Simultaneous Presentation of Wilson's disease and Autoimmune Hepatitis

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Introduction

- Wilson's disease (WD) and autoimmune hepatitis (AIH) are considered as the common causes of acute and chronic hepatitis.

- The correct diagnosis and selecting the appropriate therapy remains a clinical dilemma

AIH scoring

Liver–kidney microsomal antibody ≥1:40	2
Anti-soluble liver antigen positive	2
Total serum IgG	
>ULN	1
≥1.1× ULN	2
Liver histology	
Compatible with autoimmune hepatitis: lymphocytic infiltrates, chronic hepatitis	1
Typical of autoimmune hepatitis:[b] interface hepatitis	2

WD scoring

Table 6 Diagnostic Score in Wilson's Disease, Agreed at a Consensus Meeting.[101]

Score	−1	0	1	2	4
Kayser-Fleischer rings		Absent		Present	
Neuropsychiatric symptoms suggestive of WD (or typical brain MRI)		Absent		Present	
Coombs negative hemolytic anemia + high serum copper		Absent	Present		
Urinary copper (in the absence of acute hepatitis)		Normal	1–2 × ULN	>2 × ULN, or >5 × ULN 1 day after 2 (0.5 g D-penicillamine	
Liver copper quantitative	Normal		<5 × ULN	>5 × ULN	
Rhodanine positive hepatocytes (only if quantitative Cu measurement is not available		Absent	Present		
Serum ceruloplasmin		>0.2 g/L	0.1–0.2 g/L	<0.1 g/L	
Disease-causing mutations detected		None	1		2
Assessment of the Wilson's Disease diagnostic score					
0–1: unlikely	2–3: probable			4 or more: highly likely	

Note: In the EuroWilson Database,[103] cases scoring ≥4 are accepted as having WD

The misleading point in differentiating AIH from WD:

- Low titer autoantibody production in Wilson disease due to hepatocyte necrosis
- Abnormal 24-hour urine copper excretion
- Liver biopsy and histochemical staining

- Several cases of WD that were initially diagnosed as AIH
- partial response to immunosuppresses was achieved in these patients.

- The coexistence of these diseases in one patient, at the same time, is rare.

- Here, we present a case of acute hepatitis with dominant features of both WD and AIH

Case

- A 10-year-old boy with a history of nausea, vomiting, and tea-color urine, since days before admission.
- His parents were not relatives.
- His father was suffering from insulin dependent diabetes mellitus.
- The patient was icteric and had an ill looking appearance
- Vital signs were stable
- The spleen was not palpable, although mild hepatomegaly and RUQ tenderness were detected.
- No findings in favor of chronic liver disease

- Laboratory investigations revealed mild anemia, abnormal coagulation profile, direct hyperbilirubinemia and elevated liver enzymes
- Reversed albumin globulin ratio (albumin = 3 g/dL and globulin = 4.9 g/dL).

- There was no specific key point in his past medical history or his familial history that would guide our investigation for a specific diagnosis.
- Therefore, we evaluated him for WD, AIH and viral hepatitis, in primary investigation.
- Serologic testing for viral hepatitis were negative.

Lab Tests

Table 1. Primary Laboratory Investigation [a]

Marker	Value	Marker	Value	Marker	Value
WBC	7.1×10^3 /microL	AST	139 mg/dL	BUN	9 mg/dL
RBC	3.6×10^6/microL	ALT	133 mg/dL	Cr	0.3 mg/dL
Hb	8.9 g/L	Uric acid	1.8 mg/dL	Na	137 meq/L
Platelet	151×10^3/microL	Bilirubin (total, direct)	(7.3, 2.5) mg/dL	K	4.3 meq/L
Reticulocytes	2.7%	Alkaline phospha-tase	286 IU/L	Ca	7.8 mg/dL
MCV	99.7 fL	BS	72 mg/dL	Phosphate	1.9 mg/dL
Coombs (direct, indirect)	Neg.	PT, INR	19.5 s, 2.02	Total protein	7. 9 g/dL
ESR	54 mm/h	PTT	53 s	Albumin	3 g/dL

Lab Tests (con.)

