Pathogenesis of restricted movements in trichinellosis: An experimental study.

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Trichinellosis is a zoonosis acquired by the ingestion of insufficiently cooked pork meat containing the encapsulated larvae of *Trichinella spiralis*. Trichinellosis is presented with myalgia which affects various muscle groups; its intensity is usually related to the severity of the disease and may cause restriction of joint movement. However, joint pain in the course of trichinellosis could not be explained entirely by myositis. This study investigated the other possible causes of restricted movements of joints in animal model. We found that the histopathological changes in the joints of *T. spiralis* infected rats were in the form of inflammatory cellular infiltrates and ulceration in the synovial membrane with degeneration and ulceration of the articular cartilage. Immunohistochemical examination of the joints revealed the presence of *T. spiralis* local antigen or immune complex deposited in the synovial membrane. Leukocytosis and eosinophilia were observed throughout the experimental period but eosinophil level declined slowly but still elevated. In conclusion, the restricted movements during the course of trichinellosis seem to be not only due to direct invasion of muscles by the encapsulated *T. spiralis* larvae but also due to immune complex deposition in the joints.
Toxocara-induced hepatic inflammation: Immunohistochemical characterization of lymphocyte subpopulations and Bcl-2 expression
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Toxocariasis is a soil-transmitted helminthic disease due to infection of humans by larvae of *Toxocara canis* (*T. canis*). It is one of the most commonly reported zoonotic infections in the world. The aim of this study was to characterize the key immune cells and activity of Bcl-2 in hepatic inflammation during the course of experimental infection by *T. canis*. Mice experimentally infected with *T. canis* were divided into two groups: mice with primary infection by *Toxocara*, and those infected after sensitization by *Toxocara* excretory–secretory antigen. CD4+, CD8+, and Bcl-2-expressing T lymphocytes were identified in the liver by immunohistochemistry at different durations post-infection. Recruitment of CD4+ and CD8+ T lymphocytes within the inflammatory reaction in the liver was observed, with difference in count and localization. These cells were detected within and around *Toxocara*-induced granulomas as well as in isolated inflammatory foci in the portal tracts or within the hepatic parenchyma. The antiapoptotic protein Bcl-2 showed no significant change at different periods post-infection. On the other hand, immunization of mice with *Toxocara* excretory–secretory antigen prior to experimental infection caused earlier and more pronounced recruitment of CD4+ and CD8+ T cells to the liver and enhanced expression of Bcl-2. Moreover, CD8+ cells became more diffuse within the inflammatory infiltrate. These results suggest a dynamic change in key immune cells according to the duration of infection as well as the immune status of the host.
Interactions between *Trichinella spiralis* infection and induced colitis in mice

Inflammatory bowel disease (IBD) is a chronic relapsing inflammation afflicting any part of the bowel wall as a result of a deregulated and inappropriate immune response. In recent years, experimental and clinical evidence has demonstrated that infection with parasitic worms could protect hosts from IBD. The aims of this study were to determine if the underlying mechanism of the host immune regulation inherent to *Trichinella spiralis* infection involves Foxp3-expressing regulatory T cells, and to gain insight about time-related interactions between intestinal nematode infection and induced colitis using an experimental model for ulcerative colitis. Mice were experimentally subjected to acetic acid-induced colitis, which was either preceded or followed by *T. spiralis* infection. Assessment of colitis was done by histopathological examination of the colon and determination of pentraxin 3 levels. Immunohistochemistry was done for demonstration of Foxp3-expressing regulatory T cells in colonic tissues. It was evident that *T. spiralis* infection ameliorated the severe inflammation induced by acetic acid, evidenced by amelioration of histopathological changes and diminution of pentraxin 3 levels. The amelioration was more pronounced when *T. spiralis* infection preceded the induction of colitis. Regarding the immunohistochemical staining of regulatory T cells, *T. spiralis* infection induced recruitment of Foxp3-expressing regulatory T cells to areas of inflammation. In conclusion, *T. spiralis* regulatory mechanism can improve inflammation of the colon through the ‘inflammatory–regulatory’ axis. Finally, it would be of great importance to apply these results to the development of new therapeutic approaches for the treatment of ulcerative colitis.
Trichinella spiralis immunomodulation: an interactive multifactorial process.
Dalia S. Ashour

