Diphyllobothriasis in a U.S. Military Aviator

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BACKGROUND: Diphyllobothriasis is estimated to afflict 10–20 million people worldwide; however, this is the first case reported in a United States military aviator. Among the largest parasites of humans, the "fish tapeworm" grows from 2–15 m in length, can live >20 yr in the intestines, and is contracted through consumption of uncooked, unfrozen freshwater or anadromous fish species.

CASE REPORT: A 32-yr-old male F-22 pilot presented with mild stomach cramping, bloating, nausea, and intermittent loose stools. Symptoms were relieved with bismuth subsalicylate until several days later when the patient, during otherwise normal bowel movements, extracted multiple broken segments of tapeworm. Although physically asymptomatic, he was psychologically disturbed. Based on the large number of ova with characteristic shape, size, color, and operculum, coupled with the flattened body, yellowish coloration, and rectangular proglottids with centrally located "rosette" uteri, he was diagnosed with diphyllobothriasis (likely *D. latum* or *D. nihonkaiense*). Successful treatment with a single oral dose of praziquantel (>10 mg · kg^{-1}) was confirmed by negative stool examination over 60 d posttreatment. He likely contracted the parasite from ingesting salmon sushi or sashimi while previously stationed in Japan.

DISCUSSION: Despite only mild physical symptoms, the pilot's psychological distress and distraction from knowing about the meters-long tapeworm was significant. Prompt treatment was paramount to resumption of military operations. Aviators should be educated and encouraged to eat only well-cooked or previously frozen fish, especially when indulging in cultural cuisine.

KEYWORDS: tapeworm, fish, sushi, salmon, parasite, praziquantel.

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As aviation has expanded across the globe, pilots are increasingly exposed to the culture and gastronomy of people in foreign lands. A benefit shared by both commercial and military aircrews, this globalization affords many positive opportunities, but it also increases the risk of contracting exotic local diseases to which the aviator may not otherwise be exposed. For this reason, it is important for flight surgeons to keep a broad differential, including global health threats, when evaluating all aircrew. One such threat that may be underrecognized is that posed by foodborne parasites, such as roundworms and tapeworms.

Estimates suggest that upwards of 10–20 million people worldwide are hosts to tapeworms from the genus *Diphyllobothrium*.[5,10] Historically, nearly all infections were attributed to *Diphyllobothrium latum*, but there are now eight phylogenetically unique species which have been implicated in human infections in North America alone.[10] Growing evidence suggests that many of the infections that were thought to be from *D. latum* may actually be a different, but related species of tapeworm.[5,8,10] Most relevant to this case is *D. nihonkaiense*, which appears to be prevalent in Asia and has been found in several species of salmon in the Northern Pacific Ocean, including cherry, pink, chum, and sockeye.[8,9] Clinically, initial treatment for all species of *Diphyllobothrium* is similar. While not approved for this use by the United States Food and Drug Administration (FDA), typical therapy consists of a single oral dose of praziquantel (5–10 mg · kg^{-1}) or niclosamide (2 g).[2,3,9] However, if initial treatment fails, there is some evidence that *D. latum* is more resistant to praziquantel and may require a higher dose (25 mg · kg^{-1}) to eradicate the parasite.[9] With modern medicine and a better understanding of *Diphyllobothrium*, cure and prevention are both achievable objectives.

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While the tapeworm may seem somewhat innocuous, residing unrecognized in the asymptomatic host for decades, the oft insidious impacts of chronic diphyllobothriasis can be burdensome for an individual and community if left unchecked. Symptoms of abdominal pain, discomfort, or diarrhea are present in about 20% of infections, while less obvious manifestations include pernicious anemia, fatigue, and constipation.[9] Rarely, the parasitosis can lead to severe complications. Migration of proglottids into the biliary tract or direct attachment of the scolex in the biliary system may lead to cholecystitis or cholangitis, while infection with a very large tapeworm may precipitate a potentially lethal bowel obstruction.[2,9] All of these adverse outcomes may be avoided if the chain of infection can be broken.

