Case Report: Molecular Diagnosis of Human *Taenia martis* Eye Infection

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Abstract. *Taenia martis*, a tapeworm harbored in the intestine of mustelids, is a rarely encountered zoonotic cysticercosis pathogen. The larval stage closely resembles the *Taenia solium* cysticercus, but the natural host and thus the epidemiology of the disease is different. We here report a human eye infection diagnosed molecularly in a previously healthy female German patient. The case represents the third human infection described worldwide; the two previous cases were also European, involving eye and brain.

INTRODUCTION

Cysticercosis, a zoonotic parasitic disease due to tissue invasion of larval *Taenia* species, is in the vast majority of human cases caused by the pork tapeworm *Taenia solium*.¹ However, other *Taenia* species with different reservoirs and epidemiology, such as *Taenia crassiceps* and *Taenia martis*, may also cause human cysticercosis, but much more rarely.^{2–5} The larval stages share a highly similar morphology, and they might be virtually indistinguishable on histological sections.⁶ Still, for prognosis, prevention, and detection of parasite reservoirs, the species responsible for human disease should be determined.⁶ We here describe a human eye infection with the marten tapeworm *T. martis*, which constitutes the third human infection with this tapeworm pathogen worldwide, and the second eye infection in Germany.

CASE REPORT

A 70-year-old female patient from northern Germany presented to an ophthalmologist with symptoms of floaters in her left pseudophakic eye in July 2015. As the symptoms worsened and visual acuity in her left eye dropped significantly to hand motion in August 2015, she was referred to the Department of Ophthalmology of the Regional Clinic Hannover. Here, she presented with intraocular inflammation and vitreous hemorrhage without fundus view in the affected eye. On ultrasound, a retinal detachment was disclosed and the patient was admitted to the hospital for intraocular surgery (vitrectomy). After removal of the vitreous hemorrhage a total retinal detachment with proliferative vitreoretinopathy could be seen. In the nasal mid periphery, a large retinal defect was present. After membrane peeling, injection of perfluorocarbon liquid, and drainage of subretinal fluid, a cyst-like structure was detected under the retina. The lesion was removed from the subretinal space through the existing retinal tear. Because of spontaneous movements of the “cyst” a larval parasite was presumed and extracted from the eye for further diagnostic work-up. The retina was finally reattached by fluid-/C₃F₈(15%)-gas-exchange and endolaser photocoagulation. The specimen was fixed in 100% ethanol and send to the Bernhard Nocht Institute for Tropical Medicine in Hamburg for laboratory examination. Macroscopi-

FIGURE 1. Histological section through the cystic tapeworm larva recovered from the patient's eye. The parasite's spongy tissue is surrounded by a ruffled tegument. Periodic acid-Schiff stain, original magnification $\times 10$.

cally, the 3-mm-long semi-translucent parasite had the appearance of a typical cestode larva. Tissue sections of the specimen showed a characteristic tapeworm tegument (Figure 1), and ophthalmological cysticercosis was diagnosed. Polymerase chain reaction targeting cestode cytochrome *c* oxidase subunit 1 (*cox*),⁷ 12S rDNA,⁴ and nicotinamide adenine dinucleotide-dehydrogenase subunit 1 (NAD1)⁴ was positive. After sequencing of the 418-, 461-, and 440-bp amplicons, basic local alignment search tool analysis (www.ncbi.nlm.nih.gov/blast) revealed 100% (*cox*), 99% (12S rDNA), and 99% (NAD1) nucleotide similarities, respectively, with the marten tapeworm *T. martis*. Ophthalmological cysticercosis due to the larval stage of *T. martis* was thus diagnosed. The highest sequence similarities were found with isolates from an unspecified intermediate host from Croatia and from *Myodes glareolus* rodents from Denmark (*cox*, GenBank numbers AB731758 and EU544553; NAD1, GenBank numbers AB731758 and EU544606) and for isolates from an unspecified intermediate host from Croatia and from a human eye infection in southern Germany (12S, GenBank numbers AB731758 and JX415820). Figure 2 shows a phylogram using *cox* sequences of the current northern German isolate from the patient and *T. martis* sequences retrieved from GenBank. The sequence of our isolate is

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FIGURE 2. Phylogram of the patient's *Taenia martis* isolate and sequences from GenBank (bootstrap consensus tree). The asterisks denote *T. martis* sequences from human infections. A multiple sequence alignment using parasite *cox* sequences was generated using MUSCLE. Poorly aligned and divergent positions were removed using Gblocks with the parameter settings $-t = d$, $-b1 = 6$, $-b2 = 6$, $-b3 = 8$, $-b4 = 5$, $-b5 = h$. The final alignment comprised 396 of the original 1,620 positions from 10 sequences. MEGA 6 was used for subsequent substitution model estimation as well as phylogenetic tree reconstruction. The evolutionary history was inferred by using the maximum likelihood method based on the Hasegawa–Kishino–Yano model. The tree inferred from 500 replicates is taken to represent the evolutionary history of the taxa analyzed. Branches corresponding to partitions reproduced in less than 50% bootstrap replicates are collapsed. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the maximum composite likelihood approach, and then selecting the topology with superior log likelihood value. The analysis involved 10 nucleotide sequences. Codon positions included were 1st + 2nd + 3rd + noncoding.

closest to a sequence of a cysticercus in *M. glareolus* rodent from neighboring Denmark. Serological analysis of the patient's blood did not demonstrate antibodies to related tapeworm larvae such as *Echinococcus granulosus*, *Echinococcus multilocularis*, and *T. solium*, as investigated by immunoblot and enzyme-linked immunosorbent assay.

