

A Man with Dyspnea and Diffuse Abdominal Pain

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A 50 y/o male with a PMH significant for HIV/HCV co-infection, and chronic renal insufficiency, presented to the ED with a one week history of progressive dyspnea and diffuse abdominal discomfort. He reported resting shortness of breath without orthopnea, PND, or chest pain. His abdominal pain was diffuse, and he denied nausea, vomiting, increased abdominal girth or lower extremity edema.

He was diagnosed with HIV 3 months earlier, following an admission for septic arthritis. One month ago his CD4+ count was 125 and his viral load 200,000 copies, at which time he began antiretroviral therapy with Combivir (zidovudine/lamivudine) and Sustiva (efavirez) and prophylactic therapy with Bactrim. The patient reported strict compliance with his medical regimen.

On admission his vitals were as follows: temperature 98.9 F, pulse 107 bpm, blood pressure 112/63, respirations 28/min with an oxygen saturation of 96% on room air. The physical exam revealed a thin black male in moderate discomfort, exhibiting Kussmaul breathing with an otherwise clear lung exam. Abdominal exam revealed normal bowel sounds and mild diffuse tenderness, without rebound or guarding. There was no evidence of JVD, lower extremity edema, or S3.

Laboratory data revealed: sodium 136, potassium 5.6, chloride 112, bicarbonate 11, BUN 36, creatinine 2.6, glucose 113; WBC 6.4, hemoglobin 9.1, and platelets 193; AST 306, ALT 77, alkaline phosphatase 567, albumin 2.4. Arterial blood gas values were pH 7.33, pCO₂ 22, PO₂ 154. Finally, chest x-ray demonstrated clear lungs and EKG revealed normal sinus rhythm with T wave inversions in V1- V6.

Discussion Of The Acid-Base Disorder

- A "Normal Gap" Lactic Acidosis?

Initial review of the arterial blood gas and chemistry panel revealed a metabolic acidosis with an expected respiratory compensation (calculated PCO₂ by Winter's formula = 24+/-2). The calculated anion gap was 13, leading us to conclude that the primary disorder was a non-gap acidosis. However, prior lab studies were available for this patient, which revealed a baseline bicarbonate of 20 (presumably related to chronic renal

insufficiency) and anion gap of 5 (presumably related to hypoalbuminemia). The presence of a delta anion gap of 8 suggested a true anion gap acidosis. A serum lactate was subsequently measured, which was markedly elevated at 68.6.

Diagnosis And Clinical Outcome

The patient was admitted with the diagnosis of lactic acidosis, likely secondary to his nucleoside reverse transcriptase inhibitor (NRTI) therapy with Combivir. AST/ALT values peaked at 3621/721 respectively the morning after admission. By withholding antiretroviral therapy, the lactic acid level trended back to normal values and the patient's transaminases returned to his baseline. He continued to improve symptomatically within about 1 week and had returned to his baseline functional status.

Discussion on NRTIs and Lactic Acidosis

The development of lactic acidosis is a very rare, but often fatal, complication of therapy with nucleoside analogues. The estimated incidence of this disorder is only about 1-4 cases per 1000 person years; however it carries a sobering mortality rate of about 50%¹. Though an exact mechanism is yet to be clearly defined, it appears to be related to the inhibition of mitochondrial DNA polymerase and development of hepatic steatosis.

Perhaps of larger interest to clinicians is the ability to identify important risk factors for the development of lactic acidosis. Due to the rarity of this disorder, large-scale studies are difficult to design to evaluate this question. However, a series of case reports and cohort studies have been published. Treatment with any of the NRTIs has been associated with lactic acidosis; however the use of stavudine and lamivudine appears to confer the greatest risk^{2,3}. Another small cohort study suggests additional risk factors may include creatinine clearance of <70 mL/min and a nadir CD4+count of <200 cells/m³.⁴ Finally, pregnancy has also been targeted as a potential risk factor⁵⁻⁷.

In conclusion, the development of lactic acidosis during therapy with NRTIs is a rare but potentially lethal complication. Thus, clinicians should maintain a high level of clinical suspicion when HIV+ patients on such therapy complain of GI distress, dyspnea or general malaise, particularly in the setting of

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stavudine/lamivudine use, diminished creatinine clearance, pregnancy and CD4 counts less than 200. Furthermore the use of NRTIs should be immediately held, once the diagnosis of lactic acidosis is considered.

References

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Don't Peek!

Answers to the Clinical Quiz at the end of this edition of Jefferson Forum

Submitted by Bryan Pukenas, MD

The procedure shown above is a thoracic duct embolization. The effusion can be seen at the apex of the left lung. Radiographic dye is injected into a surgically exposed lymphatic channel in the foot. After several minutes to hours, the dye migrates to the cisterna chyli and into the thoracic duct. At this point a needle is inserted into the thoracic duct and a glue-like material is injected, essentially thrombosing the entire duct. cases of chylothorax.

Malignancy is responsible for 45 percent of total cases and 63 percent of nontraumatic cases. Lymphoma is the single most common cause of chylothorax, but Castleman's disease, sarcoïdosis, histoplasmosis, tuberculosis, lymphangiomyomatosis, multiple myeloma, and goiters are also associated with this pathology. Surgical procedures account for most traumatic cases of chylothorax.

The diagnosis is chylothorax, which is characterized by pleural fluid with a turbid or milky white appearance, secondary to high lipid content (mostly triglycerides), that enters the pleural space via disruption of the thoracic duct. Patients report gradual onset of decreased exercise tolerance, dyspnea, fatigue, and a heavy feeling in the chest. Fever and chest pain often do not occur, because of the failure of chyle to produce an inflammatory response.

E – Radiograph

Submitted by Aparna Mukherjee, MD

Skin biopsy of a discrete lesion shows a foci of multiple giant multinucleated cells within the dermis layer. This finding is characteristic of herpes simplex, which systemically disseminated in this immunocompetent patient, causing multorgan failure. With intravenous antiviral therapy, the patient made a full recovery.

D – Slide

Submitted by Jun Liu, MD

Liver biopsy of the nodules shows microabscesses with fungal elements on GMS (silver) stain. Note the extracellular beaded fungal elements embedded in debris, surrounded by fibrosed liver parenchyma.

Submitted by Carl D. Mele, MD

A 3 x 2 cm type Ia choledochal cyst is visualized at the junction of the common hepatic and common bile ducts (note the cystic duct take-off from the choledochal cyst itself). Although the patient has minimal symptoms, the cyst needs to be surgically excised because of an increased risk of cholangitis and malignancy. This is a congenital abnormality seen more commonly in women, with an incidence of roughly 1 in 15,000.

B – Radiograph

Submitted by Carl D. Mele, MD

This is a pedunculated jejunal polyp. Because the patient is asymptomatic and the polyp is less than 15 mm in size, no therapeutic intervention is recommended at this time. Patients with FJS should be screened endoscopically with EGD, colonoscopy, and small bowel evaluation at least every two years after the age of 12.

A – Capsule Image