Introduction:

Welcome to CUGH's monthly 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 Eleazar Gutierrez at egutierrez@CUGH.org.

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CASE 55 – Tragic Connections

A 20 year old woman with HIV and a history of TB presented to the hospital with the complaints of "I am coughing, my legs are swollen, my stomach is big and I need to sleep sitting up".

She was well until the Spring 2011 when she began coughing, feeling weak and "hot" and losing weight. Months later (September, 2011) in another hospital two AFB smears were positive and RIPE was started, to be monitored by family-DOT. She was also found to be HIV (+) and a month later ARVs were started. (We do not have a record of her CD4 count at the time.)

The crumpled notes she hands you and her TB "yellow card" are consistent with her present story: At two and three month follow up visits post-diagnosis of TB the fevers had ceased and she gained some weight, but her cough had only minimally improved and her sputum remained AFB positive. RIPE was continued but the patient was soon lost to follow up for the month of December and adherence was questionable. After re-engaging in care she was re-started on RIPE with streptomycin added which was continued for 2-3 months with good adherence documented until March of 2012 when repeat AFBs were negative. She was then lost to follow-up until May, 2012, at which time AFBs were again positive and RIPE was re-started. AFBs in July, 2012 were negative and she was transitioned to three-drug therapy with EHR (ethambutol, INH and rifampin) which she is currently taking for 3 months, 13 months post-initial diagnosis, with good adherence. Her CD4 count in July was 320, with good adherence to ARVs. During this long course, her cough - which didn't change with position, exertion or time of day - never significantly improved, although her fevers diminished and her weight stabilized and may have increased slightly

However, also in July 2012, 3-4 months prior to this admission, her previously unrestricted exercise tolerance gave way to dyspnea after less than one kilometer at a slow pace. 2 weeks PTA she developed progressive bilateral lower extremity swelling, followed by increasing abdominal girth, inability to sleep flat and waking at night short of breath. Four days PTA she had to sleep sitting up. She has not had fevers or chills and reports excellent adherence with ARVs, SMX-TMP, and TB treatments. Her last pregnancy was over six years ago and she does not drink. She's noted no change in the color or amount of urine.

Physical Exam:
Cachectic, in moderate respiratory distress sitting, ill appearing, diaphoretic, alert/oriented
BP 90/60 without pulsus; HR 124; T 99.9F oral, RR 56 O2 sat 78% room air
HEENT: Conjunctiva deeply red, non-icteric, PERRLA, no oropharyngeal exudate / thrush; fundi benign.
Neck: No LAD or thyroid enlargement; JVP to angle of jaw sitting, triphasic;
Lungs: Shallow and rapid breathing. Diffuse fine crackles throughout inspiration, with louder coarse crackles in upper posterior and anterior fields on R, and lower lung on L.
Heart: hyperdynamic precordium; PMI displaced to left 1cm; prominent left parasternal (RV) lift, palpable P2 parasternal 2nd RICS; split S2 with loud P2 at LUSB and apex; +S3 and +S4 at LLSB, both increased with inspiration; Gr 1 short systolic murmur RUSB; no rubs; no OS or MS in LLD
Abdomen- soft, distended with moderate shifting dullness
Firm, smooth, tender liver palpable 6 cm below the costal margin. +2 sacral edema.
Extremities: 2+ pitting edema, bilateral, extending to upper thighs and cool to touch; no calf tenderness
Neurologic: non-focal with grossly normal mental status; no fine tremor noted.

1. What is the "*frame*" of this case from the history, (i.e. the key clinical features the final diagnosis must be consistent with)?

- *HIV +, on ART and Septrim, with CD4 > 300;*
- *Prolonged duration of symptoms of (documented) TB*
- *Erratic adherence with TB treatment for over a year with an early clinical response but persistent cough*
- *Months of progressive exertional dyspnea, followed by edema, and over the last week severe orthopnea and paroxysmal nocturnal dyspnea;*

2. What are the *present clinical implications* of the patient's TB history, and how common is this sort of history in Africa? Why the persistent cough?

