Competent enough for Cryptococcus: Cryptococcus gattii Meningoencephalitis

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Learning Objective 1: Emphasize Cryptococcus gattii as an emerging pathogen causing meningoencephalitis in immunocompetent hosts.

Learning Objective 2: Recognize that C. gattii is more difficult to treat and clear than C. neoformans.

Case: A previously healthy 49-year-old African American male presented with weeks of fever, headache, back pain, and vomiting unresolved after multiple ER visits and empiric treatment with doxycycline for a tick bite. His headache persisted with new blurry vision. Examination revealed an oriented male with meningoencephalitis and bilateral nystagmus upon left lateral gaze. There was no rash, fever, seizures, history of trauma, or travel outside of Alabama in over twenty years. Immunologic work up including HIV antibody, CD4 lymphocyte assay, serum complement and immunoglobulin levels were negative or normal. Lumbar puncture (LP) revealed opening pressure of 23 mmHg, cerebrospinal fluid (CSF) protein of 129 mg/dl, and CSF glucose of 29 mg/dl. India ink was positive for encapsulated yeast. CSF cryptococcal antigen was positive (1:2048). Amphotericin lipid complex 5 mg/kg/d and flucytosine 100 mg/kg/d were administered. CSF cultures were positive for Cryptococcus species and remained positive for fourteen days despite combination therapy. His headache and blurry vision resolved with serial therapeutic LPs. Opening pressures were as high as 46mmHG, and a ventriculoperitoneal shunt was placed on day fourteen of hospitalization. MRI revealed cryptococcomas in the cerebrum and spinal cord. Interferon-gamma was initiated on day twenty for refractory infection. The Cryptococcus species was identified as C. gattii, and he received seventy-five days of amphotericin and was discharged on long-term fluconazole.

Discussion: Meningoencephalitis is one of the most serious consequences of cryptococcosis, and is a well-known pathogen among immunocompromised patients. Primary infection occurs through the respiratory tract, but it has a propensity for the central nervous system. Cryptococcus is a basidiomycetous yeast and is further classified into two species with important differences, C. neoformans and C. gattii. C. neoformans affects primarily immunocompromised, whereas C. gattii affects immunocompetent hosts. A case series from Australia showed that all cases of C. gattii were in immunocompetent hosts, and most cases presented insidiously with evolving neurologic symptoms, similar to our patient. Though C. neoformans infection has a higher mortality rate, C. gattii causes a greater number of cryptococcomas, leading to more neurological sequelae and slower response to treatment. C. gattii has been cultured from trees in Australia and was originally seen in places where those trees were sent. However, since 1999, over 200 immunocompetent cases of C. gattii infection have been reported in British Columbia and the northwestern United States with rare cases are now being reported in other areas of the US. C. gattii is known to develop resistance to antifungal agents and treatment with Amphotericin and flucytosine is often required for longer than a month. Interferon-gamma was added as adjunct therapy due to its suggested benefit in decreasing time to clearance of resistant C. neoformans in immunocompromised patients. C. gattii is still rare in most of the US but is emerging in immunocompetent hosts. Education is needed as it can present more indolently than other more common causes of meningoencephalitis and often requires lengthy and more complicated treatment regimens for successful outcomes.
Diabetic Muscle Infarction: A rare but serious complication of diabetes mellitus

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Learning Objective 1: Recognize diabetic muscle infarction as a rare but serious complication of long-standing diabetes

Learning Objective 2: Distinguish diabetic muscle infarction from other causes of thigh pain in diabetics

