Liver Failure in a Patient with Sickle-Thalassemia

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Case Presentation

- 24 y.o. AAF with sickle-β-zero-thalassemia presented to our practice in June, 2009
- Life-long history of painful crises with very high baseline narcotic requirement
  - Dilaudid PCA pump, fentanyl patches and methadone, all at very high doses
- History of liver biopsy proven “secondary biliary cirrhosis” as a child
- Had been considered for at one point for liver transplant but for her sickle cell problem
- Initial lab work…

- Hgb 8.6, Hct 27 MCV 66, Fetal Hgb 12.8
- Hemoglobin Electrophoresis:
- Reticulocyte count: 4.4%
- Chemistries
  - Creatinine 0.55
  - AST 144
  - ALT 33
  - Alk Phos 346
  - Total Protein 9 gm/dl; albumin 3.7

- Seen frequently; attempts made to rationalize and reduce total narcotic intake
- Referred to MCV for possible allogeneic bone marrow transplant with curative intent
  - Transplant physicians were concerned about abnormal liver; discussions ensued
- Sept. 2009 developed peripheral edema, treated with furosemide
- Serial chemistries….

Date	Total bilirubin	Direct Bilirubin	Hgb	Retic Count	Creatinine
9/21	14.3				0.39
10/13	10.5		9		0.39
11/11	15.7		8	8.5	0.4
12/15	70.8	25.6	8	7.3	0.45
12/23	49.1	34.92	6		
	Admitted to SNGH for exchange transfusion				
Post-exchange	13				
12/30	42.7	29.34			1.47
1/4	42		7		2.3
1/7	49				2.35
Re-admitted to SNGH hepatology service					

Further work-along the way

- Negative Hepatitis serologies (A,B,C)
- Ultrasound of liver: biliary tree not dilated; no focal lesions
- Severe coagulopathy developed with liver dysfunction precluding liver biopsy

Current Status

- Hospitalized receiving maximal supportive care
- Prognosis extremely guarded

Hepatopathy of Sickle Cell Disease

- Numerous possible etiologies:
- Acute sickle hepatic crisis, with sickling in the liver and subsequent sinusoidal obstruction
  - LFT's modestly elevated
  - Rapid self limited process
- Hepatic sequestration
  - Red cells pool in the liver leading to right upper quadrant pain, worsening anemia
  - Often requires transfusions to maintain red cell mass and blood volume

Hepatopathy, continued

- Reverse sequestration
  - Sudden release of red cells back into circulation; can lead to volume overload and heart failure
- Cholelithiasis from bilirubin stones
  - Often required gall bladder removal
- Tranfusion hemosiderosis; may require iron chelation
- Viral hepatitis – increased incidence in SCA

Hepatopathy, continued

- Cholestasis: acute or chronic
  - Hallmark is extremely elevated bilirubin
  - Can present with RUQ pain
  - Modest renal failure common
  - Treatment is said to be exchange transfusion
  - Fewer than 20 cases in world's literature, so any recommendations for therapy are based on very small sample size
  - High mortality (>50%)
  - If happens repeatedly, then called chronic cholestasis
  - Our patient was exchanged promptly but sustained only very brief benefit

