Lorenzo Azzalini

University of Padua
Medical School, Italy

“Just” an alcoholic hepatitis?

August 2005

White 10, Team C – Massachusetts General Hospital,
Boston – MA, USA

History of present illness

- 39 y.o. man w/ history of depression, HTN, alcoholism
- Admitted on 8/1 after a LOC, in a setting of EtOH withdrawal, severe dehydration, hyponatremia, hypochloremia and ARF.
- One month later, he is still in the hospital.
- Persistent hyperbilirubinemia, leukocytosis and fever of unclear etiology
- Intubated, NG tube, IV hydration and electrolytes disturbances correction
- On 8/2, transfer to the MICU.

History of present illness

- Broad spectrum antibiotic treatment: ampicillin, levofloxacin, flagyl (→ afebrile but left shift w/o clear source of infection: risk for aspiration but clear CXR, U/A –ve)
- Agitation, tachycardia and confusion → given propofol and intubated
- Diagnosis of alcoholic hepatitis (↑AST and ALT, AST/ALT > 2, ↑bilirubin and Alk Phos).
- 8/9: transfer to White 10

History of present illness

- On White 10 the patient regained consciousness. Denied abdominal pain, and was unable to recall much about the events that led up to his admission
- The pt reported that he was depressed and had drunk heavily in the last weeks. He had lost his appetite and had been eating almost nothing, and – in spite of that – had been vomiting frequently

Review of systems

- Nausea/vomiting.
- Alteration of mental status, slurring of speech.

Past medical history

- **Alcoholism and depression**
- **Hypertension** – borderline
- **?Sarcoidosis** – Presumptive diagnosis, based on CXR and chest CT

Meds on admission to White 10

- Lisinopril 10 mg PO QD
- Vancomycin 1 g IV Q12 (since 8/9)
- Cefepime 1 g IV Q12 (since 8/8)
- Flagyl 500 mg PO TID (since 8/1)
- Nexium 40 mg PO BID
- Neutra-Phos 2.5 g PO TID
- Lactulose 30 ml PO QID
- Ativan 4mg IV Q3
- Ativan 1-2 mg IV Q1 PRN
- Haldol 2 mg IV Q4 PRN
- Thiamine 100 mg PO QD
- MVI
- Fragmin 2500 U sc QD
- Senna and colace

- **Allergies** – NKDA
- **Social history** – Works in publishing, fired 2 weeks prior to admission. Recently separated from his wife because his of EtOH use, undergoing divorce. Has a 6-year-old son. Lives alone.
- **Familial history** – father w/ HTN, mother w/ ?chemical dependency

