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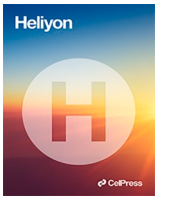

Case report

Syndrome of inappropriate anti-diuretic hormone secretion secondary to disseminated strongyloidiasis in a kidney transplant recipient: A case report

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ABSTRACT

Background: Syndrome of inappropriate anti-diuretic hormone secretion (SIADH) is associated with strongyloidiasis. Herein, a rare case of severe SIADH secondary to disseminated strongyloidiasis in a kidney transplant recipient is reported.

Case presentation: A case involving a 43-year-old male kidney transplant recipient with severe disseminated Strongyloides stercoralis infection is reported. The patient was a construction worker with a history of consuming undercooked yellow eel and sashimi. On admission, the patient presented with poor appetite, nausea, vomiting and diarrhea. Laboratory investigations revealed persistent significant hyponatremia and low serum osmolality, confirming the diagnosis of SIADH. S. stercoralis was detected in the stool and bronchoalveolar lavage fluid. He was treated with empirical albendazole because S. stercoralis was detected in the stool; however, his symptoms and hyponatremia did not improve until ivermectin was administered, after which SIADH resolved quickly.

Conclusion: This case suggests that S. stercoralis infection should be included in the differential diagnosis when a kidney transplant recipient presents with gastrointestinal symptoms and SIADH. In such situations, pre- or post-transplant screening for S. stercoralis is needed, and early ivermectin treatment is very important.

1. Introduction

Strongyloidiasis is commonly a clinically unapparent, chronic infection, but immunocompromised hosts can develop fatal disease. The manifestations of the infection range from asymptomatic eosinophilia to disseminated disease. Disseminated strongyloidiasis occurs when infective filariform larvae invade through the gastrointestinal tract and migrate to other organs, resulting in multisystem involvement and contributing to mortality rate of 80 % [1]. Previously, it has been reported in a few cases that disseminated strongyloidiasis could be complicated by syndrome of inappropriate anti-diuretic hormone secretion (SIADH), which contribute to unfavorable outcomes [2,3]. Here, we report the rare case in which a kidney transplant recipient developed severe SIADH secondary to disseminated strongyloidiasis.

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2. Case presentation

A 43-year-old male construction worker presented to the authors' hospital with a 4-day history of poor appetite and diarrhea. The patient had received a deceased donor kidney transplant with unknown cause(s) of end-stage renal disease 4 months prior. The induction immunosuppressive agent used was anti-thymocyte globulin (ATG), and maintenance immunosuppressive agents used were tacrolimus, enteric-coated mycophenolate sodium and prednisone. The patient had a history of consuming undercooked yellow eel and sashimi 8 days before admission. On admission (day 0), the patient complained of progressive loss of appetite and diarrhea. He was a febrile (temperature 36.3 °C) with a blood pressure of 124/74 mmHg, a heart rate of 92 beats/min, and a respiratory rate of 18 breaths/min. Systemic examination findings were largely unremarkable. Laboratory investigations revealed abnormal blood values, with a hemoglobin level of 9.9g/dL, a platelet count of 179 × 109/L, and a total leukocyte count of 3.71 × 109/L. A blood differential test yielded the following results: neutrophils, 85.6 %; lymphocytes, 6 %; eosinophils, 1.7 %; and monocytes, 6.5 %. Blood biochemical testing revealed significant hyponatremia (124.7 mmol/L), increased serum creatinine concentration (190.8 μmol/L), and decreased albumin concentration (3.8 g/dL). His uric acid level was 403.3 μmol/L and liver function tests were normal.

