ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΣΤΑΤΙΚΟΥ
Ασθενής 42 ετών με πυρετό και εκσεσημασμένη διάταση των ενδοηπατικών χοληφόρων

ΒΙΟΨΙΑ ΗΠΑΤΟΣ

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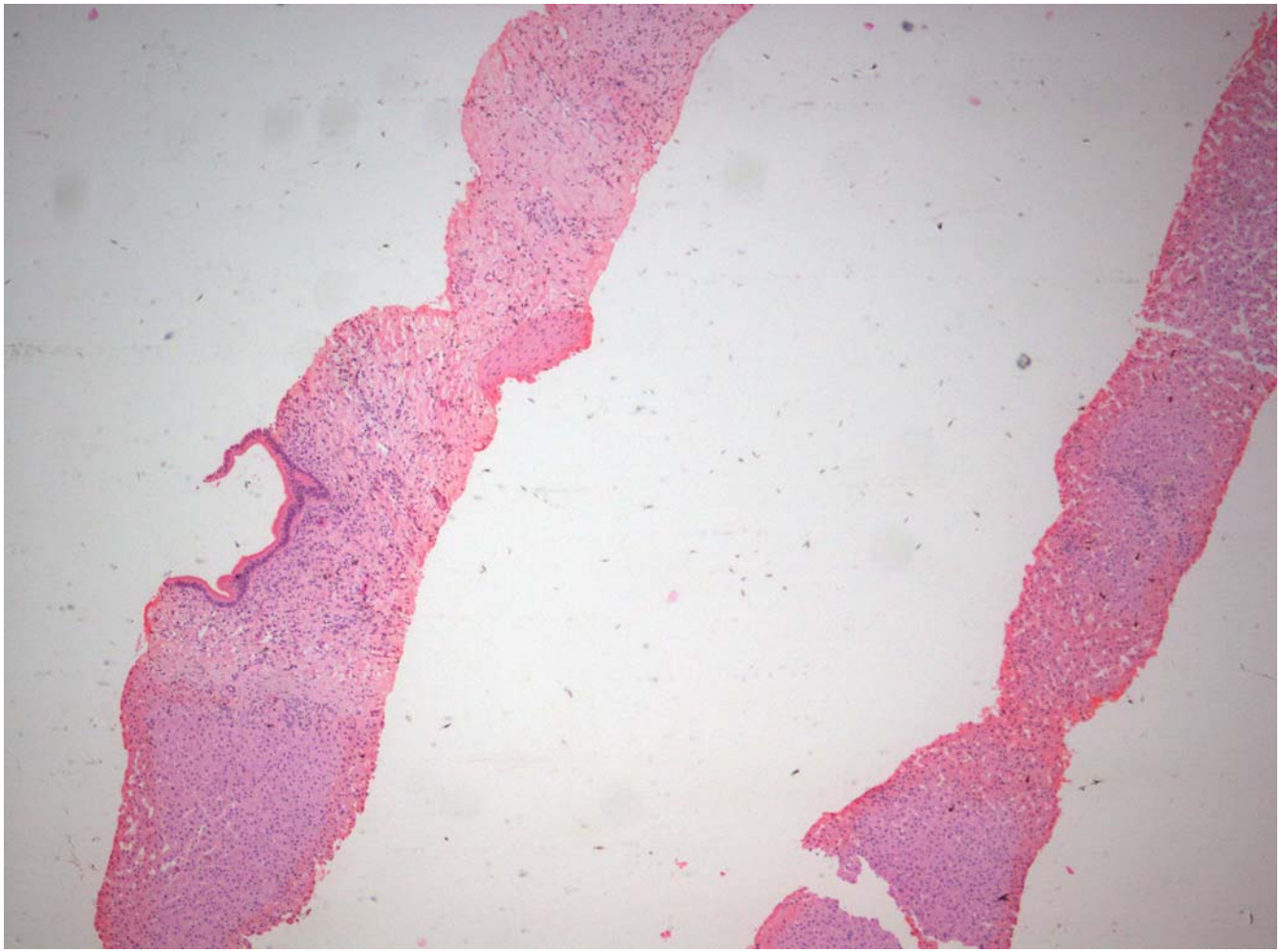
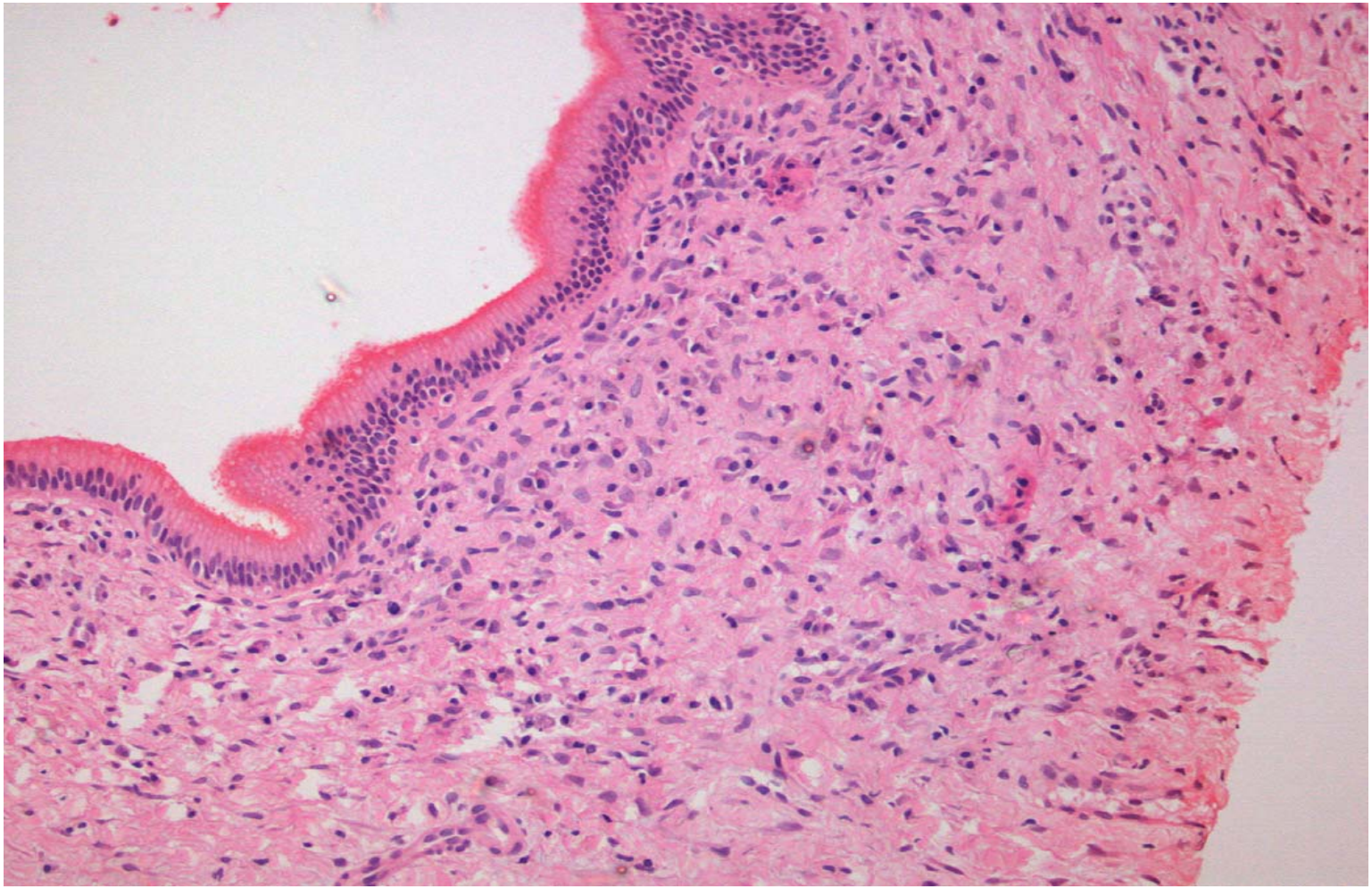
Παθολογοανατομικό Τμήμα ΓΝΑ ‘’Ο Ευαγγελισμός’’

Θεραπευτήριο: "Ευαγγελισμός"

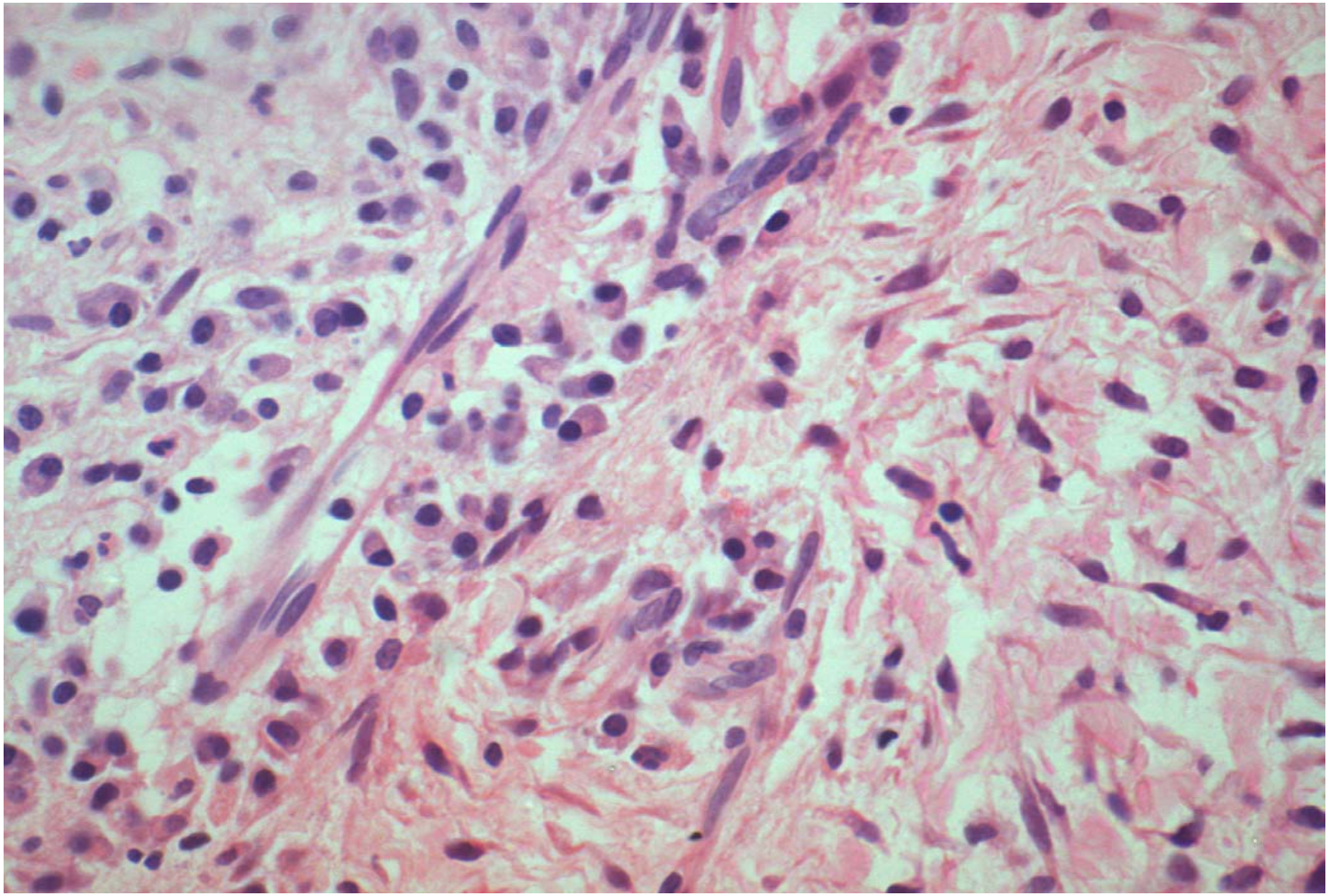
ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
Ο ΕΥΑΓΓΕΛΙΣΜΟΣ



