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Postinfectious Syndromes and Long-Term Sequelae after *Giardia* Infections

Appendix

Other Complications of Giardiasis

Possible Rare Complications of Giardiasis

In addition to the post-infection sequelae described above, there have been case reports describing rare complications involving the heart and pancreas. At least three individuals have been diagnosed with giardiasis-associated myocarditis (*1*–*3*). Two had extensive eosinophilic infiltration in the myocardium (*1*,*2*). As *Giardia* is unable to invade the intestinal mucosa, the authors proposed that these illnesses may have been related to an autoimmune-mediated process in which the immune system attacked the myocardium because of antigenic mimicry (*1*–*3*). Of note, all three cases of myocarditis occurred in the setting of an active *Giardia* intestinal infection. It is unclear whether there may be long-lasting autoimmune implications that could follow treatment and resolution of giardiasis infections.

Other authors have suggested a possible association between giardiasis and gastrointestinal cancers. Although this could be coincidental, several cases describe concurrent giardiasis and new diagnoses of pancreatic neoplasms (*4*–*7*). There is not yet a clear understanding of how the two conditions may be related. It is possible that *Giardia* infections play a role in carcinogenesis, that patients with undiagnosed neoplasms may be at increased risk of giardiasis, or that symptomatic giardiasis infections can lead to incidental detection of existing gastrointestinal cancers.

Treatment-Refractory Giardiasis

When discussing IACCIs following giardiasis, particularly PI-IBS and PI-FD, it is important to consider conditions that can occur even after treatment is administered. While most cases of acute giardiasis resolve spontaneously after two to six weeks of symptoms or sooner

with treatment, infections can persist and are very challenging to treat. Some individuals with suspected PI-IBS may have treatment-refractory giardiasis, as symptoms can mimic one another (*8*). One study followed 124 persons who had one to four courses of conventional treatment with metronidazole yet continued to experience gastrointestinal symptoms. The cohort underwent duodenal biopsies and blood and stool tests. Of those followed, 32% (n = 40) were diagnosed with treatment-refractory giardiasis (*9*). Other studies have identified young age (< 2 years), lower metronidazole doses for initial treatment, comorbidities such as HIV infection, and travel to endemic countries as possible risk factors for treatment-refractory giardiasis (*10*–*12*). Treatment strategies for metronidazole-refractory giardiasis include the use of another single agent (e.g., nitazoxanide or paromomycin) or combination therapy, using two drugs with different mechanisms of action (*13*,*14*). Several studies support quinacrine as an effective single agent, achieving cure in up to 100% of individuals with treatment-refractory giardiasis; however, challenges with quinacrine access and an unfavorable side effect profile often limit its clinical use (*15*–*17*).

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