Trans R Soc Trop Med Hyg 2020; **114**: 137–139
doi:10.1093/trstmh/trz085 Advance Access publication 5 November 2019

Persistent eosinophilia among 21 historic cases of *Strongyloides stercoralis* infection: a case for routine follow-up and repeat treatment

Paul Arkell*, Catherine Cosgrove and Peter Riley

Infection Department, St George's University Hospitals NHS Foundation Trust, Blackshaw Road, London, SW17 0QT ,UK

*Corresponding author: Tel: +442086721255; E-mail: paularkell@doctors.org.uk

Received 28 April 2019; revised 17 July 2019; editorial decision 18 July 2019; accepted 19 July 2019

Background: Strongyloidasis affects more than 100 million people worldwide and causes persisting infection.

Methods: We retrospectively reviewed 21 cases of parasitologically confirmed *Strongyloides stercoralis* infection at our centre.

Results: We found four individuals who had eosinophilia (>0.5x10^9/litre) more than 6 mo after treatment.

Conclusions: This may represent ongoing or relapsed infection. Our data support the need for continued follow-up of treated individuals, particularly those with abnormal host defences who are at risk of severe forms of the disease.

Keywords: chronic infection, eosinophilia, ivermectin, relapse, *Strongyloides stercoralis*, treatment

Background

Strongyloidasis is a neglected tropical disease caused by the nematode *Strongyloides stercoralis*, which is estimated to affect more than 100 million people worldwide.[1] Chronic infection may be asymptomatic, or cause gastrointestinal, cardiopulmonary and/or skin symptoms. In patients with specific abnormalities in host defences (most often those taking corticosteroids and those coinfected with human T cell leukaemia virus type 1), rapid replication of larvae can result in *Strongyloides* hyperinfection syndrome with up to 68% mortality.[2]

Treatment of strongyloidiasis is with ivermectin (+/− albendazole), which is well tolerated. Among individuals with chronic strongyloidiasis in randomised trials, parasitological cure (assessed at between 2 and 24 wk) was achieved in 82–100%.[3]

We reviewed all cases of parasitologically confirmed *S. stercoralis* infection at our centre, evaluating treatment response and possible markers of relapse.

Materials and methods

All individuals with *S. stercoralis* identified on wet mount microscopy between 1 January 2000 and 4 September 2018 were included. Demographic, clinical and laboratory data were collected by retrospective review of available case notes.

Individuals with positive stool microscopy at presentation were categorised as having 'parasitological treatment response' if they had a subsequent negative stool. Those with positive serology at presentation were categorised as having 'serological treatment response' if they had subsequent negative serology. Individuals with eosinophilia (>0.5x10^9/litre) at presentation were categorised as having 'eosinophil treatment response' if their eosinophil count normalised within 6 mo of receiving anthelmintic treatment. Those with one or more eosinophil counts above normal range thereafter were categorised as having 'persistent eosinophilia'.

Where the date of treatment was unavailable, the date of diagnosis with *S. stercoralis* was taken as the treatment date.

Results

Twenty-one cases of parasitologically confirmed *S. stercoralis* infection were included. Median (IQR) age was 59 (50–66) y and 13 were male. The majority of individuals were from sub-Saharan Africa. Eight were HIV-positive, two had renal transplantation, two had haemopoietic bone marrow transplantation and two had diabetes mellitus. Four individuals were taking corticosteroids at the time of diagnosis, which included both renal transplant cases and one BMT case. Serological testing for

