

A Patient with Aplastic Anemia Develops Hepatitis C and Receives Unjustified Therapy for his Hepatitis Which Seriously Worsens His Anemia.

Aplastic anemia is an inability of the bone marrow to produce enough red blood cells, white blood cells, and platelets (clotting particles), and can be total or of varying degrees of severity. His was moderately severe and was controlled with GM-CSF (granulocyte monocyte colony stimulating factor) since 1991.

I have no records from his evaluation when he first was diagnosed with aplastic anemia at age 8. Sometimes it is caused by a side effect reaction to medications, and if they were not needed or not monitored properly, there may be another source of liability. Sometimes it is by a reaction to chemicals. Since he is not yet 21, you may also want to investigate this potential cause of action.

After he began his GM-CSF therapy, his aplastic anemia was under control where he no longer needed blood or blood component (platelet) transfusions.

Unfortunately he contracted Hepatitis C, which is a viral liver infection which becomes chronic. Depending on its activity, it can kill more liver cells than regenerate, resulting in scar tissue (cirrhosis), and liver failure. It can also cause liver cancer (hepatocellular carcinoma). The cause of hepatitis C infection is usually from an infected blood transfusion, or contaminated needle.

I have no information as to how and when it was first diagnosed. The blood test for hepatitis C (non-A, non-B) is a few years old. But blood from paid sources, as opposed to volunteers, had a much higher risk for hepatitis C.

Which source were his transfusions from, and how well were those donors screened? That is another potential source of liability.

The current drug therapy of choice for treating hepatitis C is Rebetrone which consists of injections of interferon (Intron A) (an immune protein) and Rebetrol (ribavirin) (a drug that helps kill the virus). This combination of therapy has an approximate 40% positive response rate (significant reduction of the virus amount in the blood/liver), and decrease in liver cell destruction seen on a liver biopsy, twice as effective as interferon given alone.

However, the FDA and the drug manufacturer warn in bold print: "The primary toxicity of ribavirin is hemolytic anemia (destruction of red blood cells)." They also state: " It is recommended that a patient whose hemoglobin level falls below 10 g/ (gram per decaliter) have his/her rebetol (ribavarin) dose reduced to 600 mg (milligrams) daily.... A patient whose hemoglobin level falls below 8.5 g/dl should be permanently discontinued from Rebetol/ Itron A therapy (see WARNINGS)."

When there is active hepatitis C the "viral load" (the number of viral particles per milliliter: ml of blood) is often one million or more. And as liver cells die from viral infestation they burst and their protein enzyme contents enter the blood, and are easily measured on standard laboratory tests. These are LDH, SGPT, and SGOT.

Before a patient is started on Rebetrone therapy you need a reason, and often a liver biopsy is performed to actually determine microscopically what actually has occurred (scarring: fibrosis) and is (occurring active liver disease). With the standard needle biopsy through the abdomen into the liver, the major risk is bleeding, and if a patient has a very low platelet count (under 50,000, and especially under 25,000) it is contraindicated.

A liver biopsy can be performed by threading the biopsy needle via a neck (jugular) vein, past the heart and via the inferior vena cava into a hepatic (liver) vein, which eliminates bleeding into the abdomen. That was done on 3/16/2001, 15 months after the Rebetron therapy was terminated (after two weeks of therapy), and revealed "mild to moderate chronic periportal inflammation," and "mild portal (the vein that brings blood into the liver from the intestines) fibrosis (scarring)." "The hepatic lobules (liver cells) are otherwise unremarkable." This is not significantly active disease.

In his case, all the liver enzyme blood test were all normal on six studies from 7/98 through 1/3/00 and also on the eight studies after his Rebetron therapy through 10/2000 (and some were even below normal). All evidence against significantly active liver disease.

The Hepatitis C viral blood levels were 564,000 on 4/97, 700,000 on 7/13/99 and 330,000 on 11/18/99.

His hemoglobin blood levels (the oxygen carrying red blood cell pigment) showed significant anemia for years, as well as on 1/3/00 at 8.1. This is obviously below the 8.5 warning threshold level to terminate the use of this drug (ribavirin).

I know of no studies that evaluate the risks and benefits of Rebetrol in patients who have hepatitis C and aplastic anemia. Therefore, this is experimental and requires a very stringent level of informed consent.

Based on the normal liver enzymes and moderate level of hepatitis C viral particles there would be a question of therapy without a liver biopsy. But in a patient also with severe anemia, I believe that it was a departure from the standards of care to begin Rebetron therapy on 1/3/00.

