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 30 – CHEST PAIN, FOOT PAIN, & SHOCK

A 35 year old mother of six children, separated from her husband who lives in Kampala, is brought to Kisoro Hospital at 7:00 PM, carried hurriedly to a ward bed by her friends.

She is breathing rapidly and complaining of severe left chest pain under her left breast, increased with breathing and lying down. The pain began gradually in the morning but has steadily gotten worse. She's had a dry cough without sputum since yesterday, and has not noted fever. There's no history of trauma or similar pain before, no vomiting, diarrhea, or black/bloody stools.

Physical Exam:

Thin, acutely ill, in obvious respiratory distress breathing rapidly and shallowly - panting, sitting upright.

Vital Signs: BP unattainable HR 150 R 60 T 97 oral and axillary
Skin: no rashes
Mouth: no thrush
Neck: no JVP or HJR visible while lying flat;
Chest wall: significant pain elicited with firm palpation over the anterior left chest wall.
Lungs: trachea midline
clear to auscultation and percussion except on careful auscultation (repeatedly) in various positions, a short "scratchy" crackle is heard variably on inspiration under the left breast when sitting, not when supine; the scratchy sound vanished with breath holding
Heart: tachycardic at ~150, regular
PMI: neither visible nor palpable, lying or sitting
S1 S2 normal, no gallups, murmurs or rubs audible
Abdomen: benign, without hepato-splenomegaly, masses or tenderness; rectal, no stool in vault.
Extremities: no leg edema or calf tenderness; hands and right foot cool to touch;
left foot: large amount of dorsal swelling with pus oozing from crack in the skin, warm, tender ball of foot

Additional history *post-exam* (after seeing foot):

She was otherwise in her usual state of health without weight loss or night sweats until a week ago when digging barefoot in the fields, she cut her foot on a rock. The foot has grown increasingly painful and swollen.

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

    - *shock - no blood pressure attainable, with rapid tachycardia*
    - *left anterior pleuritic and positional pain, with positional crackle*
    - *no PMI palpable in any position*
    - *purulent left foot*

2. **What does the nature of the pain signify? Explain.**

    The positional and pleuritic characteristics of the pain suggest that it originates in the tissues directly involved with chest movement such as ribs or muscle, or surfaces that are stretched or brought into contact by breathing and movement such as the pleura and pericardium. While pathology in the ribs or chest muscle could cause this type of pain, short of significant trauma to the chest (e.g. a stab wound!), primary musculo-skeletal pathology would not explain the rest of this patient's presentation -- in shock.

    Left anterior, "under the breast" pain worse when lying supine suggests pericardial disease, with possible adjacent pleuritis. Pericardial pain is worse when the patient is supine because the heart's mass is then pounding against the inflamed posterior pericardium; the pain is relieved when sitting because the heart then "dangles" without beating directly on the inflamed surfaces.

3. **Why was so much attention devoted to a rather unremarkable chest exam, and what was the significance of the findings by both palpation and auscultation?**

    Special attention was paid to the auscultatory exam of the lungs, i.e. it was repeated in various positions to confirm suspected pathology in the pleura or pericardium that could explain the patient's critical illness and shock. The "scratchy sound" describes a <u>single-component friction rub</u>, confirmed by change with breathing (pleuritic) and position. Rubs are classically variable and evanescent, more so when pericardial than pleural in origin.

    Since externally applied pressure stretches inflamed surfaces, pain induced by firm palpation is also consistent with pain derived from the pleura or pericardium.

The lack of a visible or palpable PMI in this thin woman is remarkable. Although in the U.S. body habitus often obscures findings on palpation (and readily available imaging and echocardiograms have replaced whatever clinical data examination of the PMI traditionally provided), in rural malnourished Africa the PMI is obvious in the vast majority of patients, especially when the patients are physiologically "stressed", and careful examination is very useful. The absence of a PMI in this patient suggests either pericardial effusion/tamponade or lack of filling pressure in the ventricle due to shock, or both.

4. How do you differentiate the specific tissue-of-origin of the mono-phasic scratchy chest finding on PE?

The rub must be associated with either breathing (i.e. the rub disappears as patient holds her breath, both in inspiration and in expiration) or with heart rhythm (as patient holds her breath, the rub continues, timed with heart beat). If the former, it's pleural, if the latter, it's pericardial. Pericardial rubs are often best heard sitting upright, and leaning forward in exhalation. Often this isn't necessary since a pericardial rub is quite obvious if it's multi-phasic, but in this patient with a monophasic rub who's panting at 60 breaths/minute and very tachycardic, timing the sound precisely was very helpful - and its result surprising:

In this patient the scratchy sound vanished with breath holding both in inspiration and expiration, implying a pleural-based sound.

