



## **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](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 Jillian Morgan at [jmorgan@CUGH.org](mailto: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.

Gerald Paccione, MD  
Professor of Clinical Medicine  
Albert Einstein College of Medicine  
110 East 210 St., Bronx, NY 10467  
Tel: 718-920-6738  
Email: [gpaccion@montefiore.org](mailto:gpaccion@montefiore.org)

## CASE 33 – PARALYZED LEGS

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39 year old male farmer, carried to the hospital by his wife and brother, presents with inability to walk for a week. He is married, with 3 children, a native of Kisoro. The only health problem he recalled was lower back pain 14 years ago while working as a truck driver. The pain was sudden, precipitated by lifting a heavy load, worse with movement, and improved within a week with rest and “pills” . He’ s never had back pain since.

One month ago while returning from farming one evening, he had the sensation that he was “walking on air” . The sensation persisted, and over the next few weeks he started tripping over objects, not sure where his feet were. Two weeks ago his legs became increasingly weak, 4 days ago he couldn’ t walk, and two days ago he couldn’ t move his legs. Over the past 1-2 weeks he’ s noticed increasing numbness move up his legs a little every day, stopping 3 days ago at the level of his mid-belly and back. He’ s had no back pain or fever, and can feel the urge to urinate and defecate and control them normally. His arms and hands have normal strength and sensation.

He’ s not been HIV tested, has been monogamous for over 7 years since returning to Kisoro and not driving trucks, has never lived around lakes and doesn’ t swim, and hasn’ t had any sexually transmitted diseases or ulcers/blisters on his penis. He wasn’ t sick prior to the onset of these problems, and has had no weight loss, anorexia, cough, headaches, problems thinking, joint pains, skin rashes or problems with his bowels.

**Physical Exam.** Well-developed, pleasant man in no distress, using his arms to shift his body around

BP 110/70, HR 88, RR 16, T 98

Skin: normal, without rashes

Eyes: normal conjunctiva; fundi, benign without exudates, hemorrhages, papilledema

Mouth: no thrush or ulcers

Neck: no lymphadenopathy, thyromegaly, or JVP; supple

Lungs: clear

Heart: normal S1, S2, no murmurs

Abdomen: normal without masses, tenderness, distention or hepato-splenomegaly;

Extremities: no swelling, clubbing;

Musculo-skeletal: normal joints and muscles; no tenderness over spine to palpation or percussion

Neurologic: normal mental status; normal cranial nerves

rectal tone and sensation, normal

upper extremities: normal motor, sensory, reflexes, cerebellar exam

lower extremities (and abdomen):

0/5 motor strength legs bilaterally (unable to move) with rigidity on passive movement  
decreased pain but can detect, symmetric deficit up to level ~T7  
absent vibration/position legs, bilateral and symmetric reflexes: 4+ (with clonus) bilateral and symmetric; extensor plantar reflexes bilaterally

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

- *Progressive problem over 1 month, leading to complete LE paralysis*
- *Discrete level*
- *Bilateral, symmetric, both sensory (first, position) and motor, sparing the rectum with normal bladder/bowel function*
- *Hyperreflexia/clonus of lower extremities*
- *No back pain*
- *No fever or constitutional symptoms*
- *Normal mental status and upper extremity neurologic exam*

**2. As with most challenges in Medicine and Neurology, in this case there are multiple “levels” to the diagnostic question: where is the lesion, what is the pathologic process, and what is its specific etiology.**

**Where is the lesion and what is the pathologic process behind it? Explain.**

*This patient presents with loss of sensation and motor function below a discrete “level” around T7, with findings of spasticity/hyperreflexia indicative of a spinal cord process involving the sensory and upper motor neuron white matter tracts. The history of ascending numbness that seemed to follow the progressive symmetric motor weakness may suggest an ascending chronic inflammatory demyelinating polyneuropathy (a chronic “Guillan-Barre” syndrome), but the rigidity, hyperreflexia and discrete sensory level argue against that possibility.*

*The key to determining the underlying pathologic process behind a problem in any field of Medicine is an appreciation and interpretation of its “timing”, particularly its onset and evolution - in this case, the insidious progression over one month.*

*The most common cause of paraplegia in Africa is trauma from road traffic accidents – but clearly not in this case. Cord compression due to a centrally protruding herniated disc - suggested perhaps by this patient’s past history of back pain - is rare, would present*

*suddenly, and usually would be associated with pain. Spinal cord AVMs that bleed, or spinal artery infarcts (due to vasculitis, infection, atheroemboli, or compression) are other diseases of the spine that occur suddenly and are inconsistent with this presentation.*

