



Introduction:

Welcome to CUGH's bi-weekly clinical case-series, "Reasoning without Resources," by Prof. Gerald Paccione of the Albert Einstein College of Medicine. These teaching cases are based on Prof. Paccione's decades of teaching experience on the medical wards of Kisoro District Hospital in Uganda. They are designed for those practicing in low resource settings, Medicine and Family Medicine residents, and senior medical students interested in clinical global health. Each case is presented in two parts. First comes a case vignette (presenting symptoms, history, basic lab and physical exam findings) along with 6-10 discussion questions that direct clinical reasoning and/or highlight diagnostic issues. Two weeks later CUGH will post detailed instructors notes for the case along with a new case vignette. For a more detailed overview to this case-series and the teaching philosophy behind it, see [Introduction to "Reasoning without Resources"](#). Comments or question may be sent to Prof. Paccione at: gpaccion@montefiore.org

Note: If you would like to be notified when a new case is posted (along with instructor notes for the previous one), send your e-mail to Jillian Morgan at jmorgan@CUGH.org.

About the Author:

Dr. Gerald Paccione is a Professor of Clinical Medicine at the Albert Einstein College of Medicine in the Bronx, New York. His career has centered on medical education for the past 35 years – as a residency Program Director in Primary Care and Social Internal Medicine at Montefiore Hospital, and director of the Global Health Education Alliance at the school. He has served on the Boards of Directors of Doctors for Global Health, Doctors of the World USA, and the Global Health Education Consortium. Dr. Paccione spends about 3 months a year in Uganda working on the Medicine wards of Kisoro District Hospital where he draws examples for the case studies.

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CASE 24 – ABDOMINAL PAIN AND SWELLING

A 28 year old woman presents with increasing abdominal pain and swelling of 2 months duration.

The patient farms, is married and the mother of 6 children. Her husband also lives in Kisoro full time now after many years of migrant farming around Kampala 4-6 months a year.

She was well before belly pain began 2 months ago, coming on gradually, experienced as a vague discomfort in the left lower quadrant, and then after 1-2 weeks diffusely over the abdomen. It was cramping at first with some diarrhea, and then of low intensity and constant throughout the day and night. Her loose stools have become infrequent and harder, with bowel movements 2-3 times/week for the past 3 weeks. She's noticed loss of appetite, intermittent "hot/cold" sensations, and progressive weight loss. About a month ago her abdomen began to distend, and was tender when she pressed on it. She drinks about a liter of local matoke brew every night, and has had no jaundice or dark urine in the past.

She feels increasingly fatigued, but without shortness of breath, orthopnea, PND, chest pain, cough, or signs of abnormal bleeding (hematochezia, melena, hemoptysis, or vaginal bleed).

Physical Exam:

In no acute distress, sitting upright, with temporal wasting obvious

B/P 110/60 HR 100 R 20 T 100.1 oral

Conjunctiva: non-icteric; fundi: benign

skin: no spiders, palmer erythema or jaundice

mouth: ⊕ thrush;

neck: no lymphadenopathy; no JVP/HJR;

lungs; left base ?intermittent crackle, otherwise clear; no dullness;

cor: PMI 5th ICS, mid-clavicular line; S₁, S₂ normal, no murmurs, rubs

abd: no venous pattern visible

distended with shifting dullness;

tender to deep palpation and percussion diffusely; no rebound;

no hepato-splenomegaly

no edema

neuro: alert and oriented; no asterixis; no focality; reflexes + 2

1. What is the “frame” in this case (i.e. key clinical variables the final diagnosis must be consistent with)?

What is the clinical significance of each of the features of the “frame”?

- *ascites with pain (suggests inflammatory ascites)*

- *gradual development over months, with pain preceding the distention (suggests a chronic inflammatory or neoplastic process involved the pain-sensitive parietal peritoneum before inducing an inflammatory, reactive ascites.)*

- *thrush: (A marker for HIV infection. HIV increases the likelihood of TB in general and especially of extra-pulmonary TB and TB peritonitis. It also increases the likelihood of certain cancers that can involve the peritoneal cavity such as lymphoma and cervical cancer.)*

- *weight loss, other vague constitutional symptoms i.e. fatigue, anorexia, “hot/cold”: (These are consistent with a catabolic illness like chronic infection and/or cancer. They can be from HIV itself, or associated opportunistic infections or cancers.)*

- *no JVP/HJR; no signs cirrhosis - jaundice, edema, mental status change: These “negative” clinical findings markedly lower the probability of cardiac ascites (e.g. from endomyocardial fibrosis), and cirrhosis.*

1. What are the 3 most common causes of ascites in East Africa?

- *Cardiac ascites due to endomyocardial fibrosis >> rheumatic heart disease > dilated cardiomyopathy > constrictive pericarditis*
- *Cirrhosis: hepatitis B (most often transmitted in early childhood), hepatitis C, alcohol*
- *Carcinomatosis: ovarian, hepatocellular, gastric, cervical, lymphoma....*

2. a) How does the patient's belly pain and tenderness influence the differential diagnosis?

Pain signifies either inflammation from infection or neoplasm, or neoplastic impingement on mesenteric nerves.

