Raccoon on a Friday Afternoon

A Case Report

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Introduction

In both veterinary and human medicine, there are some diseases that are neglected, underrepresented, or under-studied. This may be true even for infectious organisms that have been known to medicine for many years. This paper examines one uncommonly diagnosed parasite, found in its natural host and range, and seeks to present a straightforward and thorough discussion of its natural history, pathophysiology, diagnosis, and treatment, as well as its relevance in domestic veterinary species.

History and Gross Presentation

"Frat Raccoon," as he is officially labeled, or Necropsy Case #C17-01076, was an adult male raccoon discovered outside a fraternity house on Fraternity Row at Mississippi State University. The raccoon was noted to be acting odd, and onlookers saw that he was limping and suspected a broken leg. The appropriate authorities were identified, and the MSU Campus Police gathered up the raccoon and delivered him to Mississippi State University Animal Health Center. A humane wildlife euthanasia was performed without a detailed physical examination, as is standard for wildlife presented for euthanasia. A necropsy was performed to determine the cause of death.

C17-01076 was identified as a young adult male raccoon. On external examination, the distal rear limbs were markedly swollen with pitting edema, and although no fractures could be identified, several small, superficial abrasions were discovered on the dorsal surfaces of his hind

feet. A wound on the spine showed moderate hemorrhage in the muscular and subcutaneous planes, and a fracture was identified through the spinous process of vertebrae L3.

The thoracic cavity contained some 50ml of dark red fluid. The lungs were wet and dark red in color. Thousands of pinpoint nodules, about 1mm in diameter, were disseminated throughout the lungs, lending the parenchyma a grainy texture. The heart was markedly distended through all chambers - the ventricles were especially distended and thin-walled.

The abdomen was pendulous, and a fluid wave was noted prior to opening the abdominal cavity. The abdominal cavity contained some 200 mls of clear fluid. The small intestines were corrugated and firm, with small nodules palpable through the serosa. The liver had rounded margins and a firm, grainy, fibrous texture. The mesenteric veins were dilated and tortuous. When opened, multiple worms approximately 3-5 mm in length were removed from the lumina of the mesenteric vessels. Lymphatics were similarly dilated, and mesenteric lymph nodes enlarged.

The rest of the gross examination was unremarkable.

Natural History

Schistosomiasis describes disease caused by internal parasites in the trematode superfamily Schistosomatoidea. Outside of North America, schistosomes are responsible for the infection of domestic animals, wildlife, and humans - some 600 million people are at risk in warm, water-rich

regions of 74 developing nations across the world (1). However, in North America, the only native schistosomes are *Heterobilharzia americana*, which causes infection in native mammalian wildlife and domestic animals, and several species of waterfowl schistosomes found in wild migratory birds. *H. americana* is currently the only North American schistosome relevant in veterinary care of domestic animals (2).

The life cycles of all schistosome species described in literature are similar. These parasites make use of a single intermediate host, setting them apart from other trematode species that use secondary intermediate hosts. For schistosomes, water-dwelling lymnaeid snails are the intermediate host of choice. Individual species of schistosomes utilize specific snail species, with the range of the host snail naturally defining the range of the parasite. For *H. americana,* this snail is commonly *Lymnaea (Galba) cubensis*, a freshwater aquatic snail of tropical and sub-tropical regions extending along the Gulf of Mexico and up the Carolinas along the Atlantic shore. Similar species related to *L. cubensis* can also act as effective intermediate hosts, muddying the previously-defined range of the parasite as the snails spread into new waters. (2) Wherever the appropriate snail species thrives and susceptible mammalian hosts shed waste near waterways, so can schistosomes achieve their life cycle.