Like many parasites, the lifecycle of *Diphyllobothrium* has many steps and humans are not the obligate definitive host. From the time the egg is released from the terminal end of the adult worm, the parasite develops in progressive stages of ingestion and migration through freshwater crustacean, small freshwater fish, and larger predatory freshwater trout or anadromous species, such as salmon, that return to freshwater to spawn.[2,4,10] There, in the muscular flesh of this final intermediate host, it waits as an infective plerocercoid larvae to be eaten by a human or other large carnivore.[2,4,10] Once inside a definitive host, the larvae develops and matures into the adult worm, attaching itself to the mucosal lining of the small intestine (usually at the level of the ileum) via an elongate scolex with a characteristic pair of ventral and dorsal longitudinal grooves.[2,4,9] When grown, *Diphyllobothrium* are extraordinary for their size, typically growing to 2–15 m in length, though exceptional specimens have been reportedly measured at 25 m.[9] They are also long-lived parasites, taking advantage of their human host for up to 20 yr or more.[4,9] While not known with certainty, their rate of growth is estimated to be as rapid as 22 cm/d,[9] culminating in upwards of 2000–4000 hermaphroditic proglottids,[5,9] enabling the release of 1,000,000 eggs per day.[2,9] Usually, humans are only infected with a single adult worm, though cases of infection with two or three worms have been reported.[6]

The mature worm can be identified as belonging to the genus *Diphyllobothrium* based on several morphologic features, including a flattened body with a yellowish coloration made up of wider-than-long, rectangular segments, each with their own darkly colored, centrally located, slightly elevated, classically described "rosette" uteri.[4–6] If available, ova may be seen in stool as early as 5–6 wk after infection in humans[2] and their identification may serve as the only evidence of infection. Ova are visible on iodine-stained wet mount or with standard staining with hematoxylin and eosin.[2] The eggs are ovoid in appearance, with variable sizes reported in the literature, ranging from 35–80 μm in length and 25–65 μm in width.[4,5,9] Each egg has an operculum on a narrowed pole, which serves as an escape for the embryo,[2,4,9] and a small opposing abopercular knob that can occasionally be seen under the microscope.[2] The moderately thick casing for the ova stains a tan color[2,4] while its contents will stain a very dark purple with hematoxylin and eosin. Although not directly infective from one individual to another, persistent, unfettered infection within a community ensures the perpetuation of infected wildlife and subsequent human disease burden without appropriate public health countermeasures consisting primarily of proper disposal of human waste and informed, compliant food preparation, which would break the cycle of infection.

CASE REPORT

A 32-yr-old Caucasian male, active duty, U.S. Air Force F-22 pilot presented to clinic while on a temporary assignment to Alaska with a suspected tapeworm. For the previous 2 d, he had been having mild stomach cramping and bloating, with associated nausea, but no emesis. He had a few intermittent loose stools with intervening normal bowel movements. He was taken off of flying status initially due to his bloating/cramping and was treated conservatively with bismuth subsalicylate, with reported relief of his symptoms. He had been planning to return to flying status that day; however, during his morning bowel movement, he felt something unexpected in his anus and subsequently pulled out an approximately 3-ft long worm, which he placed in a Ziploc bag and brought to clinic. Physically, he felt well and denied any fever, chills, nausea, vomiting, abdominal pain, diarrhea, constipation, hematochezia, myalgias, right upper quadrant pain, or pulmonary symptoms outside of nasal congestion due to a resolving acute viral respiratory infection. He also denied any weight loss, actually reporting a 10-lb weight gain in recent months. Psychologically, however, he was disturbed, disgusted, distracted, and anxious. When the segment was found to be 100 cm in length, with an intact terminal end, but a broken proximal end and no scolex, he was more distressed, knowing it was likely that several more meters of worm remained inside of him (**Fig. 1**). Later that same day, he pulled out another segment that was 288 cm long and was broken on both ends, validating his earlier concern (**Fig. 2**).

