Case report

A new worm infiltrating the human cornea: A report of three cases

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A R T I C L E   I N F O

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A B S T R A C T

Purpose: To characterize a new species of parasitic nematode that triggers uveitis.

Observations: Three previously healthy, relatively young people each contracted a corneal stromal nematode that, upon surgical removal and examination, did not match any known nematodes. Clinical ocular findings included corneal opacification, visible corneal worms, conjunctival injection, and uveitis.

Conclusions and Importance: The three cases presented here represent a previously undescribed parasitic infection of the cornea by an unidentified nematode. These findings may represent a previously unrecognized zoonotic infection from wildlife sources and potentially a newly documented nematode requiring description. Future clinical findings regarding this newly described nematode are needed to further develop our understanding of the disease.

1. Introduction

Ocular parasites—including protozoa, nematodes, cestodes, and trematodes—are well-documented, and ocular parasitosis has been found to be significantly more common in regions with favorable environmental factors and poor sanitary conditions. In these regions, ocular parasitosis can be endemic in the canine and feline populations, as well as in a range of wildlife species including other mammals or birds, providing a breeding ground from which arthropod vectors can transmit parasites to humans. However, it is unusual to find a live worm in intraocular structures. Nematode parasites do not usually proliferate within their definitive hosts, but rather grow, molt, mature as dioecious adults in specific anatomical sites, mate, and then produce eggs, larvae or microfilariae. During this life cycle, worms can migrate to different locations within the body, including the eye; migration takes place via blood borne carriage or through tissue to the eye or adjacent structures. The eye's immune privilege may allow further growth and development relative to other tissues and helminth parasites can infect the conjunctiva, eyelid, and intraocular cavities. A diverse assemblage of zoonotic parasites have been documented in ocular infections in people, and involve both fully developed nematodes or larval stages: for example, zoonotic species of Onchocerca have been documented to involve the cornea (probably Onchocerca cervicalis) and the anterior chamber. The following is a report of three patients from the southwestern Pacific island of Saipan, in the Mariana Islands, who presented with corneal stromal nematodes between 1997 and 2009. We believe these nematodes to be of a previously undescribed species.

2. Findings

2.1. Case I

Two weeks prior to presenting to an ophthalmologist in March 1997 on Saipan, the patient, a healthy 29-year-old Chamorro male without prior ocular, medical, or surgical history, had seen an optometrist for photophobia of 2 weeks duration in his left eye. He reported having traveled to Honolulu, Hawaii two weeks prior to development of his symptoms, but had not been outside either the Hawaiian Islands or the Mariana Islands recently. He was placed on prednisolone acetate 1% q 1 hour, and homatropine 5% TID.

On examination by the ophthalmologist, his best corrected visual
Acuity with plano lenses was RE 20/20, LE 20/25+. External exam, pupils, and motility were normal, and intraocular pressure was 10 mmHg in both eyes. Slit lamp examination of the right eye was unremarkable.

The left eye showed areas of peripheral and mid-peripheral corneal opacification. There was no injection. There was a 1.5 mm long translucent motile worm located approximately ⅔ depth within the mid-periphery of the corneal stroma (Supplemental Fig. 1). The movement of the worm was primarily undulating, and its speed through the cornea was not fast enough to note any forward or backward movement. The worm appeared to be photophobic, contracting to light from the slit lamp beam.

The anterior chamber showed rare cells and no flare. Dilated fundus exam was normal for both eyes, without evidence of vitreous cell, posterior segment parasites, or chorio-retinal tracks. The prednisolone dose was decreased to every 2 hours, and the homatropine to once daily. Complete blood count was normal with no eosinophilia. Liver function tests were also normal. Stool examination showed no mature or larval parasites or eggs.

Over the ensuing weeks, the worm was noted to traverse the mid-peripheral cornea, moving as far as 2–3 mm per day, but often remaining in the same area of the cornea: 3–4 mm from the limbus. There was no change during this period in the visual acuity, corneal opacity, or anterior inflammation. It had been hoped that the worm would move far enough to the periphery to allow a direct cut-down over the worm, in order to remove the worm with minimal refractive effect of the incision.

