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MORNING REPORT

A Man with AIDS and Abdominal Pain

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A 38-year-old man with HIV (last CD4 count 75) comes to clinic with three weeks of abdominal pain. The pain is diffuse and crampy and associated with bloating and loose stools. He reports intermittent emesis, poor oral intake, and about a 15-pound weight loss. He denies fevers or night sweats. He also notes increased urination. He does not drink alcohol or use NSAIDs.

He takes antiretrovirals and pneumocystis prophylaxis and denies any recent new medications. He has a history of cytomegalovirus (CMV) viremia. He does not smoke.

The differential diagnosis for abdominal pain in a patient with HIV and a low CD4 count is long. The two main concerns would be infections or malignancy, but we should also consider common causes of abdominal pain unrelated to the HIV.

Regarding infections, the subacute nature of symptoms (i.e. three weeks) argues against an acute bacterial or viral gastroenteritis. Subacute causes of gastroenteritis are possible such as CMV, parasites (i.e. giardia, cryptosporidium), or mycobacterial infection (i.e. TB or Mycobacterium avium intracellulare *(MAI)). He notably does have a history of CMV viremia, so gastrointestinal symptoms from CMV colitis are very possible.*

Although he lacks fever or sweats, malignancy should be considered especially with the weight loss. Lymphoma or Kaposi's sarcoma (KS) are two concerns, the latter of which can present with gastrointestinal involvement without skin disease.

Lastly, common diagnoses should be considered that are not necessarily related to HIV. Peptic ulcer disease could cause diffuse pain and weight loss via food avoidance. Gastroesophageal reflux disease should not cause weight loss, and pancreatitis would lead to a more acute presentation. Electrolyte abnormalities could cause gastrointestinal distress, such as hypokalemia or hypercalcemia, but these would not cause weight loss (although they could explain polyuria).

On physical exam, I would look for KS lesions on the skin and do a careful exam for lymphadenopathy and hepatosplenomegaly, which could suggest underlying malignancy.

On exam, his blood pressure is 107/67 with a normal heart and respiratory rate. No lymphadenopathy or skin lesions are noted. Heart and lung exam is normal. On abdominal exam, he has slight suprapubic tenderness without rebound or guarding.

Initial lab studies show white count of 3.3, hemoglobin of 12, and platelets of 80. A metabolic panel shows a creatinine of 2.3 and a calcium of 17.4.

The striking findings from the initial labs are the pancytopenia, acute kidney injury, and marked hypercalcemia. Hypercalcemia causes an inability to concentrate the urine leading to polyuria, so the patient's renal failure could simply be due to both low intake and excess fluid loss.

However, an additional concern is a bone marrow problem, such as disseminated infection or malignancy, leading to both the low blood counts and hypercalcemia.

Primary hyperparathyroidism and malignancy account for about 90% of causes of hypercalcemia, so investigation of these causes is critical. A first step in the workup of the hypercalcemia would be to get a parathyroid hormone (PTH) level, which if high or normal would suggest primary hyperparathyroidism or familial hypocalciuric hypercalcemia (FHH).

In contrast, if the PTH is appropriately suppressed, a broader list of causes of hypercalcemia should be considered, including malignancy or granulomatous due to TB or MAI, which could be related to his HIV.

For the renal failure and hypercalcemia, he should be given IV fluids and a bisphosphonate. I would recommend abdominal imaging to look for lymphadenopathy.

PTH is low at 5.4 pg/ml. CT abdomen shows prominent mesenteric adenopathy suspicious for lymphoma. No masses are seen. The patient is given IV fluids, calcitonin, and a bisphosphonate with improvement in his acute kidney injury and reduction in serum calcium.

With the appropriate low PTH, we can rule out primary hyperparathyroidism and FHH as causes of hypercalcemia. Malignancy or granulomatous disease remain the top two concerns.

The lymphadenopathy is concerning for malignancy or an opportunistic infection (i.e. TB or MAI). While fungal infections like histoplasmosis could lead to pancytopenia, the prominent adenopathy would be less common.

The patient should undergo a lymph node biopsy or bone marrow biopsy for further evaluation of the pancytopenia. Additionally, a PTHrP and 1,25-OH vitamin D should be checked, the latter of which can be elevated with some lymphomas or granulomatous disease.

A PTHrP was negative, but a 1,25-OH vitamin D returns elevated at 164 pg/mL. As there is no easy

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target for lymph node biopsy, a bone marrow biopsy is performed that demonstrates non-caseating granulomas. Rare acid-fast bacilli are visualized within the granulomas, consistent with mycobacterial infection. Cultures eventually grow MAI.

For the MAI, he is started on ethambutol, azithromycin, and rifampin. In clinic follow-up two months later, his blood counts have improved, and his calcium levels have remained normal.

Hypercalcemia has been described in granulomatous disease, most commonly in TB and sarcoidosis. Other granulomatous diseases to consider include histoplasmosis, coccidiomycosis, and other mycobacterium (such as MAI). Activated macrophages within granulomas convert 25-OH vitamin D to 1,25-OH vitamin D leading to hypercalcemia.

While primary hyperparathyroidism is the most common cause of hypercalcemia, in a patient with HIV and a low CD4 count, malignancy or granulomatous infections should be considered.

A high 1,25-OH vitamin D should suggest granulomatous disease, with treatment of the underlying infection leading to resolution of hypercalcemia.

Learning Points

1. The vast majority of cases of hypercalcemia are due to either primary hyperparathyroidism or malignancy.
2. A high or normal PTH level is due to either primary hyperparathyroidism or FHH.
3. In hypercalcemia with low PTH, granulomatous disease is suggested by a high level of activated vitamin D (1,25-OH vitamin D).

Suggested Reading

Aly ES, Baig M, Khanna D, Baumann MA. Hypercalcaemia: a clue to Mycobacterium avium intracellulare infection in a patient with AIDS. Int J Clin Pract 1999; 53(3):227-8.

Minisola S, Pepe J, Piemonte S, Cipriani C. The diagnosis and management of hypercalcaemia. BMJ 2015; 350:h2723. SGIM