The patient's history of erratic non-adherence and loss to follow-up is unfortunately common in Africa and one of the reasons for the TB epidemic continuing almost unabated in some countries. She was fully adherent to therapy for the first 3 months (the "intensive phase") when antimicrobial killing of teeming extracellular mycobacteria and clinical improvement is most rapid and the impact of treatment most obvious to the patient. Only around 10% of treatment initiates default early. However, treatment must continue for 6 months after the patient has improved to eliminate the intracellular, slow replicators and it is in this "continuation phase" when adherence is most challenging - 20-50% default from therapy at some point before the full course is finished.

Our patient had a long duration of symptoms (many months) prior to diagnosis and treatment, and her sputum smears were positive: both of these clinical observations suggest a high mycobacterial load, advanced pulmonary disease with significant parenchymal destruction and a high risk for relapse even with organisms sensitive to the administered therapy. Her sputum smears were still positive at 2 and 3 months, although the clinical significance of this latter observation is questionable. (The presence of smear positivity at 2 months is a very poor predictor of relapse, and positivity at 3 months is hardly better. The 2 month smear will be positive in ~ 20% of all smear (+) cases of TB, but an early positive smear is neither sensitive nor specific in predicting relapse: of those who will relapse, less than 40% will have had a (+) smear (sensitivity), and the persistence of dead mycobacteria which can still stain AFB(+) reduces its specificity and predictive value. Of all (+) smears at 2 months, only 25% will relapse (i.e. the positive predictive value). Microscopy at 3 months is a better predictor, but still problematic.) Culture performs better than smear but is unavailable in rural Africa: positivity at 2 months predicts a 3-fold increase in rate of relapse - but from ~2% to only 5-6%.)

Regardless, she left town during the December holidays and upon return, a 4-drug intensive phase regimen plus streptomycin (in case the organism was resistant to INH) was re-initiated. Certainly with a lower bacterial burden this second time around, she was smear negative 2-3 months later, but she again defaulted: 2 months later her AFB smear was positive and the intensive regimen with 4 drugs again re-started. Notably, all of the defaults occurred at the transition between the intensive and continuation phases, lasted from 1-3 months, and an aggressive therapeutic path – i.e. restarting from square one – was appropriately chosen by the TB monitoring team each time. She was then transitioned to a triple-drug continuation phase that includes ethambutol in addition to INH and rifampin, in case of INH resistance.

The patient's cough never disappeared, and only mildly improved. This is not unusual after successful treatment of TB. Studies show that 30-50% of treated patients have persistent respiratory complaints, most commonly cough and/or dyspnea: about 40% after 1 year post-therapy, and 15-20% after 2-3 years post-therapy. However, in the absence of other HIV-related complications, successful TB treatment should result in resolution of fever and anorexia, improvement in lassitude or weakness, and stabilization of weight loss if not weight gain.

3. a) What is the significance of the findings on Physical Exam

(i.e. *acute respiratory distress with a RR of 56 sitting upright with diffuse crackles and focally prominent coarse crackles, marked hypoxemia; JVP, hyperdynamic heart; absence of a significant TR murmur or JV cannon waves; loud and palpable P2; S3 and S4 at the left lower sternal border augmented by inspiration; absence of a left-ward displaced PMI;; deeply red conjunctiva*

b) What pathophysiologic process(es) does the exam suggest? Explain.

c) On exam, there is evidence of both chronic (> 1 month) and acute (<1-2 weeks) disease processes:

- *Identify the findings* that suggest *chronic* disease and those that suggest *acute* disease.

– *Bonus*: What is causing each of them? Identify the *unusual clinical paradox* in this case suggested by the physical exam that is key to "putting it all together".

a) The patient is in acute respiratory distress with a RR of 56 sitting upright with diffuse crackles, and is markedly hypoxemic with an O2 saturation of 78 despite extreme hyperventilation. The presentation is that of acute pulmonary edema and/or ARDS (acute respiratory distress syndrome).

The ascites and peripheral/sacral edema imply a fluid-salt retaining state that has progressed for weeks to months – consistent with congestive heart failure, nephrosis and/or renal failure, or cirrhosis. In the context of pulmonary edema and progressive symptoms of dyspnea, orthopnea and PND, and in the absence of other exam signs of uremia or cirrhosis, heart failure is likely.

