

# How skin and liver can lead to diagnosis

N. Lanthier, P. Vande Berg, A. Vande Berg, E. Harkemanne, C. Peeters, V. Havelange

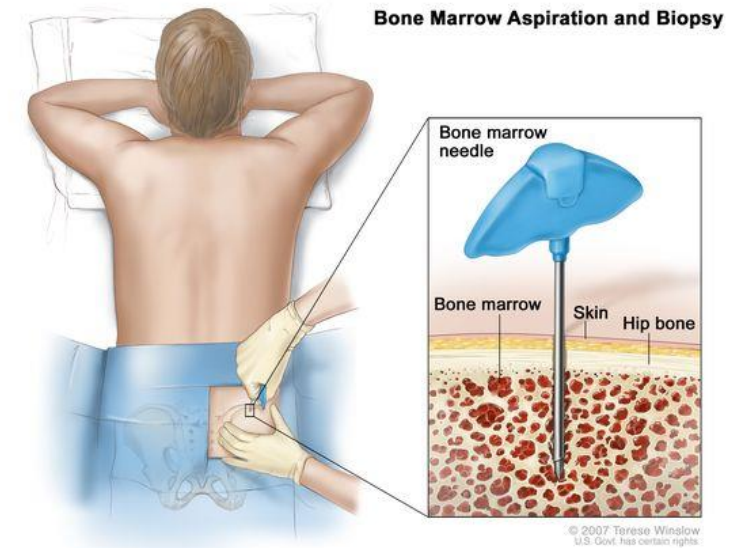
Friday, December 3, 2021

BASL meeting, Mons

# You receive a call from the haematologist...

A 73-year old woman

- Recently diagnosed with chronic myelomonocytic leukemia
  - Fatigue
  - Night sweats
  - Weight loss
  - Monocytosis
- Confirmed by bone marrow aspiration and biopsy

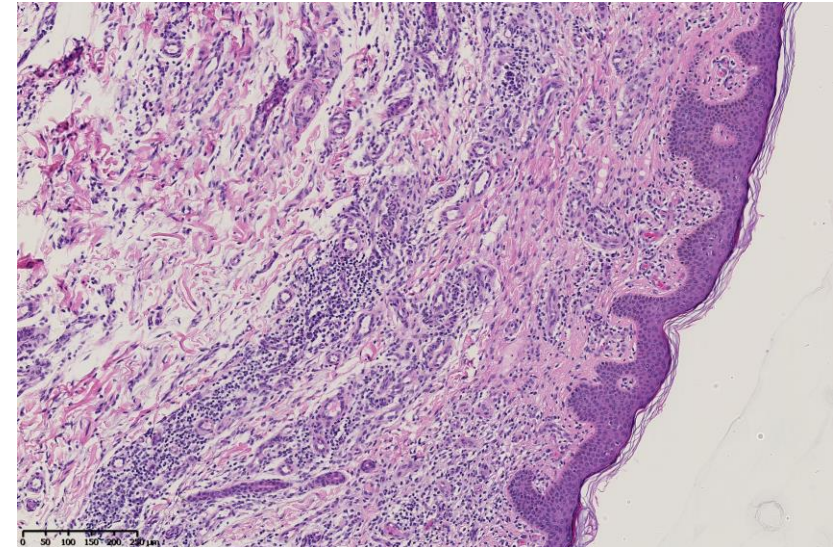


# Another feature

Erythematous firm skin nodule




- Right forearm
- Biopsy: infiltration of the dermis with a population of immature cells