Pain suggests 4 diagnoses: Carcinomatosis

Cirrhosis with spontaneous bacterial peritonitis (SBP)

TB Peritonitis

Ascites secondary to primary bacterial infection or abscess

b) What is the significance of pain preceding the development of ascites?

This sequence eliminates, on clinical grounds, the possibility of spontaneous bacterial peritonitis (SBP) - a complication of preexisting ascites from cirrhosis.

It suggests that an inflammatory or neoplastic focus came first, and over time caused edema in the peritoneal cavity.

- 3. What is the differential diagnosis in this patient and the “pros and cons” of each possibility?
What is the most likely diagnosis on clinical grounds? Explain.**

As discussed above, cardiac ascites, often seen in Uganda, does not fit the “frame” of this patient’s ascites given absence of signs of increased venous pressure, a normal cardiac exam, and presence of diffuse abdominal pain/tenderness.

Schistosomiasis, frequent in Africa, can also cause ascites without edema: however ascites is often late in the course of Schistosomiasis; usually presents in adolescence – more frequently with other complications of portal hypertension (i.e. variceal bleed or a huge spleen); and the diffuse abdominal pain/tenderness and months-long timing of the symptoms in this patient are inconsistent with this far more insidious disease.

- *Cirrhosis with SBP: although suggested by the patient’s history of regular drinking (N.B. very common in the area, most matoke beer is “half-strength”), cirrhotic ascites with SBP is unlikely given the timing: abdominal discomfort and constitutional symptoms occurring before the onset of the distention (ascites). Furthermore, there’s no leg edema, seen in >90% with cirrhotic ascites; no jaundice or history of liver problems; and no mental status change, seen in over 50% with SBP particularly with delayed access to care.*
- *“Secondary” bacterial peritonitis, an inflammatory reaction from a focal intra-abdominal infection: suggested by the onset of pain before the development of obvious ascites - but is rendered less likely by the patient’s youth, the insidious onset and long duration of symptoms, and the diffuse tenderness on exam.*
- *Carcinomatosis: fits the clinical presentation of insidious pain before overt ascites.
Lymphoma and cervical cancer are more likely in HIV-infected patients, but there’s little else to suggest lymphoma here - no lymph nodes, no spleen palpable (through the ascites), no peripheral swelling to suggest local blockage by abdominal nodes or lymphedema;*

There's no history of vaginal bleeding to suggest cervical cancer.

HCC is a major consideration in Uganda, but a hard, nodular enlarged liver isn't detectable/ballot-able, and jaundice isn't obvious at what would be a late stage of disease...

- ***Tuberculous Peritonitis (TBP):*** *TB peritonitis, which occurs in 0.1-3.5% of all patients with pulmonary TB and accounts for 4-10% of overall extra-pulmonary TB and half of abdominal TB, is the most likely clinical diagnosis in this patient. The weight loss, lack of peripheral edema, and diffuse abdominal pain suggest a non-focal intra-abdominal inflammatory process causing the ascites; the patient is HIV (+) in Africa; and the process has been progressive over 2 months.*

TBP is thought to develop most commonly from reactivation of foci seeded by prior hematogenous spread from the lungs, but also from recent spread from active pulmonary infection (which coexists with TBP in ~10-30%) or from direct extension from the intestines or fallopian tubes.

Timing is critically important in diagnosis: TBP usually develops over several weeks to months: >70% have had the disease for >4 months before diagnosis; in a series of 26 patients from Turkey, the duration of symptoms ranged 2-24 weeks, average 7-8 weeks; from Saudi Arabia in 46 patients the symptom duration was >6 weeks in 63%. In ~10% the presentation is within a week of symptom onset.

The differences among case series in the frequency of clinical manifestations of TBP probably have a lot to do with access to care and diagnostic resources. The most common symptom is a vague, poorly-localized abdominal discomfort, with distention. As with the clinical presentation of TB anywhere, the frequencies of various symptoms reported in case series range between 30-70%, with the exception of ascites or distention – usually described in 75-95% but still not universal. This “50-50” prevalence median for most symptoms means that the absence of any symptom - or even any 2 or 3 symptoms of “classic” disease - can NOT rule out TB peritonitis with certainty. One's “concept of disease” has to be broad enough to accommodate that empiric finding to avoid erring diagnostically with this serious but treatable infection.

Thus, according to the 35 case series meta-analysis (Sanai, et al, Aliment.Pharm.

Ther.2005), abdominal pain was seen in 65%, fever 60% (half of fevers only found in-hospital, not by history), weight loss 60%, diarrhea 20%, constipation 10%, ascites/distention, 75%.

The exam presentations of TBP are “wet-ascites” in over 80%; the classic “doughy abdomen” without palpable ascites (reflecting matted loops of bowel and mesentery in a still-soft inflammatory phlegmon) in 5-15%; and the more rigid, fibrotic-fixed form in 5%. About 10-15% demonstrates a palpable mass; 50% abdominal tenderness; 60% fever; 30% hepatomegaly; 15% splenomegaly. Rebound tenderness is rare.

5 . Which tests, available in a district hospital, can aid diagnosis in this patient?

