Introduction:

Welcome to the 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 4-10 discussion questions that direct clinical reasoning and/or highlight diagnostic issues. A month 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

About the Author:

I'm a Professor of Clinical Medicine at the Albert Einstein College of Medicine in the Bronx, New York, where my career has centered on medical education for the past 40 years – as a past residency Program Director in Primary Care and Social Internal Medicine at Montefiore Hospital, and global health advisor and program leader at the school. I've served on the Boards of Directors of Doctors for Global Health, Doctors of the World USA, and the Global Health Education Consortium. I spend about 3-4 months a year in Uganda working on the Medicine wards of Kisoro District Hospital which, like most hospitals in the world that serve most of the world's population, has (almost) no resources. "At the bedside", I teach Internal Medicine residents and medical students how to assimilate the elements of history, physical exam and epidemiologic probability into a diagnostic impression that, even without definitive testing, can lead to appropriate therapeutic strategies in the field.

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A 43-year-old woman presents with increasing fatigue and a “heart problem.”

She had been well, working in the fields until about 1-2 years ago when she noted that her heart was “pounding” and “racing” while she was climbing hills, and she had to slow down. The pounding and racing would happen predictably, coming on gradually and diminishing gradually if she stopped climbing.

Four months ago, she began to develop lower extremity and abdominal swelling, increased fatigue and shortness of breath with exertion, and heart racing even at rest. She went to the local health center and was given lasix and digoxin for a “heart problem”. She has taken the medication reliably and, while noting some relief, has still been symptomatic with increasing fatigue and abdominal distention over the past 2 months.

She has delivered 4 children without problems, the last 8 years ago; recalls neither prolonged debilitating illness as a child, nor lagging behind her peers; and has had no symptoms of fever, cough, weight loss, orthopnea, paroxysmal nocturnal dyspnea (PND), or hemoptysis.

**Physical Exam:**

Thin woman in no distress, lying flat in bed.

| BP: 90/60 | HR: 85 irregularly irregular | R: 15 | T: 37 |

Eyes: no proptosis or lid-lag
Mouth: no thrush, petechiae, or mucosal cyanosis;
Neck: JVP, internal and external, to angle of jaw sitting upright, with cannon V waves; palpable thyroid, no goiter
Lungs: clear to auscultation/percussion
Cardiac: barely perceptible parasternal lift; P₂ not palpable;

PMI: 1 cm lateral to mid-clavicular line, 2.5 cm. diameter
split S₁ widely heard, split S₂ at pulmonic area with different, crisp and more widely separated double sound at S₂ at the apex;
no S₃, S₄
2/4 decrescendo, diastolic murmur at left sternal border (LSB), low pitch, marked increase with inspiration to 3-4/4 with a thrill;
2/4 low pitched diastolic rumble apex, increased with expiration;
2/6 holosystolic murmur low-medium pitch, lower LSB, increased with inspiration
2/6 holosystolic murmur, high-pitched, apex to axilla
Abdomen: pulsatile, tender liver; distended abdomen with shifting dullness; no masses or spleen palpated or balloted
Extremities: + 1-2 edema to knees; no fine tremors; no clubbing or nail cyanosis.
1. **What is the clinical “frame” of this case from the history (i.e. the key clinical features that the final diagnosis must be consistent with), and their clinical/physiologic implications?**

- Onset of cardiac symptoms in the early 40’s: suggests either a process that began in her 40s or finally became symptomatic after a long, chronic course;
- Dominant symptoms of fatigue, edema, abdominal pain/distention: consistent with right-sided heart failure
- No symptoms of orthopnea/PND: no “specific” symptoms of left-sided heart failure
- Insidious progression of symptoms over >1 year, more rapid over few months: either the recently worsened symptoms reflect the end of physiologic reserve of a chronic process or a superimposed acute complication of the underlying chronic disease.

2. **What is the differential diagnosis of significant right-sided heart failure in Uganda?**

- **Endomyocardial fibrosis:** a restrictive cardiomyopathy, very prevalent in SW Uganda and East Africa, most commonly presents with signs of RV failure (although >50% of cases have biventricular involvement, and another 15-25%, LV only).
- **Rheumatic heart disease (RHD):** mitral disease, stenosis (MS) > regurgitation (MR), and/or primary or associated right-sided valve disease (tricuspid or pulmonary involvement): RHD is >10-100x more prevalent in Africa than in the West, and usually causes RV failure through LV failure - when the adaptive responses of the pulmonary vasculature and the RV succumb to the chronically high LV pressure load and RV pressures increase. However, right-sided valve involvement of the tricuspid and/or pulmonic valves can also cause RV failure. In such cases, although there may not be left heart hemodynamic stress or clinical failure symptoms, the mitral valve is almost always involved pathologically.
- **Dilated cardiomyopathy (DCM):** Much more prevalent in Africa than in the West, idiopathic or known (peri-partum, HIV, etc.) causes of DCM usually present with near-simultaneous onset within weeks to months of biventricular CHF. However, the left heart failure usually produces the first symptom, dyspnea.
- **Constrictive pericarditis:** Due to tuberculosis, chronic fibrosis of the pericardium produces signs of RV failure, JVP and ascites often out of proportion to peripheral edema.
- **Congenital heart disease (CHD):** Without the availability of modern diagnostics or treatments, in rural Africa CHD often presents in adulthood. Eisenmenger’s syndrome of severe pulmonary hypertension induced by years of increased flow through a cardiac shunt (ASD, VSD, PDA, etc) can lead to symptoms of fatigue and palpitations and signs of RV failure.
- **Other:** hyperthyroid cardiomyopathy, in Africa due most commonly to toxic multinodular goiter, presents with signs of RV failure. Usually, weight loss is evident.