→ **Skin localization of the chronic myelomonocytic leukemia**

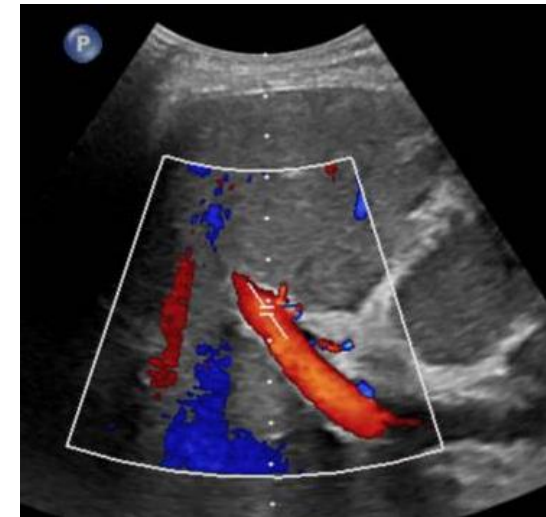
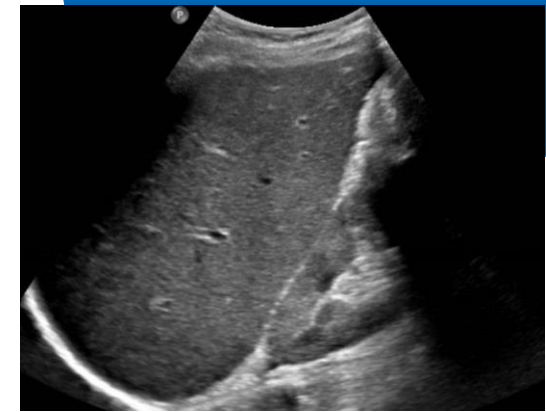
# Liver problem ?

Onset of cholestasis

	Hb	8,8 g/L
	WBC	8970/ $\mu$ L
	Monocytes	2360/ $\mu$ L
	Platelets	118000/ $\mu$ L
	CRP	33,7 mg/L
	AST	21 UI/L
	ALT	19 UI/L
	ALP	737 UI/L
	GGT	119 UI/L
	Bilirubin	0,5 mg/dL

	IgM	1,4 g/L
	IgG	20,3 g/L
	IgA	4,9 g/L
	ANCA	Neg
	M2	Neg
	ANA	1/160

 Liver ultrasound:



# What do you recommend ?

- Unclear cause, measurement of the gradient and transvenous biopsy
- Cholestasis without jaundice, wait and see
- Empirical treatment with ursodeoxycholic acid
- Suspicion of cirrhosis and portal hypertension, assessment to be completed by elastometry
- Suspicion of auto-immune hepatitis, percutaneous biopsy

# Here, the value of elastometry is limited

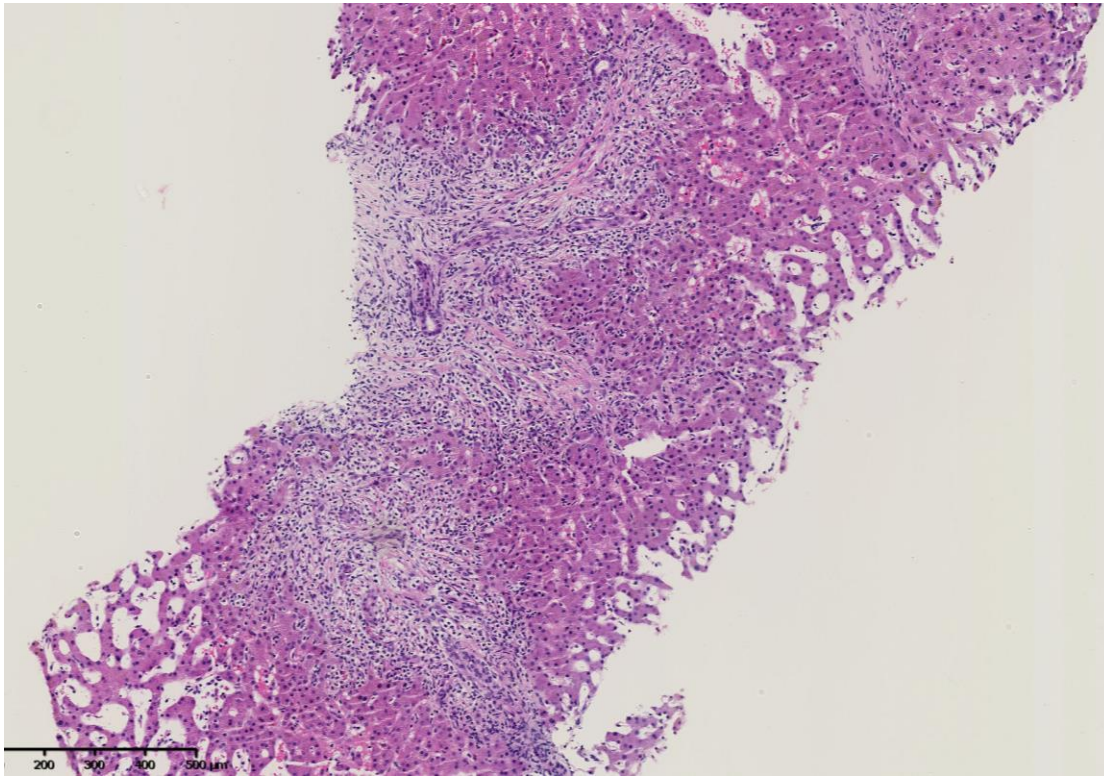
- Data on the stage of fibrosis in case of chronic viral hepatitis C, MAFLD, ALD...
- Here, suspicion of haematological infiltration, possible false-positives