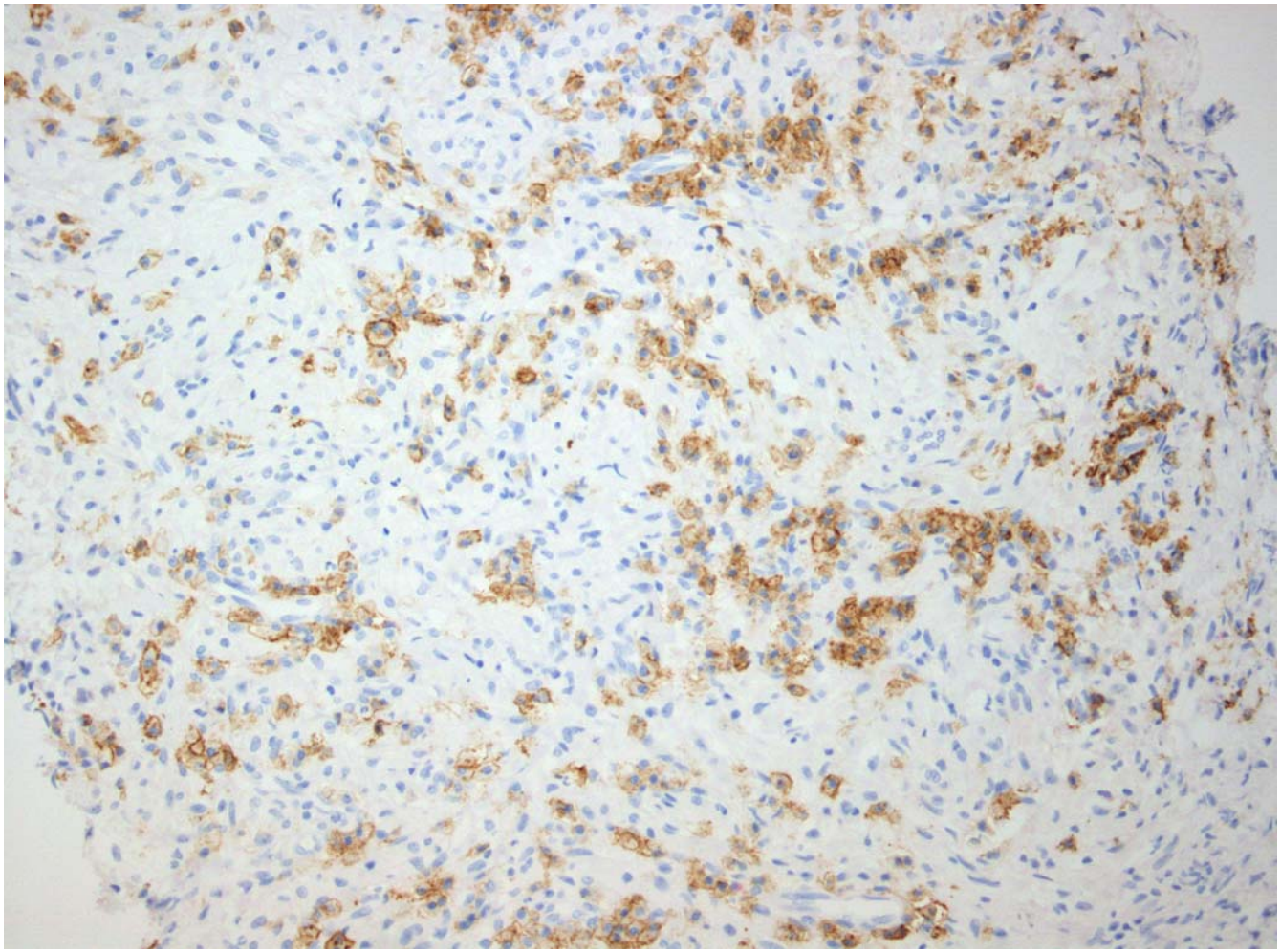
Βιοψία ήπατος & τοιχώματος χοληφόρου πόρου



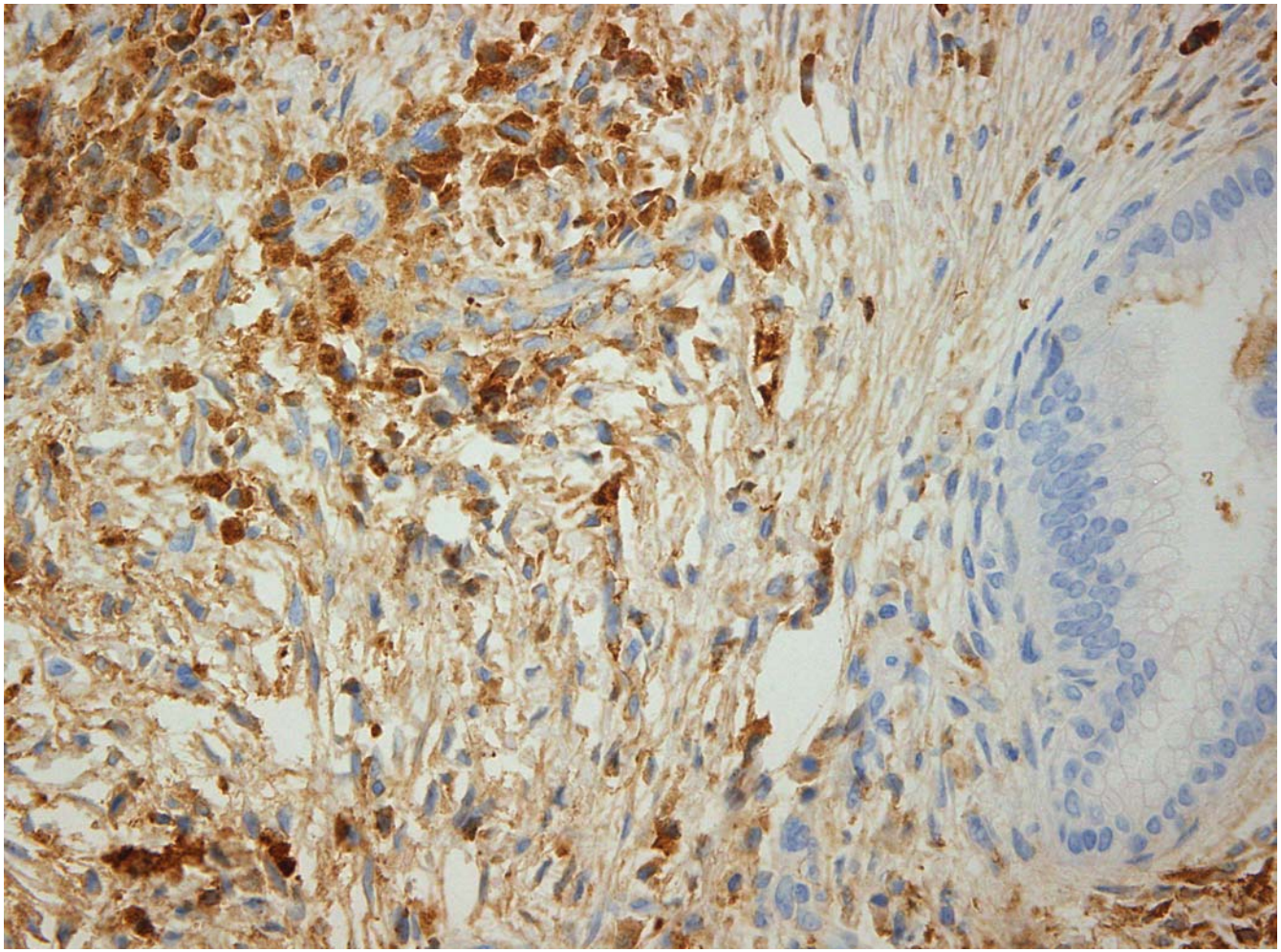
Μεγάλου (?) μεγέθους χοληφόρος πόρος το τοίχωμα του οποίου επενδύεται από υψηλό κυλινδρικό επιθήλιο. Πάχυνση και φλεγμονή του τοιχώματος.



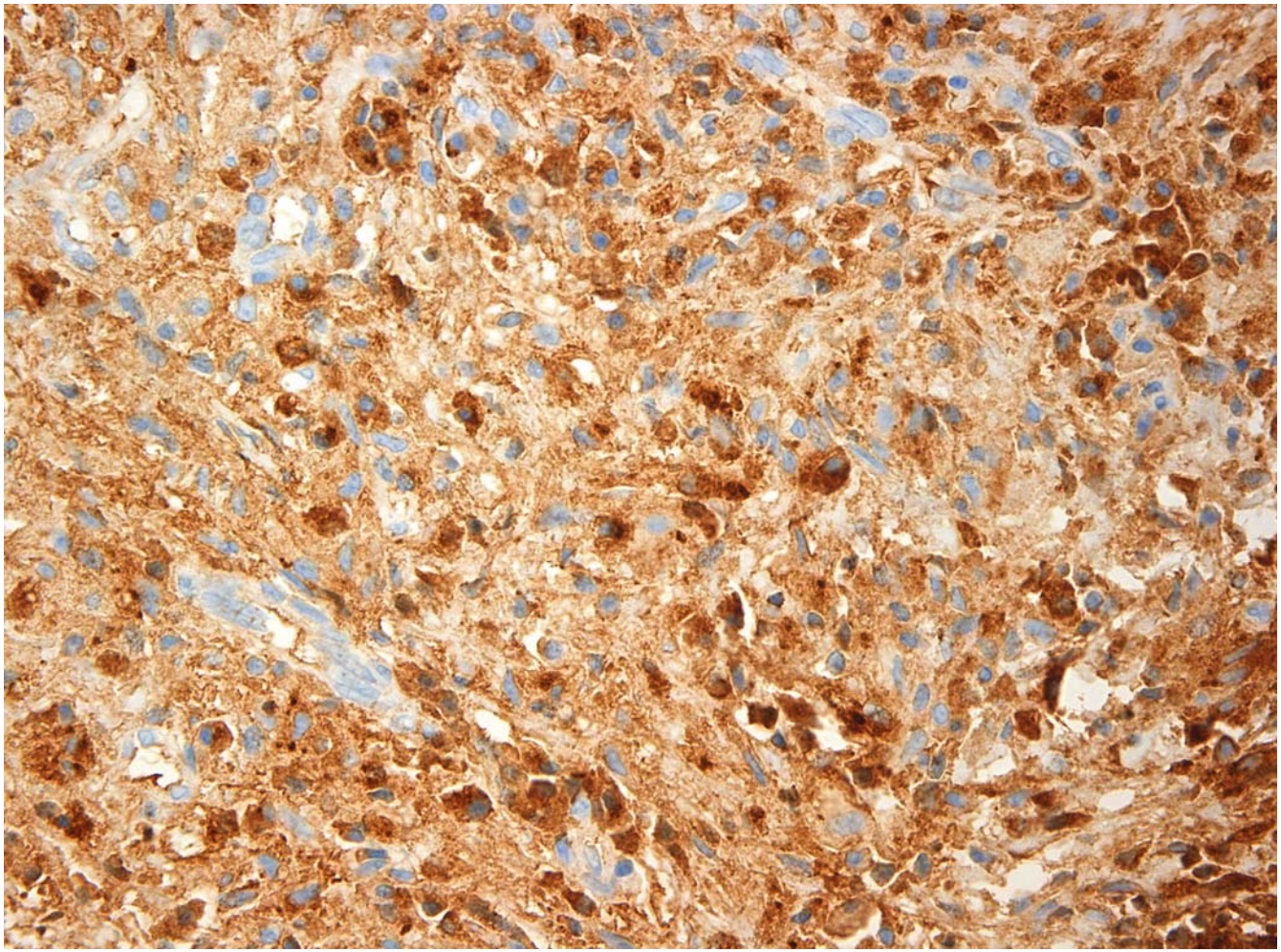
Το φλεγμονώδες διήθημα αποτελείται κυρίως από λεμφοκύτταρα, ιστιοκύτταρα και αρκετά πλασματοκύτταρα.



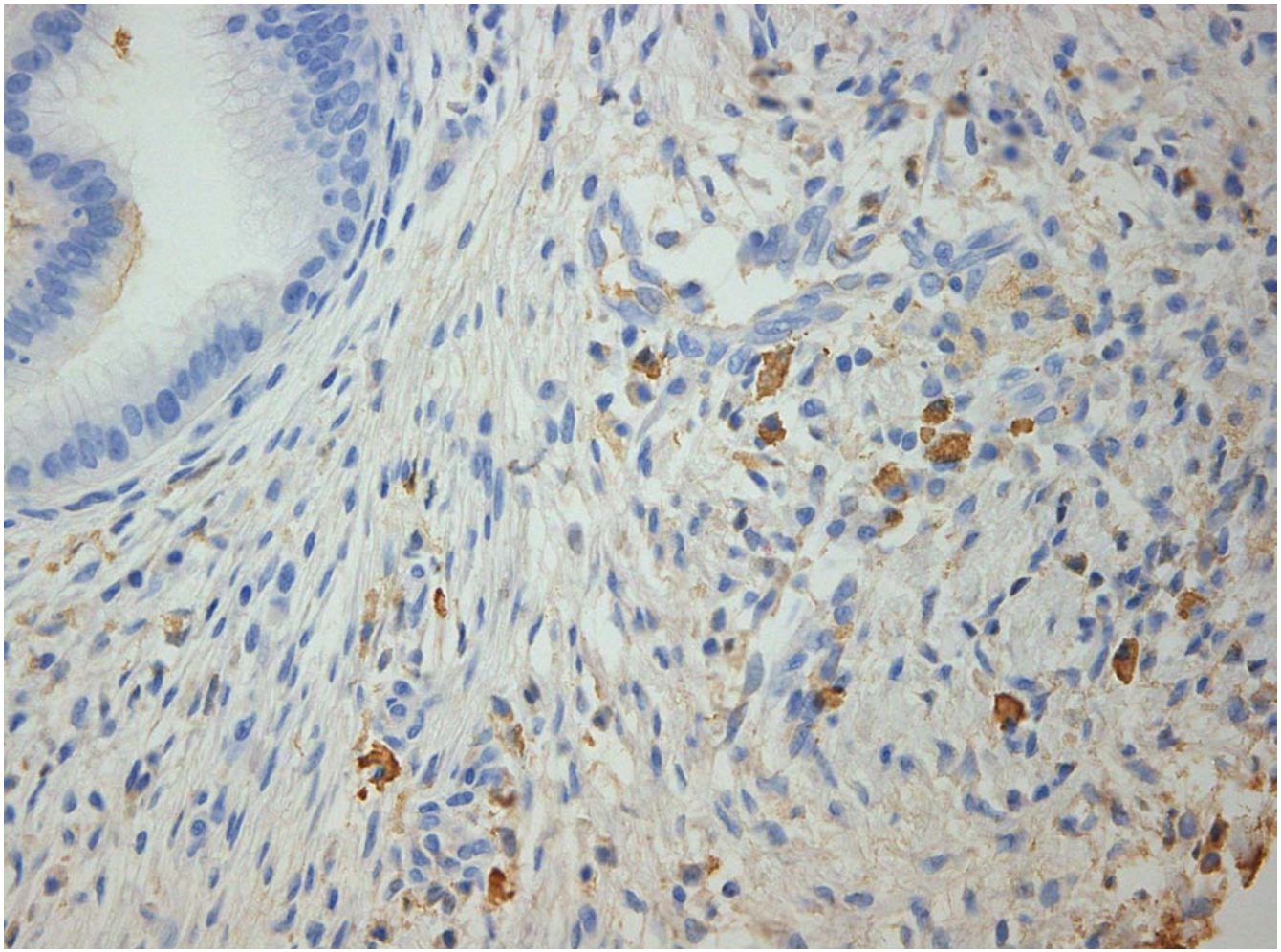
Ανοσοφαινοτυπικά τα πλασματοκύτταρα του διηθήματος αναδεικνύονται με το ειδικό αντίσωμα CD38