Table 2. Specific Laboratory Investigation [a]

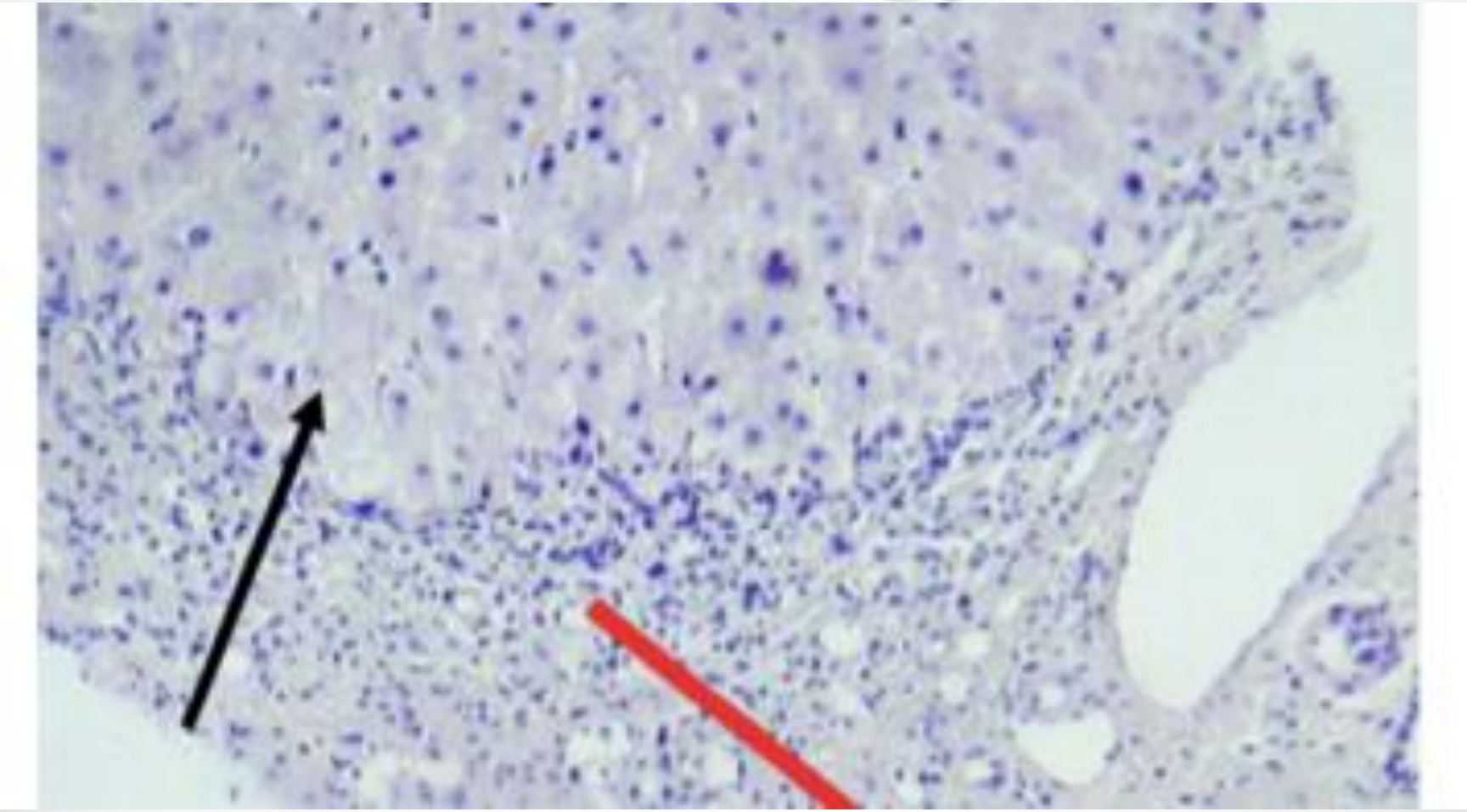
Marker	Value	Marker	Value
ANA	1/160	Ceruloplasmin	0.2 g/L
AMA	1/160	24hr Urine Copper	1600 microgr/d
ASMA	1/80	HCV-Ab IgM	0.09
Anti-LKM1	1/20	Alpha 1 antitrypsin genotyping	MM-Pi
HAV Ab (IgM)	0.3		
HBs Ag (ECL)	0.9		
HBs Ab (ECL)	23.9		