Lanthier N et al. J Hepatol. 2015.

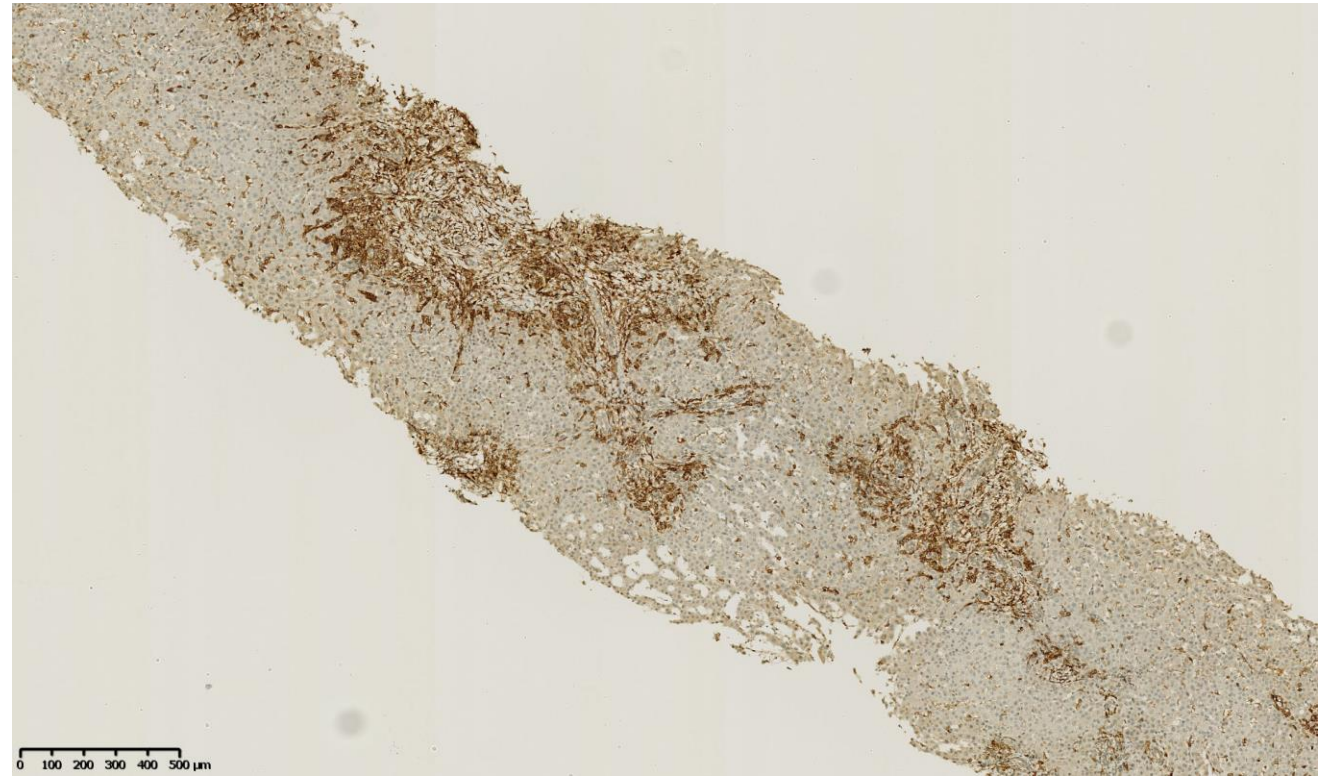
Delire B et al. Acta Gastroenterol Belg. 2020.