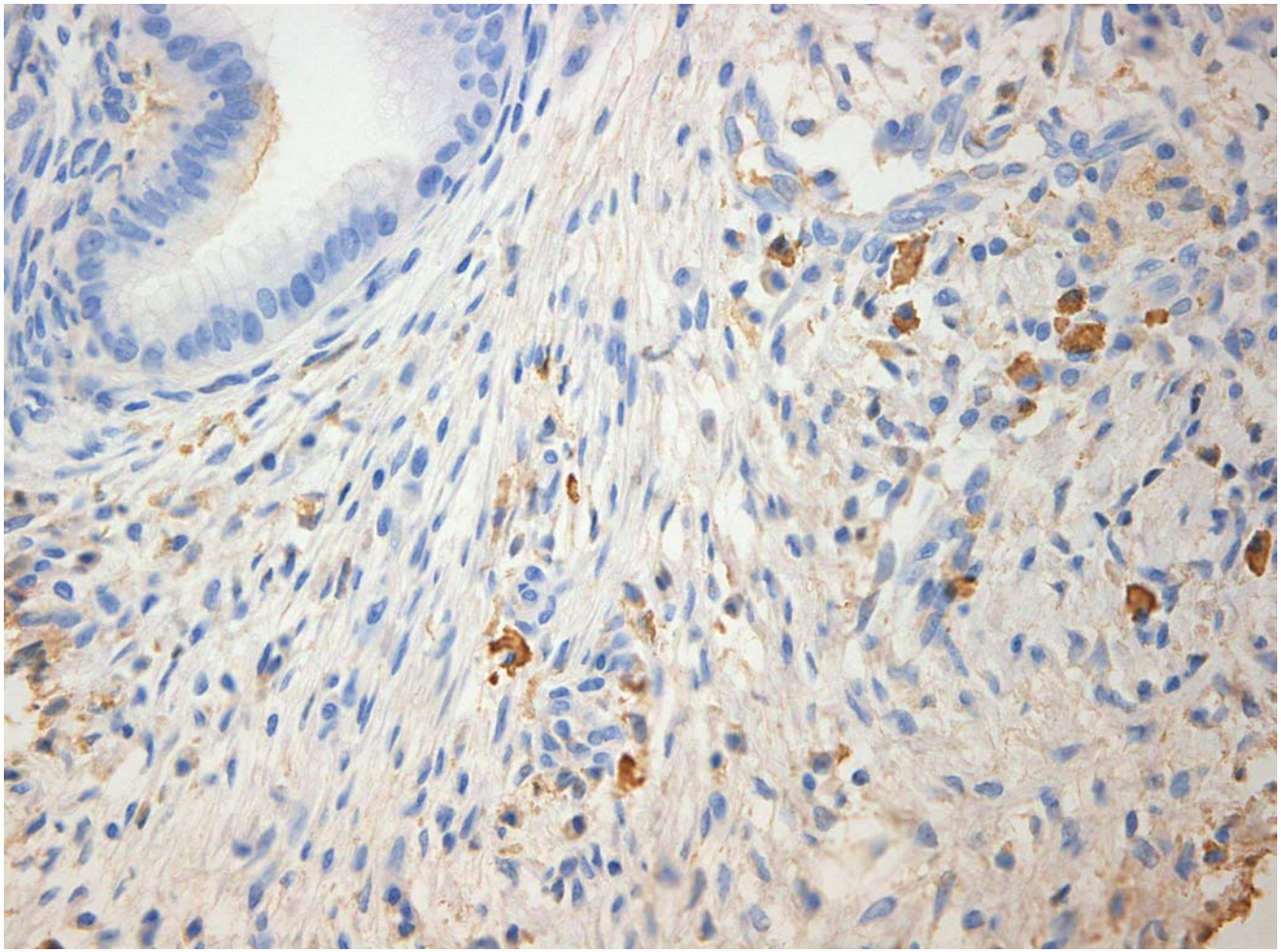
Έκφραση IgG. Συμμετοχή πολλών πλασματοκυττάρων με έκφραση ανοσοσφαιρίνης IgG.



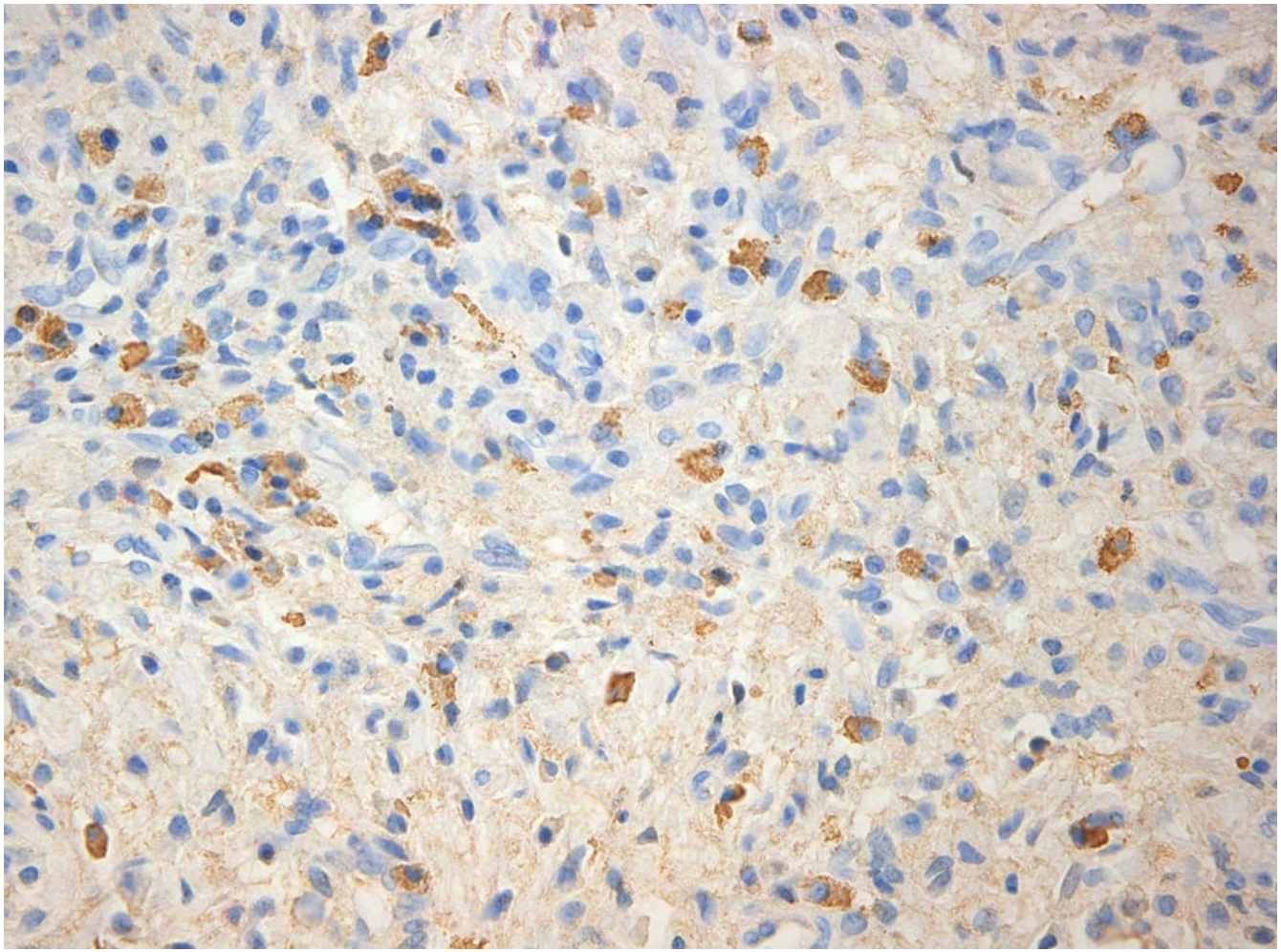
Παρόμοια ευρήματα έκφρασης ανοσοσφαιρίνης IgG με το ειδικό αντίσωμα.



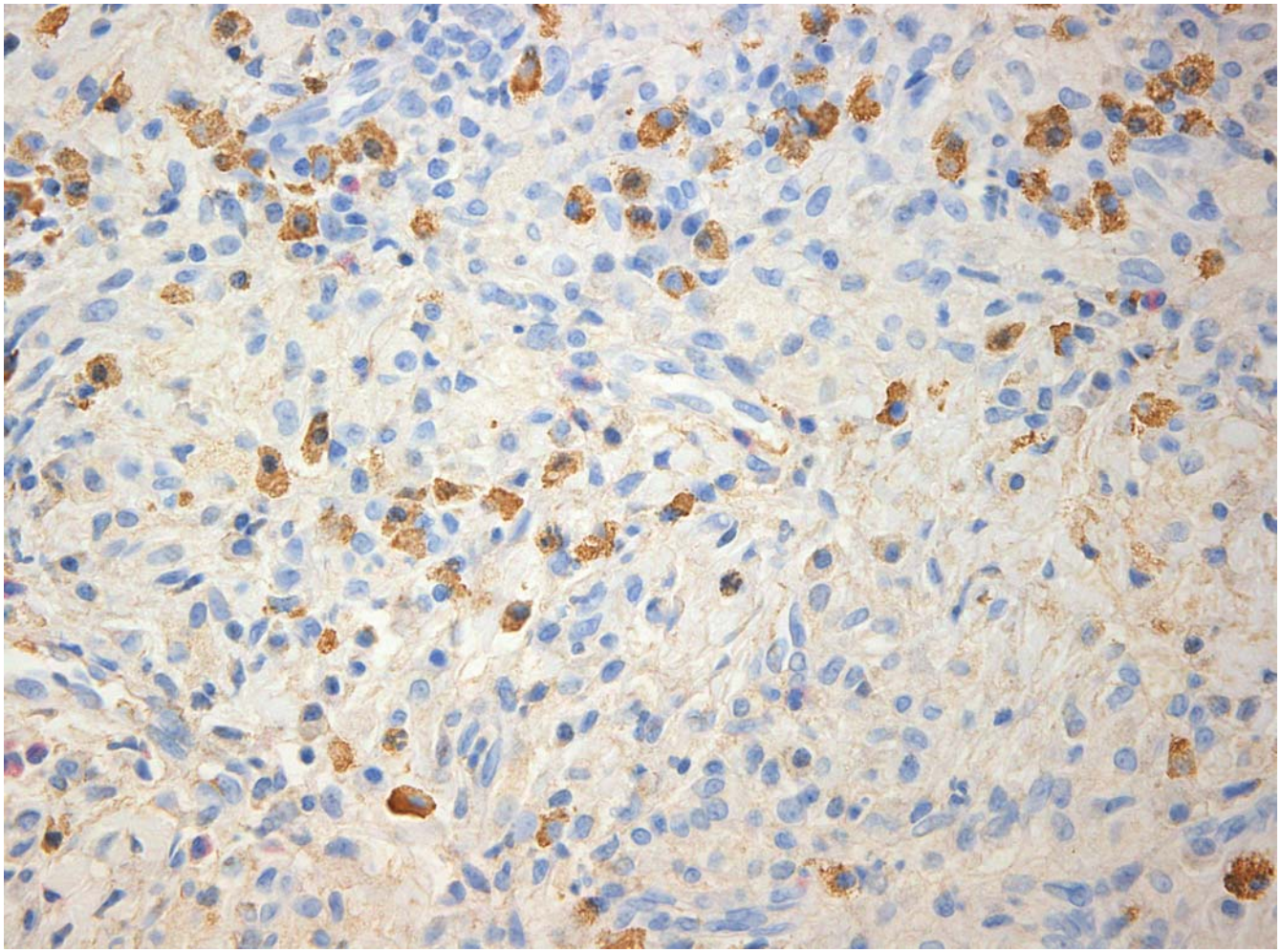
Έκφραση IgG4: Παρουσία ομοίως ικανού αριθμού πλασματοκυττάρων με έκφραση IgG4. Διακρίνεται παρακείμενα ο χοληφόρος πόρος με άθικτο επιθήλιο.



