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CASE REPORT

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Donor-derived strongyloidiasis in a Saudi pediatric kidney transplant recipient: A case report and mini-review

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Abstract

S. stercoralis infection has been identified as a donor-derived infection in cases of solid organ transplant among recipients with no prior risk factor for parasitic exposure. Worldwide and regional reports from the adult kidney transplant population highlight this indirect method of infection and caution about delayed diagnosis, severe complications, and death related to donor-derived *S. stercoralis* infection. We report a deceased-donor-derived *S. stercoralis* infection in a 12-year-old Saudi girl who underwent kidney transplantation. This is the first pediatric case reported outside the United States of America. Although she presented with mild bouts of gastrointestinal symptoms, the need for additional immune suppression put her at risk of serious complications. A literature review highlights the importance of awareness about *S. stercoralis* infections and complications in kidney transplant recipients, pretransplant screening of donors based on risk assessment, and the challenges with treatment availability and duration in this vulnerable population.

KEYWORDS

donor-derived infection, pediatric kidney transplant, pretransplant screening, *Strongyloides stercoralis*, Strongyloidiasis

1 | INTRODUCTION

S. stercoralis is an intestinal nematode that infects up to 100 million people worldwide, mainly in tropical and subtropical regions.[1] Direct skin contact with soil contaminated with the *S. stercoralis* larvae results in larval penetration of the skin followed by a migratory phase that ends in the host's small intestine.[2] Infection in the immune-competent person may be asymptomatic or may be associated with symptoms of larval migration that include a localized rash and respiratory or gastrointestinal symptoms.[2] Adult female worms develop in the intestinal mucosa and deposit eggs that hatch into larval form and are excreted in the stool.[1] Chronic infection occurs due to the distinctive ability of the *Strongyloides* larvae to reinfect the same individual by direct perianal skin penetration. This autoinfection cycle may continue for years, resulting in late or protracted clinical symptoms.[3]

Strongyloidiasis has been reported after solid organ transplantation (heart, liver, pancreas, intestine, and kidney).[4] In the transplant population, as a result of a weakened immune system, a condition of accelerated parasitic propagation known as hyperinfection may occur and lead to extraintestinal dissemination.[1] Patients are at risk of meningitis and sepsis from bacterial gut flora carried with migrating larvae; the associated mortality rate is as high as 87%.[5]

We report a case of donor-derived strongyloidiasis in a 12-year-old Saudi girl following a PKT and review the complications and treatment therapy of strongyloidiasis in transplant patients.

2 | CASE REPORT

A 12-year-old Saudi girl, who was diagnosed with congenital nephrotic syndrome in her first year of life, progressed to end-stage

Abbreviations: BAL, bronchoalveolar lavage; *C. difficile*, *Clostridium difficile*; CMV, cytomegalovirus; HIV, human immunodeficiency virus; IFTA, interstitial fibrosis and tubular atrophy; PKT, pediatric kidney transplant; *S. stercoralis*, *Strongyloides stercoralis*; SFDA, Saudi Food and Drug Authority; UTI, urinary tract infection; WBC, white blood cells.

renal disease and underwent a deceased-donor kidney transplant in July 2013. Post-transplant, she received immunosuppressive therapy that included oral prednisolone, mycophenolate mofetil, and tacrolimus.

In June 2016, 3 years after the transplant, she developed chronic rejection with severe IFTA requiring pulse steroids. This was tapered over 3 months from an initial dose of 2 mg/kg/day to a low maintenance dose of 5 mg every other day.

In November 2016, she was admitted with a *Proteus mirabilis* UTI. On the day of admission, she developed watery diarrhea and vomiting with mild colicky abdominal pain. She was afebrile with an unremarkable physical examination. Investigations included a complete blood count: total WBC 11.27 $\times 10^9$, eosinophil count 2.38 $\times 10^9$ (21%), creatinine 61 mmol/L, BUN 3 mmol/L, sodium 125 meq/L, potassium 3.1 meq/L, chloride 98 meq/L, and glucose 7.3 mmol/L. Her stool was positive for *C. difficile* toxins (A & B). Stool microscopy revealed larvae of *S. stercoralis*. Stool bacterial culture did not isolate any pathogens, and a blood culture showed no growth. Serological testing for *S. stercoralis* was not available.

A review of her history and previous investigations revealed recurrent episodes of diarrhea and mild abdominal pain along with peripheral eosinophilia of 15%-20% of her total WBC count for 1 year prior to presentation. During these bouts of gastrointestinal symptoms, stool for *C. difficile* and for ova and parasites was not requested. The family denied any travel history. Her kidney donor was a 35-year-old man from the Indian subcontinent who worked in Saudi Arabia and died in a road traffic accident.

During her admission, she did not experience clinical deterioration or evidence of disseminated strongyloidiasis. Her UTI was managed with ceftriaxone, and as her gastrointestinal symptoms could have been attributable to both *C. difficile* and *S. stercoralis*, both infections were treated. She received metronidazole and albendazole 400 mg orally twice a day for 7 days. Although her gastrointestinal symptoms resolved, a follow-up stool microscopy was still positive for *S. stercoralis* larvae. For this reason, she received a second prolonged 28-day course of albendazole. She was followed up in the clinic on a weekly basis. After completing this course, three stool samples taken on different days confirmed parasitic clearance.