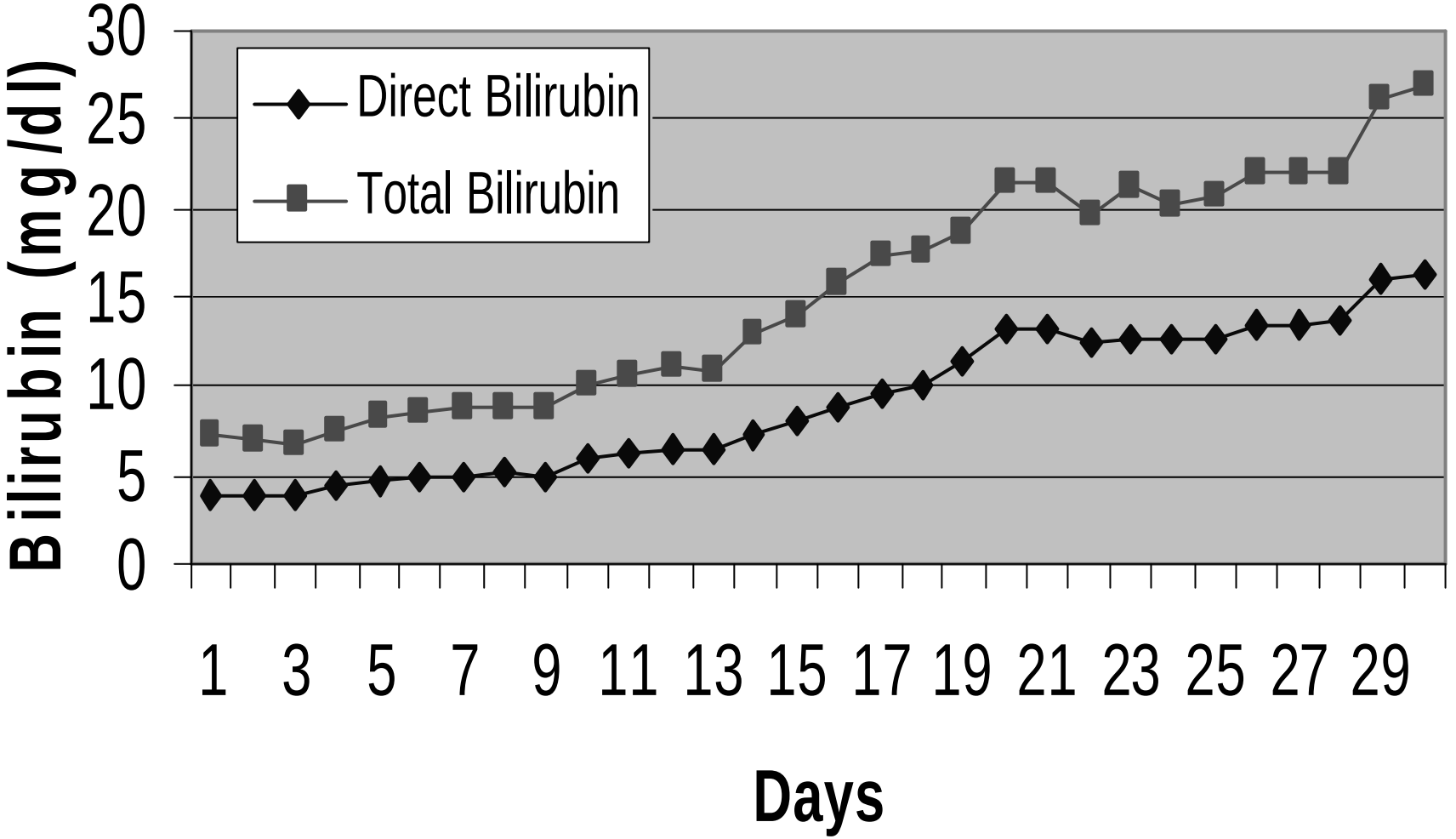
Physical exam

- Unremarkable, except for:
  - HR 107, RR 24
  - the patient was in mild distress (spoke slowly, interrupted his words to breath)
  - a JVP of 7 cm
  - abdominal distension