- Abdominal US: no space-occupying lesion and homogenous echo pattern parenchyma. Spleen size was in the upper limit of normal, with normal parenchyma.
- In slit-lamp examination by ophthalmologist, the Kayser-Fleischer ring was seen in upper and lower parts of cornea.

Liver biopsy

- fibrous bands encircling clusters of hepatocytes and regenerative nodules.
- Moderate to severe lymphocyte infiltrations and mild infiltration of eosinophil and neutrophils resulted in interface hepatitis
- Binuclear and multi-nuclear hepatocytes were seen, with feathery degeneration in several cells.
- In specific staining of tissue, no finding in favor of copper rich cells was seen.
- Histochemical analysis with rhodamine and orcein was negative.
- However, the amount of copper in dry liver tissue was about **20 times** the upper limit of normal.

Pathology



Pathology

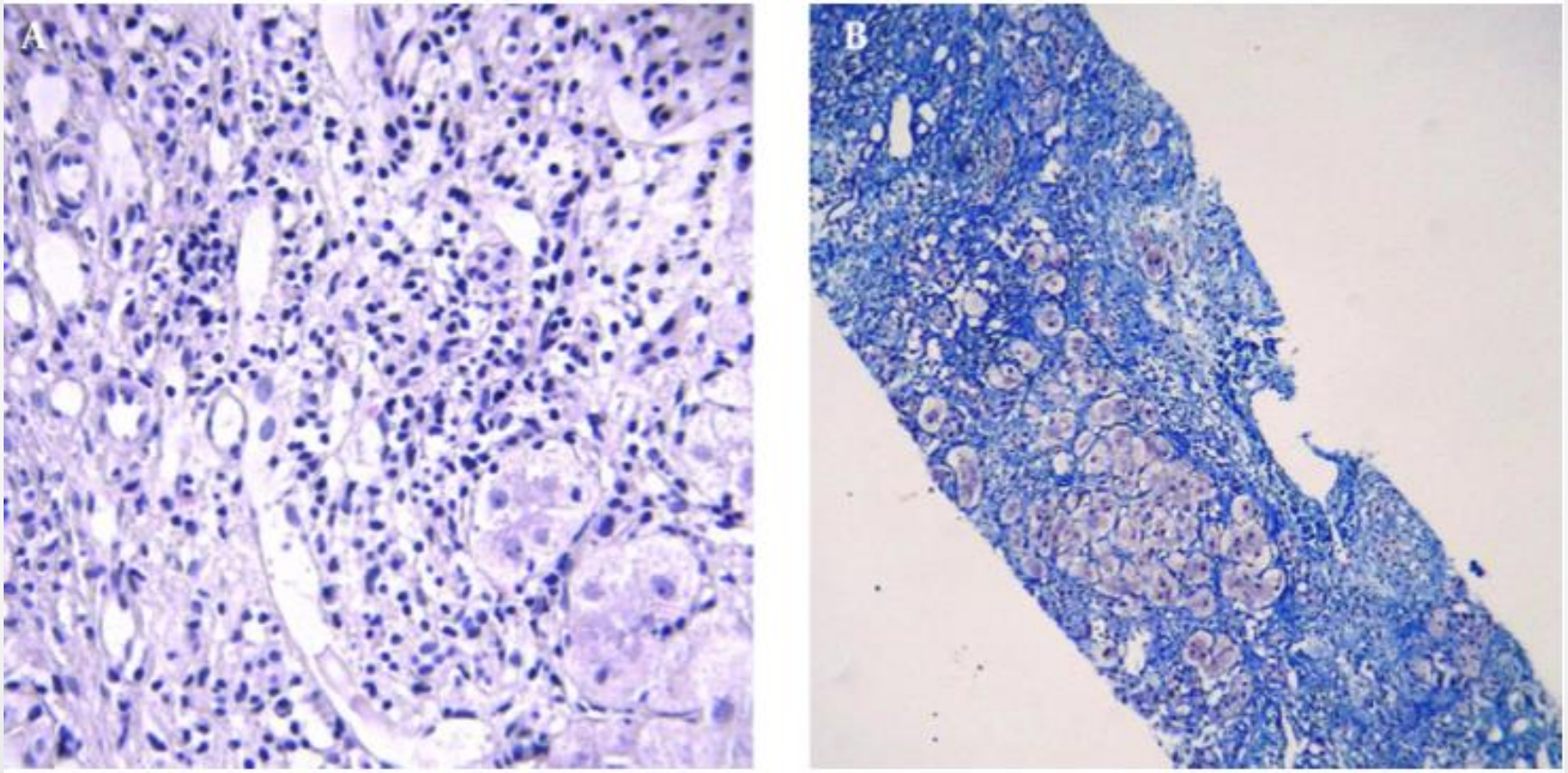


Figure 2. A, Moderate Infiltration of Lymphomononuclear Cell in Fibrous Septae, Resulting in Interface Hepatitis; B, Trichrome Stain Shows Marked Fibrosis of Liver Encasing Nodules and Single Hepatocytes (Blue Areas)

- Scoring system for this patient was done and the score of 7 was reached for him, in both of WD and AIH scoring systems
- According to the international scoring system, the score ≥ 7 are diagnostic for AIH and the score > 4 is considered positive for WD

- By considering concomitant WD and AIH, we started oral prednisolone (1 mg/Kg/day) and azathioprine (1 mg/ kg) and d-penicillamine for the patient, and an acceptable response was reached.
- Liver enzymes declined dramatically, after 20 days of treatment, and changed to near normal levels, after 6 months of medical therapy (AST= 54 mg/dL and ALT= 57 mg/dL).
- PT and INR changed to 17.5 seconds and 1.6, respectively, after administration of treatment and, at the end of 6 months of treatment, they were 14 seconds and 1.23, respectively.