Many epidemiological data support the postulate that infection with helminths might provide some protection against allergic and autoimmune diseases. Hence arises the concept that helminths strongly influence the immune system and enable protective pathways against these hyperimmune-associated disorders. This review discusses how Trichinella spiralis can make the immune system smarter in dealing with hyperimmune-associated disorders. T. spiralis possesses the capacity to direct the immune system towards a mixed Th1/Th2 phenotype with predominance of Th2 response, or it may interfere with dendritic cell maturation, induce the alternatively activated macrophages and elicit the regulatory arm of the immune response via Treg or regulatory B cells.
Heterophyiasis is an intestinal disease that remains endemic in many parts of the world, particularly the Nile Delta of Egypt and Southeast Asia, yet the populations at risk of infection expand throughout the world. The main histopathological feature of infection is villous atrophy, but the underlying factors are not well understood. Apoptosis of the villous epithelial cells was previously reported to be enhanced during intestinal parasitic infections; however, the role of *Heterophyes heterophyes* on enterocyte apoptosis was to be explored. Therefore, intestinal sections from mice experimentally infected with *H. heterophyes* were studied histopathologically and immunohistochemically for caspase-3 and NF-κB and compared to non-infected control mice. Atrophic villi covered by poorly differentiated epithelial cells were observed in the 2nd week post-infection. Also, we noted marked hyperplasia of the intestinal crypts with abundant inflammatory cellular infiltrate in the lamina propria, as well as apoptosis of cells lining the intestinal villi. Both caspase-3 and NF-κB showed positive staining in the intestinal epithelial cells with varying grades of intensity over the length of infection. Caspase-3 expression rose at the 2nd week p.i. then decreased over time, whereas NF-κB expression showed progressive increase throughout the weeks of infection. In conclusion, caspase-3 activation may be an important factor in the apoptotic pathway in early heterophyiasis, and, on the other hand, NF-κB seems to play a role in protecting the intestinal cells from excessive apoptosis. These observations may help open new avenues for tissue protective therapies that avoid or control the deleterious processes of apoptosis in various inflammatory conditions.
Inflammation, Oxidative Stress and L-Fucose as Indispensable Participants in Schistosomiasis-Associated Colonic Dysplasia
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Background: Schistosomiasis is a parasitic disease causing chronic ill health in humans with a serious consequences for socio-economic development in tropical and subtropical regions. There is also evidence linking Schistosoma mansoni to colonic carcinoma occurrence. The aim of this study was to evaluate some inflammatory and oxidative stress biomarkers, as well as L-fucose as linkers between intestinal schistosomiasis and colonic dysplasia development in mice. Materials and Methods: This study was conducted upon 80 mice that were divided the control group (10 non infected mice) and infected group which was subdivided into 7 sub-groups (10 mice each) according to the time of sacrification in the post infection (p.i.) period, 10 mice being sacrificed every two weeks from 6 weeks p.i. to 18 weeks p.i. Tumor necrosis factor alpha (TNF-α), inducible nitric oxide synthase (iNOS), and pentraxin 3 (PTX3) levels were estimated by immunoassay. The L-fucose level, and thioredoxin reductase (TrxR) and lactate dehydrogenase (LDH) activities were also evaluated in colonic tissue. Results: The current study revealed statistically significant elevation in the studied biochemical markers especially at 16 and 18 weeks p.i. The results were confirmed by histopathological examination that revealed atypical architectural and cytological changes in the form of epithelial surface serration and nuclear hyper-chromatizia at 14, 16 and 18 weeks p.i. Conclusions: inflammation, oxidative stress and L-fucose together may form an important link between Schistosomal mansoni infection and colonic dysplasia and they can be new tools for prediction of colonic dysplasia development in experimental schistosomiasis.
Upregulation of Toll-like receptor 2 and nuclear factor-kappa B expression in experimental colonic schistosomiasis.
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Role of different mediators were described in the development of the granulomatous response and fibrosis observed in intestinal schistosomiasis. However, both Toll-like 2 receptor 2 (TLR2) and nuclear factor kappa B (NF-κB) have not yet been investigated in intestinal schistosomiasis. This study aimed to characterize the role of TLR2 and NF-κB in the pathogenesis of intestinal schistosomiasis. Experimental animals were divided into two groups; group I: non-infected control group and group II: mice infected subcutaneously with S. mansoni cercariae. Colon samples were taken from infected mice, every two weeks, starting from the 6th week post infection (PI) till 18th week PI. Samples were subjected to histopathological and immunohistochemical studies. Colon of S. mansoni infected mice showed histopathological changes in the form of mucosal degeneration, transmural mononuclear cellular infiltration and granulomas formation. Immunostained sections revealed significant increase in TLR2 and NF-κB positive cells in all layers of the colon, cells of the granuloma and those of the lymphoid follicles 10 weeks PI. All these changes decreased gradually starting from 12 weeks PI on wards to be localized focally at 18 weeks PI. In conclusion, recruitment and activation of inflammatory cells to the colonic mucosa in intestinal schistosomiasis are multifactorial events involving TLR2 that can trigger the NF-κB pathways. Hence, down-regulation of both TLR2 and NF-κB could be exploited in the treatment of colonic schistosomiasis.
Infectivity of Ivermectin-Treated *Trichinella spiralis* Larvae: A New Challenge for Control
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**Background:** Despite veterinary public health efforts to control trichinellosis, the disease has re-emerged in the past 10-20 years. Although ivermectin (IVM) achieves high efficacy in trichinellosis, the possibility of disease transmission to other hosts is still present. **Objective:** Our goal was to determine the efficacy of IVM on the subsequent infectivity of *T. spiralis* larvae following prior exposure to treatment, achieved by parasitological and biochemical studies of the intestinal phase in experimental animals. **Material and Methods:** In this two-phase study, *T. spiralis*-infected mice were first treated with IVM at 5 and 10 day post infection (dpi), and larvae collected from these mice at 35 dpi were used to infect phase two naïve mice. In phase two, worm burdens and larval counts, expression levels of interleukin-1β (IL-1β) and epithelial neutrophil activating peptide 78 (ENA-78), level of vasoactive intestinal peptide (VIP) and protein carbonyl (PCO), and activities of myeloperoxidase (MPO) and superoxide dismutase (SOD) enzymes were assessed in intestinal tissues of mice. **Results:** In phase two, we found that IL-1β and ENA-78 mRNA expression levels were lower in group of mice infected by IVM treated larvae 5 dpi. This group also showed the lowest levels of VIP and PCO, as well as the lowest activities of MPO and SOD enzymes, and the lowest adult and larval counts. **Conclusion:** IVM appears to affect the infectivity of *T. spiralis* larvae. This effect was more pronounced when IVM was given early in the infection. Based on the results of our studies, IVM may be useful as a drug in both the treatment of current infection and control of subsequent infections with *T. spiralis*. 