# Transvenous liver biopsy

- Transjugular approach preferred to percutaneous approach to reduce the risk of bleeding (amyloidosis in case of ↗ ALP)
- HVPG: 10 mmHg



Cellular infiltration of the portal tracts  
Ductular damage



Massive infiltration of CD117<sup>+</sup> and CD25<sup>+</sup> cells

# What is your diagnosis ?

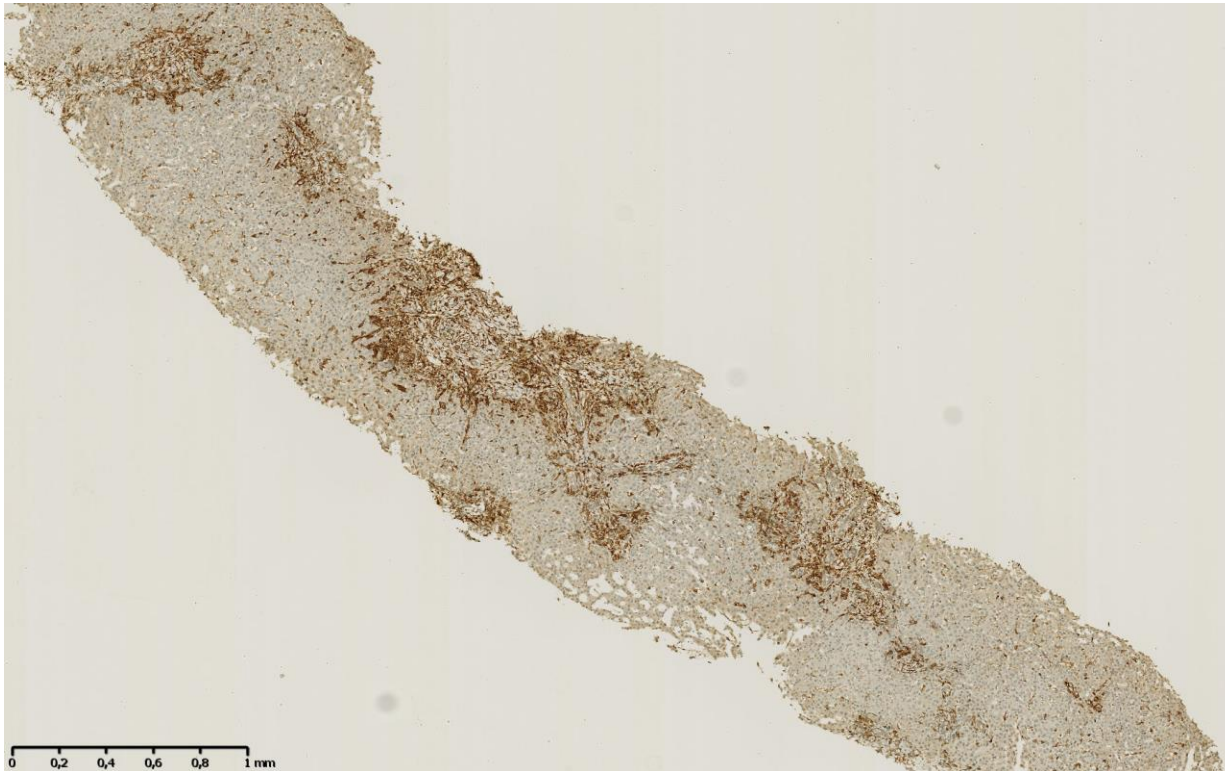
- Primary biliary cholangitis
- Vasculitis
- Lupus erythematosus
- Mastocytosis
- Histiocytosis