The marked JVP to the angle of the jaw sitting up signifies severe elevation in right-sided pressures, and the triphasic JV wave form without cannon waves suggests that TR is not prominent (or primarily causal).
The hyperdynamic heart suggests hypertrophied myocardium rather than the "weak" heart muscle of a primary cardiomyopathy, and the left parasternal lift implies RV enlargement/hypertrophy. The absence of a significant TR murmur or JV cannon waves point to an RV pressure-load rather than a volume load as the cause of the RV lift.
The loud and palpable P2 in the 2nd right ICS implies a dilated pulmonary artery and severe pulmonary hypertension (PHT) (mPAP>50). The one caveat to this is the anatomic distortion of the heart-lung-chest wall relationship caused by TB scarring, which can bring the PA close to the chest wall and make normal vigorous cardiac function seem abnormal.
The S3 and S4 at the left lower sternal border augmented by inspiration confirm their RV origin and indicate RV failure and hypertrophy respectively.
The absence of a left-ward displaced PMI or LV heave implies that the LV is relatively spared.

Pericardial constriction/tamponade, mitral valve disease, and hyperthyroidism can all cause clinical RVF. The absence of pulsus paradoxus (and the hyperdyamic precordium with clear heart sounds without a "knock") augers against pericardial disease; the absence of a murmur of MS or an opening snap suggests a non-valvular cause of the PHT; and the absence of goiter or tremor implies a euthyroid state.

Of note, the temperature is 99.9 orally in a patient in respiratory distress. The temperature should not have been taken orally as oral temps will underestimate fever in patients in respiratory distress by 1-3 degrees Fahrenheit (N.B. oral temperatures are normally 0.5 to 1 degree below rectal temperatures). Thus in this patient 99.9 orally probably indicates fever and suggests a possible acute infection precipitating cardiac decompensation, although low grade fever can also be seen in severe biventricular CHF.

The focally prominent coarse crackles that are louder and of different quality from the diffuse fine crackles heard throughout the lung, suggest that different pathologies are affecting the lung: e.g. infiltrate or scar tissue (focal crackles) vs. edema fluid (diffuse fine crackles).

The deeply red conjunctiva suggest either suffusion from viral, spirochete or rickettsia infection, or polycythemia. If the latter, damage to the lung parenchyma and chronic hypoxemia is implicated as the erythropoietin stimulus - even more remarkable in this cachectic HIV(+) patient.

b) As described above, the exam suggests pulmonary hypertension and cor pulmonale: i.e. RV enlargement due to pulmonary hypertension from pulmonary vascular and/or parenchymal pathology, leading to RV failure.

However, the diffuse rales, RR of 56, and respiratory distress suggest pulmonary edema, which is not seen usually with RV failure, and the recent and progressive symptoms of orthopnea and PND suggest that the pulmonary edema is from LV failure rather than septic ARDS.

Cardiac decompensation may well have been triggered by an acute infection, probably pneumonia.

c) Signs of chronic disease:

- *RVH signs: RV lift, palpable and loud P2, RV S4*
- *RV failure: ascites, sacral edema*
- *Red conjunctiva (if polycythemia)*
- *Coarse focal lung crackles*

Signs of acute disease:

- *Acute distress with RR 56*
- *Diffuse crackles with O2 sat 78%*

Bonus: "Putting it all together" in this case starts with recognizing the clinical paradox: how to reconcile the chronic development of right-sided cor pulmonale with the more recent development of left-sided heart failure in a patient with a non-dilated heart. (This is the reverse of what's usually seen: chronic LV failure "giving way" to RV failure after months to years of elevated pulmonary venous, and then pulmonary arterial, hypertension.).