After admission, the patient experienced severe diarrhea, nausea, vomiting and low appetite, accompanied by persistent significant hyponatremia (sodium [Na], 120.5–131.0 mmol/L). His serum osmolality was 263 mOsm/kg, urine osmolality was 396 mOsm/kg, and urine Na was 87.9 mmol/L. The laboratory investigation results were consistent with a diagnosis of SIADH (significant hyponatremia, low serum osmolality, higher urine osmolality than serum osmolality, high urine Na level, and normal thyroid-stimulating hormone and cortisol). Importantly, microscopic analysis of the feces revealed the presence of live S. stercoralis on post-admission day 3 (Fig. 1A). Furthermore, upper endoscopy (esophagogastroduodenoscopy) was performed, mucosal tissue biopsy was performed;

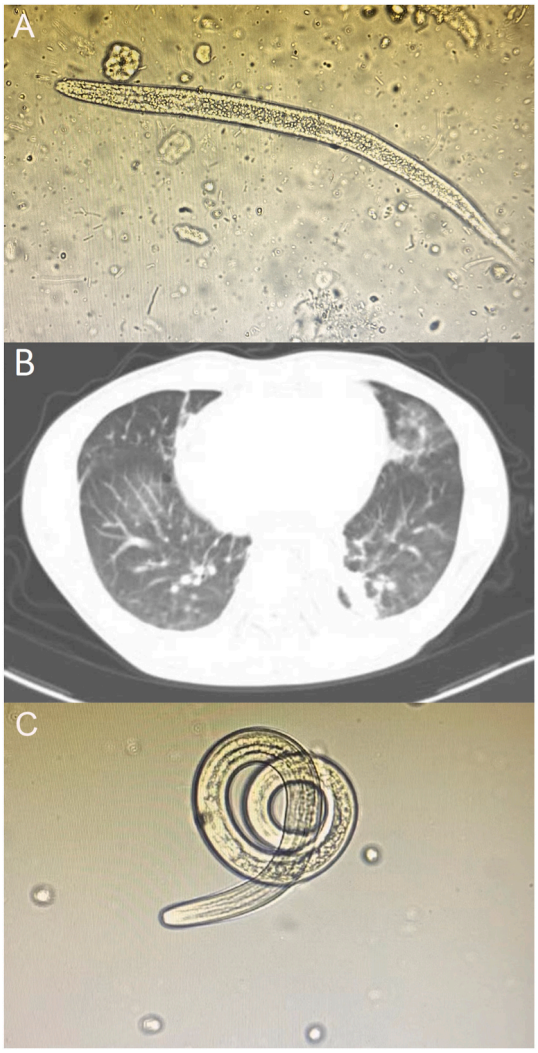

Fig. 1. Live S. stercoralis in face via microscopic approach (A). CT scan of lung involvement by S. stercoralis (B). Live S. stercoralis in BALF via microscopic approach (C).

however, S. stercoralis was not detected. On post-admission day 6, the patient developed fever, cough, sputum, and shortness of breath. Computed tomography revealed multiple patchy, high-density shadows and interstitial lung edema in both lungs (Fig. 1B). Further microscopic observations revealed the presence of live S. stercoralis in the bronchoalveolar lavage fluid (BALF) (Fig. 1C), clinical metagenomic next-generation sequencing of the BALF verified the presence of S. stercoralis.

To improve serum Na level, the patient was initially treated with aggressive electrolyte supplementation (8–10 g Na per day), and tolvaptan was administered for 4 days from post-admission day 6, but proved ineffective. After the diagnosis of strongyloidiasis was established, he underwent treatment with oral albendazole (400 mg) twice daily on post-admission day 4; however, his symptoms and hyponatremia did not improve after 1 week of therapy. Accordingly, 200 mg/kg ivermectin was administered orally daily on post-admission day 11. Five days after starting ivermectin, the patient's Na concentration normalized, and his symptoms gradually disappeared. Ivermectin was continued until he had 3 consecutive negative stool samples, and he ultimately completed a 3-week course. After 3 months of regular follow-up, the patient's symptoms improved and his Na level reached normal limits.

3. Discussion

The mean nationwide prevalence of S. stercoralis infection in China is 0.12 %, with residents in farming areas of southern China exhibiting the highest risk for infection [4]. Most transplant centers in China are located in non-endemic areas, and cases of S. stercoralis infection in kidney transplant recipients are very rare. In published cases of S. stercoralis infection in transplant patients, donor-derived infection was confirmed to account for a major proportion. Another important route of infection was travel to or residence in an area in which S. stercoralis is endemic [5]. A Brazilian study investigating screening for S. stercoralis infections in transplant candidates revealed that 10 % of fecal samples were positive [6]. Our patient was a construction worker and may have been exposed to contaminated soil before this admission; moreover, he had a history of consuming yellow eel and sashimi, which lives in field mud and may have carried S. stercoralis. Unfortunately, pretransplant screening tests and a history of parasitic infection were lacking in our case. Another problem with pretransplant screening for S. stercoralis infection is the low sensitivity of current testing methods and the specificity of eosinophilia as a diagnostic marker [7]. More importantly, the clinical presentation is variable, and the disease is often overlooked, leading to diagnostic and therapeutic delays and, consequently, unfavorable outcomes.