Cholestasis, continued

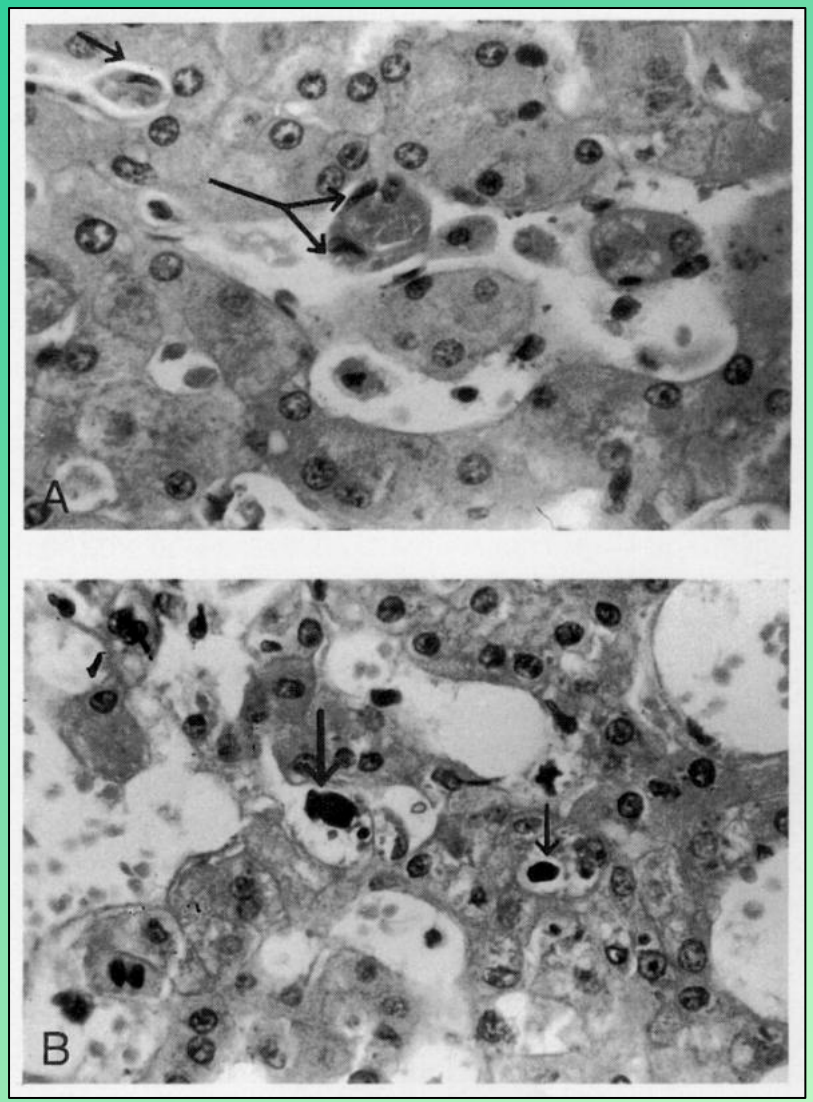
- In final analysis only extremely high bilirubin levels distinguishes this entity from other causes of jaundice and liver function abnormalities
- Only sixteen cases thoroughly documented in literature, which goes back forty years
- Little therapeutic help gleaned in reviewing that literature

Case report of patient with Sickle/ β+Thal with liver failure from cholestasis*

- 36 y.o. man admitted with liver failure, coagulopathy, hepatic pre-coma
- Liver enlarged and tender
- Treated for hepatic encephalopathy with usual supportive measures and was given packed red cells and fresh frozen plasma
- Quickly improved
- Liver biopsy performed shortly thereafter

*** Betrosian, *American Journal of the Medical Sciences* 311:292, 1996**

Liver Biopsy Findings



A: Agglutinative thrombi of sickle erythrocytes in dilated sinusoids. Swollen Kupffer cells with phagocytosed sickle erythrocytes (arrows). Hematoxylin and eosin x 400.

B: Bile plugs in dilated canaliculi (arrows). Dilated sinusoids. Hematoxylin and eosin x 400.

Distinguishing among causes of hepatic dysfunction

- In practice this is very difficult
- Frequent associated coagulopathy makes liver biopsy dangerous
- Histologic characteristics of different syndromes poorly characterized
- Treatment is supportive care in most cases with or without red-cell transfusion or exchange transfusion

Conclusion

- Severe liver dysfunction is an uncommon but grave complication of SCA
- Only exchange transfusion is thought to help, but evidence for this is very marginal
- Natural history variable but often fatal
- As in our case, liver transplantation is difficult to justify given the other chronic conditions
- Efforts at combined bone-marrow transplant and partial hepatectomy of bone-marrow donor with liver transplant have just been started at Dana Farber Cancer Institute as research trial
- No insurance reimbursement for this approach at present and no long-term follow-up data