*At the other extreme, two causes of spinal cord disease that induce neurologic symptoms much more insidiously, both seen in Africa, are HIV vacuolar myelopathy and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). As discussed below, both cause progressive symptoms over many months to years. The same is true for syringomyelia or “subacute combined degeneration” of the cord, a complication of vitamin B12 deficiency, also mentioned below.*

*Steady progressive spinal disease over weeks, as in this patient, suggests either an underlying inflammatory process/infection, or a neoplasm.*

**3. a) What is the clinical significance of the other features in the “frame” ?**

- *Complete lower extremity paralysis*  
*[Suggests poor prognosis for functional recovery no matter the cause of the lesion]*
- *No back pain*  
*[Spinal cord disease is often classified clinically as “intrinsic” – in which the primary pathology affects the spinal neurons; and “extrinsic” - in which the cord is secondarily affected by a process that invades/compresses from the outside. Most extrinsic etiologies, such as cancer, cause significant back pain preceding the neurologic deficits. Absence of pain suggests an “intrinsic” cause in this patient.]*
- *No fever or constitutional symptoms (anorexia, weight loss, night sweats)*  
*[Although perhaps surprising, most patients with bacterial or mycobacterial disease of the spine do not have fever or constitutional symptoms. Their presence would make abscess or TB more likely, but are not present in this case.]*
- *Normal mental status and upper extremity neurologic exam*  
*[Complete absence of symptoms or signs of cognitive or upper extremity dysfunction makes it less likely that such a florid manifestation of disease affecting the lower extremities is caused by a process that diffusely affects neurons in the CNS or cord, like nutritional deficiencies or some viruses.]*
- *Bilateral and symmetric, position/vibration sensory to motor neurons, sparing the rectum*  
*[Suggests that the cord is affected by an inflammatory process extending posterolaterally. It would be unusual for a mass lesion (tumor or abscess) to evolve symmetrically.]*

**b) What is the name of the clinical syndrome defined by the features of this presentation?**

*In sum, this patient is probably affected by an intrinsic focal inflammatory disease of the spinal cord that progressed over weeks, an “acute transverse myelitis” .*

**4. What is the differential diagnosis for**

- **95% of disease processes in *this anatomic location in Africa*?**
- **this *clinical syndrome* anywhere?**

**(N.B. It's useful to approach this problem from both directions, the "patho-anatomy in Africa" and the specific "clinical syndrome", as diseases common to Africa but not usually presenting this way may occasionally present atypically and should be seriously considered when the stakes are so high.)**

- *HIV vacuolar myelopathy: this is the most common HIV-associated myelopathy in the developed world, a slowly progressive painless spastic paraparesis that involves the urinary bladder and commonly causes sensory ataxia. Pathologically, vacuolar changes in the ascending and descending tracts are seen, predominantly in the thoracic cord. Clinically however vacuolar myelopathy is not a good fit in this case: it's usually a late presentation of HIV disease and parallels HIV dementia. Although this patient certainly could have HIV (and his age and past occupation as a truck driver makes that more likely), he does not have dementia nor stigmata of HIV, and has been healthy. Furthermore, vacuolar myelopathy does not present with a discrete spinal level, progresses more slowly (over many months) without causing complete paralysis, and has early bladder/bowel symptoms.*
- *HTLV 1- associated myelopathy/tropical spastic paraparesis (HAM/TSP): HTLV-1 is a retrovirus that infects over 20 million people in the world asymptotically, with only 2-5% developing overt disease, usually adult T-cell lymphoma/leukemia or immune-mediated HAM/TSP. It's common in the Caribbean and Latin America, and also in areas of Africa (e.g. S. Africa). HAM/TSP progresses slowly but steadily over many months to years with the first disability occurring after the first or second year of symptoms. It progresses faster in women; leg weakness is the first symptom in 60% - more marked proximally and steadily progressing to a spastic gait with hyperreflexia; bladder dysfunction is common early; sensory symptoms (tingling, back pain) are more common than numbness or proprioceptive errors. In this patient the time course, discrete cord level, gender, sparing of bladder/bowel, and prominence of sensory symptoms argue against chronic HTLV-1 associated myelopathy.*
- *TB myelitis: TB is common in Africa and has protean manifestations. It causes paraplegia via 3 mechanisms: a) a primary spinal radiculomyelitis, often an indolent asymptomatic meningitis (with normal CSF glucose and few cells); b) a secondary manifestation/complication of overt TB meningitis; c) secondary extension from TB osteomyelitis causing cord arachnoiditis, abscess with compression, or arteritis and infarction. Although absence of constitutional symptoms do not rule out TB, over 95% of reported cases of spinal TB have back pain as a prominent symptom, not present in this case even on exam, and the symmetric progression would be very unusual.*