4. What is the differential diagnosis of the chronic condition suggested by the exam?
…. Of the acute illness?

The chronic condition is cor pulmonale, and its differential includes:

- *Tuberculosis lung destruction and scarring*
- *HIV-related pulmonary hypertension*
- *Multiple pulmonary emboli*
- *Other secondary causes of PHT such as hepatitis B, C, etc.*

The acute illness is chronic cor pulmonale complicated by:

- *LV failure (from cor pulmonale itself), precipitated by acute pneumonia*
- *Sepsis/ARDS from acute pneumonia*
- *Acute pneumonia with history of "orthopnea/PND" caused by positional de-oxygenation when supine (apical lung scars from TB), not LVF;*
- *LV failure due to recent and independent HIV-related cardiomyopathy*
- *LV failure due to LV ischemia due to worsened hypoxemia from pneumonia;*
- *PCP developing over weeks, i.e. an independent process*

5. Which *tests* could/should be done (in a rural African district hospital) to narrow the differential? What would you predict the tests will show?
Explain their utility in this case.

- Hematocrit: if high, the hematocrit would indicate polycythemia (from hypoxemia) as the cause of the "bloodshot eyes", and also chronic hypoxia underpinning the development of PHT and cor pulmonale.

The test should not be done in the acute setting of suspected pulmonary edema, or if done acutely should be repeated when the patient is stable: hemoglobin/hematocrit measures are often (falsely) elevated in acute cardiac failure due to transudation of fluid into the alveoli with resulting hemoconcentration. Thus its measurement will be most informative days later. (The test can also be falsely negative (low) in this malnourished, cachectic patient with AIDS in whom the bone marrow might not be able to respond to high erythropoietin levels from chronic hypoxemia.)

- EKG: for signs of right atrial and/or ventricular enlargement/hypertrophy, supporting the diagnosis of cor pulmonale.

- CXR: for extent of parenchymal involvement by TB, scarring and/or acute infiltrate, and signs of acute LV failure/pulmonary edema.

- AFB smears x 2: to assess persistent activity of tuberculosis, which in this patient on therapy with multiple re-treatments would imply a high likelihood of multi-drug resistance.

- Urinalysis: for protein and casts, to check the possibility of nephrosis or nephritis/renal failure in this edematous HIV (+) patient. (N.B. HIV nephropathy usually presents without edema despite marked albuminuria. The lack of edema is due to renal interstitial disease and salt-wasting).

- CD4 count to assess likelihood of other opportunistic infections in an HIV (+) patient whose last count was 320 four months prior, who has a history of intermittent adherence, and is now very ill.

6. What treatment should be started promptly on admission and why?

The patient is acutely ill, in near-fatal respiratory distress. She would be immediately intubated if she presented to an emergency room in the U.S. In dire situations like this, especially in locations with few diagnostic resources, treating broadly for all diseases that could be fatal in hours-days if untreated, and that are consistent with the presentation, even if less likely, is indicated. Once the patient is stable, immediate withdrawal of therapy for the least likely possibilities is prudent, supplemented by close clinical monitoring.

In this patient, treatment with ceftriaxone for bacterial pneumonia/sepsis, SMX-TMP and steroids for PCP, and IV Lasix should be initiated immediately.

The patient was immediately treated empirically. After 24 hours, she was significantly better: she lost 2kg, was afebrile, in no respiratory distress, RR 28, pulse oximeter 82 (room air), with fewer fine crackles. Treatment for PCP was discontinued immediately, with close clinical monitoring.

Over the first 5 days, she diuresed a total of 7 kg from 46 to 39 kg and her lung exam improved: the diffuse crackles disappeared but focal crackles persisted in left lower and right upper anterior and posterior lung fields. She was able to sleep flat in bed for the first time in a week. After the second hospital day she was never again febrile.

Tests returned the following results by the end of the first week in the hospital:

- Hematocrit (5 days post-admission, in no distress): 55
- AFB smear negative x 2
- EKG (2nd day): HR 105, regular, right axis deviation, right ventricular hypertrophy (R>S in V1, R>5, 7mm, in V2), upright P wave V1; T wave inversion in leads III, AVF, V2-4. [EKG unchanged after clinical improvement, a week later, except for HR 92]
- CXR (No X-ray film in hospital for first 5 days; CXR done day 6 of hospitalization): Extensive infiltrates in right upper and lower lung fields with diffuse fibrotic change. Elevated right hemi-diaphragm with loss of volume right lung Streaky infiltrate left lower lobe. No significant cardiomegaly or signs of left ventricular failure. [Repeat CXR 2 weeks later unchanged except for some improvement in LLL streaky infiltrate.]
- Urinalysis: 0-trace protein, S.G. 1.020, no casts/cells
- CD4: unavailable entire admission

