



## **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 instructor 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](mailto: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 Katherine Unger at [kunger@CUGH.org](mailto:kunger@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 49 – Embarrassing and Persistent**

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32 year old man a farmer in Kisoro married with 4 children presents to the hospital with worsened symptoms of testicular enlargement and pain unresponsive to therapy for weeks.

He had been well, without past known sexually transmitted diseases or urinary infections, until 5-6 weeks ago when he noticed that his left testis was getting larger associated with a heavy dragging sensation in his scrotum. The enlargement and discomfort progressed over the next 2 weeks and he came to the hospital. At that time he claimed to have been monogamous (including during a 2 month trip to Kampala to work as a farm laborer 6 months before), and denied urethral discharge or a history of penile ulcers. The hospital notes recorded his temperature as normal, his left testis as firm, oval, 4x5 cm in size, and mildly tender. No further exam was recorded. He was treated with IM ceftriaxone and given doxycycline to take for 2 weeks, and after 3 days of in-hospital treatment he returned home not feeling any different but reassured that he would soon improve.

However, over the next 2 weeks after leaving the hospital, he didn't feel any better and now he returns. His scrotum seems larger and more painful, and he is concerned about cancer. He has taken his medications religiously, has not noted a urethral discharge, fevers, sweats or weight loss, nor any symptoms of hematuria, dysuria, diarrhea, headache or cough. He works as a digger, owns some chickens but no cattle, goats or sheep, and does not drink milk. He has not been HIV tested. He knows no other men with this type of problem in his village.

**Physical Exam:** Adult male looking stated age, thin not cachectic, in no distress but anxious.

B.P. 110/70, H.R 95, R 14, T 98.8 axillary

Skin: normal except over scrotum; no areas of hypopigmentation

Eyes: normal conjunctiva; fundi benign without exudates

Mouth: no thrush

Neck: no lymphadenopathy or thyromegaly

Lungs: clear

Heart: normal PMI; normal S1, S2,

Abdomen: no hepatomegaly; spleen tip palpable 1-2 cm below cm. non-tender, firm; no masses;

Genito-urinary: no flank/CVA tenderness or masses felt

penis normal, uncircumcised;

scrotum: swollen, with slight peau d'orange of left side

right epididymis/testis: normal, 2.5 x 3.5 cm, soft, vas deferens normal

left: testis large, oval and firm, mildly tender, 4.5x6 cm; non-transilluminating

epididymis thickened, firm-nodular

vas deferens: indurated, beaded, non-tender

prostate: firm, slightly enlarged with 1 cm. non-tender nodule felt

Lymph nodes: left groin: pair of inguinal nodes, 2x2.5, 1.5 x 2cm, non-tender, firm, mobile

Extremities: no swelling or deformities, normal

Neurologic: normal, no focality, no loss of sensation

U/A: s.g. 1.020, +1 protein, + 3 leuk.esterase, +2 blood, (-) nitrites; 20 WBC, 30 RBC; no casts

**1. What is the “*frame*” in this case (i.e. the key clinical features from the history and exam that the final diagnosis must be consistent with)?**

- *Enlarging epididymis-testes x 5 weeks*
- *Mildly tender, unilateral testis; firm, nodular epididymis and vas deferens*
- *No urethral discharge*
- *No response to ceftriaxone/doxycycline, continued progression*
- *No fever or constitutional symptoms*
- *U/A with red and white cells*

**2. What is the *differential diagnosis* in this patient, and the pros/cons for each of the possibilities? What is the *most likely* diagnosis?**

**Which diagnoses for this problem must be considered far more frequently in Africa than in the West?**

- *Chlamydia/Gonorrhea: Although GC and Chlamydia ascend the genital tract much less frequently in men to cause epididymo-orchitis (EO) than they do in women to cause salpingitis, in men younger than 35 these common sexually transmitted infections (STI's) are the most frequent cause of EO. This is no less true in Africa where STIs are a problem, than in the West.*