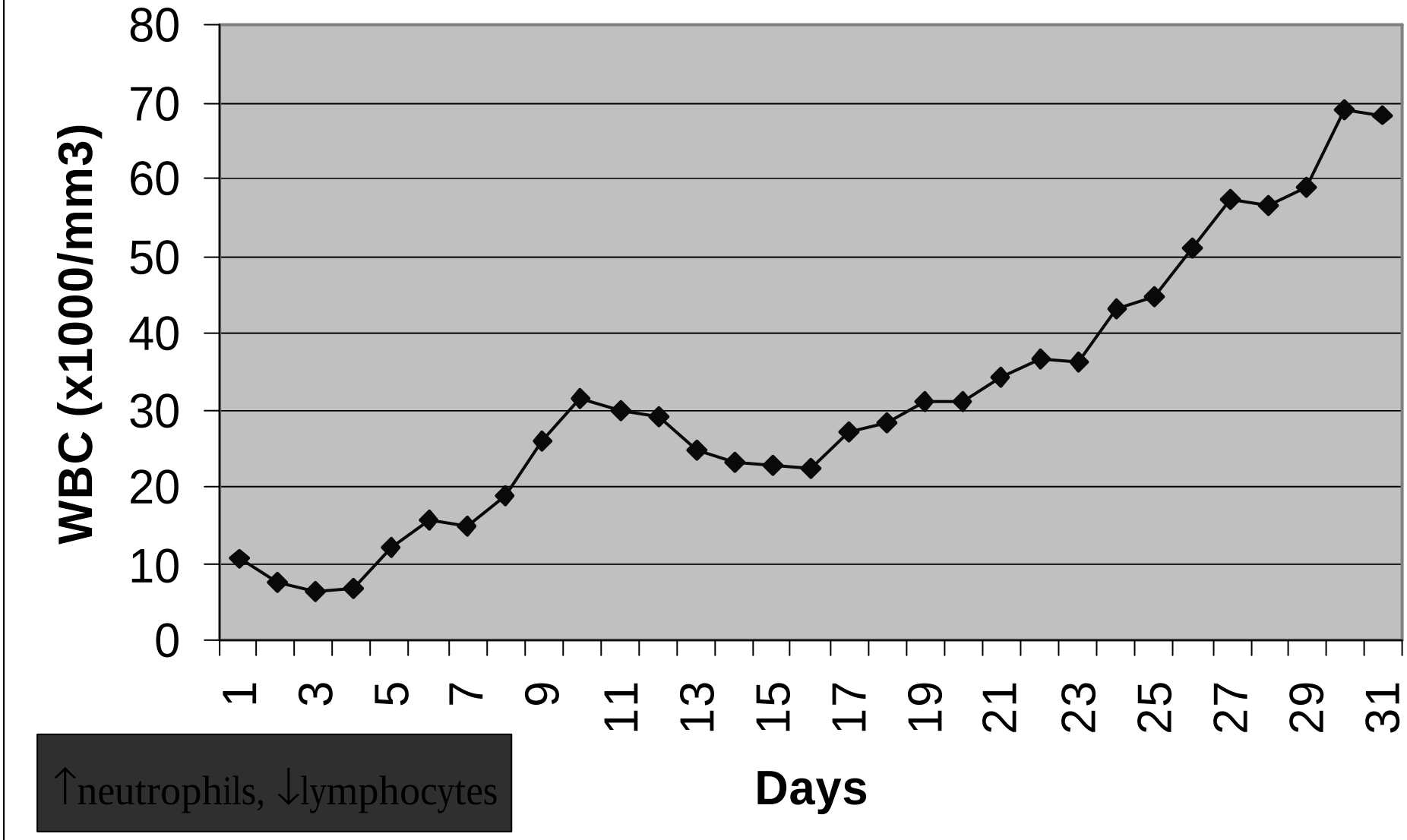
Labs and Studies on admission

- Total bilirubin 8.8, direct bilirubin 5.0
- Albumin 2.2
- AST 140, ALT 66, Alk Phos 188
- HCT 29%, Hgb 10
- WBC 26 (N 86, L 9)

Bilirubin during the month of August



WBC during the month of August



Chest X-Ray and CT

- Increased consolidation in the RUL, RML and LLL concerning for aspiration or multifocal pneumonia.
- Stable right pleural effusion with associated atelectasis.
- Chest CT negative for pneumonia, confirmed the presence of bilateral pleural effusions

Abdomino-pelvic CT

- No specific evidence for pancreatitis or its complications
- Increasing ascites
- Increasing bilateral pleural effusions

Abdominal US

- Fatty infiltration of the liver.
- Distended and thickened gallbladder.
- Small amount of ascites in the abdomen and pelvis

Other studies

- **ECG**: Sinus tachycardia
- **Head and brain CT**: No evidence of intracranial hemorrhage. No fractures seen
- **EEG**: Markedly abnormal EEG, due to the presence of diffuse, attenuated delta slowing without focal features. No epileptiform activity is present
- **Blood culture**: no growth after 7 days.

Assessment and plan

- 39 y.o. man with history of depression and alcoholism, presenting with EtOH withdrawal syndrome, in a setting of severe dehydration, metabolic alkalosis, hyponatremia, hypochloremia and pre-renal ARF.

1) Electrolytes disturbances

- ✓ Monitor lytes
- ✓ Continue IV hydration until full PO

Assessment and plan

2) Mental status

- ✓ All work up has been negative: CT, LP, EEG
- ✓ On MVIs
- ✓ ?Psychiatric disturbance → consider psychiatry consult, when 'stable‘

3) Leukocytosis

- ✓ Unknown etiology → on broad spectrum antibiotics: cefepime, flagyl and vancomycin
- ✓ Blood, sputum and urine cultures pending
- ✓ CXR read as c/w aspiration pneumonia → continue antibiotics for now and repeat CXR later on

Assessment and plan

4) Hyperbilirubinemia

- ✓ Unclear etiology. Abdomen US reveals fatty liver; CT shows worsening ascites, no evidence of pancreatitis. No evidence of hemolysis (haptoglobin normal)
- ✓ Work up for cirrhosis, hepatitis serologies, ceruloplasmin, iron studies, ANA

5) EtOh withdrawal / tachycardia

- ✓ Ativan 4 mg IV Q4

6) ARF

- ✓ Resolved with hydration

Differential diagnosis

- **Jaundice**
  - **Alcoholic liver disease**
  - **Viral hepatitis** → IV drugs? Sexual promiscuity? Travel to endemic area?
  - **Hemolysis** → rarely raises the bilirubin over 5 mg/dl. Look for an increased reticulocyte count, indirect bilirubin and LDH.
  - **Primary biliary cirrhosis** → middle aged woman, with jaundice, fatigue, pruritus. AMA + elevated Alk Phos + elevated IgM.
  - **Sepsis** → diagnosis of exclusion.