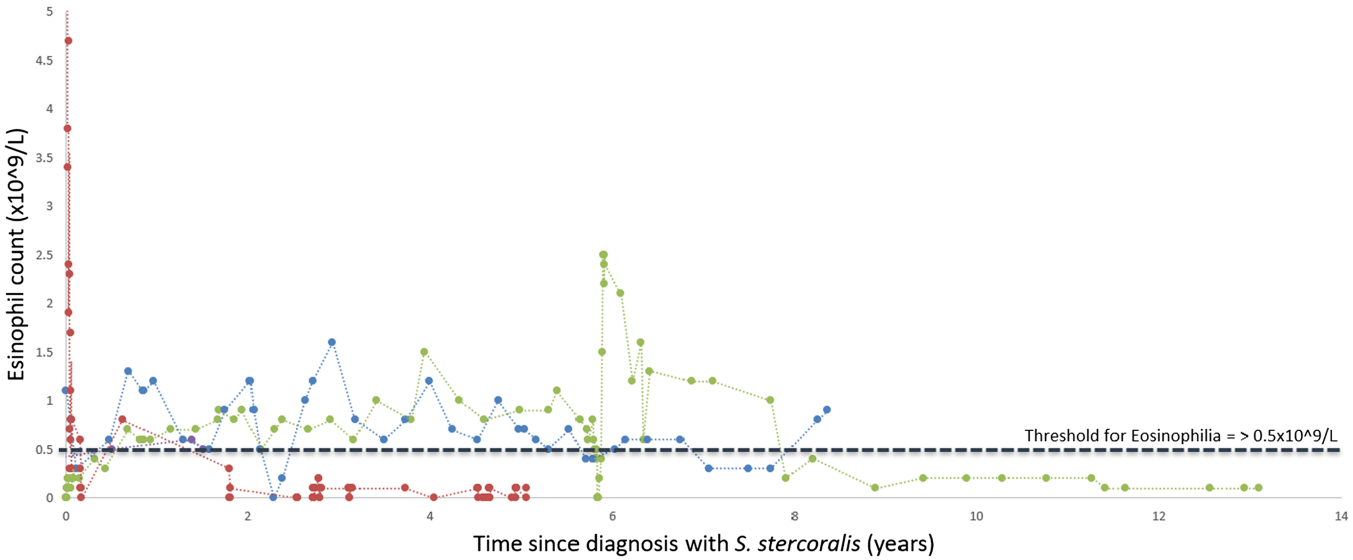

Figure 1. Retrospective follow-up of parasitologically confirmed cases of *Strongyloides stercoralis* showing four individuals who experienced eosinophilia >6 mo after treatment.

S. stercoralis was undertaken in eight cases, five of which were positive. Twelve individuals had eosinophilia at the time of diagnosis. Four individuals had a bacteraemia with an enteric organism and two were diagnosed with *Strongyloides* hyperinfection syndrome. Further baseline data are provided in the supplementary material.

Treatment was with ivermectin in nine out of 12 cases where treatment regimen was documented and albendazole in three. Individual doses and durations are provided in the supplementary material. Parasitological treatment response was demonstrated in 14 out of 21 cases while stool microscopy was not repeated in the seven other cases. Serological treatment response was demonstrated in one out of five cases, while serology remained positive in one case (at 6 wk) and was not repeated in the three other cases. Eosinophil treatment response was demonstrated in nine out of 12 cases, while eosinophil count remained positive at 6 mo in one case and was not repeated within 6 mo in the two other cases. Four individuals had persistent eosinophilia, two of whom experienced this for several years (Figure 1).

Three individuals died less than 3 mo after diagnosis with *S. stercoralis*. One was a 51-y-old male patient with renal transplantation who presented with *Strongyloides* hyperinfection syndrome and *Pneumocystis jiroveci* pneumonia.[4] The second was a 92-y-old patient admitted with candidaemia. The third was an 80-y-old with HIV infection (other clinical details were unavailable).

Discussion

In this retrospective review of parasitologically confirmed *S. stercoralis* infection, we found a predominance of individuals from sub-Saharan Africa. This is broadly reflective of the migrant communities in south London who access our hospital and is in keeping with a recent systematic review of seroprevalence studies, which found pooled *S. stercoralis* seroprevalence to be 14.6% among migrants from Africa.[5] Most individuals had a known host defence abnormality, which may have led to increased larval replication and shedding, and may have made parasitological diagnosis more likely.

