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 Eleazar Gutierrez at egutierrez@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 56 – What Now ii

A 23-year-old woman, recently homeless and abandoned by her husband, was diagnosed with HIV (CD_4 15) and miliary TB a month ago. She now presents to the hospital 4 weeks' post-discharge with increasing headaches and confusion, and a seizure on the morning of admission.

The patient had had a long wasting illness before presenting to KDH with over 2 months of dry cough, severe cachexia, inability to walk, diffuse LAD, clear lungs with no sputum production, and mild hepato-splenomegaly. She had no fever or headaches. Disseminated TB was diagnosed empirically and she responded to TB therapy with increased strength, weight gain and decreased cough, and she was sent home after 2 weeks in-hospital to be cared for by relatives, with directly-observed therapy for TB and SMX-TMP prophylaxis. Plans were made to start anti-retroviral drugs (ARVs) for HIV after 1-2 months of TB treatment when follow-up and adherence were assured.

She did well at home for an additional 2 weeks, adherent to TB DOT and SMX-TMP therapy according to the family who administered her medications. During the third week she began to complain of increasing headaches which woke her from sleep, and after 7 days of headaches appeared intermittently confused to family members. On the morning of admission, she fell to the floor unconscious, and began shaking all extremities uncontrollably and foaming at the mouth. Neither fever nor cough were noted.

Physical Exam: Carried to a bed by family members, dazed, confused, lethargic
BP 130/85; HR 60 and reg R 15 T 36
eyes: full ROM, PERRLA
fundi: white opacities (unchanged) in right eye; ? blurred discs bilaterally (difficult exam)
no thrush: tongue – swollen, lacerated, oozing blood
neck supple; posterior cervical LAD 2-3cm, increased from 1 month ago (prior to therapy)
lungs: clear; heart: normal PMI; normal S_1, S_2
abd: mild hepato-splenomegaly, unchanged, non-tender
neuro: lethargic; Cranial Nerves grossly intact;
motor: left pronator drift (repeated x 3); ? LUE 4/5; otherwise 5-/5
sensory, cerebellar, gait: unable to assess

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

2. What are the WHO (and CDC) guidelines for starting ARV therapy in newly diagnosed patients with HIV and TB?

The optimal timing of integrated HIV and TB therapy is influenced by the patient's immune status. For patients with pulmonary TB and CD4 cell counts <50 cells/mm^3, "early ART" (ie, within two weeks after starting anti-TB therapy) decreases the combined risk of an AIDS-defining illness and death [61-63].

For patients with CD4 cell counts >50 cells/mm^3 in the setting of severe HIV disease (including low Karnofsky score, low body mass index, low hemoglobin, low albumin, organ system dysfunction, or extent of disease), ART should be initiated within two to four weeks of starting treatment [62,65]. For patients with CD4 cell counts >50 cells/mm^3 in the absence of severe disease, early ART is not associated with a decreased risk of AIDS or death [61,63]; later initiation of ART (eg, 8 to 12 weeks) is associated with a lower risk of IRIS regardless of baseline CD4 cell count [61-63].

Besides immunologic status, the exact timing of ART may also depend on other clinical considerations. For example, later initiation of ART (eg, 8 to 12 weeks) may be preferred based on the patient's tolerance of TB medications and ability to swallow multiple pills. In contrast, early initiation of ART (eg, within 2 to 4 weeks) may be considered in a patient with malnutrition or wasting, regardless of CD4 cell count. Initiating ART and TB medications simultaneously is not recommended

3. What is the risk of starting ARV treatment in this patient, and why was it delayed (beyond the WHO recommendations for a patient with a CD4 count of <50)?

4. What is the *differential diagnosis* in this patient, and which clinical data are for and against each possibility?

5. What is the likely diagnosis? *Why* is it most likely? How common is it in this clinical setting? What is its pathogenesis? What are other related clinical phenomena? What are its timing and clinical features? How is it treated?