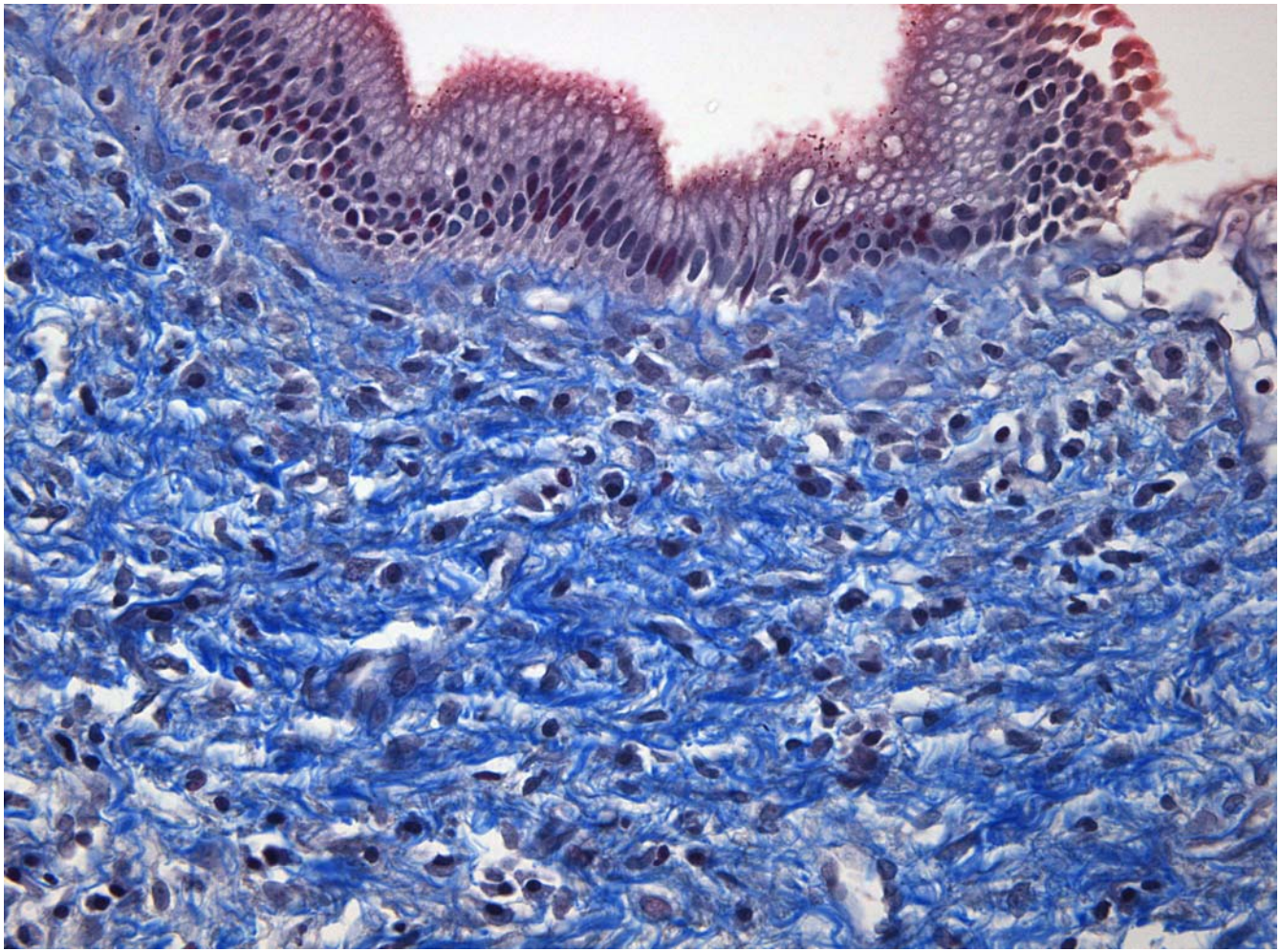
Παρόμοια ευρήματα έκφρασης IgG4 από τα πλασματοκύτταρα. Ο αριθμός τους φαίνεται να υπερβαίνει τα 10 στο οπτικό πεδίο υψηλής μεγέθυνσης (x400).



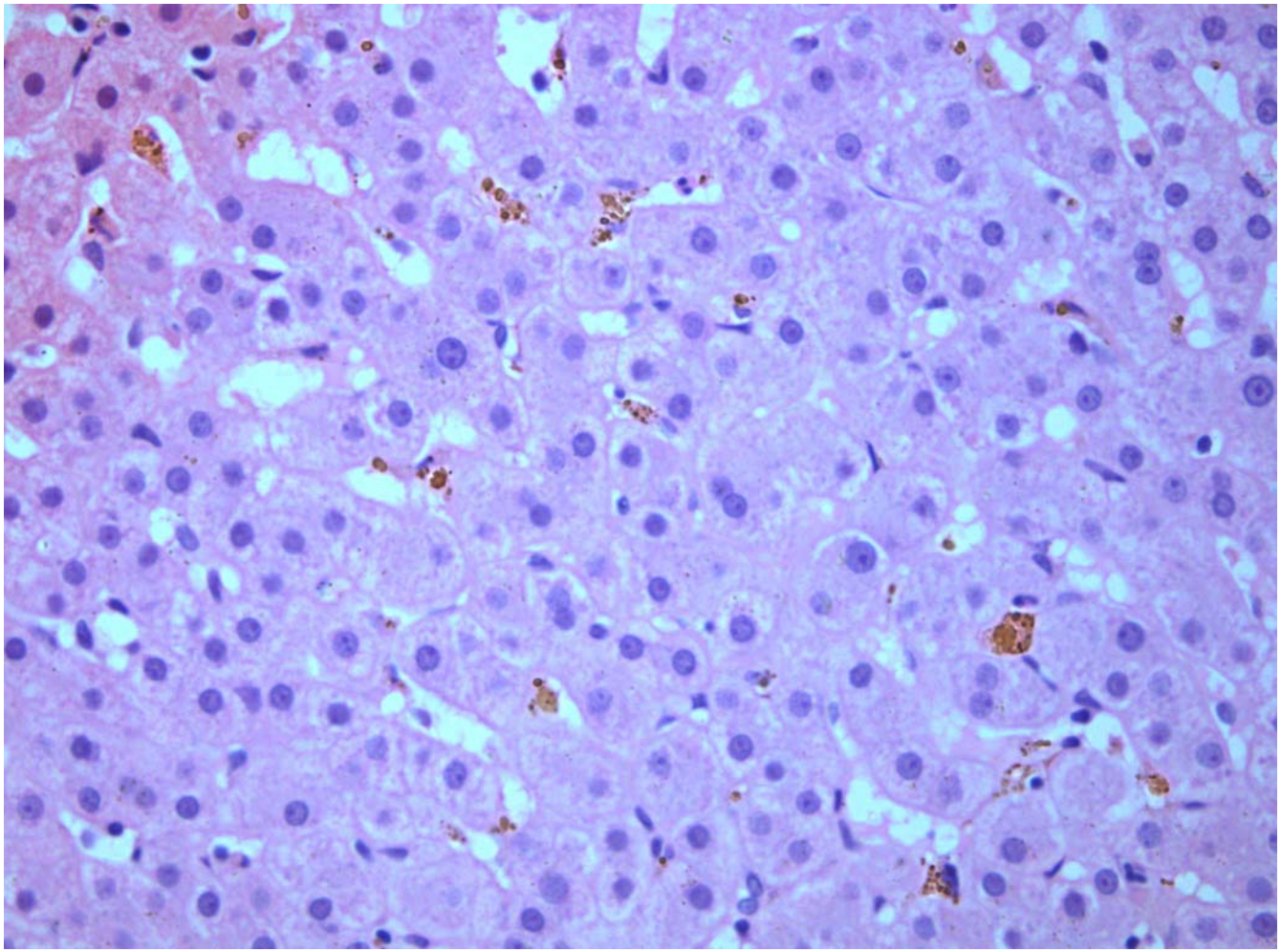
Έκφραση IgG4: Παρόμοια ευρήματα σε άλλη περιοχή. Ομοίως αριθμός πλασματοκυττάρων > 10 ανά οπτικό πεδίο υψηλής μεγέθυνσης (x 400).



