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Poster presentation

IL-10 administration reduces the severity of the CNS inflammatory reaction associated with treatment of murine *Trypanosoma brucei brucei* infection

Jean Rodgers*[1], Barbara Bradley[1] and Peter Kennedy[2]

Address: [1]Division of Infection and Immunity, University of Glasgow Veterinary School, Glasgow, G61 1QH, UK and [2]Department of Neurology, University of Glasgow, Southern General Hospital, Glasgow, G51 4TF, UK

Email: Jean Rodgers* - Jean.Rodgers@vet.gla.ac.uk

* Corresponding author

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Background

Human African trypanosomiasis (HAT) is caused by *Trypanosoma brucei rhodesiense* or *T.b. gambiense*. Infection with either parasite is fatal if untreated. The disease has 2 clinical stages, the early-stage where the parasites proliferate in the blood and lymph and the CNS-stage where the parasites establish within the CNS. The only effective drug for treatment of both forms of CNS-stage trypanosomiasis is melarsoprol. Its use can cause the development of a post-treatment reactive encephalopathy (PTRE) characterised by a severe meningoencephalitis with infiltration of lymphocytes, macrophages and plasma cells. Astrocyte and microglial activation are also apparent. Various hypotheses exist regarding the pathogenesis of the PTRE. Recent evidence indicates that the balance of cytokines within the CNS may play a role in regulating the development of the PTRE and that IL-10 helps to protect the CNS from inflammatory pathology following early CNS invasion. This study investigates the therapeutic potential of IL-10 in a murine model of CNS-stage HAT.

Methods

Two groups of CD-1 mice were infected with 2×10^4 *T.b. brucei* (GVR35/C1.8) parasites. One group was given 4 ug of IL-10 daily by intraperitoneal injection for 14-days beginning on day 17 post-infection. Both groups of mice were treated with diminazene aceturate on day 24 post-infection to precipitate a severe meningoencephalitis. The animals were killed on day 31 post-infection and the brain removed for histological evaluation using a neuropathological grading scale. Control groups, consisting of uninfected animals treated in an identical manner to the experimental animals, were run in parallel with the infected mice. Throughout the regimen all animals were assessed clinically using a visual assessment scale.

Results

We have observed that both infected groups exhibit a significantly ($p = 0.0285$, $p = 0.0009$) worse clinical picture than uninfected mice [(mean ± SE) 0.00 ± 0.00] irrespective of IL-10 administration. No clinical difference ($p = 0.6486$) was apparent between infected animals given IL-10 (1.659 ± 0.396) and those not given IL-10 (1.205 ± 0.319). However, neuropathological grading demonstrates that IL-10 administration following infection significantly ($p = 0.0229$) reduces (3.125 ± 0.248) the severity of the CNS inflammation compared to animals that did not receive IL-10 (3.875 ± 0.125). Infected groups of mice had significantly ($p < 0.0001$) higher neuropathological scores than uninfected controls (0.00 ± 0.00).

Conclusion

The results of this study highlight IL-10, as a potential adjunct to chemotherapy, through inhibiting the development of the PTRE.

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