- *Schistosomiasis: Schistosome eggs deposited by the adult S. mansoni or S. hematobium can be aberrantly deposited in the lower spinal cord via Batson's venous plexus between the urinary and portal systems (i.e. from retrograde deposition if from S. Mansoni). The ensuing granulomatous response can cause ATM. This is more common in chronically infected hosts with portal hypertension, although it can occur with acute infection and in younger hosts in their teens. It's unlikely in this case due to lack of environmental exposure in a non-endemic area, and absence of history or exam findings of schistosomiasis (recurrent rectal bleed or hematuria; hepatomegaly) or portal hypertension (splenomegaly).*
- *Nutritional causes in Africa: are unlikely for lack of suggestive environmental histories.*

  - *lathyrism: due to famine-induced cultivation and ingestion of the chickling pea, lathyrus sativus, which produces a neurotoxic amino acid that causes permanent axonal degeneration in the pyramidal tracts. Epidemics have occurred twice in Ethiopia in the past 30 years. It's more common in men.*
  - *konzo: presents in epidemics of sudden weakness with residua of spasticity and weakness in 40% of those affected, due to dietary deficiency of sulphur-containing amino acids that detoxify cyanide released from inadequately prepared cassava. Epidemics have been reported in the Congo, Tanzania, Mozambique, and Central African Republic. It's more common in women and children.*
  - *vitamin B12 deficiency: less commonly diagnosed in Africa than in Europe where autoimmune pernicious anemia is more prevalent and diagnostic resources more available, B12 deficiency may be more common in Africa than we thought in the past. It can cause "subacute combined degeneration (SACD)" of the posterior spinal columns with loss of position/vibration sense and ataxia. However, SACD is an uncommon manifestation of a probably-still infrequent deficiency in Africa; far more insidious in evolution; often associated with mental dullness and upper extremity deficits; doesn't evolve to complete symmetric paraplegia (especially in just a week), manifests absent knee jerks with extensor plantar reflexes, and is usually associated with a megaloblastic anemia (but not necessarily).*
- *Pyogenic epidural abscess (e.g Staph Aureus): Although spinal abscesses from pyogenic infections can present without fever or weight loss, usually some other preceding or associated sign of serious catabolic illness - malaise, fatigue, or sweats – is present. Also, most patients have back pain by history and tenderness elicited on exam; and a potential source of bacteremia may also be apparent (e.g. skin abscess/cellulitis, a regurgitant murmur from endocarditis, etc.) – none of these were present in this patient.*
- *Acute transverse myelitis (ATM): As discussed above, the clinical syndrome suggested by this presentation is that of ATM – subacute over days-weeks, tissue-*

*tropic (bilateral, symmetric) rather than focally invasive, involving motor/sensory white matter tracts with a discrete level in the cord, and painless.*

*The next question is what is the specific cause of the myelitis/inflammation? ATM can be caused by an infection directly involving the cord; immune-mediated inflammation, post-infectious or idiopathic (including multiple sclerosis); or an autoimmune/connective tissue disease such as lupus.*

*In this patient there are no other symptoms or signs of a systemic connective tissue disease, nor a preceding symptomatic illness. Multiple sclerosis is rare in Africa, and there are no other manifestations consistent with that diagnosis in either space or time.*

*Of the direct infections, viruses are the most frequent causes of ATM. Some of the viruses known to cause ATM are:*

- *Zoster: usually with a rash 1-2 weeks before, but not necessarily in the same region as the cord level of the ATM; it evolves over 1-3 weeks.*
- *Cytomegalovirus (CMV): usually seen in HIV; often perianal pain and decreased sensation with decreased reflexes due to lumbar-sacral root involvement.*
- *Herpes: herpes II in adults, I in children; sometimes with but usually without preceding skin lesions*
- *EBV: often with a “mono syndrome” of fatigue, pharyngitis, cervical lymphadenopathy weeks before;*
- *Enterovirus 71: in Asia especially, with hand, foot and mouth vesicles appearing with the ATM;*
- *HIV: besides the vacuolar myelopathy described above, HIV has been reported to cause ATM with a level, etc. (but this is rare). It has been reported as a complication of primary HIV seroconversion (as has aseptic meningitis, brachial neuritis, etc.)*
- *Other: most causes of ATM have not been specifically identified.*