Eosinophilia is a hallmark of chronic strongyloidiasis and hence was present in the majority of cases. Four of 21 cases had an elevated eosinophil count more than 6 mo after anthelmintic treatment. This could represent either incomplete treatment or relapse. Reinfection is unlikely as *S. stercoralis* is not endemic to the UK, although individuals could feasibly acquire reinfection when travelling abroad. Non-parasitic causes of persistent eosinophilia are possible, including HIV-related conditions (because a significant number of individuals were HIV-positive). However, there was no evidence of this in the clinical notes.

A limitation of this study is the retrospective design. Some baseline demographic, clinical and laboratory data were unavailable, despite a thorough review of the available clinical notes. In some cases, evidence of treatment regimen was not available and for those we have assumed that treatment occurred on the date of diagnosis. Diagnosis of *S. stercoralis* has always been an unusual occurrence at our centre and we believe that treatment would have been ensured in the vast majority of these cases. However, it must be noted that three of the individuals with persistent eosinophilia were in this group and therefore suboptimal treatment must be considered as a potential cause.

There are increasing case reports of confirmed relapsed *S. stercoralis* infection, including those causing severe disease.[6] Furthermore, in their recent prospective study, Repetto et al. found a high rate of persisting infection among individuals treated with ivermectin, although a major limitation to this study was significant loss to follow-up.[7]

Non-communicable diseases are an emerging pandemic globally that disproportionately affect those in low- and middle-income countries. Corticosteroids are a cornerstone treatment for many allergic, inflammatory and malignant disorders. There is a need for ongoing follow-up of individuals treated for *S.*

stercoralis, particularly those with abnormal host defences (e.g. corticosteroid use) who are at risk of severe infection. However, there is little evidence to suggest the optimal programme of testing and/or repeat treatment, or whether eosinophil count is an appropriate marker of ongoing or relapsed infection. Prolonged initial treatment and/or combination treatment with ivermectin and albendazole may be of benefit. A larger prospective study with long-term follow-up is required to address these issues.

Supplementary data

Supplementary data are available at Transactions online (http://trstmh.oxfordjournals.org/).

Authors' contributions: PA conceived the study and designed the study protocol; PA and PR carried out the data collection and analysis; PA drafted the manuscript. PA, CC and PR critically revised the manuscript for intellectual content. All authors read and approved the final manuscript.

Acknowledgements: Dr Jonathan Youngs (data collection). Dr Laura Whitney (data collection).

Funding: None.

Competing interests: Nothing to declare.

Ethical approval: St George's Research Ethics Committee indicated that specific approval was not required for this retrospective analysis of hospital records.

References

1 Bisoffi Z, Buonfrate D, Montresor A *et al*. *Strongyloides stercoralis*: a plea for action. *PLoS Negl Trop Dis* 2013;7(5): e2214.
2 Buonfrate D, Requena-Mendez A, Angheben A *et al*. Severe strongyloidiasis: a systematic review of case reports. *BMC Infect Dis* 2013; 13:78.
3 Henriquez-Camacho C, Gotuzzo E, Echevarria J *et al*. Ivermectin versus albendazole or thiabendazole for *Strongyloides stercoralis* infection. *Cochrane Database Syst Rev* 2016;(1): CD007745.
4 Pan D, Arkell P, Stone N, Delayed *Strongyloides stercoralis* hyperinfection syndrome in a renal transplant patient with *pneumocystis jirovecii* pneumonia receiving high-dose corticosteroids. *Lancet*. 2019; 393(10180):1536.
5 Asundi A, Beliavsky A, Liu XJ *et al*. Prevalence of strongyloidiasis and schistosomiasis among migrants: a systematic review and meta-analysis. *Lancet Glob Health* 2019;7(2):e236–e248.
6 Glenn K, Lindholm DA, Meis G, . Case report: a case of recurrent *Strongyloides stercoralis* colitis in a patient with multiple myeloma. *Am J Trop Med Hyg*. 2017;97(5):1619–22.
7 Repetto SA, Ruybal P, Batalla E *et al*. Strongyloidiasis outside endemic areas: long-term parasitological and clinical follow-up after ivermectin treatment. *Clin Infect Dis* 2018;66(10):1558–1565.