On 11/18/99 they noted that the HCV (hepatitis C) PCR (viral blood level) was "700,000 copies" on 7/99. But they (Dr. #1, Dr. #2 and FNP Family Nurse Practitioner #1) never noted the 330,000 HCV PCR level that was done on 11/18 until 1/3/00, and did not stop initiating the "therapy."

On 11/22 FNP #1 noted that both Drs. #1 and #2 recommended a platelet transfusion and percutaneous liver needle biopsy (into the abdomen) "before interferon therapy versus Interferon / Ribavirin therapy." They were also going to do a bone marrow aspirate biopsy. "he should also be followed by Hepatologist (Liver Specialist) for Hep C therapy." I found no such consultation. Also it was not the interferon that caused the worsening of his anemia. It was the ribavirin. Although interferon has one-half the response rate, it could be given alone. In addition, a better form of interferon, Pegasys was under development, and there was no rush in his case to begin any risky therapy.

He returned on 1/10/00 FNP #1 noted "His CBC (complete blood count) has fallen a lot since last week, but he says he forgot to take his GM-CSF last night. I emphasized to him that the Rebetron has cause some decrease in CBC and he needs to take GM-CSF every night. We will probably go up on dose next week if CBC is still decreased." There is no evidence that this negligent FNP ever brought any of this to the attention of her supervising doctors that day, or ever. His Hgb (hemoglobin) level was down to 7.7 and his white blood count was dangerously low at 1.8 (1,800) versus 2.7 the week before. He was at a serious risk for infection.

On 1/17 his Hgb was 6.0 his platelet count dropped from 16 (16,000) to 9,000 in one week. This FNP and Dr. #2 still did not stop the Rebetron therapy.

On 1/19 the Hgb was 5.6 and the platelets only 10,000. Finally the Rebetron therapy was stopped by FNP #1 and apparently some doctor (whose signature I cannot read). On 1/19 transfusions were ordered to begin with two units of RBC (red blood cells). He also was transfused two units of RBC on 2/7, 2/21, 3/14, and 4/4.

The bone marrow makes all these blood elements and some of the immature red blood cells, called reticulocytes, enter the bloodstream. His reticulocytes count pre-Rebetron on 7/12/99 was 3.0, 11/18/99 1.4 and on 1/3/00, the day of initiation of Rebetron, it was 2.6 Then it dropped to 0.6 on 1/10/00 and further decreased to 0.2 pm 1/19. On 1/31 it was 0.9. This is the opposite response of the body to hemolytic anemia where red blood cells are destroyed, and a healthy (functional) bone marrow makes more cells. This is evidence of a direct toxic effect of ribavirin on his bone marrow. Did his doctors report this to the FDA as they should have done, and did they publish their finding in any medical journals to warn other doctors of this danger?

Apparently, he will undergo a bone marrow transplant. That will complicate his hepatitis C depending on which additional drugs he will receive. Immuno-suppressive drugs do interfere with the body's ability to fight infection, including viruses. And with a damaged liver, many drugs are more toxic to his liver.

He is at risk from bleeding internally and externally from a very low platelet count. He is also at risk from complications from blood transfusions including infections and transfusion reactions.

The Defense will content that he was fully informed of all the risks, but what known risks are there with aplastic anemia, to fully inform a patient about? I now of no information on that subject. You may want to conduct a Medline search (with the National Library of Medicine) Using the key words ribavirin and aplastic anemia.

The Defense will try to claim "contributory negligence for him missing one dose of GM-CSF on 1/9/00. I doubt it made the difference to his persistent bone marrow suppression.

Since 3/4/96 has he ever missed taking any of his daily 250 mcg (microgram) injections? If so, there did not appear to be any profound effect on his bone marrow and anemia.

In my opinion Dr. #1, Dr. #2, FNP #1, their hematology clinic, and Hospital #1 (which appears to be their employer or created agents of them) are all negligent for all the reasons stated above.

You need to know that there are nutritional (herbal) alternatives to aid the liver including milk thistle (containing silymarin), and combinations of Chinese herbs. Was this option with no side effects ever discussed with him?

I would suggest that you authorize our office to obtain Board Certified Experts in Hematology, Infectious Disease and Gastroenterology to give you their opinion on negligence, causation, and damages.

He also was noted to have a probable panic attack" on in 3/00. Has he been under a Psychologist or Psychiatrist's care?

Thank you for allowing our organization to assist you with this interesting case. We continue to remain available on this case to obtain Expert Witness opinions.