*EO from GC/Chlamydia is accompanied by a history of urethral discharge, deviation of stream, or staining of underwear in ~ 50%. The presentation is acute, onset over hours to days, and the epididymis and vas deferens (and testes by extension) are swollen and tender. Frequently it starts unilaterally and becomes bilateral.*

*This patient was unlikely to have EO due to Chlamydia and/or GC: the epididymis and testis were only mildly tender, and the vas was non-tender; the infection stayed unilateral for 6 weeks; and didn't respond to appropriate antibiotic therapy.*

- *Enterobacteriaceae: Gram negative organisms from the GI tract that cause urinary infections are the most common cause of EO in older men, with the relative incidence rising after ~35 years old. Certainly at 32 this patient would be eligible for a gram (-) infection, but clinically this is unlikely: a gram (-) EO causing this degree of inflammatory enlargement would be clinically more acute and tender, accompanied by fever and prostration, and probably would have shown some response to the antibiotics he was given (though the treatment provided would not have been optimal).*
- *Brucella: EO is a focal complication of Brucellosis – a zoonotic febrile illness caused by a gm (-) intracellular coccobacillus transmitted to humans who drink the raw milk of or have occupational contact with infected domestic animals (cattle, sheep, goats, pigs). Brucella can chronically infect the reticulo-endothelial system to cause relapsing (undulating) or chronic forms of disease - an FUO or, usually later in the course, a focal infection of bones/joints (~50%), the testes (2-20%), or nervous system. In one large series of EO from Spain, the*

*median time from symptom onset to presentation/diagnosis was 30 days; all had scrotal pain and swelling; almost all had fever/sweats; half had manifestations of other focal involvement (osteoarticular 40%, cough 25%), hepatosplenomegaly (30%) weight loss (25%).*

*Although the time course fits, brucella would be less likely in this patient because of his lack of fever and constitutional or (other) focal symptoms; lack of significant environmental risk; and no response to doxycycline (which is one of the two drugs recommended as part of the 2-drug treatment regimen for brucella).*

- *Filariasis and other African possibilities:*

- *Filariasis is a mosquito-borne helminth infection that infects over 100 million people in the world, mostly in Africa, and causes disfiguring complications of lymphedema in 40%; 27 million men are estimated to suffer genital deformity caused by the preferential migration and localization of adult worms to the lymphatics of the spermatic cord from which they release microfilaria into the blood. Acute and chronic hydroceles develop when worms die, and get acutely inflamed from secondary bacterial infections. Elephantiasis of the scrotum develops from reactive hypertrophy and fibrosis.*

*A socially devastating disease (ranked second by the WHO as a cause of disability worldwide), filariasis affects communities in which the parasite is endemic and rarely presents in isolation. Although a cause of inflamed scrotum in Africa, it would be very unlikely in this male from a non-endemic area with a firm, non-transilluminating, mildly tender mass presenting for the first time.*

- *Guinea worm, dracunculiasis: endemic in many areas of West Africa, the genitals scrotum can be the endpoint of migration of the adult female worm, which, having matured in the gut after ingestion of larvae-contaminated water by its human host, is looking to break through the skin and hatch new larvae in fresh water.*

*Usually, an intensely inflamed papule/blister containing the worm develops on the lower extremities, but the worm can emerge anywhere, genitals included, inducing scrotal inflammation (often with intense pruritus) for a painful period of weeks.*

- *Leprosy: in lepromatous leprosy, the mycobacteria preferentially localize and cause disease in cooler areas of the body: thus, hands and feet lose sensitivity, the nose to the larynx become involved, and eyelids and testes are targets of early disease. Sometimes, EO can be one of the first manifestations of leprosy in young men, but usually there are other signs of the disease at presentation.*

- *Toxoplasmosis in HIV: Toxo is a common opportunistic infection in AIDS, and can cause orchitis rarely, usually in the presence of other manifestations of AIDS.*

- *Viruses:*

- *Lymphocytic choriomeningitis (LCM): an arenavirus found in North America, Europe and Russia but thought to be prevalent worldwide, this rodent-transmitted pathogen causes an acute febrile illness sometimes with orchitis and/or aseptic meningitis.*