5. a) What "test" can readily be done to help clarify the diagnosis?
b) What potential test findings, observed in this patient, would be specific for the one cause of a mono-phasic scratchy chest exam sound that you are looking for with this test?
c) What is the differential diagnosis that test finding?

a) EKG, looking for changes of pericarditis

b) The EKG can be specific for pericarditis - as it was in this case - by showing sinus tachycardia, decreased voltage (<5mm standard, <10mm precordial leads), ST elevation in all leads – concave upward and most marked in V4-6, upright blunted T waves, depressed PR segments. There was no electrical alternans. These changes are diagnostic of acute pericarditis (without the rare but specific findings of tamponade, electrical alternans).

c) The differential diagnosis of ST elevations include myocardial infarction (MI) and "early repolarization".

In an MI, the elevations are concave downward (dome-shaped) and the T waves which are often peaked initially, invert prior to the STs returning to baseline. T waves in

pericarditis are flattened early on. They also invert - but only after the STs have returned to baseline.

Young Africans (and African Americans) have a high prevalence of "early repolarization" changes in which the QRS j-point has a high take-off. This leads to a pattern of ST elevation that can also occur diffusely. However, in early repolarization, the ST segments are elevated mostly in V1-3 and the T waves are tall; in pericarditis, the ST's are elevated maximally in V4-6, and the T waves are modest.

If the ratio of the height of ST elevation to the height of T waves in V5 or V6 is >.25, it's likely to be pericarditis, with a specificity of > 95%.

d) What is the apparent inconsistency between the exam and the test findings and how can it be explained?

Of interest, the rub in this patient was actually a pleural-based rub despite obvious pericarditis on EKG (which was likely causing her pain).

In many cases of pericarditis there is associated adjacent pleuritis and a left-sided pleural effusion (over 40%).

6. a) What is the (etiologic) differential diagnosis of this disease process in Africa and how does it contrast with the differential diagnosis in developed nations?
b) How would the differential be influenced if she were HIV (+)?

a) Two representative papers in the last 5 years demonstrate the contrast between Africa and developed nations vis-à-vis etiology of pericarditis:

Reuter el al (QJM 99:827, '06) reported a series of 233 patients from South Africa between 1995-2001 with the following distribution of etiologies: Tuberculosis 70%; neoplastic 10%; autoimmune 5%; septic 2%; idiopathic/other 14%
And from Italy, Imazio et al reported a series of 453 patients (Circulation 2007, 115:2739): "idiopathic/other" 83%; neoplastic 5%; autoimmune 7%; tuberculosis 4%, septic 1%.

1. Tuberculous Pericarditis: This is by far the most prevalent etiology of pericarditis in Africa, over 70% of all cases, and over 90% in HIV + patients. TB involves the pericardium through retrograde lymphatic spread from nodes in the mediastinum or less commonly through hematogenous dissemination, and most of the effusion and later pathology are due to the ensuing hypersensitivity reaction to the tubercle bacilli. It usually presents insidiously, with symptoms developing over weeks. Of interest, it's the second most common cause of "CHF" in South Africa, after rheumatic heart disease (more common than hypertensive or dilated cardiomyopathies). 1-8% of all cases of pulmonary TB in Africa reportedly involve the pericardium.

2. Neoplastic pericarditis: The most common neoplasms metastatic to the pericardium are breast, lung, melanoma, lymphoma and sarcoma. Usually these cancers are obvious on physical exam or by history, particularly in Africa where patients' access to care is delayed.

3. Autoimmune diseases: SLE, rheumatoid arthritis, scleroderma, etc. can all cause pericarditis but usually as part of a broader rheumatic/connective tissue presentation.

4. Septic pericarditis: is rare, usually due to strep or staph from another source, and usually is acute and progressive over days to a week. It's commonly associated with pain, fever (median>102), and EKG changes; and lethal without prompt open surgical drainage.

5. Other non-infectious etiologies: uremia and radiation pericarditis are seen frequently in the West, but radiation therapy and therefore its side effect of pericarditis, is not available in rural Africa. Uremia is seen in Africa however, almost always associated with a compatible spectrum of other uremic symptoms not seen in this patient.