# Many diseases can affect the liver and skin

Disease	Skin manifestation	Liver finding
<b>Hemopathies</b>		
Lymphoma	Pruritus, erythematous patches, plaques and nodules	Nodules, mass
Langherans cell histiocytosis	Brown to purplish papulonodular eruption	Diffuse liver infiltration, nodules, sclerotizing cholangitis
Malignant histiocytosis	Ulcerated lesions, erythematous plaques	Peliosis hepatis
Systemic mastocytosis	Maculopapular eruption, mastocytoma, pruritis	Portal hypertension, cholestasis
<b>Systemic diseases</b>		
Sarcoidosis	Papular lesions, nodular lesions, plaque-like lesions, lupus pernio, erythema nodosum, subcutaneous nodules	Cholestasis, cirrhosis, hepatic vein thrombosis, portal hypertension
Crohn's disease, Ulcerative colitis	Erythema nodosum, pyoderma gangrenosum Sweet syndrome	Primary sclerosing cholangitis
<b>Vasculitis</b>		
Periarteritis nodosa	Erythematous nodules, ulcerated lesions, purpura, petechial rash, livedo reticularis	Aneurysm of hepatic artery
Giant cell arteritis	Erythematous nodules, ulcerated lesions, purpura	Cholestasis, nodules, biliary stenosis
<b>Autoimmune disease</b>		
Lupus erythematosus	Butterfly shaped facial rash, discoid lesions, papulo-squamous lesions	Hepatitis
Systemic sclerosis	Pruritus, hyper- or depigmentation, ulcerations, skin sclerosis, subcutaneous calcifications	Overlap with primary biliary cholangitis (Reynolds syndrome)
Sjögren's syndrome	Raynaud's phenomenon, purpura, ichthyosis, association with other auto-immune diseases i.e., systemic lupus erythematosus, systemis sclerosis	Cholangitis, hepatitis

# When skin and liver histology are confronted

Multifocal CD25<sup>+</sup> clusters of abnormal mast cells

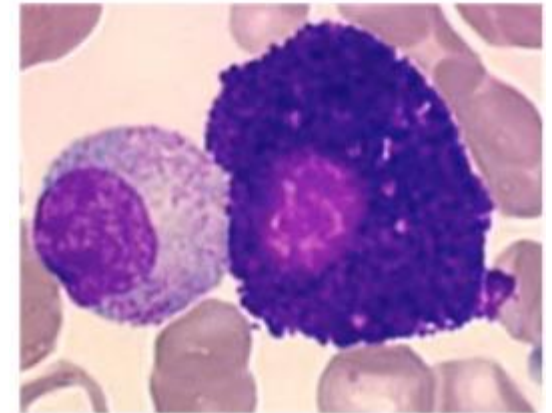


**Diagnosis:** Systemic mastocytosis with an associated hematologic neoplasm (SM-AHN).

# Systemic mastocytosis

## Infiltration of different organs by mast cells

- Common liver damage
  - Hepatomegaly
  - Disturbance of liver enzymology
  - Portal hypertension
  - Hepatocellular insufficiency
- Histology
  - Infiltration of the portal tracts or sinusoids
  - Cholestasis, cholangitis
  - Nodular regenerative hyperplasia, septal and perisinuoidal fibrosis
  - Veno-occlusive disease or secondary hematopoiesis
- SM-AHN: SM + myeloproliferative syndrom/myelomonocytic leukemia/myelodysplasia
  - ✎ The diagnosis of SM-AHN in bone marrow can be difficult



# Evolution of the patient

- KITD816V mutation: present
- Serum tryptase: elevated (192 µg/L)
- Start treatment with midostaurine
  - Non-responder
- Second-line therapy with avapritinib
  - Normalization of liver tests
- Patient still alive, after 2 years of follow-up
- Life expectancy: 24 months (SM-AHN), 15 months (SM-CMML)

