HSV Hepatitis as the Initial Presentation of Acquired Immune Deficiency Syndrome

by Jean Ong Kian Koc, Ronald Miick, Nikroo Hashemi

A 28 year-old female without significant prior medical history presented with five days of right upper quadrant abdominal pain, vomiting, fevers up to 39.3 and chills. Physical examination revealed right upper quadrant tenderness. Initial laboratory data revealed normal complete blood count and comprehensive metabolic panel. Intravenous antibiotics were started for suspected biliary infection. Hyperdense gallbladder sludge, dilated biliary ducts and multiple hepatic hypodensities, suspicious for abscesses, were noted on computed tomography (CT) scan. Laparoscopic cholecystectomy was performed for suspected acalculous cholecystitis. Abdominal MRI on post-operative day 2 confirmed rim-enhancing lesions around the mildly dilated biliary system. Due to the extent of the abscesses, a human immunodeficiency virus (HIV) test was performed. It was positive and the absolute CD4 count was 4 cells/mm3. Her liver enzymes started to increase on post-operative day 7 and endoscopic retrograde cholangiopancreatography (ERCP) was performed; it was normal but a small sphincterotomy was made. She remained febrile and her liver enzymes peaked by post-operative day 20 [alkaline phosphatase 487 IU/L, total bilirubin 0.7 mg/dL, alanine aminotransferase (ALT) 1517 IU/L and aspartate aminotransferase (AST) 2137 IU/L]. She underwent diagnostic laparoscopy with wedge resection of hepatic segment five. Histology showed extensive hepatocellular necrosis, particularly in the subcapsular regions, with ground glass nuclear morphology and intranuclear (Cowdry type A) inclusions suspicious for herpes simplex virus (HSV) cytopathic effect.

The whole blood HSV 2 DNA PCR viral load was above the upper limit of detection for the assay (1 x 108 DNA copies/mL). A thorough physical exam revealed herpes labialis. Intravenous acyclovir (10 mg/kg q8h) was immediately started and she defervesced rapidly with normalization of liver enzymes on day 14. On day 19 of acyclovir treatment, she was diagnosed with cytomegalovirus (CMV) co-infection with neurological involvement. The acyclovir was changed to ganciclovir to cover both infections. She completed three months of antiviral treatment. Repeat abdominal CT scan two months after initiation of treatment showed interval decrease in the hepatic abscesses and liver enzymes remained normal.

Our patient presented with acute, anicteric hepatitis clinically mimicking acute cholecystitis. Histology was consistent with HSV hepatitis, a treatable cause of liver failure. Prompt initiation of antiviral treatment strongly correlates with improved survival.[1] Patients present with fever, high aminotransferases, normal bilirubin, leukopenia, thrombocytopenia, abdominal

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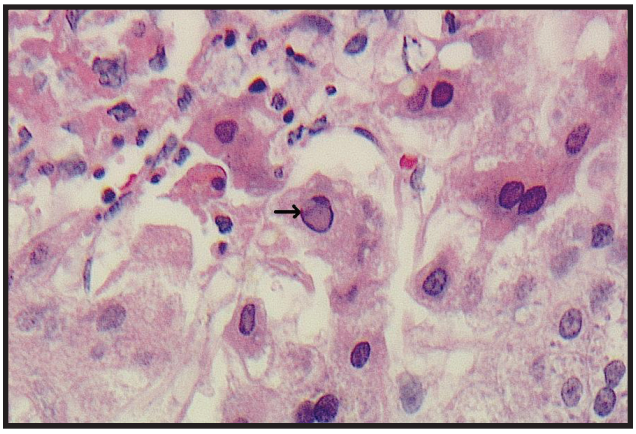

Figure 1. Liver segmentectomy demonstrating intranuclear "glassy" inclusions with chromatin margination in infected hepatocytes. Hematoxylin and eosin, 400x.

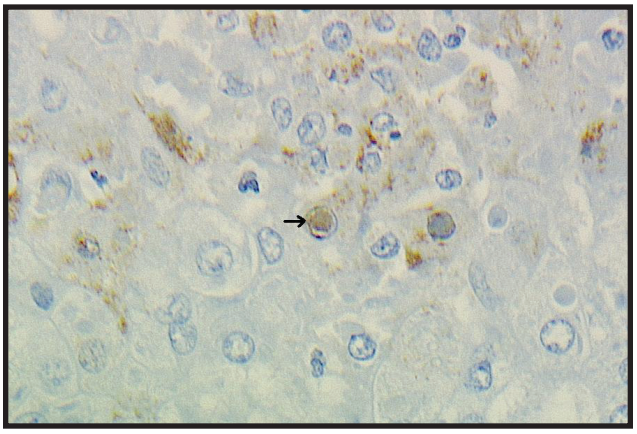

Figure 2. Immunoperoxidase stain for Herpes Simplex Virus showing positive (brown) staining in a Cowdry type A inclusion (400x).

pain and acute renal failure. Herpetic lesions are present in 57% of cases.[2] Liver biopsy is the gold standard for establishing the diagnosis. Immunosuppression, major surgery, trauma or pregnancy can reactivate HSV infection. Our patient's recently diagnosed HIV/AIDS could have predisposed herpes virus dissemination to the liver causing hepatitis.

There are limited number of HSV hepatitis cases in the literature thus there is no guideline as to the duration of antiviral treatment. Existing case series demonstrated varying lengths of treatment ranging from 3 weeks to 6 months, depending on clinical response.[3] Data supports empiric antiviral treatment with acyclovir for all patients with acute hepatitis of unclear etiology until HSV infection is excluded.[1] ■

References

1. Novell JP et al. Herpes Simplex Virus Hepatitis: An analysis of the Published literature and Institutional Cases. Liver Tranplantation 2007; 13: 1428-1434.
2. Kaufman B et al. Herpes Simplex Virus Hepatitis: Case Report and Review of Related Literature. Clinical Infectious Disease. 1996; 24: 334-338.
3. Berrington WR et al. Clinical Correlates of Herpes Simplex Virus viremia among Hospitalized Adults. Clinical Infectious Disease 2009; 9: 1295-1301.

Answers to this month's crossword puzzle:

1 S	U	2 C	R	3 O	S	4 E	■	5 M	U	6 T	A	7 T	E	8 D
P	■	E	■	E	■	L	■	I	■	A	■	O	■	I
9 O	C	C	U	R	■	10 M	Y	C	O	B	I	O	M	E
R	■	U	■	S	■	■	■	R	■	U	■	L	■	T
E	■	11 M	E	T	A	■	12 C	O	A	L	E	S	C	E
■	13 F	■	■	E	■	14 Z	■	B	■	A	■	■	■	D
■	O	■	15 A	D	M	I	N	I	S	T	E	16 R	S	■
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20 C	D	I	F	F	21 I	C	22 I	L	E	■	23 C	D	N	A
U	■	B	■	■	N	■	C	■	■	24 C	■	I	■	R
25 P	U	R	G	26 E	■	27 P	U	L	M	O	N	A	R	Y
■	■	O	■	C	■	S	■	■	■	C	■	T	■	■
28 H	I	S	T	O	L	O	G	29 Y	■	30 C	R	I	C	31 K
I	■	I	■	L	■	A	■	E	■	Y	■	O	■	I
32 D	Y	S	B	I	O	S	E	S	■	33 X	E	N	O	N