Case study

A 32-year-old Caucasian woman presented to her primary care physician with a

- 3 month history of anorexia, weight loss, fatigue and arthralgia. BMI 23
- she experienced a constant vague discomfort in the right upper quadrant of the abdomen.

She was referred to us because laboratory testing had revealed abnormal liver enzyme values

Her medical history was otherwise unremarkable.

Family history was positive for hypothyroidism on mothers side.

No use of drugs, herbals or dietary supplements

No risk factors for viral hepatitis

No history of traveling

Laboratory investigations

ESR	12 mm/h
WBC	8.7 x 10^9/mm3 (reference 3.5 – 11.0)
Hb	8.3 mmol/ml (reference 7,5 - 10)
Platelets	237 x 10^9/mm3 (reference 150 - 450)
Bilirubin	68 µmol/L (normal < 20)
ALT	691 IU/L (normal < 30)
AST	509 IU/L (normal < 45)
Alk Phos	130 IU/L (normal <100)
GGT	69 IU/L (normal <60)
INR	1.2
Albumin	38 g/L

Creatinin, Urea and electrolytes are normal

Additional tests:

IgG: 20 g/L (reference 5.5 – 16.0)
IgM: 1.2 g/L (reference 0.23 – 2.5)

Viral serology:

HAV IgM	-
HAV IgG	+
HBsAg	-
anti-HBc	-
Anti-HCV	-
HIV	-

Ceruloplasmin: 31 mg/dL (reference 25-35)
Ferritin: 150 ng/mL (reference 40 to 200)
alpha 1 antiptrypsin: 200 mg/dL (reference 150-350)

Abdominal ultrasound: normal

Differential Diagnosis

Conclusion: Acute hepatitis with jaundice

Obstruction:	Choledocholithiasis, malignancy
Viral hepatitis:	Hepatitis A, B, C, E, CMV, EBV, HIV
Toxic:	(prescription) drugs, alcohol
Autoimmune:	AIH, primary biliary cholangitis, primary sclerosing cholangitis
Metabolic:	Wilsons Disease, Haemochromatosis, a1-antitrypsin deficiency

Which antibodies do you expect in this patient?

A. ANA and smooth muscle antibodies

B. LKM-1 and LC1 antibodies

C. SLA and LP antibodies

Which antibodies do you expect in this patient?

A. ANA and smooth muscle antibodies (75%)

B. LKM-1 and LC1 antibodies

C. SLA and LP antibodies

Case

Liver biopsy was done

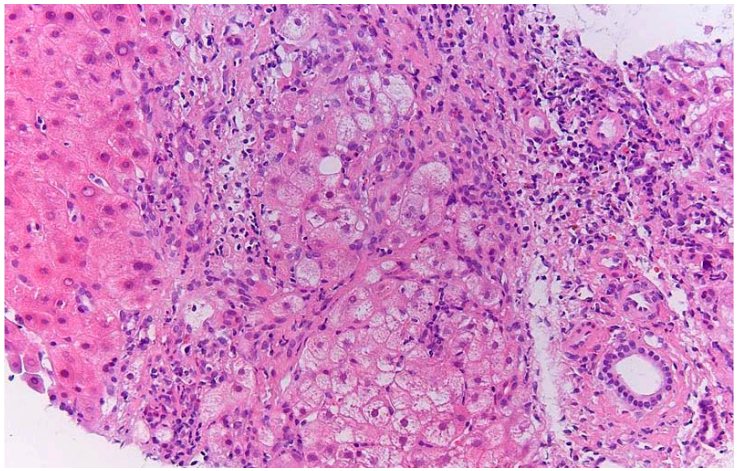
Which histological feature is typical of AIH?

A. Interface hepatitis

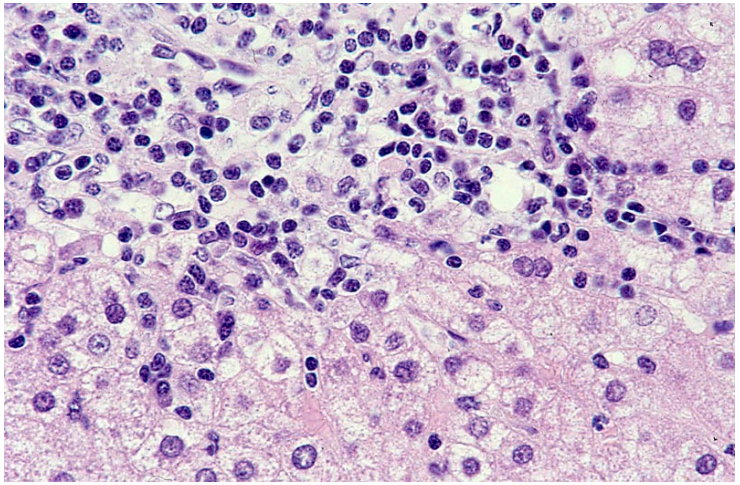
B. Plasmacellular infiltration

C. Emperipolesis
(at least one complete inclusion of a mononucleated inflammatory cell with visible cytoplasm in a hepatocyte)