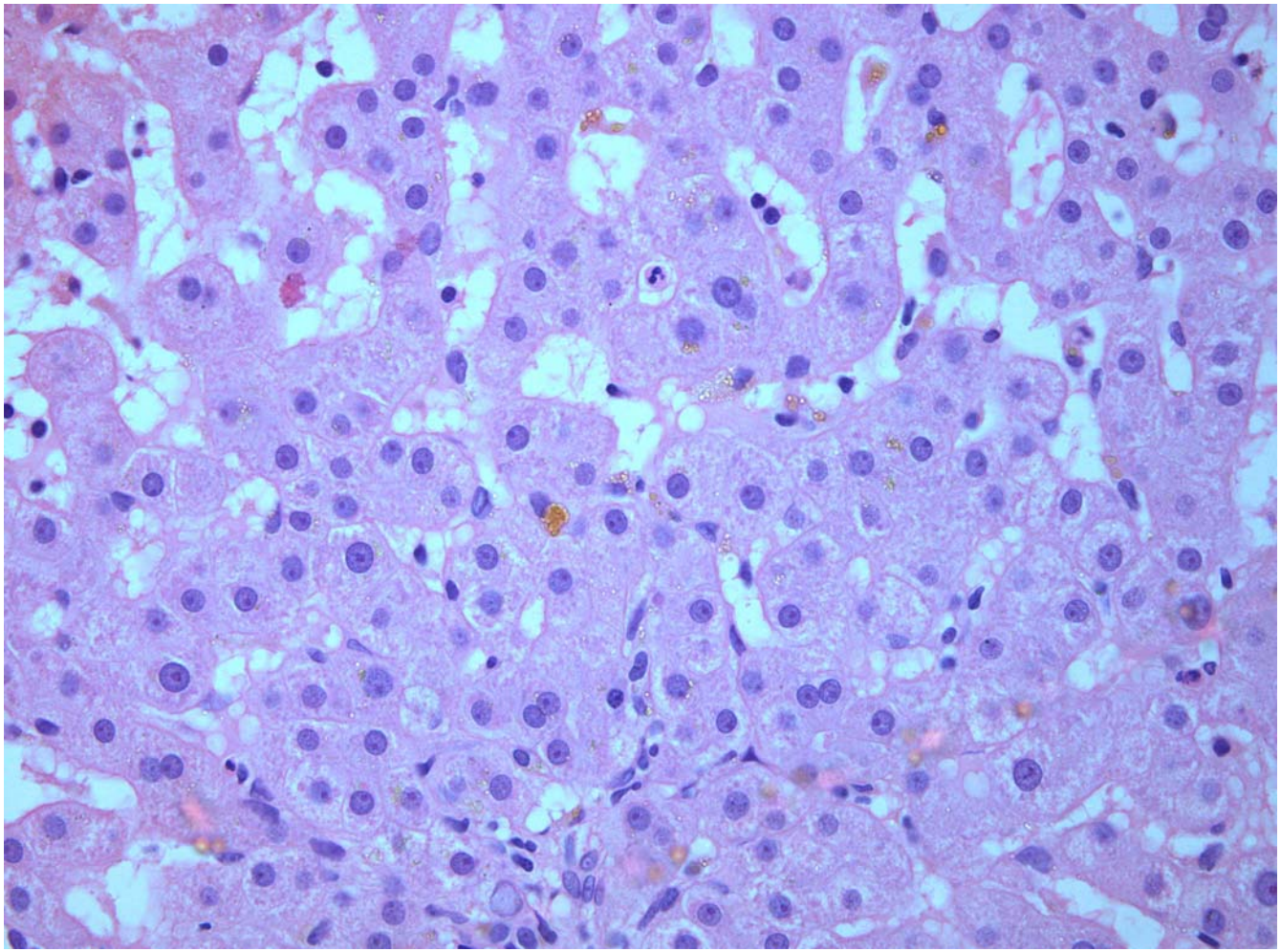
IgG4: Παρόμοια ευρήματα



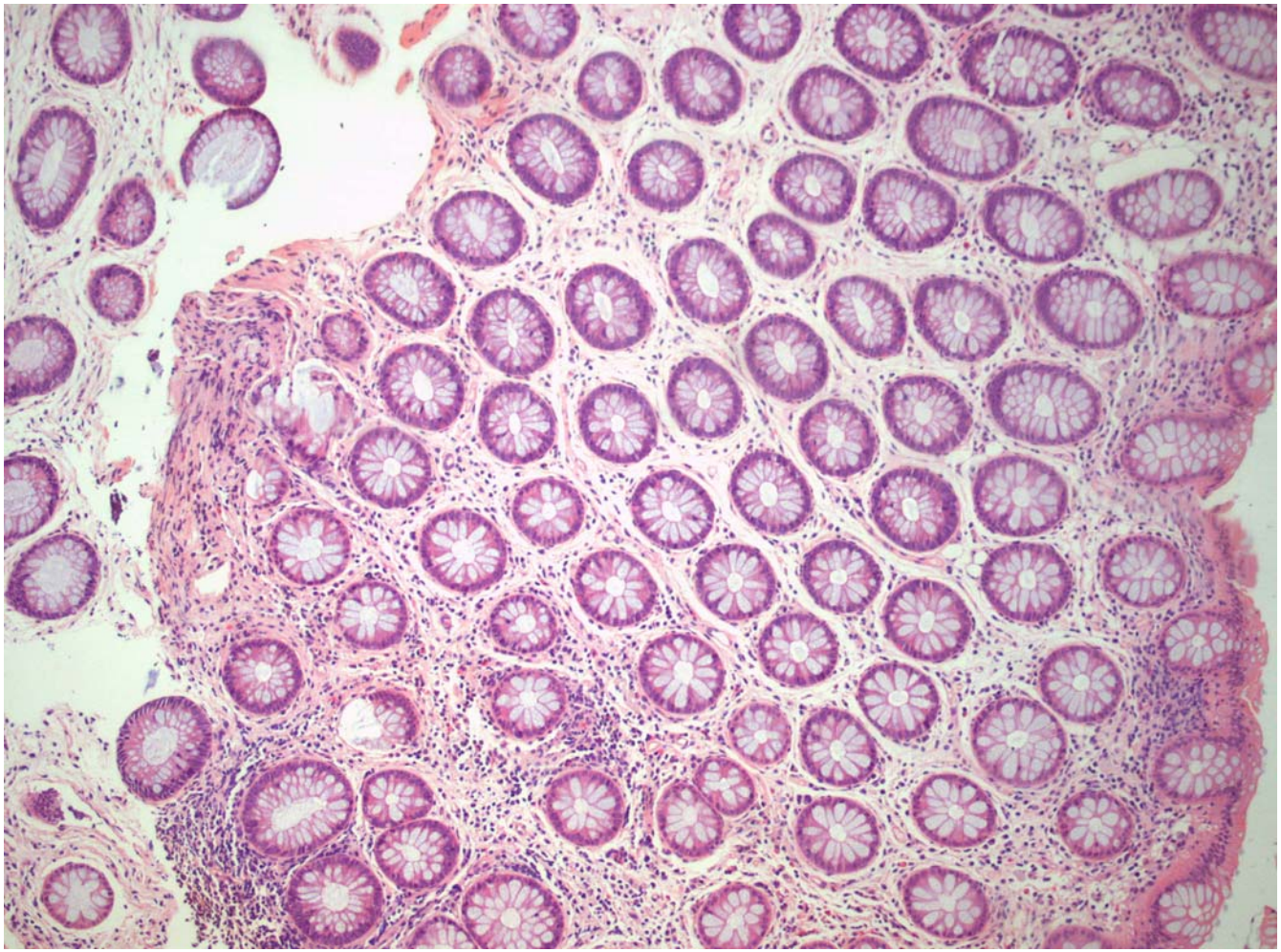
Αξιοσημείωτη ίνωση στο τοίχωμα του χοληφόρου πόρου η οποία αναδεικνύεται με την ειδική εξέταση με την χρώση CAB.



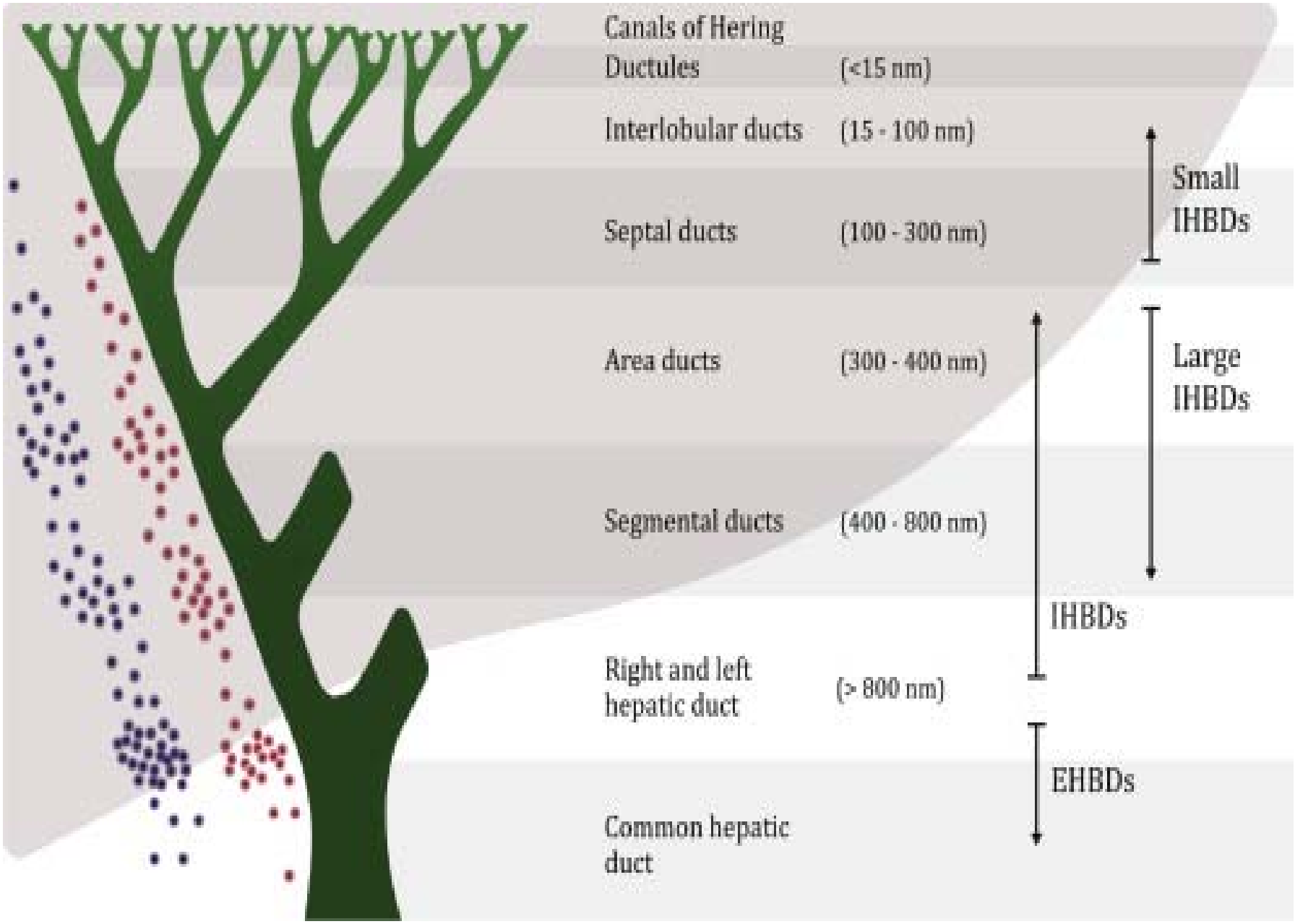
Ευρήματα χολόστασης σε κολποειδή [Cholangiolar cholestasis]. Απουσία ευρημάτων αλκοολικής νόσου του ήπατος.

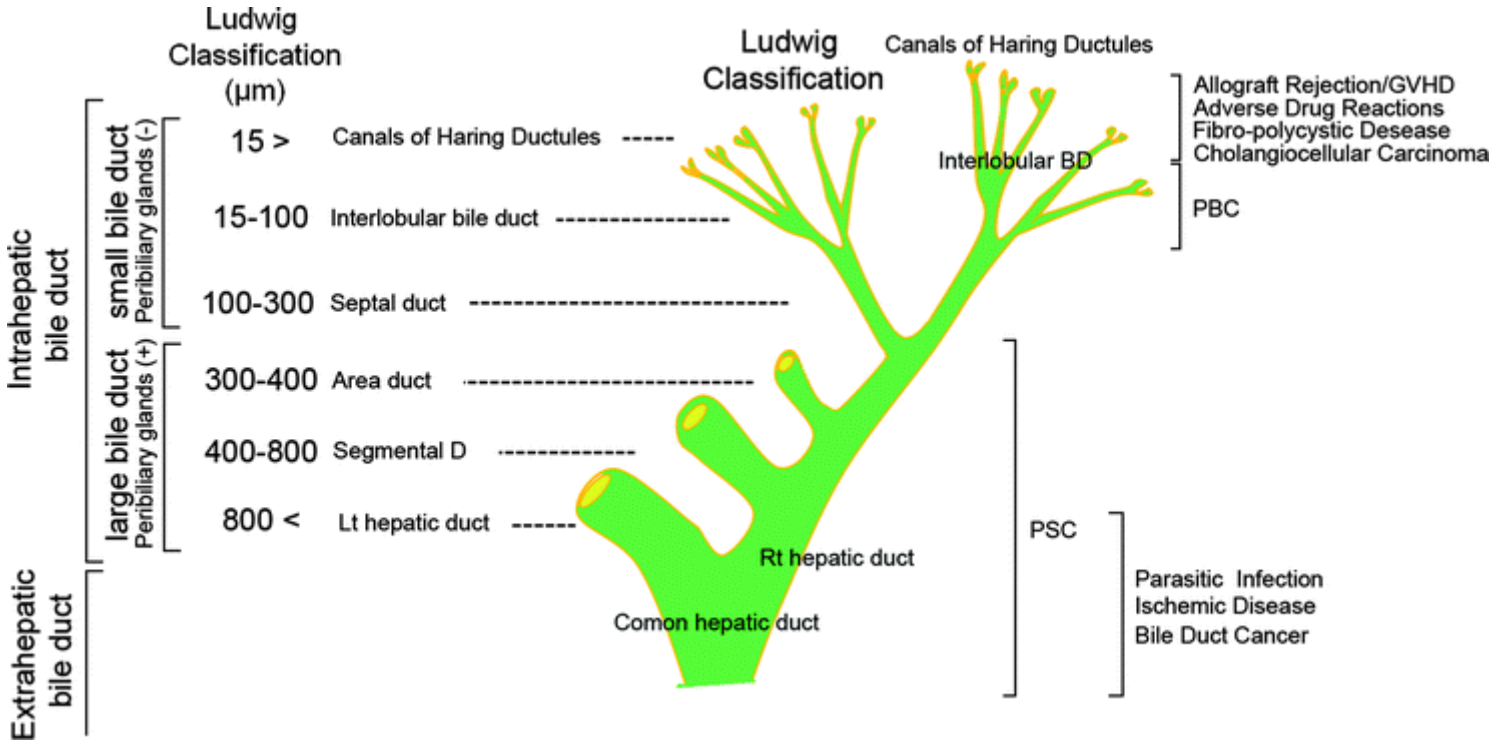


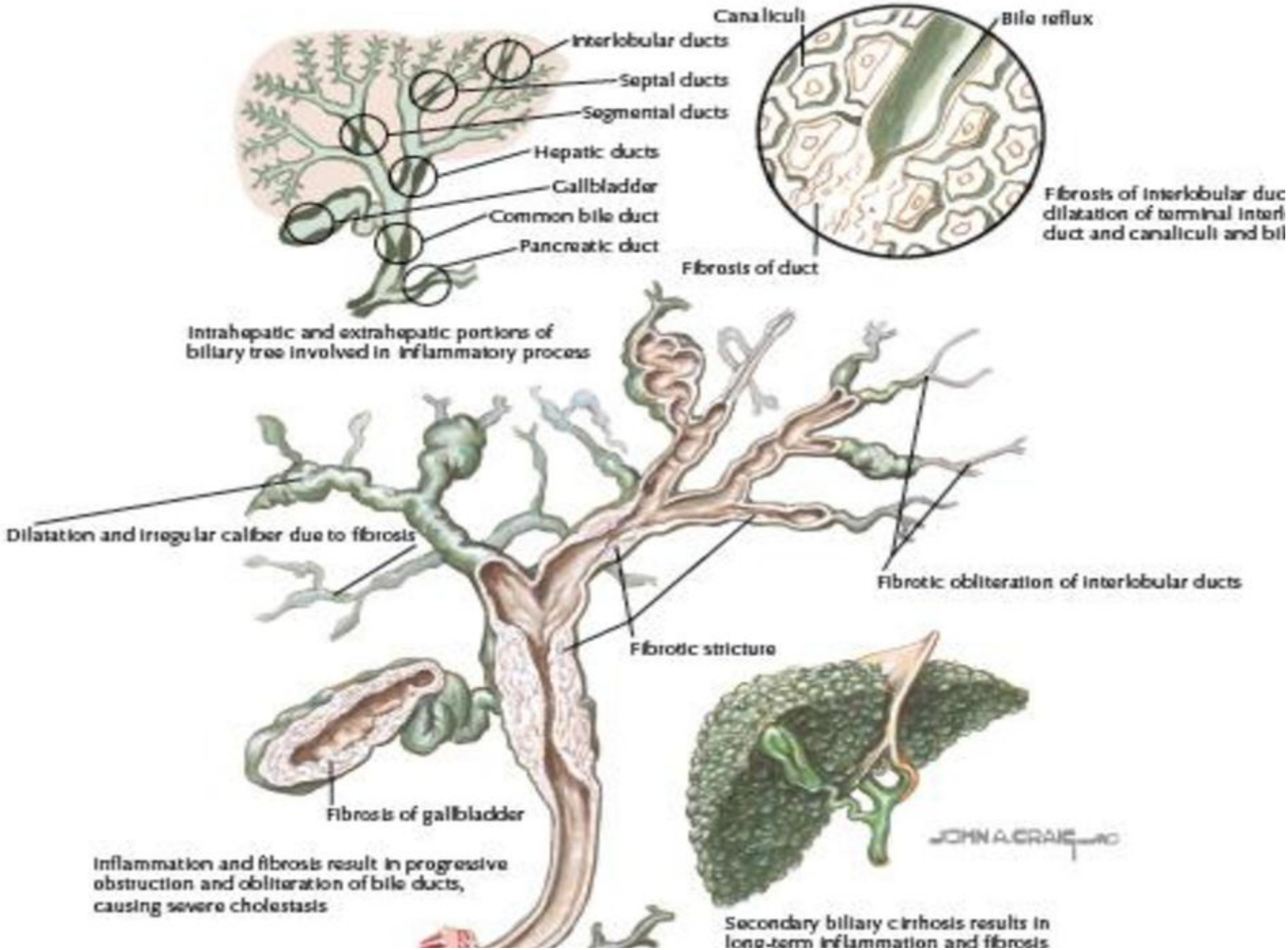
Ευρήματα χολόστασης. Διακρίνονται στα κολποειδή αθροίσεις ουσίας με χαρακτηριστικά χολής [bile concretions].