The patient, a retired office worker, lives in a small village in a rural area west of the city of Hannover. Since 1972, together with her husband, she has inhabited an old half-timbered house constructed in 1860. They had never owned pets. Martens have frequently been seen on the premises, in the house itself and in the nearby village, littering and caus-

ing damage to cars and housing. Rodents are also ubiquitous. The patient and her husband had often worked in the garden, handling stuff of many kinds, and had grown vegetables. The patient had never removed marten feces herself, but had left the task to her husband. After surgery, the retina remained reattached, intraocular inflammatory reaction regressed, and corrected visual acuity eventually returned to 20/30 (Figure 3). Computed tomography and magnetic resonance imaging did not reveal any lesions in the brain or the abdomen. We nevertheless administered oral albendazole (400 mg, twice daily) for 7 days to treat any tapeworm larvae which might have been missed by imaging.

FIGURE 3. Left eye after surgical removal of subretinal *Taenia martis* cysticercus. (A) Close-up view showing conjunctival injections 4 weeks after vitrectomy. (B) Fundoscopy displaying retinal scar 8 weeks after fluid-gas-exchange and endolaser treatment. (C) Fundoscopy showing reattached macular area 8 weeks after vitrectomy.

DISCUSSION

Adult strobilar *T. martis* tapeworms inhabit the intestine of mustelids, which are their definitive hosts and which comprise martens, badgers, and weasels. Infective tapeworm ova are excreted with mustelid feces and contaminate the environment. Oral uptake of parasite ova by intermediate hosts, such as voles, muskrats, and other rodent prey for mustelids, in the natural life-cycle of the tapeworm leads to hatching of larva in their intestine. Subsequently, after blood-borne dissemination, cysticerci develop in pleural and peritoneal cavities. When the intermediate hosts fall prey to mustelids, the parasite's lifecycle is complete.⁸ Human infection with *T. martis*, where the human serves as dead-end intermediate host, is very rarely seen and only two cases have been reported so far.^{4,5}

In 2010, the first described human infection with larval *T. martis* had occurred in a 43-year-old woman living in a small village in southwest Germany.⁴ The patient had complained of flashing light sensations in her left eye, and a *T. martis* larva had been found subretinally similar to our case. After surgical excision, retinal detachment had occurred which had also been treated by pneumatic retinopexy. Visual acuity had been completely restored after surgical treatment and administration of albendazole and dexamethasone. The second human infection with *T. martis* had been diagnosed in 2012 in a 44-year-old woman in eastern France.⁵ A single lesion had developed in the left temporal lobe of the brain, causing aphasia and hemiparesis. The parasite had been removed surgically and an oral antiparasitic regimen with albendazole and praziquantel had been administered, leading to full recovery. Similar to our case, the parasite had been diagnosed molecularly in the previous two human infections after surgical removal. All three human cases were successfully managed clinically, combining surgery and antiparasitic chemotherapy, with favorable outcomes. In none signs of immunosuppression were present (which is in contrast to most larval *T. crassiceps* infections in humans³), but the larvae were found in special anatomical compartments, the eye and the brain, where immunological surveillance is naturally low and surgical removal is difficult. Whether these are sites of predilection for *T. martis* in humans remains uncertain at the moment. Especially in such anatomical sites, molecular parasite species identification should be attempted, as different larval tapeworm species (especially as the morphologically similar *T. crassiceps*) have different disease prognoses.⁶

In addition to human cases, two nonhuman primate infections with *T. martis* larvae have been described very recently in an Italian zoo⁹ and in a French primate center.¹⁰ In the animals (a ring-tailed lemur that died of the infection and a macaque that survived, respectively), peritoneal infection had developed. Both cases had also been diagnosed molecularly. The macaque had been treated successfully with praziquantel intramuscular monotherapy, as surgery and a regular oral treatment regimen were not possible.

The risk factors for human *T. martis* infection are unknown. In all three human infections, the patients had no recent travel history and all had been living in rural areas with rodents (acting as marten prey) observed in abundance. There are only very scarce and punctual data about the epidemiology of *T. martis* in final and intermediate hosts in Europe; no such data are available for the area where the patient lives. In the previous two cases reported,^{4,5} the patients had kept dogs (one also additionally cats), but, when examined, pet feces did

not contain *T. martis* ova. In our case, martens and marten litter were frequently observed on the patient's premises, making a fecal contamination of the environment with *T. martis* ova likely. Environmental contamination was also assumed in the two nonhuman primate infections. As a general preventive measure, thorough hand washing before food consumption and proper disposal of animal feces is strongly advisable, especially in areas with high marten populations.

In summary, we here describe the third human case of *T. martis* cysticercosis. With the more widespread application of molecular diagnostic tools, more unusual zoonotic larval tapeworm species will likely be detected. More information on the epidemiology and clinical disease will thus become available and more effective prevention methods can be implemented.

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