Syndrome of Inappropriate Anti-Diuretic Hormone Secretion Secondary to *Strongyloides stercoralis* Infection in an Allogeneic Stem Cell Transplant Patient: A Case Report and Literature Review

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ABSTRACT

Syndrome of inappropriate anti-diuretic hormone (SIADH) has been reported to be associated with systemic *Strongyloides stercoralis*. Here, we report a case of a stem cell transplant (SCT) recipient who developed severe SIADH secondary to systemic *S Stercoralis*. The SIADH resolved quickly after treating the systemic *S Stercoralis* with ivermectin. A systematic review of the literature was performed by PubMed, Scopus, and Cochrane database search. Only eight cases of *S Stercoralis* in allogeneic SCT recipients have been previously reported. To our knowledge, ours is the first reported case of SIADH secondary to *S Stercoralis* infection in an allogeneic SCT recipient. Prior to transplantation, even if asymptomatic, patients from endemic regions should be screened with strongyloides immunoglobulin (Ig)G serology. Pretransplantation eosinophilia should be evaluated by screening multiple stool samples for ova and parasites. Transplant candidates with positive serology or stool tests can be treated pretransplantation to eradicate infection. Patients at risk for *S Stercoralis* who develop nonspecific gastrointestinal complaints, rash, pulmonary infiltrates, or gram-negative bacteremia or meningitis may have *S Stercoralis* hyperinfection syndrome. Our case indicates that the development of SIADH may be an additional clue to this diagnosis. Appropriate diagnostic studies, including repeat stool and other body fluid sampling, should be expedited and ivermectin therapy initiated rapidly to prevent significant morbidity and mortality.

STRONGYLOIDES stercoralis is endemic in tropical and subtropical regions and occurs sporadically in temperate areas. Manifestations of infection range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease in the immunocompromised host. Syndrome of inappropriate anti-diuretic hormone (SIADH) has been associated with *S Stercoralis*; the mechanism is unknown, although it has been attributed to central nervous system (CNS) or pulmonary involvement [1,2].

Here, we report a case of an allogeneic stem cell transplant (SCT) recipient who developed severe SIADH secondary to infection with *S stercoralis*. Our patient did not have CNS features or pulmonary infiltration, and the mechanism by which *S stercoralis* caused SIADH remains unclear. *S stercoralis* infection in allogeneic SCT recipients has been previously reported in eight patients. To our knowledge, this is the first reported case of SIADH secondary to *S stercoralis* infection in an allogeneic SCT patient.

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CASE REPORT

A 68-year-old man was diagnosed with Philadelphia chromosome–positive B-cell acute lymphocytic leukemia (ALL) in December 2012. He was originally from Colombia, but had lived in Miami for 17 years. He was treated with hyper-CVAD (cyclophosphamide, vincristine, doxorubicin [Adriamycin], and dexamethasone) chemotherapy and imatinib and achieved remission. Following that, he underwent matched-unrelated SCT. Graft-versus-host disease (GVHD) prophylaxis included tacrolimus and low-dose methotrexate.

Eight weeks prior to SCT (day -56), he had persistent significant eosinophilia for 4 weeks. Eosinophilia peaked at 67% with absolute eosinophil count of 7.9×10^3. Serum strongyloides immunoglobulin (Ig)G and single stool test for ova and parasites were negative. Given anticipated SCT and chemotherapy, he was treated empirically with Albendazole 400 mg orally twice daily × 3 days. Eosinophilia resolved and did not recur in the early post-transplantation period.

Four months after transplantation (day 120), while on tacrolimus, the patient presented with epigastric pain, nausea, and vomiting. Upper gastrointestinal (GI) GVHD was suspected. He was admitted. Upper endoscopy (EGD) was performed and showed diffuse mild inflammation in the gastric body and duodenum (Fig 1) and biopsy specimens were taken. After the EGD, he was started on prednisone 20 mg orally twice daily and budesonide for a presumed clinical diagnosis of acute GI GVHD [3].

Recurrence of eosinophilia was noted approximately 2 weeks prior to his admission (day 106; Fig 2). He developed a progressive increase in his eosinophilia to levels disproportionate to that typically seen in the setting of GVHD (from <5% [0.14×10^3] to around 16% [0.7×10^3]). His eosinophilia level peaked at 31% (1.1×10^3) at the time of admission and EGD, and the possibility of infectious etiologies was considered.