3. **What is the pathophysiologic significance of the sequence of symptoms in the clinical history of this patient?**
• Despite a raucous heart with many murmurs on PE, the patient bore 4 children without a problem and was without symptoms until her 40’s. When symptoms first developed, they were predominantly those of right-sided heart failure (fatigue, edema, abdominal distention), and palpitations that came on predictably with exertion.

• The sequence of symptoms carries diagnostic significance:
  1) Given the absence of significant preceding left-sided heart failure symptoms (dyspnea on exertion, orthopnea, PND), the RV symptoms were unlikely to be caused by increased pulmonary artery pressures in response to chronically elevated left-sided pressures.
  2) The racing/pounding heart that came on predictably with exertion may have been caused either by sinus tachycardia associated with a failing heart under stress, and/or atrial fibrillation (AF) conducting through the AV node at very fast rates via exercise-induced catecholamines. Both possibilities would be consistent with the occurrence of subjective palpitations only with exertion, unlike the more variable onset seen with paroxysmal supraventricular or other re-entry tachycardias which often happen at rest.

4. What is the pathophysiologic significance of the physical exam findings?

• Irregularly irregular rhythm: atrial fibrillation. Development of AF months ago could have precipitated symptomatic deterioration, particularly in ventricles dependent on atrial contraction (stiff hypertrophic ventricles or stenotic valve lesions (e.g. MS, TS)).
• JVP to angle jaw sitting marked elevation of right-sided pressures; cannon waves in the JVP, and a pulsatile liver: tricuspid regurgitation is present.
• Barely perceptible parasternal lift: not a markedly enlarged chronically hypertrophied right ventricle despite right-sided symptoms. This finding is strong exam evidence against both pulmonary hypertension and pulmonic valve-mediated causes of RV failure both of which would usually produce a significant parasternal lift even after the ventricle begins to fail.
• PMI: slightly displaced, slightly enlarged: the LV is dilated somewhat, but not much; there is no LV heave.
• 2/6 holosystolic murmur, high-pitched, apex to axilla: mitral regurgitation. In light of the high pitch of the murmur (which indicates a high pressure gradient between the LV and LA) and the only-slightly displaced, modest LV PMI without a heave noted above, the MR is mild-moderate and unlikely to be the principle cause of the symptoms;
• 2/6 holosystolic low-medium pitch murmur LSB, increased with inspiration: tricuspid regurgitation (TR). The increase with inspiration identifies right-sided murmurs. TR, often better seen in the neck than heard in the chest, is also visible in this patient in the cannon V waves and pulsatile liver mentioned above.
• Diastolic low-pitched decrescendo murmur at the lower left sternal border, markedly increased (with a thrill) with inspiration: tricuspid stenosis plus tricuspid inflow from TR. As noted above, the increase with inspiration identifies right-sided murmurs, but in this case in diastole; the low pitch suggests a low pressure gradient during blood flow between the 2 chambers (the RA and the RV in diastole), and the marked augmentation in inspiration clearly defines the murmur as TS rather than MS.
• The degree of augmentation suggests that the TR plays a significant role by increasing flow across the deformed orifice, and thereby murmur intensity. The murmur of pulmonary regurgitation (PR) from either a primary valve lesion or secondary to pulmonary hypertension from associated MS would also increase with inspiration, but the lack of an RV lift strongly mitigates against that.

• 2/4 diastolic rumble at the apex, increased with expiration, and the widely separated sharp “double sound” at S2: mitral stenosis with an opening snap (OS). Although it’s possible that the diastolic rumble is transmitted TS and not MS, the change with respiration that is opposite to that of the diastolic murmur at the LSB, the OS heard at the apex (though a mitral OS is often heard at the LSB as well, but not in this case), and the pathologic observation that the vast majority of TS is accompanied by at least some MS, all point in favor of this apical murmur originating from MS. The wide A2-OS interval and the displaced PMI in the presence of MR suggest that the MS is neither severe nor the dominant mitral lesion - consistent with the absence of a history of prior MS symptoms of dyspnea, orthopnea, PND, hemoptysis.

5. How does the physical exam help the clinician determine the cause of right-sided heart failure in Uganda (see question #2)?
What is the most likely etiology of this patient’s clinical presentation and how common is it?
What “tests” should be ordered?