Case: A 48 year-old African American female presented with a 2-month history of progressive left thigh pain and swelling. She had long-standing type 2 diabetes mellitus complicated by end stage kidney disease requiring hemodialysis, severe peripheral neuropathy, retinopathy, and hypertension. Two months prior to admission, the patient reported left medial thigh pain. One month later, she reported persistent left medial thigh pain that worsened with movement and hemodialysis. The pain was constant, accompanied by intermittent swelling, and she noted a masslike sensation. She denied paraesthesias, fevers, or joint symptoms. Interval work-up included doppler ultrasounds that were negative for deep vein thrombosis and the recommendation of physical therapy. In the week prior to admission, her pain intensified to the point that she could not walk so she presented to the emergency department. On examination, her left anteromedial thigh was swollen and exquisitely tender to palpation without palpable masses, erythema, crepitus, or inguinal adenopathy. Pertinent laboratory studies included a WBC of 7.1 K/uL, CPK of 447 U/L and negative blood cultures. Given her severe pain, we obtained an MRI. It revealed diffuse intramuscular and perifascial edema of the left vastus medialis and vastus intermedius without focal fluid collections. Similar, but less severe findings were seen in the right thigh adductors and vastus medialis. We managed the patient conservatively with rest and pain control, and her symptoms gradually improved.

Discussion: Diabetic muscle infarction (DMI) is a rare vascular complication of poorly controlled, long-standing diabetes mellitus. It results from ischemic necrosis of skeletal muscle with local inflammation. It is slightly more common in women(59%) and type 1 diabetics(62%). As in our case, patients typically have microvascular complications, such as nephropathy(71%), retinopathy(57%) and neuropathy(55%). Common symptoms include pain(80%), swelling(76%), mass(34%), and fever(10-50%). DMI usually occurs in the thigh, most commonly the vastus lateralis and medialis muscles. Bilateral involvement occurs in 8-30% of cases. Laboratory data is non-specific but can include leukocytosis and an elevated creatinine kinase or erythrocyte sedimentation rate. MRI shows a hyperintense signal on T2-weighted images. Muscle biopsy showing microvascular disease with muscle necrosis and inflammation can confirm the diagnosis.

As with our patient, diagnosis is often delayed due to the rarity of the disease and misdiagnosis of more common etiologies such as infections or neuropathies. The differential diagnosis includes focal myositis, polymyositis, pyomyositis, deep vein thrombosis, necrotizing fasciitis and calciphylaxis. Our patient's case highlights features that suggest DMI, including her characteristic pain and swelling associated with typical MRI findings. MRI findings are generally confined to a single muscle or muscle group and lack the focal, well-demarcated intramuscular fluid or gas collections of pyomyositis or necrotizing fasciitis. Our patient also lacks the rapid progression of severe systemic symptoms that herald necrotizing fasciitis or pyomyositis. Other helpful diagnostic features include the absence of dermal and subcutaneous fat necrosis seen in calciphylaxis.
MMM: Mysterious Medication Mania

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Learning Objective 1: Describe common manifestations of baclofen withdrawal particularly acute psychosis.

Learning Objective 2: Understand and be able to explain to patients that baclofen should never be stopped abruptly.

Case: Introduction: Baclofen is commonly prescribed to alleviate pain in patients with muscle spasms. Abrupt withdrawal of baclofen can lead to frank psychosis.

Case Presentation: A 60-year-old male with hypertension, diabetes mellitus and chronic lumbago presented with an episode of fatigue, shaking, abnormal speech and altered mental status. The evening prior to admission, the patient had been exhausted from performing physical labor at his home and fell asleep without taking his medications. He awoke the next morning still tired and very shaky, to the point that he could not hold a glass of water without spilling it. The day progressed and his wife noticed his abnormal speech. He developed memory problems. EMS found him to be hypotensive at 73/40 but normoglycemic with a blood glucose of 102. Admitting physicians did not want medications to complicate his altered mental status and held his home medications of gabapentin, zolpidem, citalopram and baclofen. An extensive work-up for metabolic, cardiac, and neurologic causes of altered mental status revealed only an elevated CK of 2022. By hospital day 3, his mental status had deteriorated to the point that three separate episodes of psychiatric codes were called on him. He was found to be screaming, tremulous, rigid, hyper-religious and having visual hallucinations. His acute psychosis caused concern for a toxidrome and poison control was called. After discussing the case with poison control, his baclofen was restarted. Within a few hours, he returned to his normal self.