3 | DISCUSSION

The global prevalence of *S. stercoralis* ranges between 10% and 40% and is as high as 60% in resource-poor tropical and subtropical regions.[1] Available prevalence studies on intestinal parasites based on stool microscopy have not reported *Strongyloides* detection in the Saudi population.[6,7] In a study conducted on HIV-seropositive patients in the capital city Riyadh, *Strongyloides* larvae were detected in 2.2% of tested individuals[8]; however, the nationalities of the included cohort were not described. A review of expatriate workers in the western regions of Al Baha and Al-Madinah Al-Munawarah identified a prevalence of 2.59% and 3.5%, respectively.[9,10]

Expatriates make up one third of Saudi Arabia's population with the majority originating from South Asia.[11]

Donor-derived *Strongyloides* infection, although not common, has been reported among adult solid organ transplant recipients. A recent publication has identified a total of 27 donor-derived *S. stercoralis* infections after solid organ transplantation.[4] Most case reports highlight the fact that donors have been from areas where strongyloidiasis is highly prevalent.[5] Within Saudi Arabia, most reports have come from the Eastern Province.[12-14] In one report, three cases of post–kidney transplant *Strongyloides* infection were from the city of Dammam, where BAL specimens, a duodenal biopsy, and stool specimens revealed *S. stercoralis* larvae.[12] In all three cases, the donors were from Bangladesh. Two cases reported in Riyadh were of Saudi adult post–kidney transplant recipients who were ultimately diagnosed with *S. Stercoralis* hyperinfection. In one case, the patient had presented with recurrent *Streptococcus bovis* meningitis followed by *E. coli* chest infection, and in the other case, the patient had recurrent *E. Coli* urosepsis and CMV reactivation.[15,16] These cases highlight the risk of morbidity associated with migrating larvae. Regionally, in the Middle East, three fatal cases of *Strongyloides* hyperinfection post–kidney transplant have been reported from Kuwait.[17] All three donors were from the Indian Subcontinent.

In the pediatric transplant population, there have only been two reported cases of donor-derived *S. stercoralis* infection from the United States. One report was from 1981 of a 10-year-old girl post–kidney transplant who presented with fever, cough, diarrhea, abdominal pain, and persistent eosinophilia and was found to have disseminated strongyloidiasis.[18] The other kidney recipient from the same donor developed similar symptoms and was also confirmed to have *Strongyloides* hyperinfection.[18] The second reported pediatric case was of a 14-year-old boy who had presented with fever, vomiting, diarrhea, and a buttock rash 72 days post–kidney transplant. In this case, the Puerto Rican donor was implicated in infecting three transplant recipients with *S. stercoralis*.[19] Our case is the first reported donor-derived *S. stercoralis* infection in the pediatric population in Saudi Arabia. Although she presented with mild gastrointestinal symptoms possibly attributable to strongyloidiasis, her unexplainable and persistent eosinophilia raises the concern for an undiagnosed parasitic infection.

Kidney transplantation began in Saudi Arabia with living-related donors in 1979.[20] In 1984, the first Saudi deceased-donor kidney transplant was performed from a deceased adolescent boy to two young female recipients.[20] By the end of 2015, a total of 9790 kidneys were transplanted, with 2838 kidneys from deceased donors.[21] Saudi Arabia leads the Arab world in terms of annual numbers of deceased-donor PKT.[22] Although the numbers are modest in comparison with European program counterparts, 69 deceased PKTs were conducted between 2014 and 2016.[23] National and regional case reports of adult patients with severe and fatal donor-derived infections raise the concern for a similar risk in the PKT recipient.

Pretransplant *Strongyloides* screening for recipients is recommended by several internationally recognized medical societies.[24-26] Screening includes serological testing and stool microscopy for

recipients from endemic areas and for those presenting with unexplainable eosinophilia or gastrointestinal symptoms prior to organ transplantation.

Unlike recipient screening, widespread support for *Strongyloides* donor screening has not been adopted by most medical societies. The American Society of Transplantation and the American Society of Transplant Surgeons do however recommend pretransplant donor screening of living and deceased donors with history of residence or travel to areas of *S. stercoralis* endemicity or if found to have unexplained eosinophilia.[24] A combination of serological testing and stool microscopic examination is recommended.

Donors and recipients with positive screening and those with confirmed *S. stercoralis* infection or disease require antiparasitic therapy. Ivermectin is the first-line therapy, as it is effective at eradicating both adult and larval stages of the parasite and has the least side effects among therapeutic options.[27] A repeated dose at 2 weeks improves cure rates.[27] Ivermectin is not currently approved by the SFDA and is not available as a treatment option.[28] Most case reports from Saudi Arabia document treatment with albendazole.[12,13,15] Albendazole has an efficacy of 45%-75% and is considered a second-line agent.[29] The recommended dose is 400 mg orally twice a day for 7 days, although treatment durations in reported cases are varied.[29] Our patient received a total of 5 weeks of albendazole (an initial 7 days as the recommended dose, followed by a 28-day prolonged course) before stool clearance was documented. In the immunocompromised patient, treatment failures have been reported with parasitic clearance taking up to 21-30 days.[19] Based on this, some authors have advocated for maintenance antiparasitic therapy, prolonged doses, or combination treatment when patients require additional immunosuppressive therapy or are presenting with hyperinfection or disseminated infection.[4,19,26,27]

We report a case of *S. stercoralis* infection in a deceased-donor PKT who did not have a severe presentation; however, the need for additional immune suppression put her at risk of complications. She presented with unexplained and prolonged eosinophilia and recurrent abdominal pain and diarrhea which should have prompted a sooner suspicion and evaluation for parasitic infections. This case highlights the need for awareness about *S. stercoralis* infections in PKT recipients and the need for screening and adequate treatment to avoid delays in diagnosis and infection-related morbidity and mortality. As screening for donors in non-endemic areas is not routinely advocated, we recommend screening deceased donors who originate from a *S. stercoralis* endemic country. Additionally, prompt *S. stercoralis* testing is warranted for symptomatic recipients on immunosuppression therapy or if presenting with unexplainable eosinophilia. It remains essential to establish recipient and donor screening protocols based on risk assessment and to have access to first-line therapy options for this vulnerable population.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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