CASE REPORT

Strongyloides Hyperinfection Secondary to High Dose Steroids and Chemotherapy

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A 37-year-old male initially presented with gross hematuria. He underwent urologic workup revealing a low grade urothelial carcinoma with no evidence of muscle invasion. He had no known risk factors for bladder cancer, was a lifelong non-smoker with no significant second hand smoke exposures, occupational exposures or medication exposures. He underwent transurethral resection of the bladder tumor followed by adjuvant course of BCG and active surveillance with cystoscopy with no evidence of local recurrence.

Three years later the patient developed acute onset of left sided facial and left upper extremity paralysis, and was found on imaging to have a right frontal hemorrhage. He underwent urgent surgical decompression as well as high dose corticosteroids. Pathology was consistent with urothelial carcinoma based on immunohistochemistry. He underwent staging CT scans of the chest, abdomen and pelvis with no evidence of intrathoracic abnormalities with the exception of a small calcified granuloma of right middle lobe. Abdominal imaging revealed bilateral adrenal metastases, multiple retroperitoneal and pelvic lymph nodes, and mild thickening of the superior portion of the bladder. Biotheranostics Cancer TypeID was performed and returned with 96% probability of urinary bladder as site of origin. He underwent stereotactic radiation to the resection cavity and to four additional lesions. He was eventually started on cisplatin and gemcitabine as part of a palliative regimen. He completed one full cycle of chemotherapy with mild neutropenia.

The patient started his second cycle of cisplatin with gemcitabine and four days later presented to the emergency department with headaches. Dexamethasone was increased and lab testing revealed severe hyponatremia at 118. At the time, this was felt to be a combination of SIADH from intracranial disease as well as from renal losses with recent platinum chemotherapy and mannitol. After initial clinical improvement following correction with 3% saline, he suddenly became unresponsive, and hemodynamically unstable. His acute course, included septic shock with enterobacter aerogenes bacteremia, requiring intubation and mechanical ventilation. He developed acute small bowel obstruction with bowel wall thickening, diffuse bilateral pulmonary infiltrates, initially thought to be secondary to aspiration, as well as a diffuse maculopapular rash most prominent on his chest wall and abdomen. Due to his bowel obstruction, exploratory laparotomy with surgical gastric tube and lysis of adhesions was attempted. His post-operative course was complicated by worsening anemia and aspiration of degraded blood products through the nasogastric tube. EGD was performed revealing a severely inflamed duodenal bulb with viscous material in stomach. A random biopsy of duodenum, returned revealing a helminth compatible with strongyloides species. Despite maximal support and diagnosis, the patient was unable to make a meaningful recovery and died.

We reviewed all of our patient's complete blood counts from time of diagnosis up to and including his final hospitalization, and a peripheral eosinophilia was not noted. He was born and raised in Mexico, emigrated to California over a decade prior, with no recent travel. He had no pets at home, and did not complain of a chronic cough prior.

Strongyloides infections in humans can be transmitted through fecal-oral transmission or skin exposures to the filariform larvae. The organism has global distribution. In the US the prevalence is low at 2.7% but, it can be higher in certain refugee populations by much as 40.4%.[1] Although felt to be underestimated, the estimated global burden has been reported as high as 100 million people infected.[2] In addition to an enteric life cycle, where eggs and larvae are excreted by the adult parasite, the filariform larvae have a second autoinfection life cycle of penetration through the intestines or perianal skin and migrating via bloodstream to the lung. They will then perforate the alveolar sacs, ascend the tracheobronchial tree and be swallowed entering the GI tract. In patients with impaired immune systems, this autoinfection lifecycle can become accelerated, with increasing burden of parasites, labelled as hyperinfection.[3] Hyperinfection itself is often accompanied by sepsis and respiratory failure and has a mortality as high as 85% in immunocompromised patients.[3,4] Although more prominent in chronic infections, peripheral eosinophilia is often not present in acute or hyperacute infections, and may only be seen in 20-30% of the cases.[4]

We present this case for review given the unexpected infectious complication of immunosuppression with steroids for intracranial metastases as well as chemotherapy. The patient's case is unique with the unlikely appearance of metastatic bladder cancer given his initial presentation with low grade non-muscle invasive disease, his age, and absence of risk factors for bladder cancer. He was presumably chronically colonized with strongyloides prior to initiation of high dose steroids and chemotherapy, without obvious risk factors or exposures to place him at elevated risk of helminths

colonization. He showed no historical or laboratory evidence of possible chronic infection even in retrospective review. Finally his clinical course, pulmonary findings, gastrointestinal findings and bacteremia with enteric organisms were fairly classic for acute hyperinfection in retrospect. Although chemotherapy likely contributed, his immune impairment was likely more related to high dose steroids in the preceding months. Hyponatremia and meningitis can occur as part of hyperinfection[3] and likely were the first unrecognized symptoms in our patient.

Even assuming that prevalence of global infection is higher than reported, the large number of patients treated with corticosteroids, global infection rates of HIV and volume of patients treated with chemotherapy, suggests that development of "hyperinfection" even in those infected is chronically rare. However, specialties caring for immunocompromised patients, should be vigilant for this infection, particularly in recent immigrant populations.

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