Discussion: Baclofen has a short half-life of 3-4 hours. Symptoms of withdrawal can develop within 12-72 hours of cessation. Patients can present with symptoms of tachycardia, autonomic instability, seizures, hyperthermia and spasticity. Spasticity can lead to rhabdomyolysis. If baclofen is not restarted, patients can develop frank psychosis or even die from the withdrawal. The exact cause is unknown, but thought to be due to baclofen causing continuous inhibition of monoamine neurotransmitters. The neurotransmitter receptors become highly sensitive to monoamines and once baclofen is stopped and norepinephrine and dopamine reach the receptors, it leads to autonomic arousal and delirium. Readministration of baclofen leads to rapid resolution of delirium. When baclofen is prescribed, patients should be advised to never stop it abruptly. If baclofen needs to be discontinued, it should be tapered over 1-2 weeks to prevent withdrawal. Finally, it is important to remember to continue baclofen when patients are hospitalized, even for those with altered mental status.
Kaposi’s Sarcoma Presenting as Atypical Conjunctivitis

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Learning Objective 1: Recognize ocular Kaposi’s sarcoma (KS)
Learning Objective 2: Identify indications for systemic chemotherapy in KS

Case: A 35 year-old African-American male presented to clinic with a 2-week history of progressive right eye redness with associated nasal congestion. Redness had spread to the left eye several days before. The patient had been diagnosed with AIDS five months prior, with an initial CD4 count of 4, and viral load of 140,000. Physical exam was notable for bilateral conjunctival erythema, with thickening of the right lacrimal caruncle. Moderate nasal mucosal edema was noted. Further exam did not reveal additional mucosal or cutaneous lesions. On laboratory evaluation, viral load was now undetectable on boosted darunavir and fixed-dose tenofovir/emtricitabine.

The patient returned to clinic 1 month later with worsening bilateral eye redness and facial edema. Physical exam revealed a beefy-red, crescent-shaped right conjunctival mass with mildly dilated surrounding vasculature. Violaceous nodules were present in the posterior oropharynx and left superior gingiva. There were two small (~1 cm) hyperpigmented plaques on the right thigh and upper abdomen. Marked facial edema and narrowing of the nasal passages had developed. Though no respiratory or constitutional symptoms were present, chest X-ray revealed diffuse nodular infiltrate, with perihilar predominance.

A clinical diagnosis of Kaposi’s sarcoma (KS) related to immune reconstitution was made, with pulmonary involvement. Due to a shortage of doxorubicin, chemotherapy consisting of paclitaxel was administered the following day. The patient reported rapid improvement in symptoms over the next few days.

Discussion: KS is a well-known complication of AIDS, associated with human herpesvirus 8 infection. Visceral involvement is common, with predilection for the oral cavity, GI tract, and lungs. Ocular disease is seen in approximately 20% of cases, affecting the conjunctiva, eyelids, and lacrimal sacs. Conjunctival lesions are usually bright red or violaceous in color, slightly raised, and may bleed. The inferior fornix is the most common site of involvement. Early lesions may appear similar to subconjunctival hemorrhage. Eyelid KS is more common, typically presenting as a raised purple lesion, similar to an ecchymosis. Associated lymphedema is common with KS and may be severe, possibly explaining the facial edema and nasal congestion seen in this case.

Treatment with systemic chemotherapy is indicated for KS in the following settings: extensive cutaneous disease, lymphedema, symptomatic visceral disease, and immune reconstitution inflammatory syndrome (IRIS). In this patient, KS manifested after 6 weeks of antiretroviral therapy, supporting a diagnosis of IRIS. IRIS refers to unmasking or worsening of an opportunistic infection with response to combined antiretroviral therapy (cART). It occurs in about 10% of patients with AIDS starting cART. Affected patients usually have low baseline CD4 counts and high baseline viral loads. KS is among the most common underlying diseases in IRIS, presenting as early as 3 weeks to as late as 1 year following initiation of therapy. In one case series, IRIS occurred in 12/41 (29%) cases of pre-existing Kaposi’s sarcoma. Visceral KS occurring in IRIS tends to be aggressive, with potential for chronic lymphedema, and mortality estimated at 50%. Systemic chemotherapy with doxorubicin or paclitaxel is potentially life-saving in such patients.
Mystery Case

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Case: A 24 year old woman presented with recurrent numbness, headaches, slurred speech, tremors and drooling.