Generally, S. stercoralis infection causes nonspecific symptoms in multiple organ systems, predominantly gastrointestinal, dermatological, and respiratory. Among transplant recipients, gastrointestinal (79.6 %) and respiratory (33.3 %) symptoms are the most common, while skin rash (20.3 %) and fever (30 %) are less common, and only 1.9 % of recipients are asymptomatic [5]. S. stercoralis infection in our patient involved the gastrointestinal and respiratory systems and was therefore defined as disseminated strongyloidiasis. The infection was not detected early because the signs and symptoms of S. stercoralis infection in the gastrointestinal tract can mimic other post-transplantation intestinal complications, including other infections, drug toxicity, and acute rejection. SIADH was the most notable complication in this patient, and was not responsive to conventional treatment until ivermectin was administered. To date, the mechanism by which S. stercoralis causes SIADH has not yet been elucidated. Studies have suggested that the translocation of strongyloidiasis can result in SIADH, which may be associated with the central nervous system, gastrointestinal tract and pulmonary infiltration [2,3,8,9]. Studies have reported that patients with tuberculosis can develop SIADH because tuberculous lung tissues can release anti-diuretic hormone (ADH) or ADH-like substances [10,11], implying that S. stercoralis may have infiltrated the tissue and released ADH or ADH-like substances autonomously in our patient. Another study reported that anorexia resulting from chronic S. stercoralis infection was responsible for increased ADH secretion [3].

Ivermectin kills adult Strongyloides rather than the larvae; As such, repeated dosing is necessary. There is an autoinfective cycle of approximately 2 weeks, during which ivermectin must be readministered, and additional dosing is necessary because it will not kill S. stercoralis in the blood or larvae deep inside the bowels [1]. In real-world practice, the duration of treatment is based on patients' condition, with daily ivermectin administered until symptoms resolve and stool tests are negative for at least 2 weeks (i.e., 1 autoinfection cycle) or longer if the patient remains immunosuppressed. A six-month maintenance course of ivermectin has been recommended in patients with a high risk for relapse and high tolerance [12,13]. In our patient, the administration of albendazole alone did not effectively control the disease, and the addition of ivermectin resulted in better efficacy because the two drugs administered killed S. stercoralis via different mechanisms.

Interestingly, there is some evidence that cyclosporine is active against S. stercoralis in vitro, and its use in immunosuppressed patients has prevented Strongyloides hyperinfection in kidney transplant patients, however this effect has not been confirmed clinically [7]. A few case studies have reported that tacrolimus is associated with SIADH, because switching from tacrolimus to cyclosporine resulted in remission of SIADH, however, the mechanism remains unclear [14,15]. Based on the above evidence, cyclosporine appears to be the better choice when S. stercoralis infection occurs in kidney transplant recipients.

4. Conclusion

In SOT clinical practice, the unique challenge in treating strongyloidiasis is due to the underrecognition of a particular history of parasite exposure and underappreciation of the potentially fatal complications. Pretransplant screening to identify S. stercoralis infection in donor/receptor pairs is needed due to the presence of this infection in nonepidemic areas. Clinicians should have a high index of suspicion when ill-defined gastrointestinal symptoms, respiratory symptoms and obscure hyponatremia are present, and they should consider strongyloidiasis as a differential diagnosis.

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Ethical approval statement

Ethics approval was not required for this study. Written informed consent was obtained from the patient for publication of this report and any accompanying images.

Data availability statement

The clinical data utilized in this report are described in this article. Further details will be made available on request.

