Case of the month

A 33 year old woman with pre-existing diabetes on oral medication presented to an Emergency Department complaining of nausea, vomiting and inability to take her medication for 3-4 days. The day prior to being seen she noted that her urine was getting very dark and that her stools were getting lighter in color. Her presenting complaint to the ED was nausea, vomiting and diarrhea. She also stated that she had not taken her metformin because she ran out of her prescription, but stated that she had taken one dose of her boyfriend's expired metformin 3 days prior. She also complained of diffuse, crampy, lower abdominal pains of the same duration. Her emesis was described as green/yellow mucous with moderate frequency and her diarrhea as watery and mild. The only medications disclosed by the patient at this time were metformin and albuterol.

In the ED she was awake, although lethargic and appeared jaundiced. Her physical examination was significant for scleral icterus, dry mucous membranes and lower abdominal tenderness. Her initial laboratory results showed: blood glucose 347 mg/dl, creatinine 0.5 mg/dl, Na 129 meq/L, K 6.4 meq/L, total bilirubin 10, her AST was 5055 and ALT 4523 iu respectively, her INR was 1.3. She was started on IV fluids and insulin coverage. Two hours later her K was 3.8 meq/L, her Anti-HBS was negative, AntiHBCore was positive, and Hepatitis C AB was negative as was her HAV IGM. Blood drawn 11 hours after coming to the ED revealed her acetaminophen level was <2 as was her salicylate level and repeat AST and ALT were 3036 and 3419 respectively and her LDH was 6080. Her bilirubin was repeated and was reported as 10.6 with 6.4 direct. The following day her HBSAG from blood drawn 2 hours after admission to the ED was reported as positive.

Nearly 9 hours after her ED evaluation the patient was admitted to the medical service with a diagnosis of hepatitis. At this time the patient stated, to the admitting resident, that she was taking "Extra Strength Motrin" 3 tablets 3 times daily. Extra Strength Motrin is a preparation that consists of 300mg ibuprophen tablets that is available OTC in Canada, but not available in the United States. The resident contacted NJPIES with concern over possible acetaminophen toxicity, with both an unknown dose and an unknown time.

With elevated LFTs, hyperbilirubinemia and a possible history of supertherapeutic acetaminophen ingestion, NJPIES recommended treatment with n-acetyl cysteine ((NAC). Dosage for PO and IV NAC formulations were relayed to the admitting resident by NJPIES at this time, with the recommendation that IV be used.

Orders were written for oral NAC, which was discontinued for an unknown reason. This was followed by a written order for IV NAC, but this was also canceled prior to any doses being administered. The patient was admitted to a medical floor and as of NJPIES communication 19 hours after the patient presented, the patient had not received NAC, in either oral or IV formulation.

The patient was eventually started on oral NAC after at least 26 hours in the hospital. The following day she was clinically asymptomatic, her transaminases dropped to 1439 and 2486 respectively and her INR stayed at 1.1. 3 days later, NAC was discontinued at the recommendation of the hepatologist. The patient felt well, and was discharged from the hospital on the following day with hepatology clinic follow-up for her viral hepatitis. After the patient's discharge HBV DNA was detected in a sample of her blood by PCR. No proof of the actual preparation consumed was ever obtained.

This was a truly complicated presentation. There is little doubt that she has "hepatitis" with both a defect in ability to conjugate bilirubin and significant transaminitis. She also has a hepatitis profile which is indicative of recent hepatitis B infection. Three days after presentation in the ED her transaminases dropped to 711 and 1647 respectively for AST and ALT and again to 528 and 1310 on the 4th hospital day. While it is possible to have an acute hepatitis that presents with transaminase elevations such as this, the rapid decline is not consistent with viral hepatitis, thus a toxic hepatitis is the most important etiological factor in this case.

In the initial history the patient actually denied taking "Tylenol," but when one considers the lack of availability of a preparation of "Extra Strength Motrin", is it possible that this was "Extra Strength Tylenol?"

Apparently there was some concern from the admitting resident, but should this have been considered earlier in the work-up? NAC has proven effective when used in an early presentation of acetaminophen toxicity, and there is reasonable evidence to suggest its advantage in reducing mortality in late-presenting acetaminophen-associated fulminant hepatitis and perhaps non-specific fulminant hepatitis as well.[1, 2] The mechanism by which NAC benefits patients in late-presenting acetaminophen toxicity is poorly understood: it may result from such actions as free radical scavenging or its ability to increase tissue oxygenation.[1, 2] The lack of a detectable acetaminophen level does not rule out acetaminophen toxicity. In a recent presentation at a national toxicology conference, 21% of patients presenting with the history of repeated super therapeutic doses of acetaminophen had no detectable acetaminophen in their blood, as was described in this case (NACCT 2008). The effectiveness of NAC in treating acute viral hepatitis is less clearly supported. Though it may not be a standard therapy for acute viral hepatitis, and we have been unable to find any documented benefit to treating acute viral hepatitis with NAC, there is no documented harm caused by therapeutic dosage of NAC in these patients.[3] When one considers that this patient, who has an acute viral hepatitis, was also likely ingesting chronic doses of acetaminophen, the choice to start NAC is without question.

Also in the United States, acetaminophen toxicity is the most common cause of acute liver failure, representing 46% of all cases.[4] This includes the cases without a history of acetaminophen ingestion as well as cases where serum levels of acetaminophen are negative. As such, it is reasonable to treat with NAC in the setting of acute hepatitis, even without a clear etiology.

Citations:

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3. Gunduz H, Karabay O, Tamer A Ozaras R, Mert A, Tabak OF.N-acetyl cysteine therapy in acute viral hepatitis. World Journal of Gastroenerol. 2003 Dec;9(12):2698-700.

4. Lee, William M., Squires, Robert H. Jr., Nyberg, Scott L., Doo, Edward, Hoofnagle, Jay H. Acute Liver Failure: Summary of a Workshop Hepatology 2008;47:1401-1415