Hymenolepis nana
A case report of a perfect IBD camouflage warrior
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Abstract
Rationale: There is evidence that parasitic helminths can ameliorate colitis in animal models and humans. Although infections with Hymenolepis sp. are clinically benign, the immunomodulatory interactions between host and parasite are largely unknown.

Patient concerns: In this study we examined the intestinal mucosa of an adult asymptomatic patient harboring adult and larval dwarf tapeworms (Hymenolepis nana) who underwent surgery for an unrelated reason.

Interventions: Routine histology and immunohistochemistry were performed to characterize the host’s response to the parasite. Parasitic DNA was sequenced to identify the tapeworm species.

Diagnoses: Morphological and immunohistochemical studies showed a nearly complete absence of an anti-parasite host immune response. The outer surface of the parasite also showed prominent cross-reactivity with various tested leukocyte antigens. Our findings closely resemble experimentally obtained data from the H. diminuta-infected rat at the state of persistent colonization.

Outcomes: Cross-reactivity of parasite-borne molecules with anti-human-leukocyte antibodies indicates a potential functional role in active modulation of the host’s immune response.

Lessions: We believe that better understanding of the host-cestode interaction will certainly extend our knowledge on auto-aggressive disorders such as inflammatory bowel disease and might provide potential treatment options.

Abbreviations: IBD = inflammatory bowel disease, IRB = institutional review board.

Keywords: alternative treatment, chronic inflammatory bowel disease, hymenolepis nana, IBD, parasite

1. Introduction

Cestode infections are widespread within the animal kingdom in most vertebrate and arthropod species, including humans.[1] These infections are often asymptomatic in the definitive host and even the encysted larval stages in the appropriate host invoke only sparse immunological responses.[2] From an evolutionary stand point, it makes sense to the parasite to harm the definitive host as less as possible. A particularly successful example in these terms is Hymenolepis nana. It is responsible for the majority of tapeworm infections in humans with estimated 50,000,000 to 75,000,000 carriers worldwide.[3] In spite of the large number of carriers, little clinical impact is caused by this silent passenger in the digestive tract. This anatomic hallmark underlines their extreme specialization. Besides prevention of cestode-induced zoonoses such as echinococcosis, the primary reason for cestode research is their potential for therapeutic intervention against autoimmune and autoaggressive disorders such as inflammatory bowel disease (IBD). Since it is known that parasitic helminth infections have the ability to ameliorate colitis,[1] the elucidation of the responsible immunomodulatory mechanisms bears the potential to identify new molecular targets and offer new treatment options for patients with IBD.

Hymenolepis spp are well-established models in cestode research, specifically, the rat tapeworm H. diminuta.[10] Due to obvious technical limitations, rodents are currently the mainstay for experimental mammalian cestode research.[14] To our knowledge, there are no studies that have analyzed the immune response in humans against H. nana.

In this study, we analyzed a Meckel’s diverticulum which was removed from an immunocompetent 40-year-old female patient undergoing surgery for acute appendicitis that harbored H. nana. We used this opportunity to study the human immune response to H. nana.

2. Ethics statement

All specimens used in this study were examined for diagnostic reasons and therefore, an institutional review board approval was not required.