CRediT authorship contribution statement

Maozhi Tang: Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Qiongyao Peng:** Formal analysis, Data curation. **Bangqin Hu:** Formal analysis, Data curation. **Ming Tang:** Formal analysis, Data curation. **Linguo Shen:** Formal analysis, Data curation. **Wenqian Huo:** Project administration, Methodology. **Keqin Zhang:** Resources, Methodology, Conceptualization. **Ling Liu:** Writing – review & editing, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] D.J. Gonzales, R.K. Chakraborty, A. Climaco, in: StatPearls (StatPearls PublishingCopyright © 2023, StatPearls Publishing LLC., 2023.
[2] T.S. Reddy, J.W. Myers, Syndrome of inappropriate secretion of antidiuretic hormone and nonpalpable purpura in a woman with Strongyloides stercoralis hyperinfection, Am. J. Med. Sci. 325 (5) (2003) 288–291.
[3] E. Hayashi, N. Ohta, H. Yamamoto, Syndrome of inappropriate secretion of antidiuretic hormone associated with strongyloidiasis, Southeast Asian J. Trop. Med. Publ. Health 38 (2) (2007) 239–246.
[4] C. Wang, J. Xu, X. Zhou, J. Li, G. Yan, A.A. James, et al., Strongyloidiasis: an emerging infectious disease in China, Am. J. Trop. Med. Hyg. 88 (3) (2013 Mar) 420–425.
[5] C.L.R. Abad, E. Bhaimia, A.N. Schuetz, R.R. Razonable, A comprehensive review of Strongyloides stercoralis infection after solid organ and hematopoietic stem cell transplantation, Clin. Transplant. 36 (11) (2022) e14795.
[6] R.C.B. Gryschek, M.A. Corral, R.B. Sitta, M. Gottardi, L.C. Pierrotti, S.F. Costa, et al., Strongyloides infection screening in transplant candidates: what is the best strategy? Transpl. Infect. Dis. : an official journal of the Transplantation Society (2023) e14153.
[7] O. Meira Dias, N. Belousova, N. Sharif, I. Brasg, L.G. Singer, J. Tikkanen, et al., Strongyloides hyper-infection in a lung transplant recipient: case report and review of the literature, Journal of the Association of Medical Microbiology and Infectious Disease Canada = Journal officiel de l'Association pour la microbiologie medicale et l'infectiologie Canada 7 (2) (2022) 150–156.
[8] D. Aregawi, D. Lopez, M. Wick, W.M. Scheld, D. Schiff, Disseminated strongyloidiasis complicating glioblastoma therapy: a case report, Journal of neuro-oncology 94 (3) (2009) 439–443.
[9] S. Vandebosch, F. Mana, A. Goossens, D. Urbain, Strongyloides Stercoralis infection associated with repetitive bacterial meningitis and SIADH: a case report, Acta gastro-enterologica Belgica 71 (4) (2008) 413–417.
[10] C. Bal, D. Gompelmann, M. Krebs, L. Antoniewicz, C. Guttmann-Ducke, A. Lehmann, et al., Associations of hyponatremia and SIADH with increased mortality, young age and infection parameters in patients with tuberculosis, PLoS One 17 (10) (2022) e0275827.
[11] M. Hashimoto, S. Kuriiwa, A. Kojima, K. Shinhuku, A. Sato, R. Sasaki, et al., Mild lung tuberculosis in a patient suffering from status epilepticus caused by the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), Intern. Med. 56 (4) (2017) 429–433.
[12] A.C. Roxby, G.S. Gottlieb, A.P. Limaye, Strongyloidiasis in transplant patients, Clin. Infect. Dis. : an official publication of the Infectious Diseases Society of America 49 (9) (2009) 1411–1423.
[13] E.M. Mokaddas, S. Shati, A. Abdulla, N.R. Nampoori, J. Iqbal, P.M. Nair, et al., Fatal strongyloidiasis in three kidney recipients in Kuwait, Med. Princ. Pract. : international journal of the Kuwait University, Health Science Centre 18 (5) (2009) 414–417.
[14] K. Takagi, T. Yagi, S. Shinoura, Y. Umeda, R. Yoshida, D. Nobuoka, et al., Syndrome of inappropriate antidiuretic hormone secretion following liver transplantation, Acta Med. Okayama 71 (1) (2017) 85–89.
[15] T. Azuma, H. Narumi, K. Kojima, Y. Nawa, M. Hara, Hyponatremia during administration of tacrolimus in an allogeneic bone marrow transplant recipient, Int. J. Hematol. 78 (3) (2003) 268–269.