulac-Sage,
Romano Colombari, James M. Crawford, Amar Dhillon,
Linda Ferrell, Ryan Gill, Maria Guido, Prodromos
Hytiroglou, Yasuni Nakanuma, Valerie Paradis,
Pierre Emmanuel Rautou, Christine Sempoux,
Dale C. Snover, Neil D. Theise,
Swan N. Thung, Wilson M.S. Tsui & Alberto Quaglia

6. Key issues

- We lack a single universal definition of and guidelines for ALCF, a syndrome currently based on clinical, i.e. non-tissue pathology data.
- Considering the multiple variables, an overemphasis on the need for a single universal definition of ACLF may be a complex challenge, whereas a broader definition that assists in recognition of the ACLF syndrome may be more important for prognostic and transplant indications.
- The literature on the histology of ACLF is as yet scarce, although it has been recognized as a frequently occurring entity (25-40% of cirrhotics).
- Histology may help in differentiating between acute and chronic liver injury in the context of common clinical scenarios but its limitations need to be recognised.
- Clinico-pathological studies on ACLF should be etiology based.
- Liver biopsy in patients with ACLF may have a diagnostic and prognostic role.

Hospital das Clínicas

Faculdade de Medicina da

Universidade de São Paulo

Pathology

Prof. Venâncio A. F. Alves Dr. Evandro S. Mello

Dra Fabiana Lima Dr Ryan Tanigawa

Dr. Renan Ribeiro Dr. Sebastião Martins

Dr. Dafne Andrade Dr.Arthur Volpatto

Hepatology

- Prof. Flair J. Carrilho
- Prof. Suzane K. Ono-Nita Prof. Alberto Q. Farias
- Prof.Claudia PM. Oliveira Prof. Eduardo Cancado
- Dr. Denise C. Paranaguá Vezozzo
- Dr Mario Guimarães Pessoa Dra. Aline L. Chagas
- Dra. Regiane S. M. Alencar Dra. Karla Toda

After mitigating the acute injury, spontaneous recovery is more likely in those with ACLF than ESLD due to a higher baseline hepatic reserve. After acute insult or injury, the condition of a patient with ACLF is likely to rapidly deteriorate .

In the first 1–2 weeks after injury onset,the patient could also develop sepsis.

This intervening period is a therapeutic 'golden window' to ameliorate the acute injury, supplement liver regeneration, to modulate the patient's immune response to prevent sepsis and to prevent multiorgan failure and death.

Jindal A,Rastogi A, Sarin S:
Exp. Rev. Gastroenterol & Hepatology, 2016