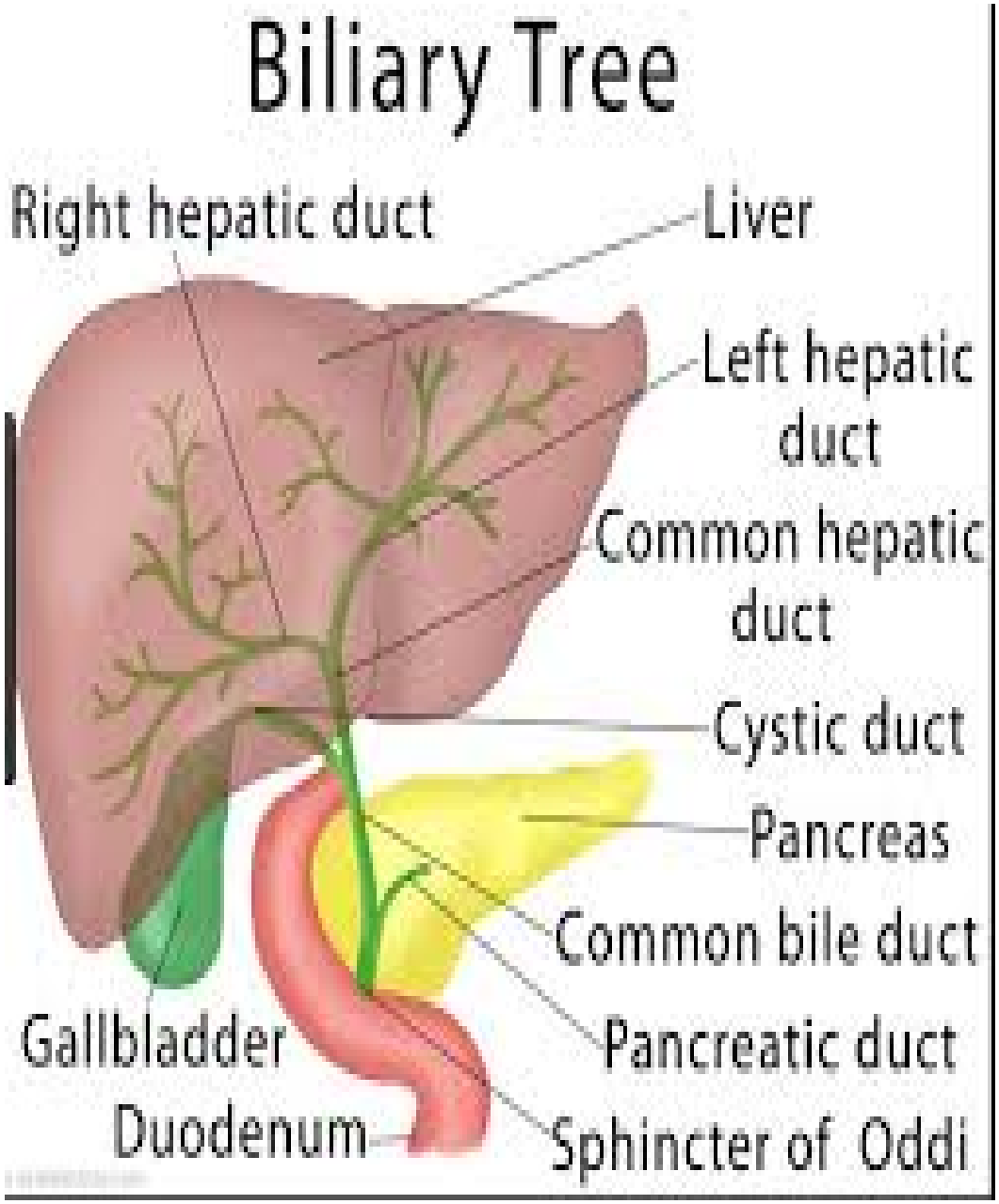


Βιοψία παχέος εντέρου με απουσία αξιοσημείωτων μικροσκοπικών ευρημάτων – εικόνα στα πλαίσια του φυσιολογικού.


Canals of Hering
Ductules
(<15 nm)
Interlobular ducts
(15 - 100 nm)
Septal ducts
(100 - 300 nm)
Area ducts
(300 - 400 nm)
Segmental ducts
(400 - 800 nm)
Right and left hepatic duct
(> 800 nm)
Common hepatic duct
Small IHBDs
Large IHBDs
IHBDs
EHBDs


Ludwig Classification (μm)
Intrahepatic bile duct
small bile duct
Peribiliary glands (-)
large bile duct
Peribiliary glands (+)
Extrahepatic bile duct
15 >
Canals of Haring Ductules
15-100
Interlobular bile duct
100-300
Septal duct
300-400
Area duct
400-800
Segmental D
800 <
Lt hepatic duct
Ludwig Classification
Canals of Haring Ductules
Interlobular BD
Rt hepatic duct
Comon hepatic duct
Allograft Rejection/GVHD
Adverse Drug Reactions
Fibro-polycystic Desease
Cholangiocellular Carcinoma
PBC
PSC
Parasitic Infection
Ischemic Disease
Bile Duct Cancer


Canaliculi
Bile reflux
Interlobular ducts
Septal ducts
Segmental ducts
Hepatic ducts
Gallbladder
Common bile duct
Pancreatic duct
Fibrosis of duct
Fibrosis of interlobular duc
dilatation of terminal interl
duct and canaliculi and bil
Intrahepatic and extrahepatic portions of
biliary tree involved in inflammatory process
Dilatation and irregular caliber due to fibrosis
Fibrotic obliteration of interlobular ducts
Fibrotic stricture
Fibrosis of gallbladder
Inflammation and fibrosis result in progressive
obstruction and obliteration of bile ducts,
causing severe cholestasis
Secondary biliary cirrhosis results in
long-term inflammation and fibrosis



Συμπέρασμα:
Πρόκειται για νόσημα των χοληφόρων πόρων με εικόνα στα πλαίσια σκληρυντικής χολαγγειΐτιδας [sclerosing cholangitis] στο οποίο παρατηρείται:

1. Χρόνια φλεγμονή και περιπορική ίνωση του τοιχώματος του χοληφόρου δένδρου [chronic inflammation and periductal fibrosis of the walls of the biliary tree].

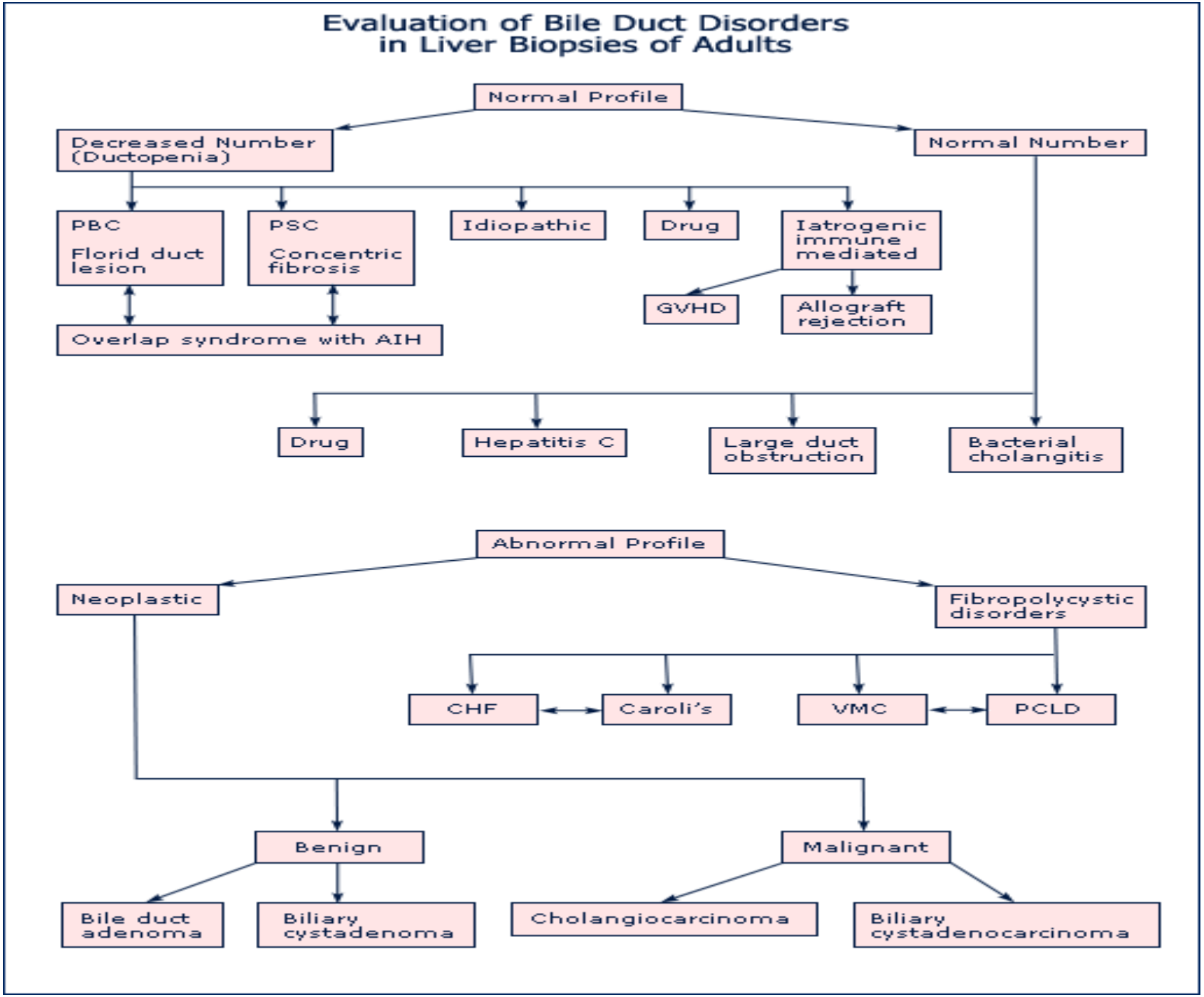
2. Βλάβη μεγάλου ? ενδοηπατικού πόρου [large? intrahepatic bile duct]

3. Συμμετοχή ικανού αριθμού πλασματοκυττάρων IgG4 (+) [> 10 ανά οπτικό πεδίο υψηλής μεγέθυνσης].

4. Αναλογία IgG (+) / IgG4 (+): < 40%

5. Storiform fibrosis ? Periductal concentric fibrosis?

6. Obliterative phlebitis?


Evaluation of Bile Duct Disorders in Liver Biopsies of Adults
Normal Profile
Decreased Number (Ductopenia)
Normal Number
PBC
Florid duct lesion
PSC
Concentric fibrosis
Idiopathic
Drug
Iatrogenic immune mediated
GVHD
Allograft rejection
Overlap syndrome with AIH
Drug
Hepatitis C
Large duct obstruction
Bacterial cholangitis
Abnormal Profile
Neoplastic
Fibropolycystic disorders
CHF
Caroli's
VMC
PCLD
Benign
Malignant
Bile duct adenoma
Biliary cystadenoma
Cholangiocarcinoma
Biliary cystadenocarcinoma


ΕΥΧΑΡΙΣΤΟΥΜΕ ΠΟΛΥ
ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ
ΣΑΣ

Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is a **chronic cholestatic liver disease** characterized by **chronic inflammation and periductal fibrosis** of the walls of the biliary tree.

The typical PSC patient is a 30–40-year-old male with **inflammatory bowel disease**, but advances in diagnostic imaging have allowed PSC to be diagnosed at all ages including childhood.

Primary sclerosing cholangitis usually affects **large intrahepatic and/or extrahepatic bile ducts,** but in 5% of cases, only **small intrahepaticbile ducts** are involved; this is called small-duct PSC.

A liver biopsy is not necessary to diagnose large-duct PSC in the presence of typical cholangio-graphic findings.

Patients who present with clinical features and a liver biopsy compatible with PSC but with a normal cholangiogram are classified with small-duct PSC.

Liver function tests show cholestasis.

Elevated serum alkaline phosphatase (ALP) is a characteristic biochemical finding.

Anti-neutrophil antibodies in a perinuclear pattern (p-ANCA) are found in approximately 80% of PSC patients, although this test lacks sensitivity and specificity.

Although the clinical course varies widely, **progressive obliteration of the biliary tree eventually leads to biliary cirrhosis**, and Liver Transplantation continues to be the only therapeutic option for patients with end-stage PSC

Typical liver histologic findings in PSC are:

A. Fbro-obliterative bile duct lesions characterized by an "**onion-skin"-**like periductal fibrosis around medium-sized or larger bile ducts.

B Epithelial lining cells are seen to be atrophic and degenerative.