Differential diagnosis

- **Leukocytosis and fever**
  - **Persistent infections**
  - **Mycobacterial or fungal infections**
  - **Neoplasms** → solid tumors and lymphoproliferative disorders
  - **Primary hematologic disorders** → myeloprolipherative disorders (e.g., polycythemia vera), leukemias, chronic hemolysis
  - **Chronic inflammation states** → rheumatic fever, SLE, thyroiditis, myositis, drug reactions, pancreatitis

Work up

- Liver function tests → acute hepatitis, sepsis, leukemia, lymphoma, metastatic carcinoma
- Amylase → significant elevations (>10 times the normal values) are suggestive of biliary disease
- Hepatitis serology → HBsAg, IgM anti-HBcAg, IgM anti-HAV, Ig anti-HCV
- Other tests → ANA, AMA, SMA, ceruloplasmin, iron studies, α_1-antitrypsin

Work up

- Blood analysis and blood smear → quantitative and/or qualitative alterations of blood cells
- Cultures → blood, urine, CSF, sputum (to r/o infectious cause)
- Abdomen CT +/- US → to r/o cholelythiasis, cholecystitis, pancreatitis, etc
- ERCP or PTC → if an extra-hepatic obstruction is suspected
- CT scans → abscess, masses, LAD, organomegaly, other types of lesions

Work up

- Chest X-ray → acute pneumonia, masses, mediastinal abnormality
- Tumor markers → leukocyte alkaline phospatase (LAP), vit B_{12} levels, tests for monoclonal Ab to carcinomas
- Bone marrow aspiration and biopsy → to exclude a primary bone marrow disorder, metastatic tumor, chronic infections

Hyperbilirubinemia

- Liver Team consult → confirmed our diagnosis of alcoholic hepatitis. Persistent Alk Phos and bilirubin high levels were still of unclear etiology.
- HCV and HBV serologies were negative.
- ANA were negative. No evidence of autoimmune hepatitis, primary biliary cirrhosis, Wilson's diasease, hemochromatosis, or α_1-antitrypsin deficiency.
- HIDA scan → wrong indication (no excretion of tracer due to hepatic insufficiency).
- Cholecystotomy tube → presumptive acalculus cholecystitis. No improvement of jaundice. Bilirubin even increased.

Infection?

- Pt treated with broad spectrum antibiotics in the MICU for presumptive sepsis.
- On White 10, antibiotics were stopped, as sepsis was not likely. Cefepime and vancomycin were used for 5 days upon a diagnosis of aspiration pneumonia.
- Blood, urine, CSF, pleural liquid, bile, ascitic liquid, sputum cultures were repeatedly negative.

Infection?

- During the whole hospitalization, the pt's temperature remained almost always between 98 and 101°F. When antibiotics were d/c, there was an increase of the temperature. But neither the leukocytosis nor the hyperbilirubinemia were influenced by the antibiotic treatment.
- For this reason, **ID ruled out infection as a possible etiology of the pt's fever, leukocytosis and hyperbilirubinemia.**

Hematologic disorder?

- Hematology consult
  - This patient's anemia is likely anemia of chronic disease (low TIBC and high ferritin) or some marrow suppression in the setting of infection and inflammation.
  - Macrocytic anemia of vitamin B_{12} and folate deficiency is a possibility (MCV in the upper limit of normal interval).
  - Although the patient has elevated bilirubin and appears icteric, he is unlikely to have a hemolytic process (as his haptoglobin and LDH are normal).

Hematologic disorder?

- The leukocytosis is likely a leukemoid reaction in the setting of chronic inflammation or infection.
- Other considerations on the differential diagnosis of leukocytosis include CML, hematologic and non-hematologic malignancies.
- To differentiate CML from a leukemoid reaction → leukocyte alkaline phosphatase (LAP) score:
  - high in infection, inflammation, and polycythemia vera (PV)
  - low in chronic myelogenous leukemia (CML)

Hematologic disorder?

- When the marrow is directly invaded by tumor, fibrosis, or granulomatous reactions, neutrophilia can be associated with circulating immature granulocytes, nucleated red cells, and teardrop-shaped erythrocytes, with or without thrombocytosis.
- Leukocyte alkaline phospatase (LAP) score → 89 (normal: 40-100)
- Blood smear → normal (except for some target cells).
- **The combination of anemia and neutrophilia is often associated with chronic infection or inflammation, and this is our leading diagnosis for this patient's hematologic pathology.**

A sad story

- During the last days of August, the patient developed hepato-renal syndrome (Cr 5.9 mg/dl), massive ascites and hepatic encephalopathy; his blood cultures grew gram +ve cocci. He was transferred to the MICU.
- MELD score was 41 on 9/1 (calculated as 91% mortality at 90 days per the Mayo Clinic website calculator).
- Goals of care were discussed with the family.