Post-admission 8 days, her exam revealed JVP in the lower neck sitting 6 cm above the angle of Louis; the RV lift was present but diminished, the P2 no longer palpable; the S3 at the LLSB disappeared, the S4 was audible but diminished. The coarse crackles persisted unchanged, but the diffuse crackles on admission disappeared.
Oxygen saturation had improved to 86% upright, dropping to 82% lying flat for 20 minutes. With exertion (rapid walking 200 yards, which she performed comfortably) she desaturated to ~82.

7. From the above narrative, identify the "*clinical tests*" the team performed and explain their diagnostic significance.
Explain the diagnostic significance of the *lab/imaging tests* noted above.

The clinical response to empiric therapy and careful observation (and measurement) of exam findings over time are among the most important diagnostic "tests" in resource-poor areas.

The clinical observations noted above carry the following diagnostic significance:

- *Response to the first 24 hours of empiric therapy: i.e. weight loss with diuretics; absence of respiratory distress with a halving of the respiratory rate and improvement of O2 saturation, fewer crackles. [Significance: The diffuse crackles were indeed from edema fluid responsive to diuresis, implying LV CHF - not bilateral pneumonia or sepsis/ARDS. The ability of the kidneys to respond vigorously to diuresis implies a normal or near-normal creatinine and renal function.]*
- *Total diuresis of 15-20% of body weight with disappearance of fine crackles but persistence of coarse crackles. [Significance: corroborates the suspicion of 2 causes of crackles, edema fluid and inflammation, fibrosis]*
- *Afebrile after the 2nd hospital day [Significance: probably had an underlying pneumonia]*
- *Ability to sleep flat and exercise [Significance: Corroborates the diagnosis of LV CHF that improved with both diuresis and treatment of acute infection.]*
- *Diminution of overt PE signs of PHT and cor pulmonale [Significance: Pneumonia increased cardiac output and along with LV decompensation and pulmonary venous hypertension, acutely raised PA pressures precipitating acute-on-chronic cor pulmonale. The "acute" phase is now resolved as are the florid exam signs present on admission.]*
- *Positional desaturation [Significance: V/Q mismatch and hypoxemia worsen when more blood flows to un-aerated segments of the lung when the patient lies supine, in this case the right apex fibrotic from Tuberculosis. Although such positional desaturation could have contributed to her "orthopnea/PND", symptomatic resolution was rapid with diuresis suggesting CHF as the main cause of her acute symptoms.]*

- *Lack of overt dyspnea on exertion despite O2 saturation of 82% [Significance: She is well-adapted to chronic hypoxemia.]*

Lab-imaging:

- *Hematocrit:55, performed when the patient's pulmonary edema resolved, corroborates the polycythemia of chronic hypoxemia, and cor pulmonale secondary to parenchymal lung disease;*
- *EKG: with RAH and RVH, corroborates the clinical suspicion of cor pulmonale secondary to PHT;*
- *CXR: extensive multi-lobar infiltrates/fibrosis from TB; the left lower lobe streaky infiltrate that partially resolved may have been the nidus of the acute bacterial infection causing cardiac decompensation. On this x-ray a week later, there was no evidence of pulmonary edema.*
- *AFB smears negative: no active TB apparent (though smears are only ~60% sensitive).*
- *Urinalysis: no protein or active sediment implies no nephrosis/nephritis; renal failure (not suspected) is even less likely;*

8. After day 8, the team decided to *discontinue furosemide and observe the patient.* What plausible reasons would support that decision?

Furosemide was discontinued to evaluate:
a) The relative contribution of acute infection vs. chronic fluid retention to her recent presentation, especially given the dominant chronic findings of cor pulmonale.
How much of the LV failure was induced by the infection, either directly - through worsening hypoxia and LV ischemic dysfunction, or indirectly - through precipitating acute cor pulmonale which then affected LV filling pressures (see below)? In the absence of infection, would she remain stable off diuretics?
b) If she needed the diuretics, how rapidly would she regain fluid weight? This is a critical issue in low resource settings in general, and particularly in this patient with a history of non-adherence when feeling well. How closely must she be followed?