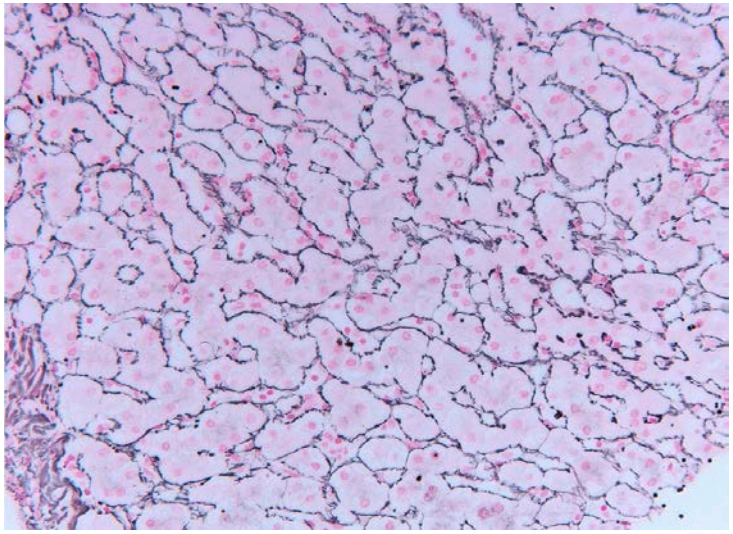
D. Rosette formation
(small groups of hepatocytes arranged around a small, sometimes not visible, central lumen: best seen on reticulin stain)



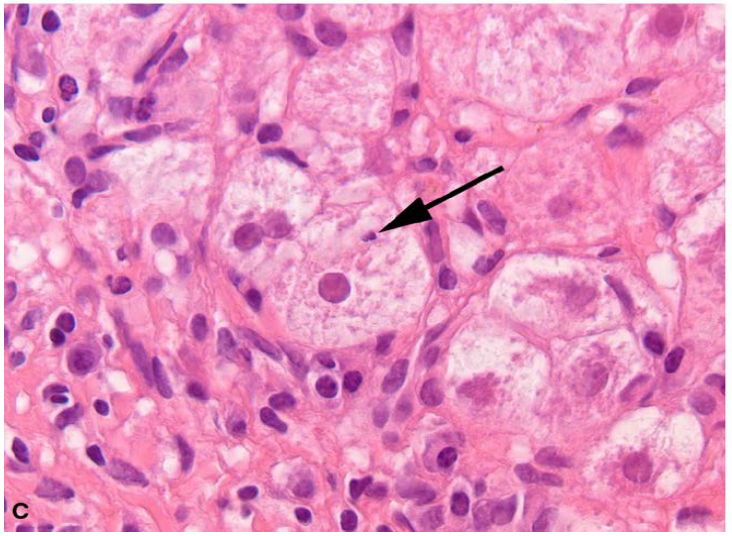
Interface hepatitis



Plasma cells infiltrate



Rosette formation



Emperipolesis

De Boer et al, Histopathol 2014

Liver biopsy

Feature	Score
A. Periportal or periseptal interface hepatitis (piecemeal necrosis)	
Absent	0
Mild (focal, few portal areas)	1
Mild/moderate (focal, most portal areas)	2
Moderate (continuous around <50% of tracts or septa)	3
Severe (continuous around >50% of tracts or septa)	4
B. Confluent necrosis	
Absent	0
Focal confluent necrosis	1
Zone 3 necrosis in some areas	2
Zone 3 necrosis in most areas	3
Zone 3 necrosis + occasional portal-central bridging	4
Zone 3 necrosis + multiple portal-central bridging	5
Panacinar or multiacinar necrosis	6
C. Focal (spotty) lytic necrosis, apoptosis and focal inflammation	
Absent	0
One focus or less per 10X objective	1
Two to four foci per 10X objective	2
Five to ten foci per 10X objective	3
More than ten foci per 10X objective	4
D. Portal inflammation	
None	0
Mild, some or all portal areas	1
Moderate, some or all portal areas	2
Moderate/marked, all portal areas	3
Marked, all portal areas	4
Maximum score	**18**

Ishak 1995

Liver biopsy

There is evidence of severe interface hepatitis, with marked presence of plasma cellular infiltrates in both the portal areas and lobules. HAI 12. The bile ducts are intact. Reticulin stain shows the presence of rosettes. Emperipolesis is observed at least twice. There is some extension of collagen fibres from the portal areas, consistent with moderate fibrosis.

Conclusion: Histological changes, typical for acute autoimmune hepatitis, but consistent with viral hepatitis and toxic injury. HAI: 12, Stage 2 fibrosis.

Is this autoimmune hepatitis?

A. Yes

B. No

Feature/parameter	Discriminator	Score
ANA or SMA+	≥1:40	+1
ANA or SMA+	≥1:80	**+2**
Or LKM+	≥1:40	
Or SLA+	Any titre	
IgG or immunoglobulin level	>Upper limit of normal	+1
	>1.1× Upper limit	**+2**
Liver histology	Compatible with AIH	+1
	Typical of AIH	**+2**
Absence of viral hepatitis	No	0
	Yes	**+2**

≥6 points: probable AIH;

≥7 points: definite AIH

Case study questions

1) In case of *starting prednison*, what would you do to **protect bone metabolism?**

2) Would you do a **liver biopsy**

- after obtaining 2 years of clinical remission, in order to decide to wean / stop therapy?

3) *In case of long-term immunosuppression;*

Are there **risks** associated with long-term use of immunosuppression?

Would you do specific **evaluations** to identify these risks?