Eggs of *H. americana* hatch quickly in contact with fresh water, which releases the free-swimming miracidium stage (2). Miracidium burrow through the soft mantle of host snails and encyst in sporocysts, which split multiple times into daughter sporocysts as they develop cercariae. Roughly four weeks later (1), cercariae emerge from the snail to penetrate the skin of a

suitable mammalian host - prominently, raccoons, rabbits, and bobcats, although they have also been identified in dogs, horses, and a llama (2). All schistosome cercariae are free-swimming, and emerge from the egg with a tail to maneuver them through the water in search of a mammalian host. Cercariae appear to find prospective hosts largely by chance, although in the case of human schistosome larvae, they exhibit positive tropism toward arginine, an amino acid present on the surface of the skin. Once in contact, cercariae penetrate the epidermis in about 30 minutes with a combination of proteolytic enzymes and physical friction, losing their tails in the process. (1)

After entering through the integument, the immature schistosomules migrate to the lungs, and finally to the liver. Development in the liver is brief, and at maturity, flukes reside in the mesenteric veins. Adult schistosomes are sexually dimorphic, which is unique among trematodes, with adult females held in a specialized “gynecophoric canal” along the ventral aspect of the larger male (1). Eggs produced are more or less spherical, and lack either a spine (as in most schistosome eggs) or an operculum (as seen in the eggs of other trematode species), which is helpful for identification and differentiation (2). Eggs are released into the lumen of the mesenteric veins to enter the intestines and shed in the feces, and upon contact with fresh water, will hatch to continue the uncomplicated schistosome life cycle (2). In total, the prepatent period from skin penetration to egg production lasts 5-8 weeks (1).

Pathophysiology

Schistosome ova are deposited by the female directly into the vessels, and from the vessels must burrow through the small intestine to reach the lumen and outside environment (2). Eggs are thought to travel through tissue using proteolysis, likely in a similar manner to the method used by cercariae to enter the epidermis (4). As with many aspects of schistosome biology, egg migration is in need of further study. In human infections, it is thought that about ⅔ of all eggs fail to reach the intestinal lumen (1). Similarly, in some animal cases, schistosome eggs seem to disperse around the body and lodge in other organ systems during their quest to reach the small intestines. Common sites for wayward ova in raccoons are the peritoneal viscera, like the pancreas and liver, but they are also frequently found in the lungs (3). The spread of eggs throughout the body is known as disseminated schistosomiasis.

Three Louisiana raccoons necropsied with evidence of naturally-occurring *H. americana* infection showed lesions that mainly affected the liver. Livers were generally firm and fibrous, with white granular foci, similar to those identified in C17-01076. Reproductive pairs of the parasite were removed from the mesenteric veins of all three animals. On microscopic evaluation, the ova seemed responsible for the majority of the granulomatous tissue damage. Schistosome ova were identified on histology of the liver, small intestines, pancreas, lungs, and vessels. Ova were surrounded by granulomatous reactions, characterized by collagenous isolation of the eggs from host tissue, and eosinophilic and lymphocytic infiltration. All three of the raccoons showed evidence of infection with several other parasite species, mostly nematodes, which is to be expected in wildlife necropsy. (3)

Several anine infections with *H. americana* are documented. Cases of canine disseminated schistosomiasis posted for necropsy have lesions similar to those found in raccoons. One dog necropsied grossly exhibited the characteristic pale, shrunken liver with pinpoint white foci, and abundant abdominal free fluid. Clusters of *H. americana* ova were identified histologically in the liver, lungs, pancreas, and small intestines, surrounded by the classic lymphoplasmacytic granulomatous reaction. The ova present in this dog were all calcified, especially so in the small intestine, where mineralization could be appreciated grossly and radiographically. Tissue mineralization appears to be a characteristic of chronic infection. This dog was euthanized due to its poor condition and poor prognosis, and although schistosomiasis was not considered ante-mortem, the disseminated granulomatous disease associated with ova-tissue interaction is thought to be the cause of its clinical signs. (4)

A clinical case described in a llama in Texas had clinical signs of bronchopneumonia and dilated cardiomyopathy prior to humane euthanasia. On necropsy, it exhibited thousands of 2-4mm granulomatous nodules on the lung surface and liver, as well as several in the heart. Ova were visible histologically from tissues of all major organs, and *Heterobilharzia americana* infection confirmed with polymerase chain reaction. (5)