C. Fibro-obliterative lesions eventually replace the bile duct with **fibrous scarring** and inconspicuous inflammation.

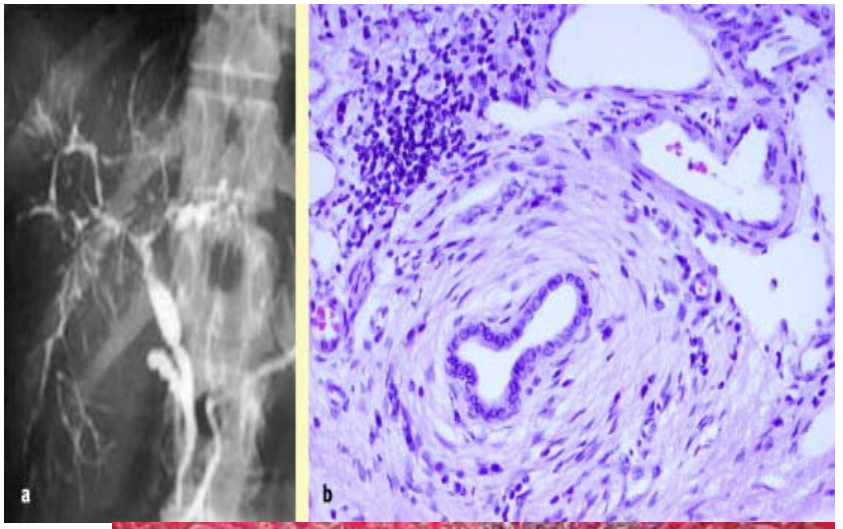
D. Small interlobular bile ducts may also be affected and replaced by fibrous scars in addition to the involvement of larger ducts.

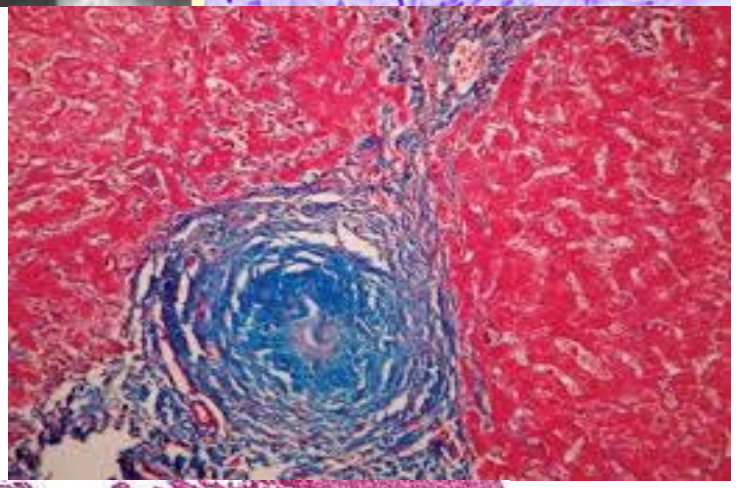
Involvement solely of small interlobular bile ducts can lead to the diagnosis of the **small-duct variant of PSC.**

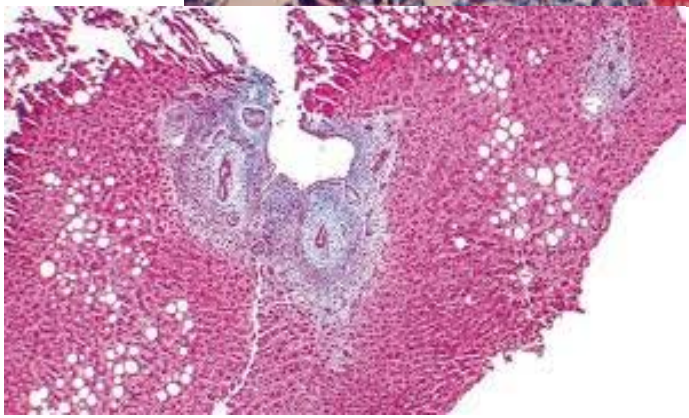
E. Lymphoplasmacytic **inflammation** involving the hilar bile ducts and intrahepatic bile ducts is variable.