- Also, the total and direct bilirubin changed to 0.7 and 0.2 mg/dL, at 6 months.

Discussion

- Acute hepatitis has a wide variety of etiologies.
- The correct diagnosis and selecting the appropriate therapy remains a clinical dilemma

- There are few cases with classical manifestations of WD and several features of AIH, simultaneously:
- Milkiewics and co-workers (2000) reported two cases of WD with superimposed autoimmune features
- *Wozniak and co-workers also in 2002 reported two cases of WD initially diagnosed as AIH*

Differentiating these two entities

- Autoantibody can be positive in WD due to hepatocyte necrosis, especially in early stage of this disease.
- Liver biopsy and histochemical staining: despite elevated hepatic copper content, these stains are frequently negative in patients with WD.

- The 24-hour urine copper:
- This test is abnormal in 80 - 85% of untreated patients with WD.
- However, in any severe icteric hepatitis, abnormal copper metabolism may occur. Although the 24-hour urine copper in acute icteric hepatitis is occasionally increased, the *level does not exceed the value of 200 microgram/24 hour.*

- In relation to a certain degree of overlapping between WD and AIH, it is highly recommended to screen for WD, particularly when poor response to steroid treatment is seen in patients with AIH

- On the other hand, there are several cases of WD patients, who are suffering from superimposed manifestations of AIH.

- In this group of patients, combination therapy with penicillamine and steroid may be of benefit

Conclusion

- This case highlights, although rare, the coexistence of Wilson's disease and autoimmune hepatitis and the need to maintain a high level of awareness of this problem.
- Therefore, it is reasonable to consider this type of hepatitis in rare patients, with dominant features of both diseases at the same time.

Thanks for your attention