How accurate are they for the diagnoses under consideration?

What is the most definitive “test” for this disease in actual practice in rural Africa?

The tests most likely to be available in a district hospital include direct tests on the ascitic fluid, and indirect tests that look for manifestations of TB in other organs:

- *Paracentesis and ascitic fluid analysis*
- *Chest x-ray*
- *ESR*

Analysis of the ascites starts with its color:

- *Pink or red: pink fluid has ~10K RBCs per mm³, and grossly bloody fluid has many tens of thousands of RBCs. HCC has bloody ascites in 50%; other cancers ~20%; other cancers with metastases to both peritoneum and liver ~70%; TB peritonitis ~ 10% bloody.*

- *Cloudy/turbid: Clear ascitic fluid usually means no infection present: Turbidity indicated SBP (defined as >250 WBC/mm) with a sensitivity of 98%, specificity 23% in >900 patients (Am J. Emerg Med 2007;25(8):934-7). Although not studied in TBP, it's likely that the observation, based on cell counts, holds. One problem with "cloudy" fluid as an indication of infection is the "opalescence" conferred by as little as 50-100 mg/dl triglyceride, which is common in cirrhosis (almost a third of specimens in one study had elevated TG concentrations making the fluid look cloudy (AmJPath 1991)).*
- *Milky: A white "milky" color signifies a TG concentration >200 mg/dl, and most often >1000 . This is "chylous ascites", in the past thought to be a manifestation of tumor blocking the lymphatics/thoracic duct. However, other studies have shown that cirrhosis itself is 10x more likely to be the cause of chylous ascites than is cancer, and that 1/200 cirrhotic ascites are chylous.*

Ascitic fluid analysis in TBP reveals:

- *500-1500 cells, but can demonstrate <100 cells in 10-20% of cases.*
- *lymphs predominate, but only in 70% of cases: poly predominance can be seen in early TBP and is to be expected in patients with TBP and chronic renal failure;*
- *protein is >2.5 gm/L in nearly 100% with TBP without cirrhosis, but only 50% in the presence of co-morbid cirrhosis (which is common in patients with TBP, an especially significant risk factor for TBP in the developed world). N.B. Although protein can't be determined in most district hospitals, in low resource areas the urine dipstick has been used to estimate, with good accuracy, the cell count, protein and glucose in the CSF to predict meningitis (Lancet 95; 345, 1290-91).*
- *glucose is low in TBP. Two studies have shown that an ascitic/serum glucose ratio of <0.96 is 100% accurate (!) in predicting TBP vs. cirrhosis (Tubercle 1984, 65:47-52), but no patients with SBP were in the control group with cirrhosis. However, since most patients with SBP (i.e. $>90\%$) have a total protein <2.5 (i.e.transudate), the combination of a low glucose*

ratio and a high protein can provide strong evidence for the diagnosis of TBP over cirrhosis and SBP. The problem is differentiating, by basic fluid analysis alone, TBP from peritoneal carcinomatosis – which can cause both low glucose and high protein in the ascitic fluid.

- AFB smear (culture) is positive in only ~3% of cases, thus useless most of the time. Although not available in most district hospitals, even TB culture of the ascites is positive in only about a third of cases of TBP.

“Indirect” tests such as the chest x-ray for evidence of co-existing pulmonary TB or the ESR are equally disappointing as powerful predictors of disease:

- CXR is suggestive of TB in 20-50% of patients with TBP, more commonly (~50%) in children.
- ESR ranges between 20-120 and is >60 in ~50% of cases of TBP.

Clinical suspicion, guided by a broad disease model, is the most important element in diagnosis of TBP. The usual “definitive” test available in district hospitals in Africa is also clinical: **empiric therapy for TB**.

With empiric therapy, pain and fever should decrease within a week, and distention/ascites slowly resolve over weeks.

Suggested Readings:

Burack, W, and Hollister, R.; Tuberculous Peritonitis A Study of Forty-Seven Proved Cases Encountered by a General Medical Unit in 25 Years AJM 1960 (4):pp.510-523

Karney, W.W., et al. The spectrum of tuberculous peritonitis *Chest* 1977;72;310-315

Wilkins, E.G.L.; Tuberculous Peritonitis: Diagnostic Value of the Ascitic/Blood Glucose Ratio; *Tubercle* 65 (1984) 47-52

Sheets, E. et.al CPC NEJM:1998; 338 (4):248-254

Muneef, M.Al et.al. Tuberculosis in the Belly: Review of Forty-six Cases Involving the

Gastrointestinal Tract and Peritoneum Scand J Gastroenterol 2001 (5):528

Demir, K., et.al; Tuberculous peritonitis - reports of 26 cases, detailing diagnostic and therapeutic problems Eur J Gastroenterol Hepatol 13:581-585

Sanai, F.M., Bzeizia, K.I.; Systematic review: tuberculous peritonitis – presenting features, diagnostic strategies and treatment Aliment Pharmacol Ther 2005; 22:685–700.

Dinler, G. et.al; Tuberculous peritonitis in children: Report of nine patients and review of the literature World J Gastroenterol 2008 December 21; 14(47): 7235-7239