The gross lesions described above in C17-01076 are classic when compared to those found in the three Louisiana raccoons, the dog, and even the llama. Histologically, trematode eggs were found prominently in the lung parenchyma, pancreas, mesenteric lymph nodes, and all layers of the small intestines. The ova were encircled by rings of fibrous connective tissue. Lymphocytes

and reactive macrophages, along with a few eosinophils, infiltrated the tissues surrounding the ova. Some ova clusters showed evidence of early tissue mineralization. Eggs were present in the alveoli and occluded pulmonary arteries, forming thrombi. Adult trematode pairs were removed from the mesenteric veins during gross dissection, and adult males and pairs were visible histologically in multiple mesenteric veins. One pulmonary artery also contained an adult male schistosome. Comparatively, the liver contained only a moderate amount of schistosome eggs embedded in the hepatic parenchyma. While inflammatory cells were present, the central fibrosis, thrombi, and hepatic cell loss evident on histopathology of the liver is not entirely attributable to the parasites, but rather our raccoon's diseased heart.

There are two notable differences between C17-01076 and the above-documented natural raccoon infections. The three raccoons examined above had similar hepatic fibrosis and granulomatous reactions, but all three exhibited small, shrunken livers. C17-01076 exhibited marked hepatomegaly, with rounded liver margins that extend well past the costochondral arch. This change can be attributed to the second difference between C17-01076 and other cases - his heart. While cardiac pathologies were not noted in the other raccoons or in dog cases, C17-01076 exhibits a heart dilated in all chambers. The hepatomegaly, clear abdominal fluid, and dependent edema of the rear limbs are likely evidence of congestive heart failure from severe myocarditis, but seem to be more or less unrelated to the schistosomes or their eggs. Grossly, there is no clear-cut cause to the heart disease. However, in wildlife necropsy, infection with more than one parasitic species is to be expected - and microscopic examination found that second parasite in our raccoon's heart. Schizonts and merozoites of an unidentified protozoal organism were found

clustered in the myocardium. Cardiomyofibers were degenerate and edematous and infiltrated by large numbers of lymphocytes and macrophages. The myocardium was thin, consistent with dilated cardiomyopathy. (7)

Frat Raccoon's finders described odd behavior and limping. While some lethargy and malaise can be attributed to his generalized state of disease, we also suspect that he was hit by a car or another vehicle not long before his euthanasia, causing the small abrasions on his hind limbs and the fracture and hemmorhage associated with the L3 vertebrae.

Diagnostics

Diagnosis is straightforward when eggs are shed in the feces. Sedimentation in 0.85% sodium chloride solution is an important tool, since eggs hatch rapidly when in contact with fresh water. If allowed to hatch, miracidia can also be identified microscopically (2). However, eggs are shed sporadically, and may shed less often as infection continues into chronic stages, as ova lodge in tissues rather than being voided in the feces (1). While diagnosis via fecal sedimentation is possible, it is not a perfect tool, as infections will be missed when patients are not actively shedding eggs. Polymerase chain reaction of sampled intestinal tissue is a straightforward and accurate method of diagnosis. Eggs are easily identifiable histologically, so an ideal biopsy sample would include enough tissue for sectioning as well as PCR. (4)

The most difficult aspect of diagnosing *H. americana* in canine or other patients is that veterinarians must be looking for it. While annual fecal flotations are performed on many dogs,

schistosome ova will not be identified without sedimentation, so even actively shedding animals will go undiagnosed. The most common clinical signs are nonspecific signs of disease such as vomiting, diarrhea, and lethargy. Blood work may be abnormal, but there is no pathognomonic formula for discovering *Heterobilharzia* on CBC and chemistry. However, about half of all documented canine cases have presented with hypercalcemia (6). In cases of severe granulomatous reactions, tissue may mineralize around ova, revealing pinpoint hyperechoic foci that are visible on abdominal ultrasound. On radiographs, mineralization may be visible along the intestines outlining ova trapped in granulomas as they attempt to reach the lumen (4).

With such nonspecific clinical signs, it can be difficult to justify an expensive PCR for a scarcely-diagnosed parasite. Rarely does hypercalcemia in dogs bring to mind parasitic causes, so veterinarians treating hypercalcemic patients may fall down the rabbit hole of endocrinopathies or neoplasia before *H. americana* is considered. Since *H. americana* is primarily found in the southeastern United States, it should be considered as a causative agent in dogs with nonspecific gastrointestinal signs and a history of visiting bodies of freshwater, and may be more suspect when hypercalcemia or tissue mineralization is identified. Interestingly, the patient profile identified by current literature is young adult, large breed dogs that spend most of their time indoors (8).