After 2 weeks of observation, surgical intervention was considered. Removal of the worm was attempted with a slit lamp, as visualization under the operating microscope was impaired. A 22-degree SuperBlade™ was used to place a 2 mm horizontal incision ⅔ depth into the cornea directly over the worm, at the 5:00 mid-periphery. As the incision was made, it was noted that the intracorneal worm was moving vigorously away from the incision site. Viscous lidocaine was placed into the incision, and the worm stopped moving. However, the light reflexes from the corneal stroma and the incision made it difficult to distinguish the worm from the corneal stroma. Fluorescein dye was placed, which did not significantly highlight the worm. After multiple attempts to grasp and remove what may have been the worm through the incision, the decision was made to cease further manipulations. The cornea and anterior chamber were carefully examined, and it was noted that the parasite was not visible in either, so it was presumed to be present in the area of the incision. The partial thickness incision was left unsutured. Antibiotic ointment and a patch were placed, and the patient discharged.

On postoperative day 1, visual acuity decreased to 20/40. There was 3 + conjunctival injection. The horizontal incision site at 5:00 was well approximated, and at 3:00 in the mid-periphery, the live worm was visible. The patient and his wife were highly distressed. The decision was made to attempt to kill the worm.

An argon laser was used through an Abraham lens, at a spot size of 100 μm, and duration of 0.1 msec. Beginning at 80 mW, the power was titrated up to 400 mW, focusing treatment on the ends of the worm. A total of 35 spots were placed along the length of the worm, and at the end of the treatment, the worm had ceased moving. The following day, the worm had moved to the 2:00 mid-periphery. It was motile and continued to contract when exposed to the slit lamp beam.

The patient was referred to a corneal specialist for further evaluation and management. The worm was measured at the slit lamp to be approximately 1500 μm long, at ⅔ depth into the paracentral cornea.

It was considered that destroying the worm by cryoablation or phacoablation might incite a severe immunologic reaction, and for this reason, the decision was made to proceed with surgical removal. Because topography showed that the previous vertical incision had resulted in astigmatism, it was elected to use an astigmatically neutral lamellar surgical approach and “bring the organism to the surface”.

Six weeks after presentation, the patient was brought to the operating room, and under local anesthesia, a disposable Katena™ Barron-Hessburg suction trephine was used. The trephine was centered to include the worm, and trephination done to approximately 300 μm. The parasite was removed intact and passed directly to the parasitologist. The specimen, however, was lost during processing.

Prednisolone and homatropine were gradually tapered. Four months after surgery, there were no signs of active inflammation. Visual acuity was 20/50, correctable to 20/20. The patient showed no signs of systemic or further ocular parasitic infection.

2.2. Case 2

In November 2005, a healthy 8-year-old Chamorro male presented on Saipan with a 3 week history of redness, itching, glare sensitivity and blurred vision OD. He had no past ocular or medical history. He had traveled one month prior to Houston, Texas, and 10 months prior to that to southern California.

His visual acuity was RE 20/30, correctable to 20/25 (−0.50 + 1.00 × 005), LE 20/20. External exam, pupils and motility were normal. Slit lamp exam of the right eye showed diffuse + 1 conjunctival injection. The cornea showed diffuse subepithelial opacities from the 11:00 limbus to 2:30, with surrounding cell (Supplemental Fig. 2). The corneal epithelium showed no staining or ulceration. Within the corneal stroma, at the 2:30 o'clock position mid-periphery, a 1 mm long motile worm was visible. It was translucent with tapered ends and seemed to have a visible cavity through the center along the longitudinal axis. This translucency was presumed to be an intestine. The worm contracted to light. The anterior chamber showed no cell or flare. The iris and lens were normal. The slit lamp exam of the left eye was unremarkable. Intraocular pressure was normal in both eyes. Dilated retinal exam was normal in both eyes, with no vitreous cell, and no signs of retinal or choroidal tracks.

Systemic evaluation by a pediatrician was normal, as were laboratory examination of stool for parasites, complete blood count including eosinophils, abdominal ultrasound, and serum chemistries.

The patient was referred for removal of the corneal worm. Exams during the ensuing 2 weeks showed that the worm remained in the same area of the cornea, though it rotated its orientation relative to the limbus, from 90° to the limbus to 60° to the limbus. The worm was extracted in December 2005 through a freehand lamellar dissection with a limbal incision into the cornea. The worm, however, was not removed intact, and there was no specimen available for pathological or parasitological examination.