3. Case report

Hematoxylin and eosin-stained sections of the Meckel’s diverticulum showed adult intestinal tapeworms. Proglottids, attached to a scolex with suckers and hooklets, were found in the
intestinal lumen, as well as a number of free eggs. The protoscolices within the embryonated eggs showed up to 6 hooklets (Fig. 1A–F). Serial sections revealed an encysted worm larva within the mucosa (Fig. 1A). A polymerized chain reaction (PCR) with standard PCR conditions and a cestode-specific primer pair within 18s rDNA (forward primer 5’ TCAGCTATGGTTTATTGGATCA3’; reverse primer 5’ CCGACTGC-GATCTGTAACAA3’; product size 184bp) was performed to confirm the diagnosis of infection with Hymenolepis spp. Routine histology and immunohistochemistry (Table 1) were performed to characterize the host’s response to the parasite. There was no inflammatory change, specifically eosinophilia, in the tapeworm-infected patient as compared to a series of 6 control Meckel’s diverticula. Inspection of the cestodes revealed no changes associated with rejection by the host such as loss of normal architecture, edema, mixed cell infiltrate, or areas of epithelial erosion.[4] The host immune reaction to the parasite was assessed by immunohistochemical staining for T and B lymphocytes as well as macrophages. The larva was surrounded by CD3-positive T lymphocytes. Besides this, few CD68-positive macrophages were sparsely scattered around the larva. No changes were observed in the diverticular mucosa adjacent to the adult tapeworm. The brush border of the tegument stained unexpectedly positively with an anti-CD68 antibody and the tegument cells showed cytoplasmic positivity with an anti-CD3 antibody. Embryos with condensed and small nuclei—indicating a late stage of development—stained positively with an anti-CD4 antibody. Other embryos with less condensed nuclei, located within the same range of proglottids, stained positively with an anti-CD8 antibody. No parasitic structures showed positive staining with an anti-CD20 antibody (Fig. 2).

4. Discussion

The results suggest structural similarity of parasite components to certain host proteins. Alternatively, absorption or uptake of host molecules or fragments thereof could have taken place that might explain the cross-reactivity within the tegument but not the embryos.[5]

The cross-reactivity of key players in the host’s initial immune response and parasite-borne molecules indicates a potential functional role in active modulation of the host’s immune response. This reflects the perfect camouflage of H nana at the level of conventional histology and immunohistochemistry. The IBD hygiene hypothesis connects the high hygienic standards and the absence of macroparasites to the increased incidence of IBD.[6] Experimental studies and clinical trials[7] with living helminths have shown the beneficial effect of parasites in such disorders. Thus, it is tempting to therapeutically administer further species like H nana, which can generally be left untreated due to their asymptomatic persistence in the host while they are invasive enough to modulate the microenvironment within the intestinal mucosa and have an effect on IBDs. Thus, we suggest that this predominantly indolent human-specific macroparasite may be a candidate to be administered in selected, immunocompetent patients suffering from IBD, even though there are few reports about severe complications of H nana infections in HIV patients and malnourished children.[8]

Table 1

| Antigen | Manufacturer | Dilution | Clone | Antigen retrieval program |
|---------|--------------|----------|-------|--------------------------|
| CD3     | Novocastra   | 1:100    | LN10  | H2 (20/100)              |
| CD4     | Novocastra   | 1:40     | 1F6   | H2 (20/100)              |
| CD8     | Novocastra   | 1:40     | 4B11  | H2 (30/95)               |
| CD20    | Dako         | 1:600    | L26   | H2 (20/95)               |
| CD68    | Dako         | 1:100    | PG-M1 | E1 (5)                   |

The antibody stains were performed on a Bond III (Leica Biosystems, Germany) automated immunostaining system. Kits were used according to the manufacturer's specifications.
Figure 2. Morphology and immunohistochemistry of cestode in Meckel’s diverticulum. (A) Column “adult” represents a cross-section through mature proglottids and adjacent intestinal mucosa. There is cross-reactivity between most of the antibodies and parasite structures. Column “larva” shows a lymph follicle with an intramucosal larva. There is no notable difference in goblet cell population between the samples. Column “reference” shows intestinal mucosa from another diagnostic specimen of a Meckel’s diverticulum. (B) Adult tapeworms, scolex, (C–E) proglottids, (F and G) neck region of 2 individuals. Scale and objective: A: column “adult”: 20, bar 100 μm, columns “larva”, “reference”: 10 ×, bar 100 μm; B–D: 40 ×, bar 50 μm; E: 10 ×, bar 200 μm; F and G: 20 ×, bar 100 μm.
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