

A Curious Case of a Doxycycline Deficiency

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Case: A 36-year old Mexican laborer with no known past medical history was admitted as a transfer from an outside hospital after being found down in a sugarcane field where he was working. Witnesses reported the patient complaining of shortness of breath and feeling “heated,” with seizure-like activity and subsequent bowel and bladder incontinence. Upon arrival at a rural ED, the patient was noted to be hyperthermic to 104.7F and hypotensive with GCS 3. He was intubated, started on pressors, and received empiric vancomycin and piperacillin-tazobactam prior to transfer. Upon arrival to UMCNO, the patient was found to have a normal WBC count with lactic acidosis (14.2), mild rhabdomyolysis (CPK 1123) and an AKI (Cr 2.6). On physical examination, he had substantial bilateral conjunctival hemorrhages. A lumbar puncture showed 0 WBC, 381 RBC and an elevated total protein and glucose. History was limited for the first few days but it was known that patient was working as a laborer in a sugarcane field and also that he was living in a dilapidated cabin in rural Louisiana with possible wild animal and insect exposures. Three days after admission, blood cultures resulted positive with gram negative bacilli not identified on the identification PCR panel. Infectious diseases team was consulted at this time and recommended doxycycline addition to cover for zoonotic/rickettsial infections given his clinical history. Cultures eventually resulted with *Brucella melitensis*, prompting his antibiotics to be tailored to ceftriaxone, doxycycline and rifampin at meningeal doses, and the teams later learned from family that the patient frequently ate unpasteurized cheeses made on his family’s farm in Mexico. MRI brain revealed rhombencephalitis consistent with neurobrucellosis with extensive micro-hemorrhages in the spine concerning for arachnoiditis. Patient initially required dialysis for acute renal failure but his renal function slowly recovered throughout his admission. His hospital course was complicated by prolonged delirium, an acute upper GI bleed and ESBL *E.coli* complicated UTI. He completed a 6-week course of this 3-drug antibiotic regimen with improvement noted in serial lumbar punctures. Though he did not return to his baseline mental status, the patient was eventually discharged home with family after 90 days in the hospital on an ongoing 6-month course of doxycycline and rifampin.

Discussion: *Brucella* is a small gram-negative coccobacillary organism associated with domestic mammal populations in Mediterranean countries, the Middle East, Central and South America and India. Species that cause human disease are linked to exposures to sheep/goats (*melitensis*), swine (*suis*), cattle/bison (*abortus*), and dogs (*canis*). *Brucella melitensis*, as identified in this case, notably accounts for the majority of cases seen worldwide. Transmission is associated with eating undercooked meat, consuming unpasteurized or raw dairy, organism inhalation (particularly in a laboratory setting) and penetration of bacteria through open skin wounds or mucus membranes. The incubation period is highly variable with cultures often requiring up to 21 days for growth. Clinical presentation remains heterogeneous with dissemination to the central nervous system, heart, bones and joints commonly described along with the not infrequent sequelae of rhabdomyolysis and acute renal failure, as noted in this case. Neurobrucellosis is not uncommon and typically presents with heterogeneous neuropsychiatric symptoms with long term sequelae. Neurobrucellosis is treated with combination drug therapy with parenteral agents for at least 6-weeks followed by prolonged oral therapy for an average of 6-months. This case describes not only a rare zoonotic infection but also highlights the importance of acquiring a detailed exposure history including recent travel and ingestions prior to developing a differential diagnosis and treatment plan.