- *Mumps: an uncommon complication of mumps but nevertheless a common cause of bilateral orchitis in non-vaccinated youth, becoming infrequent with vaccination in Africa, usually associated with parotitis.*

- *Ebola, viral hemorrhagic fever: orchitis can be seen with Ebola infection, often in the recuperation phase of this frequently fatal epidemic illness.*

- ***Tuberculous Epididymo-orchitis:*** *This patient presents with male genital tuberculosis (MGTB), an uncommon subset of genitourinary TB. As an organ “system” from kidney to urethra/vagina, genito-urinary TB is the second most common manifestation of extra-pulmonary TB worldwide, (after lymphatic TB). In the U.S., male genital TB - involving prostate, seminal vesicles, vas deferens, testes, epididymis, or penis - accounted for 1.5% of total TB cases. In endemic areas, MGTB is thought to be at least twice as common: e.g. in Russia, MGTB increased from 5.3% to 9.4% of total TB cases between 1979 and 1993.*

*Most MGTB results from reactivation of quiescent foci that have lay dormant for years, although once reactivated, direct spread to adjacent areas or via infected urine from the kidney, can occur.*

*Reactivation of a quiescent focus in the genital tract explains why most patients with MGTB do not have constitutional symptoms of fever or weight loss – these symptoms would suggest coexisting extra-genital disease.*

*Symptoms are insidious and often mild at onset: prostatic TB causes typical “chronic prostatitis” symptoms with frequency, slow stream, nocturia, dysuria, hematuria and hematospermia. EO usually causes a painless scrotal mass beginning usually in the epididymis and later extending to the testis which may become mildly tender and come to clinical attention after many weeks of insidious growth.*

*On exam, the epididymis and possibly testis is enlarged, firm, and non-tender, and the vas deferens is thickened or beaded. Some scrotal edema and inguinal adenopathy may be present. The exam is remarkable for lack of heat, erythema, or pain. In most cases, TB is only considered after therapy for GC/Chlamydia has failed.*

*This patient fits the clinical picture, the history and exam, of EO due to TB very well and did not have findings suggestive of alternative causes of EO.*

- *Other non-infectious causes: two other non-infectious causes of scrotal swelling must be kept in mind: testicular cancer and testicular torsion. This patient was unlikely to have either: cancer is usually slower growing, presents at a younger age, and doesn't involve the epididymis or the vas, both thickened and beaded in this patient. Torsion is the opposite: much more acute and painful than seen here, presenting in males between 15 and 30 years old*

*with an acutely painful scrotum that's considered a surgical emergency within 6 hours to prevent testicular infarction.*

*Of the above causes of EO, brucella, filariasis, guinea worm, leprosy, ebola and TB are all much more prevalent in (or unique to) Africa than the West.*

- 3. What is the most frequent mis-diagnosis of patients with this disease in district hospitals in Africa, and why?  
What test is indicated, and what is the appropriate therapy in this case?**

*It was notable that none of the practitioners in the district hospital had ever treated TB EO, and was unaware it existed. This is a hospital that sees ~100 male cases of TB/year, and based on reports of its prevalence in the literature, there should be between 2-6 cases of male genital TB annually on the wards. Usually, in therapeutically unresponsive EO, an orchiectomy has been performed for suspected abscess, and since there are no culture or histopathology resources available, definitive diagnosis is never uncovered. Since MGTB usually represents focal reactivation, surgery can be curative.*

*Appropriate therapy in this case is treatment for TB (with RIPE).  
An HIV test should be drawn (it was negative in this patient).*

*The patient began responding with decreased size of the epididymis/testis and the mild tenderness was gone after about a week of treatment.*

### **Suggested Reading:**

Jacob JT, et al., Male genital tuberculosis Lancet Infect Dis 2008; 8: 335–42

Hagley M. Epididymo-orchitis and epididymitis: a review of causes and management of unusual forms. *Int J STD AIDS* 2003; **14**: 372–78.

Gorse G, Belshe R. Male genital tuberculosis: a review of the literature with instructive case reports. *Rev Infect Dis* 1985;7: 511–24.