Off furosemide, the patient steadily gained ~0.5 Kg/day, and after 6 days was in respiratory distress again with O2 saturation of 80, a respiratory rate of 42, and crackles diffusely. (This was only 2 days after she exercised vigorously without labored breathing despite an exertional pulse Ox of 82. Since then, she had a 1.1 Kg further weight gain.)
She was again diuresed and, with a loss of 1kg over 24 hours appeared well, in no distress, with only the coarse focal crackles in the same areas previously noted.

9. a) What is the pathophysiology underlying the development of her *chronic* illness?
b) How common is this chronic condition in patients with a similar history of TB?
c) What are the risk factors for its occurrence post-TB?
d) How can the most recent clinical observations off diuretics be explained coherently in the context of her overall illness?

a) The patient has clear evidence on physical exam and EKG of RV hypertrophy due to pulmonary hypertension. The PHT is not due to congenital intra-cardiac shunts or mitral valve disease, and the extensive scarring in her lung and the chronic hypoxia she lives with suggests primary parenchymal destruction from TB over primary vascular etiologies such as PHT due to HIV-related immune arteriopathy, multiple pulmonary emboli or "primary pulmonary hypertension".

TB causes PHT and cor pulmonale in treated patients by leaving in its wake fibrosis, emphysema, bronchiectasis and vascular distortion and obliteration.

b) Residual pulmonary impairment is common post-TB.

Representative studies have defined the scope of the problem:

- *There is a 15-50% prevalence of cor pulmonale in inpatient or autopsy series of patients with severe TB (as reviewed in Ind J Tub., 1986, 33:167);*
- *In India, cor pulmonale was 4 times more frequent in patients with CXR evidence post-treatment of fibrotic "solid lesions" than in patients with clear x-rays, but nevertheless 20-25% with cor pulmonale had only minimal CXR evidence of residual TB. 1/3 had less than 1 lobe involved, and only 1/4 had TB in more than 1 lung. (Ind J Tub., 1986, 33:167)*
- *In Texas, restrictive defects were seen in 30% post-TB; 50% had a >20% decrease in VC; 10% had >50% decrease in VC, enough to cause chronic disability;(Chest 2007; 131:1817)*
- *In Indonesia, 40% had an FEV1 < 60% predicted at diagnosis, decreasing to 25% of patients after successful treatment; (Indian J Tuberc 2009; 56:132)*
- *In Latin America, TB survivors had a 2-4x increase in diagnosed COPD;(EurRespJ 2007;30:1180)*
- *In South African miners, a population at very high risk for TB, loss of lung function was greatest 6 months post-treatment onset and stabilized after 12-18 months. Pulmonary impairment was highly correlated with the number of episodes of TB: e.g. FEV1 decreased 326 cc 6 months after the first episode, stabilizing at 153 cc loss after 18 months; after a 3rd episode, FEV1 was 583cc below controls, stabilizing at 410cc. 20% had an FEV1 <80% predicted after 1 episode, and 35% after 3 episodes. In a 15 year follow-up of this cohort, prior TB was shown to accelerate age-related loss of VC and FEV1 by 40 cc/year on average, and more in those who presented later and/or had worse disease. (Thorax 2000; 55:33 and Thorax 2010; 65:1010)*

c) The risks for the occurrence of PHT and cor pulmonale post-TB treatment are:

- *Duration of illness pre-treatment and delay in receiving appropriate therapy:*
  In one study, patients with MDR-TB who had prolonged symptomatic disease had only 2/3 the residual lung function of other treated patients and a 1/3 decrease in 6 minute walking distance which correlates with increased mortality.(Rev.Port Pneumol 2011; 17:216)
  Delays in treatment are common with TB. In Brazil, an average of 7 weeks elapses between the first medical visit for TB symptoms and the onset of therapy, and 10-12 weeks between symptom onset and treatment. The delays are undoubtedly longer in rural Africa.
- *Extent of disease on CXR*
- *Smear positivity (which correlates with extent of disease)*

d) Our patient had all the risk factors for the development of severe pulmonary dysfunction post-treatment: delay in seeking treatment initially; extensive radiologic changes in at least 2 lobes; smear positivity; and erratic treatment adherence with recurrent evidence of active smear (+) disease over the period of a year.