*Non-viral infectious causes of ATM include:*

- *Syphilis: the cord can be involved in secondary syphilis, or tertiary gummatous disease*
- *Borrelia, Lyme*
- *Mycoplasma*
- *Tuberculosis and Schistosomiasis as mentioned above*

**5. What tests, available in many district hospitals in rural Africa, would be appropriate ? Explain why?**

- *HIV: although this is not the presentation of HIV-associated vacuolar myelopathy, HIV infection increases the probability of many of the other infectious causes of ATM.*

*The HIV test provides an essential clinical context for most differential diagnoses in Africa.*

- *X-ray of thoracic spine: although an x-ray would have very low yield in the absence of back pain, if available it'd be warranted to support the clinical impression, especially given the high stakes; would help assess cancer, abscess and TB which could involve vertebral bodies.*
- *X-ray of chest: low yield in absence of symptoms, but in 20-40% with spinal TB, evidence of active or inactive TB would be seen on x-ray.*
- *LP, CSF: this would be a non-specific test since lymphocytes and elevated protein would be expected with all relevant diagnoses. CMV often presents with polios in the CSF; and TB with a very low glucose and high protein (but these are often not seen).*
- *VDRL, RPR: >90% sensitivity in secondary, ~50% in tertiary syphilis, but in late latent syphilis, close to 100% with neuro-syphilis have a +VDRL ; a positive result however would be non-specific since other inflammatory diseases frequently cause a false positive result.*

*Results: The HIV test was positive! Spine and chest x-rays were normal. CSF showed ~50 lymphocytes, normal glucose, and high protein. The VDRL was negative.*

*HIV increases the probability of HIV myelitis (rare), TB, syphilis, herpes II, zoster and CMV. One report of myelopathy in 33 South African HIV (+) patients revealed vacuolar myelopathy in only 1. HTLV1, endemic in the KwaZulu/Natal region, was seen in 12, TB in 6, Zoster in 3, syphilis in 2 (both responded dramatically to penicillin), schistosomiasis in 2, and enterovirus in 3 (2 of whom had another cause identified).(Bhigijee, A, et al; Neurology 2001; 57:348)*

## **6. How should this patient be treated?**

*The guiding principles of empiric therapy when confronted with a disastrous illness, are:*

- a) to treat whatever is reasonable and treatable;*
- b) if there is a response to broad-based therapy and the duration of recommended treatments are feasible, continue **all** therapies until the end of their courses;*
- c) if there is a response, but the duration, side effects or expense of therapy for some possibilities make a shotgun approach difficult to maintain, re-assess the likelihood of various diseases and tailor therapy accordingly.*

*In this patient, the tempo of disease had been recently very aggressive, and his paralysis complete. Despite a clinical impression of non-specific viral or idiopathic ATM as most likely, he was treated broadly:*

- *penicillin for syphilis was started (inexpensive, efficacious in neuro-syphilis and of limited duration)*
- *ART therapy for HIV was begun (and a CD4 count ordered, which would take weeks)*
- *IV acyclovir was procured, and started for HSV and VZV, for 14 days;*



- *anti-TB therapy was started despite the very low likelihood of TB (no pain, etc.)*
- *praziquantel for schistosomiasis was given (efficacious, and only a few doses necessary)*
- *vitamin B12 was administered IM*
- *steroids were started for post-infectious/idiopathic ATM. Steroids might also prevent IRIS from developing post-ART, and help with viral or TB-induced inflammation.*

*(Penicillin and acyclovir were completed and stopped, without improvement. The steroids and TB treatment were continued for 2 months, steroids tapered, TB therapy continued a 3<sup>rd</sup> month and stopped without effect. ART was continued with an initial CD4 count of 220.)*

### **Suggested Readings:**

Frohman, E.M., Wingerchuk, D.M. Transverse Myelitis *N Engl J Med* 2010;363:564-72.

Irani, D.N. Aseptic Meningitis and Viral Myelitis *Neurol Clin* 2008 26(3):635

Freilich, D., Swash, M. Diagnosis and management of tuberculous paraplegia with special reference to tuberculous radiculomyelitis *Journal Neurology, Neurosurgery, and Psychiatry*, 1979, 42, 12-18

Araujo, A.Q.C., Silva, M., The HTLV-1 neurological complex *Lancet Neurol* 2006; 5: 1068–76