A PCR was not necessary on our raccoon, since both granulomatous ova and adult fluke pairs were beautifully visible histologically in multiple tissue sections. Immunohistochemistry was submitted in an attempt to identify the protozoal organism found in his heart, which was of

unclear origin when microscopically examined. Tests for *Toxoplasma gondii* and *Sarcocystis neurona*, two usual protozoal suspects in the southeast, returned negative. *Neospora* and *Trypanosoma cruzi* are two more protozoal considerations, but further testing was not performed due to scarcity of racoon-associated funds.

Treatment

Treatment is straightforward, provided the parasite can be identified. Common medications administered to canine patients include fenbendazole (40 mg/kg orally SID for 10 days) and praziquantel (25 mg/kg orally BID for 2-3 days), which can be given in separate treatments or concurrently (8). Historic treatments used appear to vary for both dose in mg/kg and period of treatment. Some dogs presented with confirmed cases of *H. americana* and hypercalcemia treated at Texas A&M University showed reversal to normocalcemia within a few days of treatment (6). Infections have been confirmed in horses and a domestic llama, but so far, no medical treatment has been described in these species - the llama was euthanized with no treatment, and infection seemed to be incidental and not causing primary disease in several infected horses (5, 10).

If *H. americana* is definitively diagnosed or even suspect based on clinical signs, repeat fecal sedimentation after the treatment period may be valuable in identifying elimination of adult flukes and efficacy of treatment. Eggs shed into a wet environment can rapidly hatch and re-infect other potential mammalian hosts, so animals that are actively shedding should be kept away from water sources, and their feces should be disposed of until shedding is no longer

evident in feces. Treatments for *H. americana* and other schistosomes (which are also treated with praziquantel) are adulticidal and will not eliminate the schistosomule stage. In human schistosome infections, breeding adult schistosome pairs are thought to live some 20-30 years (1).

With the rapid reversal of at least some clinical and diagnostic signs, it may not be uncalled for to initiate treatment while waiting on definitive results. Long-term clinical control and outcomes are not currently well-understood, especially since it can be difficult to diagnose infections in the first place. However, treatment with praziquantel and fenbendazole appears overall positive. The precise course of treatment is not well-described, so repeat fecal sedimentation, resolution of clinical signs, and favorable response to treatment are currently the most important considerations for resolution of disease.

Human Health

The cercarial stages of avian schistosomes present in waters of the Southeastern United States are well-known to cause cercarial dermatitis, or swimmer's itch. In bodies of freshwater and along Gulf Coast beaches, these avian schistosome cercariae penetrate aberrantly into human skin, and cause sensitization and a localized allergic immune response without any patent parasitic infection. Cercarial dermatitis is pruritic and uncomfortable, and can be temporarily unsightly, but ultimately is not harmful (9). While the full range of schistosome species capable of producing this response is currently not well-described, *H. americana* is thought to behave similarly to the avian schistosomes in this regard (1).

Outside of the United States, schistosomes cause much more human harm than just an irritating rash. As described above, populations of 74 nations are at risk for human schistosome infection. Damming of rivers and building of reservoirs for fresh water an agriculture allows snail species to proliferate, and infection spreads and becomes endemic in the area. The population most at risk for severe disease appears to be young men in their twenties, perhaps due to water recreation and agricultural pursuits. Both acute and chronic infections are problematic. Currently, there is no vaccine or preventative medication, and as with nonhuman patients, diagnosis is difficult and best achieved by fecal sedimentation in individuals actively shedding eggs (1). With the similarities between disease courses and treatments, comparisons between human and animal infections are valuable and should be kept in mind whenever schistosomiasis is considered in future cases.

Conclusion

Even in its home range in the southeastern United States, documented cases of *H. americana* are rare. With the associated vague clinical signs, it is understandable that fecal sedimentation, a PCR, and intestinal biopsy to search for trematode eggs are not at the forefront of every veterinarian's mind. For the time being, this parasite will likely remain under-diagnosed. However, it should not be unknown, and veterinarians within the Southeastern United States should seek to be aware and knowledgeable of the only mammalian schistosome found in North America.

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