6. Other infectious etiologies: In the West, the most common cause of pericarditis is "idiopathic", likely due to infection with a virus. Of the known viruses, Coxsackie and echo lead the list, but many others such as adenovirus or mononucleosis are possible. Non-viral causes include spirochetes - syphilis and borrelia (lyme); and "atypicals", Chlamydia and mycoplasma.

b) HIV infection both makes TB more likely, and adds to the spectrum of etiologic possibilities for pericarditis: lymphoma, Kaposi's sarcoma, Cryptococcus, Nocardia, HSV, CMV, MAI, and Staph have all been reported to cause pericarditis in HIV+ patients.

7. What is the *emergency* in this case? What is its differential diagnosis and what are some pros and cons for each possibility?

- *Shock is the emergency. Assessing its severity is complicated by an expected "low normal" BP in this thin, malnourished woman from rural Africa.*

- *The differential diagnosis is:*
  - septic shock: plausible because of the obviously infected foot. The focal pleuritic pain could be from a superimposed pneumonia. Auguring modestly against septic shock are the patient's cool extremities (suggesting low cardiac output and vasoconstriction peripherally) and lack of confusion.
  - pericardial tamponade: suggested by the anterior pleuritic pain and obvious pericarditis on EKG, the lack of a palpable PMI, and the cool extremities. It's not likely to be the sole cause of shock because of the lack of obvious JVP/HJR.
  - volume depletion: likely contributes to her hypotension through increased insensible respiratory losses, and is supported by her cool extremities (and possibly intact mentation). Although volume depletion can cause change in mental status, shock from sepsis is more likely to do so.

8. What treatment should be emergently administered?

- *<u>Rapid "fluid challenge</u>": In a hypotensive patient the first liter(s) of fluid should be administered as a diagnostic test as well as a therapeutic maneuver: this means rapidly (!), monitoring BP and HR. Since both the interstitial and intravascular spaces are depleted when volume loss causes hypotension, giving fluid too slowly, even at "vigorous hydration" rates of 200-300 cc NS/hour, may be slow enough for the fluid to transudate into the depleted interstitium nearly as fast as it's infused, hardly raising the blood pressure or lowering heart rate. One then risks a "false negative" interpretation of the effect of volume on shock, and unnecessarily delays cardiac, renal and CNS re-perfusion.*

  Thus a "fluid challenge", for both diagnosis and therapy, requires giving fluid rapidly enough so that it all stays in the intravascular space while its effect on BP and HR is assessed: 500 cc of normal saline over 10-15 minutes. In hypovolemic shock, one sees a brisk rise in BP >10-15 and a reflex decrease in HR >10-20 after the 15 minute infusion. In septic shock, the BP usually rises < 5-10 mm. To be safe, if you see an increase >5 mm, repeat the "challenge". Hypovolemia will continue to respond to fluid. Although early sepsis may be volume responsive, in late septic shock BP will rise sluggishly and slightly if at all: If the rise is initially <5, it's likely to be septic shock or adrenal insufficiency (usually caused by TB/HIV in Uganda).

  In pericardial tamponade complicated by hypovolemia, the BP should increase and neck veins appear.

  If an appropriate fluid challenge is positive for hypovolemia, infuse 1-2 liters of normal saline promptly and keep hydrating aggressively at 300-500 cc/hour for the next few hours; and if the challenge is negative, slow down to a maintenance rate that keeps BP above 65, assessing neck veins, lungs and vital signs.

- *<u>IV antibiotics</u>, broad spectrum combination, covering strep/staph and gram negative organisms given the "can't miss" urgency of the patient's presentation.*

9. If the blood pressure becomes measurable, what physical exam maneuver is appropriate?

Pulsus paradoxus, a sign of hemodynamically significant tamponade, is appropriate. Along with raised JVP and tachycardia, pulsus paradoxus is one of the cardinal clinical features of tamponade. Although echo-defined indentation or collapse of the RA or RV free wall in diastole is the technologic "gold standard" for diagnosing tamponade, many feel that it's too sensitive a standard for "tamponade", picking up clinically insignificant degrees of hemodynamic compromise. Although pulsus >10 is found in >95% of patients whose cardiac output has been compromised by pericardial effusion, studies (e.g. Reuter,

QJM 99:827, 2006) in which tamponade was diagnosed by echo have found that only 20-30% with echo-defined tamponade had pulsus.

With fluids the patient's BP became attainable, and her HR dropped to 110; the BP demonstrated a pulsus paradoxus of >20. Over 24 hours, there was a marked increase of the JVP to the angle of the jaw.
A clear-cut triphasic pericardial "friction rub" (cycling with the heart rhythm) appeared.
CXR showed massive water-bottle heart and clear lungs with a left pleural effusion.