Postoperatively, the patient did well, with visual acuity returning to 20/20 within one week. Slit lamp exam showed no visible worm remnants. The patient has been followed for 10 years postoperatively, and his vision has remained 20/20, with slight corneal scarring superimodially. There have been no signs of recurrence of the ocular worm during this period.

2.3. Case 3

In December 2008, a generally healthy, 34-year-old Chamorro woman with a history of soft contact lens wear for myopia presented to an optometrist with blurred vision in her right eye for one week. Her travel history was negative except for a one week trip to San Diego, California, 3 weeks prior.

Her visual acuity with soft contact lenses was 20/30 OD, 20/20 OS. Slit lamp exam OD noted no injection, +2 diffuse superficial punctate keratitis with staining, and +1 diffuse central stromal haze. There were no anterior chamber cells or flare. The anterior segment of the left eye was normal. It was assumed that the signs were related to the contact lens, and the contact lenses were discontinued, with instructions to return in 3 days. No improvement was noted, and the patient was referred to an ophthalmologist.
On examination, her visual acuity with glasses was 20/50–2 OD (−2.75 sph), and 20/20 OS (−3.00 sph). Slit lamp exam OD showed trace conjunctival injection. The cornea showed diffuse epithelial haze extending to the anterior stroma with 2–3+ central endothelial keratic precipitates. Inferiorly in the mid-ribera, a 1 mm long and very thin translucent motile worm was poorly visible.

Fig. 1. Intrastromal haze and poorly visible worm inferiorly (circled) in Case 3. There is diffuse epithelial haze extending to the anterior stroma with 2–3+ central endothelial keratic precipitates. Inferiorly in the mid-peripheral stroma, a 1 mm long and very thin translucent motile worm is poorly visible.

Gross microscopic examination at the AFIP revealed an intact white translucent adult male nematode which was 1050 μm in length and 90 μm in diameter (Fig. 3). It was uniform in diameter with slight tapering at both ends, and bluntly rounded cephalic and caudal extremities. The cuticle was 2 μm thick and finely striated (Supplemental Fig. 6). The mouth or stoma leads to a cuticular-lined esophagus that was about 350 μm long and occupied about 1/3 of the length of the worm (Supplemental Figs. 7–9). The base of the esophagus revealed no glandular or muscular modifications. The intestine was a thick tube about 35 μm in diameter (Supplemental Fig. 10). The anus was about 30 μm from the posterior tip of the worm. The posterior end of the worm had 2 spicules: a long, jointed spicule measuring 65 × 17 μm, and a short simple spicule measuring 40 × 12 μm (Supplemental Fig. 11). It was attempted to perform histological examination; unfortunately, however, the specimen was lost in processing.

3. Discussion

Although a specimen for pathological examination was obtained from only one of the patients, it is presumed that all 3 were infected with the same genus and species of nematode, based on the clinical presentation, course, and morphology on slit lamp examination. All 3 patients were otherwise healthy, relatively young and living on the island of Saipan in the Mariana Islands when infected with an ocular worm. Each patient presented with mild ocular symptoms (such as mild blurred vision, redness or photophobia) and was found to have only corneal stromal inflammation. None of the patients had signs of posterior segment or systemic infection.

In each case, there was a single motile translucent intrastromal corneal nematode, with a relatively robust or stout body, not tapering strongly in the caudal and cephalic extremities, and ranging in length from approximately 1 to 1.5 mm. The worms had features common to all nematodes: specimens are round with bilateral symmetry of the body and radial symmetry for the cephalic region, and possess a complete digestive tract, separate sexes and a protective nonliving cuticle. The base of the esophagus is not modified, and accessory esophageal glands were not evident. Phylum Nematoda and particularly the monophyletic Class Chromadorea (formerly within the paraphylectic Secernentea) and the Class Dorylaimae contain the most parasitic worms infecting humans and otherwise is a very large group of mega-diversity. The only specimen available for gross examination was a completely developed adult male nematode with fully cuticularized spicules, which are accessory copulatory organs. The length of the morphologically dissimilar spicules (65 μm and 40 μm) is the most specific feature apparent that can be used in identification.