On admission, his sodium (Na) level was 128 mmol/L (baseline Na was 135 mmol/L). His Na decreased to 115 mmol/L over the next 4 days. He was clinically euvolemic, and his laboratory work-up was consistent with SIADH (low serum osmolality [238 mOsm/kg], inappropriately high urine osmolality [308 mOsm/kg], high urine Na [103 mmol/L], and normal thyroid stimulating hormone, cortisol, and serum creatinine).

Duodenal biopsy pathology showed duodenal mucosa with *S stercoralis* (Fig 3A) and repeat stool sampling for ova and parasites was positive (Fig 3B). Serum strongyloides IgG continued to be negative. The presumed diagnosis of GVHD was revised and the diagnosis of strongyloides hyperinfection syndrome (HS) was made instead of GVHD. Accordingly, he was treated with ivermectin 200 mg/kg orally daily. Ivermectin was continued until he had three consecutive negative stool samples after the two consecutive positive samples post-transplantation, ultimately completing a 2-week course. One week after starting ivermectin, the patient's Na normalized and the eosinophilia improved (Fig 2).

REVIEW OF THE LITERATURE AND DISCUSSION

A systematic review of the literature was performed by a PubMed, Scopus, and Cochrane database search limited to English language articles. Including our present case, only nine cases of *S stercoralis* in allogeneic SCT recipients have been reported (Table 1) [4–11]. There was an additional case reported by Safdar that was specifically excluded given the lack of post-transplantation immunosuppression in the autologous setting. Four patients received their transplants in centers in North America, one in Brazil, three in Europe, and one in India.

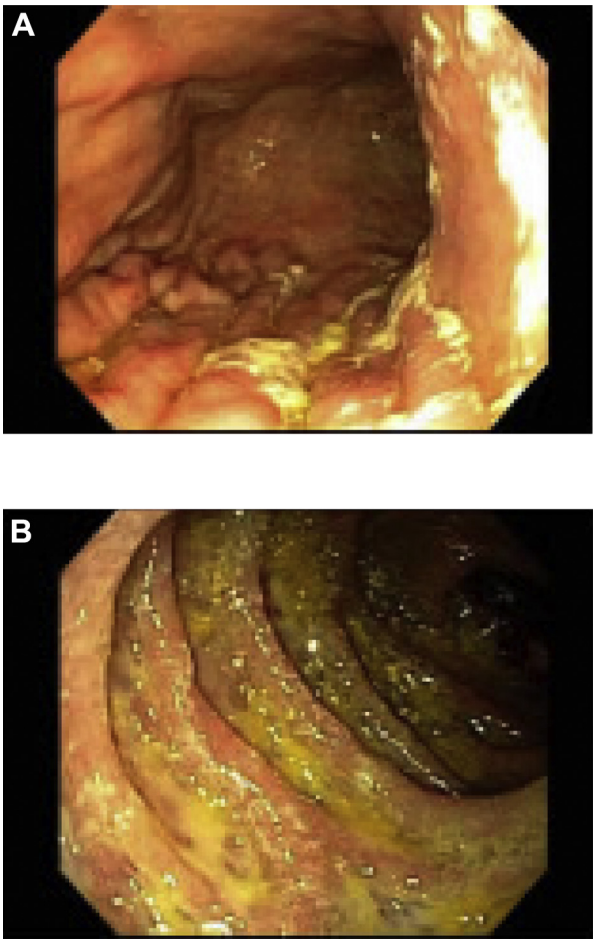

Fig 1. EGD showed diffuse mild inflammation characterized by erythema in the gastric body (**A**) and diffuse moderate inflammation characterized by congestion (edema), erythema, and granularity in the entire duodenum (**B**).

Only two patients presented with clinical signs possibly related to the *S stercoralis* infection before SCT. Those two patients had pretransplantation eosinophilia. Their pretransplantation stool screening failed to detect the parasite (one patient had single stool testing and one had multiple stool testing). There was no report of strongyloides antibody screening pretransplantation in these patients.

The median time for development of signs of strongyloidiasis was 25 days after transplantation (range, 2–121 days). The disease presented as pulmonary (HS) in four cases, GI symptoms in four, and urinary tract symptoms in one patient. Five patients died; the parasitic infection was considered the cause of death in three cases (all with HS). Our patient was treated with tacrolimus as GVHD prophylaxis at the time of diagnosis. The other surviving patients (including a patient with HS) were all receiving cyclosporine as GVHD prophylaxis.