Regarding his dietary history, he enjoyed fish and said he had eaten tuna sushi, smoked salmon, and grilled halibut in the days and weeks prior to his diagnosis. He began a 3-yr assignment stationed at Kadena AFB, Japan, 6 yr ago. He also spent an additional 3 mo there 2 yr ago on temporary duty assignment.

Fig. 1. Terminal end of the tapeworm. Note the germinate uteri extending to the last proglottid segment. Total length of initial segment: 100 cm. [Color figure available online].

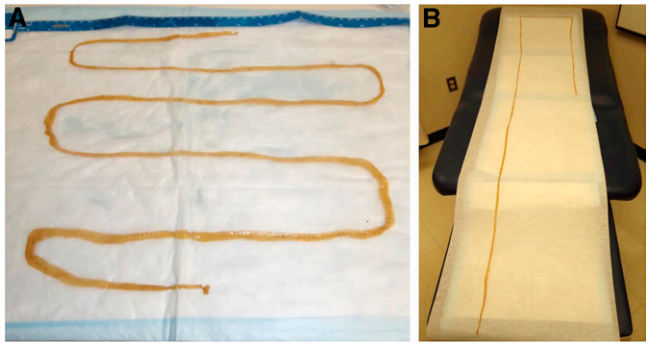

Fig. 2. The second expelled segment. A) Note that both ends are torn, indicating that the scolex remained in the patient. Total segment length: 288 cm. B) Putting that length into perspective on an exam table. [Color figure available online].

Although recollection of his exact diet over these periods was not possible, he recalled eating a "fair amount" of sushi, usually a spicy tuna roll, but occasionally sashimi, which he said may have been salmon. He also remembered a specific meal 2 yr previous where he ate undercooked tilapia at a local restaurant in Virginia, even sending the fish back to the chef, but only after he had eaten around the areas that he thought had been uncooked. He had a history of pinworms as a child, but no other known parasites.

Physical exam was fairly benign, with normal vital signs and only mild abdominal tenderness to palpation in the left lower quadrant. At 188 cm tall and 98.5 kg (body mass index of 27.9), he had an athletic build and was not visibly malnourished. While it was likely that the patient had harbored the parasite for many years, knowing that it was present was extremely bothersome to him and distracting enough that he did not feel comfortable resuming any kind of flying duties while the tapeworm remained alive inside of him.

A complete blood count, looking for possible megaloblastic anemia or eosinophilia, and comprehensive metabolic panel, looking for evidence of possible parasitic hepatic involvement, were both sent to the lab and returned with all values within normal limits. Due to the known infectious agent and suspected high ova burden, examination of his stool for ova and other parasites was able to be completed using only a small sample of fecal material attached to the expelled worm segments. Staining with hematoxylin and eosin revealed many tan colored, approximately 55–65 μm by 35–50 μm, ovoid shaped eggs, with a single operculum located at the vertex, characteristic knob at the abopercular end, and darkly stained, unembryonated contents (**Fig. 3**, A-D).

Phone consultation and transmitted images of the worm segments (**Fig. 4**) with an infectious disease specialist at Naval Medical Center Portsmouth and the director of Tropical Medicine at Uniformed Services University of the Health Sciences, as well as detailed inspection at the local Pathology Department, confirmed suspicion of infection with *Diphyllobothrium*. Laboratory resources to further differentiate between the two most likely species—*D. latum* vs. *D. nihonkaiense*—by molecular analysis were not available. Testing of preserved specimens at a later date was deemed too costly and clinically unnecessary. Whereas the exact source of infection could not be determined