• Endomyocardial fibrosis (EMF): One of the rare causes of valve stenosis is EMF. The endocardial fibrosing process can involve the chordae and commissures of the AV valves resulting in stenosis (though more commonly regurgitation). Stenosis occurs far less frequently in EMF than in rheumatic heart disease, BUT… EMF is very common in Uganda and “uncommon presentations of common disorders are more frequent than common presentations of rare disorders” (a colloquial, qualitative version of Bayes Theorem). Furthermore, ascites is very prominent in EMF and the lack of an RV lift is consistent with this restrictive cardiomyopathy.

• However, RHD is also common in Uganda, and the simultaneous stenoses of both mitral and tricuspid valves, to-be-expected in RHD involving the tricuspid valve but (doubly) rare in EMF, favors RHD, as does the opening snap.

• Dilated cardiomyopathy (DCM): although DCM can cause MR and TR by secondarily dilating the AV orifices, prominent diastolic murmurs or snaps would not be part of the picture.

• Constrictive pericarditis: Chronic fibrosis of the pericardium produces a heart that is normal to modestly enlarged (consistent with this patient’s). Furthermore, the sharp sound around S2 thought to be an OS may instead be a “pericardial knock” with similar timing in diastole - due to the heart “knocking” against the fibrotic/calcified pericardium in diastole. However as with DCM, prominent murmurs (in this case systolic or diastolic) and/or snaps would not be heard.

• Congenital heart disease (CHD): Eisenmenger’s syndrome of severe pulmonary hypertension induced by years of increased flow through a cardiac shunt (ASD, VSD, PDA, etc), could manifest both diastolic and systolic murmurs due to increased flow across normal valves or turbulence across the shunts (e.g. an ASD could cause a diastolic
murmur (with inspiratory augmentation) due to increased flow across a normal tricuspid valve. However, by the time the RV fails in an ASD, the flow murmur across the TV should decrease or disappear as ventricular and atrial pressures equalize. Furthermore, the S2 should be prominent and fixed in an ASD, unlike this patient.)

- Most importantly, almost all with CHD presenting with right-heart failure have a notably hyperactive precordium and ventricular hypertrophy from years of volume and/or pressure overload; and cyanosis or clubbing would be expected. None of these signs were present in this patient.

- Other: hyperthyroid cardiomyopathy would be very unlikely in this patient with a normal thyroid gland, no fine tremor, no lid-lag, and a HR in AF of only 85 in a young patient, albeit on digoxin (N.B. AF due to hyperthyroidism is usually resistant to medication and hard to control)

**Rheumatic heart disease (RHD): Tricuspid Stenosis**

- The multiple murmurs and the OS make it very likely that the underlying disease in this patient is RHD, a rare disease in the West but still ravaging Africa and the 3rd World as it once did everywhere before modernization. In both Africa and S.E. Asia 2-6% of school-aged children have echocardiogram evidence of RHD, mostly “silent”, and mostly involving the mitral valve. Our patient has 4 murmurs, and exam evidence of involvement of both the tricuspid and mitral valves with different degrees of stenosis and insufficiency.

- The absence of preceding left-sided symptoms and the dominance of right-sided symptoms and PE findings suggest that although mitral disease is also evident on PE, it is not symptomatic. Although some patients with MS respond to the chronically elevated left atrial pressure with an unusual degree of pulmonary vasoconstriction and hypertension leading to early RV failure which then may decrease left-sided symptoms, a preceding history of left-sided symptoms and exam evidence of RVH (e.g. lift) or PHT (e.g. increased P2) would be expected, as would a preceding history of left-sided symptoms from MS especially during one of her 4 pregnancies. The remarkable observation in this patient is the how “normal” the chest wall is on palpation despite the severity of the (right-sided) symptoms and the presence of regurgitant murmurs. The heart’s just not receiving that much blood!

- Right-sided valvular lesions are uncommon in rheumatic heart disease (~5% of clinical presentations, 10-20% of pathological diagnoses in patients with RHD), they’re almost always found in association with mitral pathology and rarely dominant clinically - - but that’s probably the case here: tricuspid stenosis with regurgitation (most tricuspid RHD is a mix of both), possibly becoming more overtly symptomatic with the loss of the atrial kick after the development of atrial fibrillation.

- Of the two right-sided murmurs, TS is probably dominant: with only a mild RV lift (consistent with patient’s thin frame), TR is less likely to be the principle hemodynamic dysfunction. However, the TR is sufficiently severe to transmit pulsations to the chronically congested liver and the internal jugular vein, and to increase the flow across the tricuspid valve in diastole accentuating the murmur of TS.

- An EKG showed atrial fibrillation and normal R-wave progression without evidence of either RV or LV hypertrophy corroborating the clinical suspicion of dominant TS. An echocardiogram was unavailable.
Suggested Reading:

Essop MR et al., Rheumatic and Nonrheumatic Valvular Heart Disease: Epidemiology, Management, and Prevention in Africa. Circulation. 2005;112:3584-3591

Hurst JW (ed) The Heart

Constant, J. Bedside Cardiology 4TH Ed. Little, Brown and Co. 1993