We considered the nematodes that have been reported to infect the cornea, anterior segment or bulbar conjunctiva of humans and pri- mates, and a range of other mammals and birds. Among these, all of those that occur as adults in mammalian hosts can be excluded because of the length or morphology of their spicules and site of localization in the definitive host (Table 1). The dorylae nema and especially the Muspineidea (miniscule parasites occurring in tissues of bats and mice) due to the presence of esophageal glands in the basal region of the esophagus, which are lacking in the specimen from Saipan.16

We considered the possibility that some nematodes that could infect the eye in the juvenile stage might under unusual circumstances mature to the adult stage in this aberrant anatomic location. Most of these worms can also be excluded because of the morphology or considerably greater length of spicules in adults (Table 2). Other potential Rhabdi- tida or Pangrolaimida including some genera and species in the families Rhabditidae and Cephalobidae can also be excluded based on distinct morphological attributes. Males remain unknown among some cepha- lobes such as Helicephalobus.25

We suspect that, although the specimen examined was an adult having completed the 4th molt, the worm had not reached its complete length perhaps because it had recently molted or because it was in an
unusual anatomic location and host. Identification of the worm would require collection of another specimen in order to develop comparative DNA sequence data which could be diagnostic, and examination of the distribution of caudal papillae in male specimens, an important morphologic feature in classification. Although we are unable to identify the genus and species of this worm, it has morphological features that are consistent with some genera and species referred to the Superfamily Filarioidea (order Spirurida) especially within the Family Onchocercidae. Specific attributes consistent with such a provisional identification include a strongly rounded head, lack of cephalic development or expansion, a cuticular-lined, undivided, esophagus that occupies one-third of the worm’s length, absence of modification in the basal region of the esophagus, dissimilar spicules of different lengths (left longer than right, and with a joint separating the shaft from the lamina), and a very short, blunt and rounded tail lacking apparent alae or ventral genital papillae. Furthermore, among many Onchocercidae (including some number of genera typical of bats, such as species of Litomosa, and species of Dipetalonema and Onchocerca in mammalian hosts of diverse orders), the left spicule is considerably longer than the right and possesses a characteristic joint separating the shaft and lamina. Most of the species in Tables 1 and 2, encompassing those reported in ocular infections, belong to the Family Onchocercidae.

There are many vertebrate parasites in the Onchocercidae that have not yet been shown to cause zoonotic eye infections in humans, but which may have the potential to do so. Overall there are about 70–80 genera of onchocercids partitioned across 8 subfamilies including the Onchocercinae which contains the greatest taxonomic diversity for species circulating in birds or mammals. For example, species of at least 16 genera of filaroid nematodes, in addition to those of Pelecitus, have been described as parasites of wild birds alone.44

Because of the rarity of this infection and the fact that it has not been described previously, it is likely a zoonotic infection. The mode of transmission is unknown. Parasites can reach the cornea either by migration from the anterior chamber or by direct inoculation from the external environment. It is most likely that the worm penetrated the cornea from the anterior chamber, which would imply that the worm was inoculated into the patient as a larval form by an arthropod vector and then developed into an adult worm somewhere in the body before migrating to the anterior chamber and finally the cornea (Cameron J, personal communication, 2016).

Most zoonotic nematodes that have a tropism for the eye reach the eye by migration through the host tissue (possibly through the optic

Fig. 2. Scheimpflug showing the depth of the intrastromal worm in Case 3.

Fig. 3. Entire worm in Case 3. An intact white translucent adult male nematode measuring 1,050 μm in length and 90 μm in diameter with slightly tapered ends, visualized by microscope.
nerve) or through the circulation while in the larval stage. It is not known which route is more common or which are the preferred or aberrant routes. The eye is an immune privileged site that may allow for growth and development of a parasite beyond what could occur in other tissues. Among filarioids, the transition from microfilaria to larva occurs in an arthropod host; therefore, if this worm is a filarioid, it did not migrate to the eye as a microfilaria.

Larval stage filarial nematodes such as those of Onchocerca spp., Loa loa, and Dirofilaria spp., are inoculated by arthropod bite into the definitive host. The development of microfilariae requires co-feeding of mature adult male and female worms. None of the 3 patients reported here was found to have microfilaria or peripheral eosinophilia suggesting that fully developed adult nematodes were not present in other anatomical sites. Some other nematodes, such as Gnathostoma spp., and Toxocara canis, are acquired through the ingestion of eggs or larvae, sources of which include contaminated water, soil and undercooked meat and vegetables.

It is rare for nematodes to infect the eye by direct inoculation, such as Thelazia sp. Because the human eye has a number of defense mechanisms in place to protect against microorganism breach, trauma is usually required for parasites to enter through this route. Though this may have been a mechanism in one patient who was a contact lens wearer (Case 3), there was no source of trauma or microtrauma in the other two cases. Rare corneal involvement has been documented with onchocerciasis and gnathostomiasis.