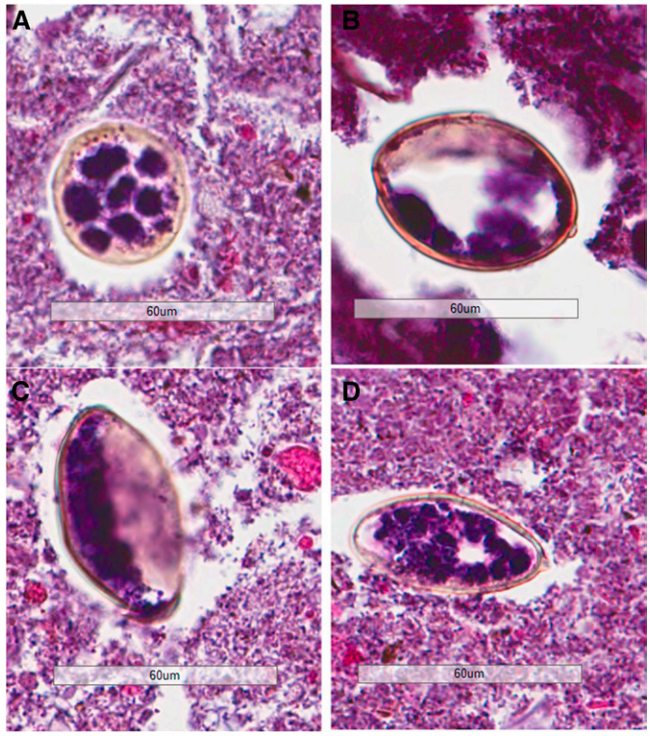

Fig. 3. *Diphyllobothrium* ova stained with hematoxylin and eosin, all from the same fecal sample. [Color figure available online]. A) En face view, illustrating the thick yellowish casing and dark purple unembryonated contents. B) Longitudinal view with a distinct abopercular nub (right side); also illustrative of variable ova width. C) Longitudinal view with a visible operculum, seen with a slightly lifted edge (lower side). D) Longitudinal view with intact casing and abopercular nub; the operculum is not visible. All images obtained using Aperio ScanScope at 40× magnification and viewed with ImageScope v12.2.2.5015 at 40× zoom.

with certainty, it was clear that there were many opportunities for the patient to ingest uncooked freshwater or anadromous species over the previous 6 yr. Based on his history, he most likely contracted the *Diphyllobothrium* from salmon sushi or sashimi, as this was a repeated dietary indulgence.

The patient was treated with a single dose of oral praziquantel, 1200 mg (approx. 12 mg · kg^{-1}). While the goal dose was

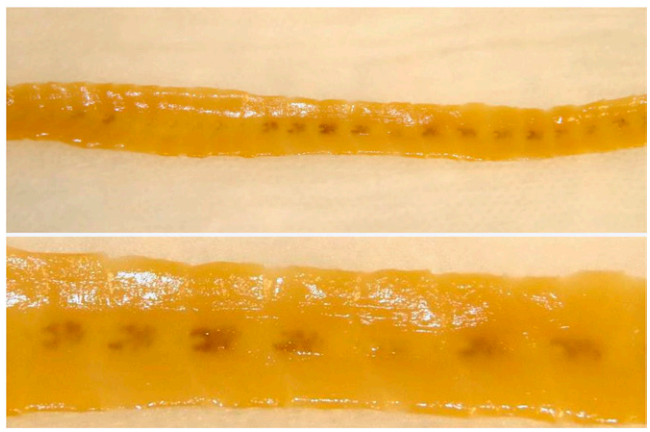

Fig. 4. Up-close view of a section of *Diphyllobothrium*. Note the wider-than-long, rectangular proglottids, with darkly colored, centrally located, "rosette" uteri. The lower image is a zoomed in version of the upper view. Proglottid width was variable, generally between 4–8 mm. [Color figure available online].

10 mg · kg^{-1} (98.5 kg), praziquantel comes in 600-mg tabs and is generally well tolerated. Following treatment, he passed several smaller broken segments of worm within his feces, but never identified the scolex. He denied any symptoms from treatment, including urgency or diarrhea. Of greater significance, he reported feeling much better psychologically, knowing that the worm was likely dead. Although he did not have any symptoms, due to his occupation as a fighter pilot in a single seat airframe and a nearly 8-h sortie ahead for the return flight home, an electrocardiogram (ECG) was completed to evaluate for possible arrhythmia (including bradycardia or ventricular fibrillation) from the praziquantel. The ECG showed normal sinus rhythm with normal intervals, axis, and morphology.