Diagnosis of shock: combination of pericardial tamponade and hypovolemia (due to increased insensible losses).

10. What is the physiologic and/or anatomic origin of the multi-phasic sound ausculted after the patient was hydrated?

The multi-phasic sound is the "complete" pericardial friction rub.
A pericardial rub can have one, two or three components. The 3 components are, in descending order of frequency, 1) ventricular systole; 2) atrial systole; 3) ventricular relaxation.
15-20% of rubs are monophasic (just ventricular systole), 30% biphasic (ventricular and atrial systole) and 50% are triphasic with all 3 components present.
The rub was not heard on admission due to the patient's marked hypovolemia which impaired cardiac filling and likely caused too weak an impulse against the pericardium to generate the rub.

11. What was the most likely *etiologic* diagnosis for the pathologic process in this patient? Explain your reasoning.

The most likely diagnosis in this patient is ***septic/purulent pericarditis****.*

Although far less common than Tuberculous Pericarditis in Africa, the purulent foot with cellulitis/acute osteomyelitis makes hematogenous spread to the pericardium/pleura of a pyogenic (?staph) organism most likely in this patient.

The very tight temporal relationship of these 2 uncommon acute processes in the foot and the chest dominate the clinical reasoning process here.
Although absence of fever is notable, the time course over days, the absence of any illness prior to cutting her foot, the acute severe pain, the marked EKG changes, and the rapid progression to tamponade are all consistent with purulent pericarditis.

Of note, although textbooks emphasize the prototypical acute presentation of purulent pericarditis – with chest pain, friction rub and EKG changes in the majority – a recent literature review (Medicine 2009, 88:52-65) reported that only 30-45% of the patients documented in case series of purulent pericarditis since the 1960's had each of those 3

features taken separately; however, >80% had fever (median 102) recorded, the median duration of illness was 7 days; 65% of infections were gram positive, 30% gram negative. (The disconnect between the clinical descriptions in textbooks versus the literature probably reflects either a textbook bias towards the "classic case" or a literature bias of "publication" in which the more unusual presentations of disease are reported, or a little of both.)

12. What is the appropriate treatment, and what happened in Kisoro?

- *The appropriate treatment is antibiotics and urgent pericardiocentesis followed by a surgical pericardial drainage procedure to maximize the chance of cure and prevent both the high rate of recurrence otherwise and constrictive pericarditis. Even with these procedures the condition is fatal in 20-40%.*

- *We didn't have a pericardiocentesis needle, or the expertise to do the procedure safely. We checked at the only other hospital in the district, and neither did they. In the meantime, we kept up the broad spectrum antibiotic coverage, and explored and drained pus from her foot (which were gram (+) cocci in clusters on smear, presumably Staph).*

  We also started therapy for tuberculosis, the most common cause of pericarditis in Africa, 35 times more prevalent than purulent pericarditis - just in case! (You can't be a diagnostic purist in emergencies when life hangs in the balance and definitive testing is out of reach. Even if coexisting TB was only 5% likely, it would be worth the low risk of TB antibiotic toxicity.)

  And we decided she needed to make the 10 hour journey to the capital Kampala for appropriate care: we'd collected money to support her trip, her attendant, someone to care for her 6 kids, and the medical/surgical costs in the "big hospital".
  After 3 days, the patient was (unfortunately) feeling better. She could stand up. The fluids, antibiotics, painkillers were working, though the pulsus hadn't diminished, the rub was loud, the JVP elevated, and the fever persistent.
  She adamantly refused to venture outside the district, much less the capital, and she insisted on returning home. We enlisted her relatives and her evangelist in the cause. No one could convince her to take up the offer and adopt our strategy.

  On the 6th day, she was given a stash of oral antibiotics against Staph and TB and a follow-up appointment (that was never kept), and we watched her limp out of the ward to her soon-to-be-orphaned children.

Suggested Readings:

Parikh, S, et.al. Purulent Pericarditis: Report of 2 Cases and Review of the Literature

Medicine 2009; 88:52-65
Spodick DH. Pericardial diseases. In: Braunwald E, Zipes DP, Libby P, eds. Heart disease: a textbook of cardiovascular medicine, 6th edn. Philadelphia: WB Saunders, 2001: 1823–76
Reuter, H. et. al; Diagnosing tuberculous pericarditis Q J Med 2006; 99:827–839.
Imazio, M. et. al; Indicators of Poor Prognosis of Acute Pericarditis Circ 2007, 115:2739
Troughton, R.W., et.al Pericarditis Lancet 2004; 363: 717-27