Hypoxemia was caused by V/Q mismatch in perfused but unventilated segments of her lung (possibly exacerbated by shunting through a silent patent foramen ovale, not uncommon in the general population, as the PHT developed). Hypoxemia's impact on oxygen delivery to the tissues and exercise tolerance was probably mitigated for a while by polycythemia, in effect "doping" with endogenous erythropoietin.

PHT was a product of interstitial fibrosis, direct obliteration of the pulmonary vasculature, and the pulmonary vasoconstrictive response to hypoxemia and poorly ventilated airways. Worse with lower pO2 throughout the night when supine and sleeping, her RV gradually failed in systole, causing increased systemic venous pressure, hydrostatic edema in her legs and sacrum, and congestion of the liver with hepatic tenderness and ascites.

The RV progressively dilated and the intra-ventricular septum moved to the left, encroaching on the left ventricle and raising pressure in the LV cavity now as well. If her albumin level was depressed by her malnutrition and hypercatabolism, common in AIDS patients in Africa but unmeasurable in Kisoro, edema would form in her lung at lower LV pressures than normally necessary to cause CHF. Edema from raised LV pressures, caused initially by intra-ventricular interdependence and septal shift, would further compromise alveolar oxygenation, exacerbate pulmonary vasoconstriction, raise PA pressures, shift the septum even more, and establish a vicious cycle of ever-increasing LV pressures, pulmonary edema, and hypoxemia. The progressive hypoxemia, insensible volume loss and hypotension, and tachycardia could provoke myocardial ischemia and further impair LV function.

In our patient this hemodynamic downward spiral was probably accelerated by a superimposed pneumonia to which lung distortion by fibrosis, bronchiectasis, impaired ciliary clearance, wet lungs, and HIV all contributed. The pneumonia increased her cardiac output and with it, both RV and LV pressures leading to biventricular cardiac decompensation and the severe respiratory distress she presented with initially. On presentation she had florid signs of both acute cor pulmonale and acute pulmonary edema.

Unfortunately, treatment of the acute pneumonia was not sufficient to stave off the vicious cycle of fluid retention-hypoxia-raised intra-cardiac pressures that commenced again after diuretics were stopped. She clearly would be a candidate for long-term oxygen therapy if it were available in rural Africa.

She was discharged on furosemide with close follow-up planned, although her prior history of intermittent adherence and the rapid onset of pulmonary edema bode poorly for her long-term prognosis.

Suggested Reading:

Kapoor, S.C. Pathogenesis of Cor Pulmonale in Pulmonary Tuberculosis Ind. J. Tub., 1986, 33, 167

Pasipanodya, J.G., Pulmonary Impairment After Tuberculosis CHEST. June 2007;131(6):1817-1824

Hnizdo, E., Chronic pulmonary function impairment caused by initial and recurrent pulmonary tuberculosis following treatment Thorax 2000;55:32–38

Lee, J.H., et.al. Lung function in patients with chronic airflow obstruction due to tuberculous destroyed lung Respiratory Medicine (2003) 97, 1237–1242

Di Naso F.C Functional evaluation in patients with pulmonary tuberculosis sequelae Rev Port Pneumol. 2011;17(5):216---221

Bloomfield, G.S., et al., Conditions That Predispose to Pulmonary Hypertension and Right Heart Failure in Persons Exposed to Household Air Pollution in LMIC Global Heart 2012; 7 (3): 249

Ross, J., et al. Excess lung function decline in gold miners following pulmonary tuberculosis Thorax 2010;65:1010

Menezes, A.M.B., et al Tuberculosis and airflow obstruction: evidence from the PLATINO study in Latin America European Resp. J 2007; 30 (6): 1180