As the patient felt well both physically and psychologically, he was returned to flying duties and successfully completed the extended sortie back to home station without issue. Repeat stool examination for ova and parasites was completed greater than 60 d posttreatment and was negative, confirming treatment success.

DISCUSSION

This case is a reminder that the public health warnings about undercooked or unfrozen fish should be earnestly heeded, especially by those tasked with operational flying missions. Servicemembers should thus be appropriately educated about the risks posed by foodborne illness, including parasites, prior to temporary or permanent assignments. This is especially important in regions where ingestion of cultural cuisine which does not meet FDA standards, such as sushi and sashimi, is likely.

For personal and commercial use, the FDA has published publicly available guidelines for safe handling of fish species that may harbor parasites, including *Diphyllobothrium*.[11] If cooking the fish thoroughly is not desired, then proper freezing can eradicate the infective plerocercoids. The temperature and length of time are both important considerations. Freezing fish and storing at −4°F or below for 7 d, freezing at −31°F until solid and then storing at −31°F for 15 h, or freezing at a temperature of −31°F and then storing at −4°F or below for 24 h are all acceptable regimens to kill any parasites that may be present.[11] Eating uncooked, undercooked, or fish that has never been frozen to these specifications—such as advertised "never frozen" salmon sushi or sashimi—increases the risk of infection and ought to be avoided.

If a tapeworm is suspected, accurate identification is important to ensure that proper treatment can be administered. While there are many known species of *Diphyllobothrium*, it is expensive to differentiate them genetically as they appear morphologically similar. Identification to the species level requires analysis of the mitochondrial cytochrome c oxidase 1 (μ1) gene by PCR.[8,10] At present, the United States Department of Defense does not have a reference laboratory that performs this type of testing, necessitating use of commercial resources if identification is required. Clinically, distinguishing between the multiple species of *Diphyllobothrium* is not usually necessary, as patients typically respond well to a single dose of praziquantel, 5–10 mg · kg^{-1} (best if taken with liquid during a meal).[2,4] If initial treatment is not successful, some recommendations call for up to 25–50 mg · kg^{-1} of praziquantel.[9] Though not available for human use in the United States, a single dose of niclosamide, 2 g for adults or 50 mg · kg^{-1} for children, may be equally effective.[2,3] If neither of these is an acceptable alternative, some success has been noted with the use of intraduodenal gastrografin, which causes the expulsion of the entire living worm.[9] As noted previously, although not FDA approved for the treatment of diphyllobothriasis, use of praziquantel is widely accepted among specialists and is listed as treatment on the DPDx website for the Centers for Disease Control and Prevention—a well-known, reliable, and freely available reference for general clinicians looking for information on parasitic diseases globally.[2]

While the mechanism of action in the treatment of *Diphyllobothrium* has not been elucidated, in schistosomes—its FDA approved use—praziquantel works by inducing rapid contraction of the worm's musculature by increasing cell membrane permeability to calcium, leading to paralysis.[1] Presumably, parasitic paralysis leads to dislodgement from the mucosal lining and subsequent discharge from the body. Niclosamide, on the other hand, is believed to lead to energy depletion in the cells by uncoupling mitochondrial oxidative phosphorylation and inhibiting anaerobic ATP production.[7,12] Both medications are generally well-tolerated, with few side effects. Aeromedically, the low, but present risk of arrhythmia following administration of praziquantel warrants an electrocardiogram be performed prior to resumption of flying duties, particularly in single-crew aircraft.

Despite the absence of other reported cases of diphyllobothriasis in U.S. military aviators in the literature, with thousands of pilots and aircrew stationed in the Pacific, it is likely that this patient is not the only individual affected, even in this narrow demographic. Screening stool samples in asymptomatic pilots would be cumbersome, labor-intensive, and may lead to undue psychological stress. A reemphasis on education and prevention, spearheaded by flight surgeons embedded with the operational units stationed in the region, would be an inexpensive way to mitigate the risk of infection in those individuals newly assigned or not yet afflicted by this relatively common, often silent, freeloading cestode.

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