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 questions 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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64. Finally Fungating

42-year-old man presents to the hospital with a large, foul-smelling mass on his right foot and inability to walk.

He was fine, married with 5 children working as a potato farmer in Kisoro his entire life, until about 4 years ago when he started noticing intermittent right foot swelling. The swelling was mild, not always present, worse at the end of the day, and associated with a feeling of leg heaviness, but not pain. He had no fever, prominent veins, skin changes or shortness of breath.

About a year ago, he noticed a solid dark painless nodule on the back of his right foot near his ankle which grew in size to about 3 centimeters over a few months, with 2 other smaller similar lesions appearing on the edges of the nodule. They became softer as they grew, and the nodules merged with each other. He went to a traditional healer who, over the course of the last few months tried various herbs both orally and directly applied to the growing lesion. Two weeks ago, the lesion formed a crater at the top, and began to ooze yellow pus and to smell bad. When walking induced pain on the top of the foot, he decided to come to the hospital. He has been monogamous, and has not had fever, anorexia, diarrhea, weight loss, or other skin conditions.

Physical Exam:

Thin but not cachectic, in no distress, unwrapping a pus-filled, soiled rag from around his right foot and ankle, filling the ward with a pungent “rotting” smell.

BP: 110/80 HR: 95 T: 98 R: 18

Skin normal, except for lower right leg (see below)

Mouth: no thrush;

Neck: no lymphadenopathy, JVP, or thyromegaly

Lungs clear,

Heart normal PMI; normal S1, S2;

Abdomen: without hepato-splenomegaly or tenderness

Groin, right: two 1-2 cm tender lymph nodes

Neurologic: intact mental status, CN, motor, sensory, cerebellar, reflex exams

Extremities: arms and left leg, normal without edema

Right leg: mild pedal edema

8 cm diameter fungating, verrucous, multicolored (pink, brown-black, purple), firm-fleshy mass 5 cm tall, topped by a 2 cm diameter pus-filled ulcer; adherent fleshy-soft, bleeding, 1-2cm smooth broad-based polyps around the perimeter; fleshy mass is fixed to underlying tibia and non-tender; surrounded by a firm, indurated, hyperpigmented plaque base ~ 2 cm. in diameter;

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

- Non-tender, progressively enlarging mass x 1 year, fixed to bone
- Bleeding polypoid lesions surrounding the mass, on an indurated base
- Adult male, Uganda
- On lower legs
• Pain is recent, with pus and malodor, tender nodes
• Preceding edema for years
• No thrush or HIV risks

2. What is the (rather restricted) differential diagnosis, and the pros and cons of each of the possibilities mentioned?

The progressive growth of this huge fleshy mass over a year suggests either a malignancy or exuberant inflammatory tissue. It’s too rapidly growing, fixed and aggressive (with bleeding) to be a benign neoplasm.

The pain, pus, malodor and tender nodes that more recently developed suggest secondary bacterial infection and shouldn’t distract from consideration of the primary process. As for the primary process, the bleeding and lack of pain suggest malignancy over chronic inflammation, but if it were inflammatory it would likely be stimulating granulomatous pathology (painless, indolent), and be fungal in origin.

Two organisms must be considered: chromoblastomycosis, and mycetoma.

• Chromoblastomycosis is a fungal infection of cutaneous and subcutaneous tissues that begins as a pink papule at the site of dermal inoculation of the fungus, and slowly and progressively grows into a plaque and then into a verrucous nodule with a cauliflower appearance. It spawns satellite lesions which can coalesce through lymphatics, invades the subcutaneous tissue, and induces multiple bouts of secondary infection resulting in induration and lymphedema/elephantiasis. Ulceration can occur with secondary bacterial infection.

  o Chromoblastomycosis is relatively rare, but ubiquitous in the tropics, seen in both South and Central America and sub-Saharan Africa (especially Madagascar), and extremely difficult to treat.

  o This patient had a more aggressive course than usual for chromoblastomycosis and smooth fleshy polypoid lesions and bleeding would be very uncommon with this infection; the lesion in this patient began as a nodule that followed years of swelling, not an expanding papule/plaque with later edema.

• Mycetoma is a firm swelling of the subcutaneous tissues with granule-discharging sinuses caused by higher filamentous bacteria (actinomyces) or fungi. It is relatively frequent in the tropics, usually occurring in adult men (5:1) on the feet and lower extremities and is painless.

  o This patient’s presentation is not that of a mycetoma in which the skin is smooth and shiny and the indurated deforming mass is marked by sinuses open to the skin discharging granules.

**Endemic Kaposi Sarcoma (KS)**

This patient’s presentation is classic for endemic KS, a heavily vascularized tumor of spindle-shaped cancer cells induced by herpes virus 8, or Kaposi Sarcoma-associated herpes virus (KSHV). A similar histopathology is seen in 4 clinical types of KS, now known to all be caused by the same agent: the “classic” KS of older men primarily of Mediterranean decent; endemic KS in Africa; transplant-related KS; and epidemic-AIDS-related KS.
KSHV is found in 10% of U.S. blood donors, ~30% of Italian blood donors, and ~ 50% of East African blood donors. The presence or absence of immunosuppression leads to different degrees of tumor aggressiveness and patterns of visceral involvement extending beyond the dermal and mucosal involvement of classic and endemic KS. Following the prevalence of KSHV, East Africa - around Western Uganda, the Congo, Rwanda and Burundi - has the highest incidence of endemic KS. While sexual transmission is dominant in the West, in Africa infection can occur via maternal-infant transmission and during childhood and adolescence. KSHV is in saliva. Prior to the HIV epidemic, KS caused 3-9% of all cancer in Uganda, but in the AIDS era, KS (both endemic, non-HIV-associated KS and HIV-associated KS) makes up ~50% of the cancers in Uganda.

Endemic KS (non-HIV related) is a disease of adult men (10:1 gender ratio) over age 25, increasing in incidence with age up to 55-65 years, primarily of the lower legs and feet, and is often localized at presentation in ~50%. It can involve the subcutaneous and lymph tissues initially, producing edema before any overt skin lesions appear. Prior to the AIDS epidemic, endemic KS was classified into 4 types: “nodular”, with a benign clinical course; “florid” – exophytic, more extensive, 1 or more extremities, invading bone; “infiltrative” – penetrating deep and stimulating fibrosis; and in children (much rarer), “lymphadenopathic”, with concomitant skin and salivary gland involvement in adolescents. By that classification, this patient has the more aggressive florid “exophytic” presentation, probably involving underlying bone.

3. What tests should be ordered? What therapy is appropriate?

The main test of significance is an HIV test, which would differentiate endemic from epidemic-AIDS-related KS.

This is of central importance both prognostically and therapeutically, with AIDS-related KS being more viscerally widespread and aggressive usually, but also therapeutically amenable to reconstituting the immune system with ART therapy.

In this patient, the HIV test was negative.

An X-ray of the right lower leg for signs of bony invasion is also indicated.

Although the presentation is classic for endemic KS, since definitive therapy involves surgery (with possible amputation), or transport to a referral center for chemotherapy and/or radiotherapy (with an 80% response rate expected), a biopsy should be taken of the lesion for confirmation.

Prior to that however, the lesion must be cleaned and debrided, and antibiotics given for 10-14 days for the complicating secondary bacterial infection.
Suggested Readings:
Antman, K, Chang Y, Kaposi’s Sarcoma NEJM 2000; 242: 1027-38
Matondo P. Kaposi’s Sarcoma in Africa Clinics in Dermatology Y 1999;17:197–207