In brief, all three patients presented with mild anterior segment inflammation, and were found to have a motile translucent corneal intrastromal nematode 1–1.5 mm in length. The one specimen that was successfully retrieved was a completely developed male nematode. Because the specimen was lost in processing prior to histological examination, only its morphological features are known. In this specimen, the spicules, a form of accessory copulatory organs, are the most specific feature that can be used for identification. Based on this and other morphological features, all nematodes known to infect the anterior segment in humans, primates, and a range of other mammals and birds, either as adult nematodes, or in a juvenile state, can be excluded. This nematode’s morphological features are consistent with some genera and species in the Superfamily Filarioidea, especially the Family Onchocercidae. Based upon the rarity of infection, it is likely a zoonotic nematode.

Table 1
Characteristics of nematodes reported to infect the eye as adults.

| Species                                      | Usual site in definitive host | Range of length of spicules (µm) or distinctive morphology |
|----------------------------------------------|------------------------------|------------------------------------------------------------|
| Ancylostoma caninum                          | Intestine in dog and cat     | COPulatory bursa                                          |
| Angiostrongylus cantonensis                  | Lung in rats                 | 1200                                                       |
| Dracunculus medinensis                       | Skin in human               | 490-730                                                   |
| Loa loa                                      | Heart in rats                | 65-80                                                      |
| Setaria labiatopapillosa                    | Subcutaneous in human        | 123                                                       |
| O. reticulata                                | Soft tissue in monkeys       | 120                                                       |
| O. mansoni                                   | Subcutaneous in human        | 287-360                                                   |
| O. lupi                                      | Peritoneal cavity in dog     | 92-104                                                     |
| O. cervicalis                                | Ligaments and tendons in horse (O. cervicalis) | 64-295                                                   |
| O. dewitie japonica                         | Subcutaneous in boar (O. dewitie japonica) | 116-360                                                   |
| O. gutturosa                                 | Ligament in cattle (O. gutturosa) | 360                                                       |
| O. jakutensis                                | Subcutaneous in deer (O. jakutensis) | 170                                                       |
| O. lini                                     | Sclera in dog (O. lini)      | 270                                                       |
| O. reculata                                  | Ligament in horse (O. reculata) | 112                                                       |
| Oxyspirura species                          | Conjunctival sac, nasolacrimal duct, nictitating membrane in birds and primates | 145-220                                                   |
| O. mansonii                                  |                             |                                                            |
| O. youngi                                    |                             |                                                            |
| Parafilaria bonica                          | Subcutaneous in castle       | Single spicule                                             |
| Peltecus species                             | Soft tissue in birds         | 62-66                                                     |
| Setaria labiopapillosa                      | Peritoneal cavity in cattle and buffalo | 82                                                       |
| Thelazia californiensis                     | Conjunctiva and nictitating membrane in cat, dog, rabbits, carnivores | 250-280                                                   |
| Wuchereria bancrofti                        | Lymphatics in human          | 150-187                                                    |

* Species belonging to Family Onchocercidae.

Table 2
Length of spicules of nematodes reported to infect the eye as larvae.

| Species                                      | Usual site in definitive host | Range of length of spicules (µm) |
|----------------------------------------------|------------------------------|----------------------------------|
| Baylisascaris procyonis                      | Raccoon                      | 380-620                          |
| Gnathostoma species                          | Carnivores                   | 400-800                          |
| Toxocara cati                               | Cat                          | 1700-1900                        |
| Trichinella spiralis                         | Human, swine, bears, raccoon, foxes | No spicules                   |
into the cornea.

4. Conclusions

The 3 cases presented here represent a previously undescribed parasitic infection of the cornea by an unidentified nematode. The gross description of the worm does not match those of previously reported ocular parasites. Infections represented in these cases are likely attributable to a single species, which may represent a previously unrecognized zoonotic infection from wildlife sources and potentially a newly documented nematode requiring description. Resolution of the source and identity of these nematodes can be based on early recognition of infection, and collection of archival specimens from the Southwest Pacific suitable for detailed comparative morphological study and comparative molecular-based analyses.

Patient consent

Informed consent was obtained from the patients for the use of their health information.

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Conflicts of interest

None.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.01.013.

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