F. Biliary sludge or microstones are deposited in some affected bile ducts.

G. Xanthogranulomatous changes or severe parenchymal necroinflammation with interface hepatitis is usually not prominent

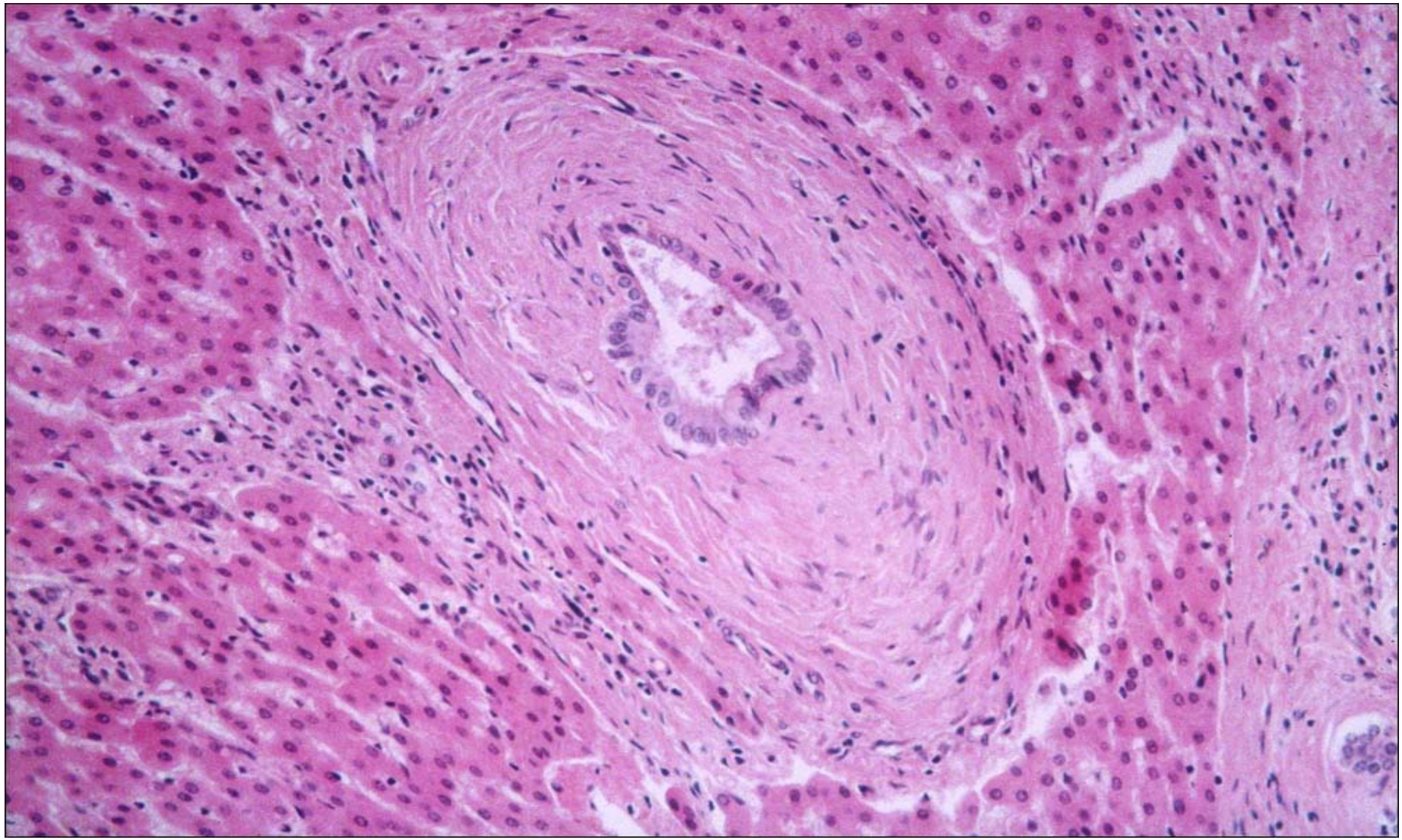




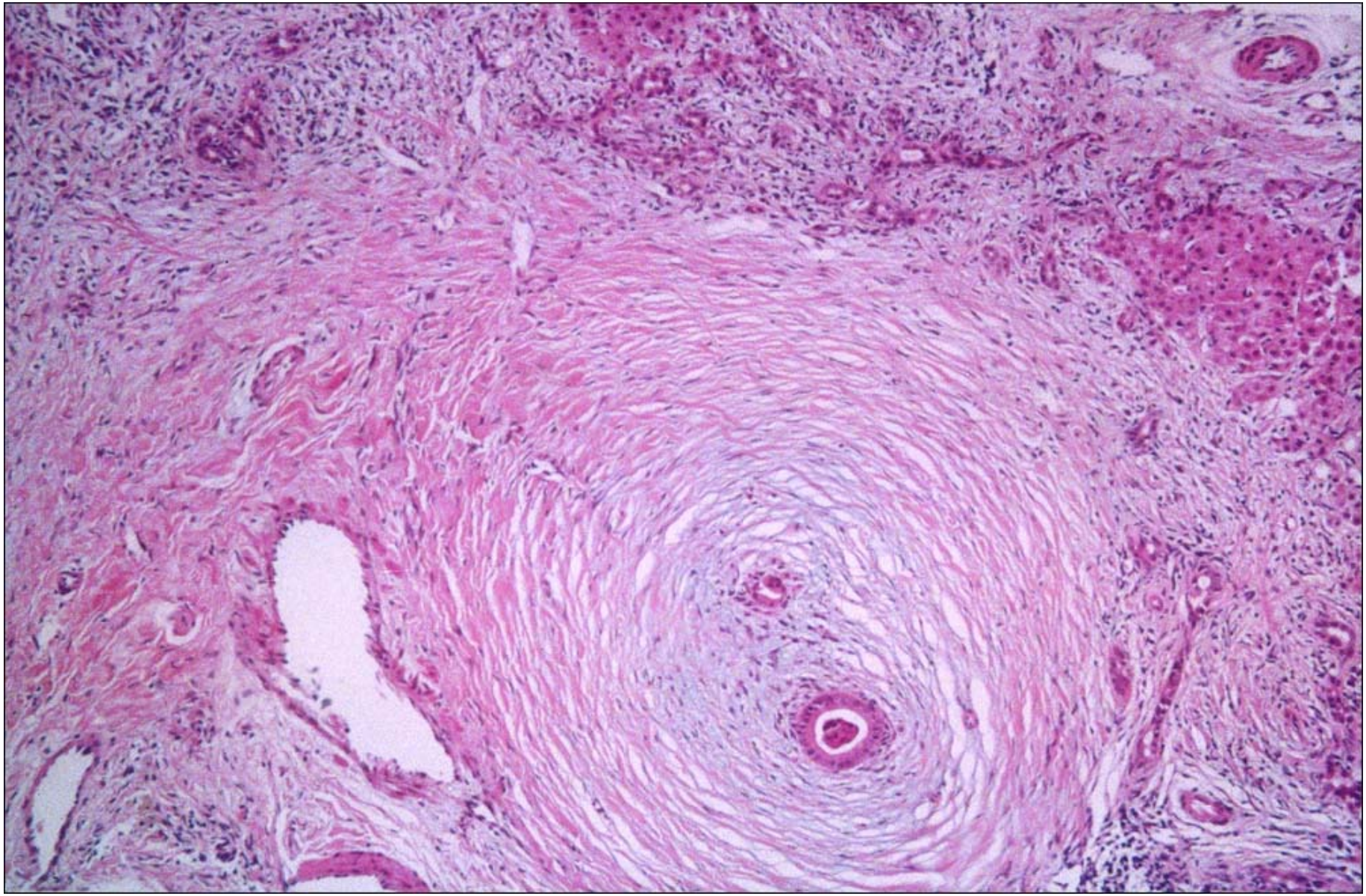


Primary Sclerosing Cholangitis

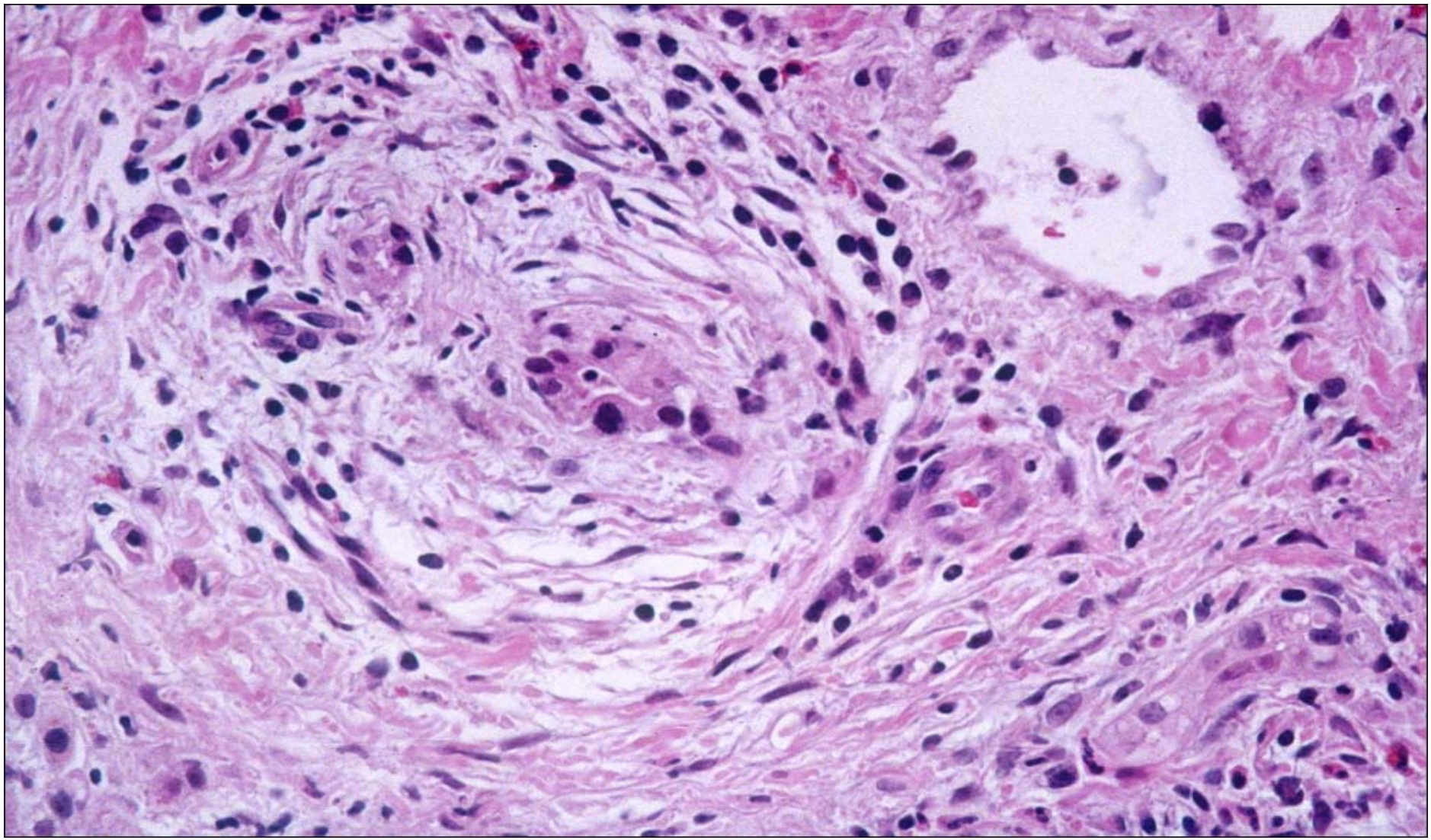
Concentric **periductal "onion-skinning" fibrosis** with atrophy and injury to bile duct epithelium is the classic lesion seen in **primary sclerosing cholangitis**, but this pattern of ductal injury is not seen in all cases and may be **absent in needle biopsy** specimens.



Sclerosing Cholangitis Associated with Primary Immunodeficiency Sclerosing cholangitis-type changes may be seen in patients with immunodeficiencies, as in this case of **common variable immunodeficiency**. Such lesions are also seen in patients with **AIDS**. Various **infectious agents** such as Cryptosporidium, cytomegalovirus, and microsporidium have been implicated etiologic agents, although none was identified in this case.



Sclerosing Cholangitis Associated with Primary Immunodeficiency
The interlobular bile duct shows **degenerative changes,** such as pyknosis, and is surrounded by loose **concentric fibrosis**.



IgG4-Related Sclerosing Cholangitis

Many lymphoplasmacytic infiltration and fibrosis, particularly IgG4-positive plasma cells.

IgG4-associated AIH is characterized by extensive parenchymal necroinflammation in addition to portal and periportal hepatitis with many IgG4-positive plasma cells.

A majority of pathological changes of IgG4-hepatopathy may be secondary to IgG4-SC **and/or type I autoimmune pancreatitis (AIP).**

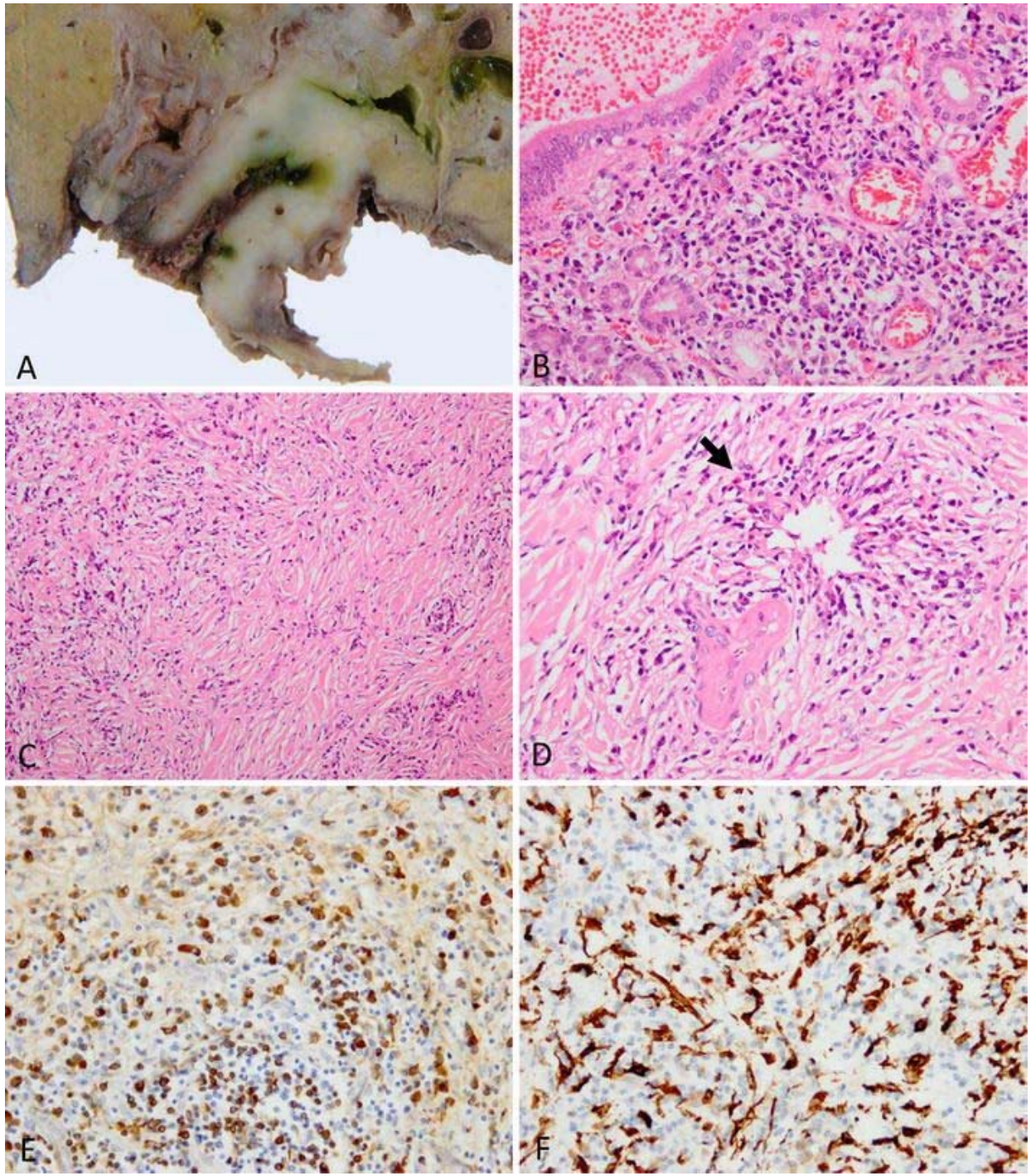
Pathologically, marked **lymphoplasmacytic infiltration**, including a large number of IgG4-positive plasma cells, and **storiform fibrosis** usually resulting in a tumorous lesion and **obliterative phlebitis** are common characteristic findings.

Eosinophilic infiltration is also noted in most cases, whereas neutrophils, abscess, and necrosis are not.

IgG4-RD in a given organ is occasionally associated with another IgG4-related disease in **other organ**, either synchronously or metachronously.

In the hepatobiliary system, IgG4-sclerosing cholangitis (IgG4-SC) is considered an IgG4-RD and mainly involves the **extrahepatic bile ducts and occasionally the hilar and intrahepatic large bile ducts.**

In addition, IgG4-related inflammatory pseudotumor, IgG4-hepatopathy, and IgG4-related autoimmune hepatitis have also been described as IgG4-RDs. Of note, type 1 AIP and IgG4-SC frequently develop **in the same patient**.



Pathology of IgG4SC.

a The **hilar bile duct** shows extensive wall thickening.

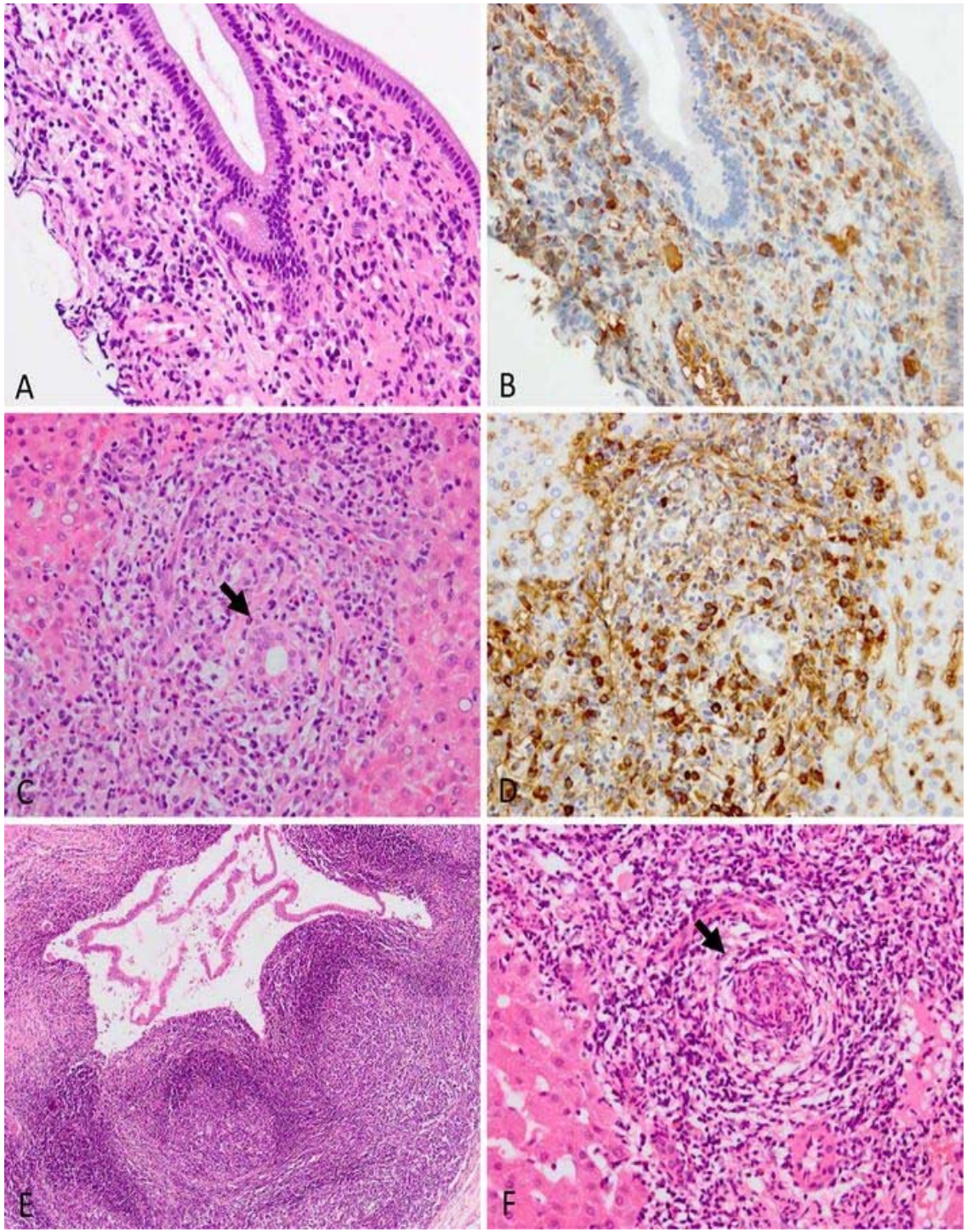
b Plasma cell-rich inflammation is noted beneath the intact lining epithelium.

c Collagen fibers are arranged in a **storiform pattern**.

d Lymphoplasmacytic phlebitis (arrow) represents an early sign of **obliterative phlebitis.**

e IgG immunostaining demonstrates many **IgG** - positive plasma cells.

f Many **IgG4**-positive plasma cells have infiltrated the tissue.



Biopsy findings and differential diagnoses of IgG4SC.

a Bile duct biopsy shows the infiltration of **lymphocytes and plasma cells** in the bile duct stroma. The lining epithelium is well preserved.

b Many **plasma cells** appear to be positive for **IgG4**, indicating the diagnosis of ISC.

c In this liver biopsy, the portal tract is expanded with a dense inflammatory infiltrate containing lymphocytes, plasma cells, and eosinophils. The arrow indicates a **slightly damaged bile duct**; however, bile duct injury is less conspicuous than that in PSC.

d IgG4 immunostaining shows many IgG4-positive plasma cells, in keeping with ISC.

e Follicular cholangitis is characterized by dense lymphocytic infiltration with many lymphoid follicles.

f Sclerosing cholangitis with **Granulocytic Epithelial Lesion** shows intraepithelial **neutrophilic** infiltration and periductal fibrosis (arrow) / type 2 autoimmune pancreatitis.