1	Case Report
2	Human Ocular Thelaziasis: A Case Report from Indonesia
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9	Short title: Human Ocular Thelaziasis: A Case Report from Indonesia
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20	Number of Tables: 0 (none).
21	Number of Figures: 2 (two) figures.
22	Word count: 1,707 words.

23 Keywords: Thelaziasis, *Thelazia callipaeda*, human ocular, Indonesia.

24 Abstract

25 Thelaziasis is a parasitic disease caused by a nematode of genus Thelazia, which is rare in the 26 world, including Indonesia. The definitive hosts for Thelazia are canids, felids, mustelids, and other 27 mammals, while the vector is drosophila flies. Consequently, this study reported an uncommon 28 occurrence of human ocular thelaziasis in Indonesia. Based on the patient's complaints and 29 physical examination, we found a living worm that move actively in the anterior chamber, then 30 documentation is carried out both during the examination at the polyclinic and in the operating 31 room. The surgery was performed using topical anesthesia, clear corneal incision, and removing 32 worm through the main port. Morphological examination from the parasitology laboratory 33 showed that the worm was *Thelazia callipaeda* species. Following this intervention, the patient 34 was given an oral anthelminthics drug, topical and oral antibiotics, topical steroid and surgical 35 treatment. There was no recurrence or appearance of any other symptoms was reported in two 36 months of follow-up.

37 Introduction

38 The epidemiology of parasitic ocular diseases can be explained by the causative organism's habitat 39 as well as the patient's habits and health status. Furthermore, an ocular examination may provide 40 information about the underlying infection, and knowledge of the possibilities of travel-related 41 pathology may explain the disease symptoms.(1) Thelaziasis is a parasitic condition caused by a 42 nematode of the genus Thelazia, which infects the eyes of wild and domestic animals. The species 43 associated with this disease include Thelazia californiensis and Thelazia gulosa, which have been 44 reported in the United States, along with *Thelazia callipaeda*, which is common in Asia and affects 45 humans.(2) Meanwhile, canids of domestic and wild origins are concerned as the primary 46 definitive hosts for Thelazia callipaeda, though infections in mustelids, lagomorphs, and felids 47 have been identified.(3) Thelazia californiensis infections have been detected in several 48 mammals, mostly domestic and wild canids, as well as cervids, jackrabbits (Lepus californicus), 49 bears, sheep, and felids. The intermediate vectors or hosts for these parasites are drosophilid 50 flies, which consume lacrimal secretions (lacrimophagous). Fannia spp., including Fannia 51 benjamini (canyon fly) and F. canicularis (lesser house fly), are the hosts of T. californiensis, while 52 Phortica variegate and Phortica okadai are the primary intermediate vectors of T. callipaeda. The 53 vectors feed on the conjunctival secretions of infected animals, thereby ingesting the parasite's 54 first-stage larvae, which are produced from the eggshell and covered in sock-like membranes.(4) 55 Subsequently, the parasites mature into the third larval or infective stage in 2–3 weeks while in 56 the vector before migrating to the fly's trunk for transmission to a new host. These flies, which 57 are active during the daytime, land on the eye area and release infective larvae onto the 58 conjunctiva while feeding on lacrimal fluid.(5)

The first case of human thelaziasis was discovered in Asian countries, owing to the disease's spread in the former Soviet Union and Far East countries, including Korea, Nepal, China, Thailand, India and Europe.(3,6–10) This contrasts with Southeast Asian countries, such as Thailand, Myanmar, Vietnam, and Indonesia, where only a small number of ocular thelaziasis cases have been reported.(11,12)

This work has been reported in line with the improved SCARE checklist (Supplementary Material
1). The SCARE guidelines were published in 2016 and modified in 2018 to provide a structure for
surgical reports.(13)

67

68 Case Presentation

A 49-year-old man with the complaint of a moving worm in the left eye was referred to Hasanuddin University Hospital. The initial symptom was blurred vision, followed by redness and an itchy feeling in the left eye that began about 2 weeks later. A history of trauma, systemic disease, and previous ocular symptoms were denied. According to the information obtained, the patient was a farmer who resided in a district about 500 km from the capital city, where humans and animals coexisted, and no similar history had been reported in his neighbourhood.

Subsequently, the visual acuity (VA) of the right and left eyes were 20/20 and 1/60, while the intraocular pressure measured with non-contact tonometry obtained 11 and 10 mmHg, respectively. The slit-lamp examination, revealed conjunctival hyperaemia, corneal and palpebral oedema, minimal lens opacification at the anterior capsule, and a living worm in the anterior chamber of the left eye. In addition, the assessment indicated that the right eye was normal, the funduscopic examination showed a normal posterior segment, and routine investigations, including chest X-rays and blood tests, were conducted to rule out systemic disorders.

82 The surgical was performed under topical and intracameral anesthesia of lidocaine, the worm 83 then extracted from the patient's eye via a clear corneal incision made at the superior with a 84 keratome blade. The injection of Ophthalmic Viscosurgery Devices (OVD) rouse positive pressure 85 in the anterior chamber resulting the worm moved out through the main incision as shown in 86 figure 1. The worm transferred immediately into the tissue container then identified in the 87 Parasitology Laboratory of The Faculty of Medicine of Hasanuddin University and The University 88 of Indonesia. This involved submerging the organism in a formalin solution, resulting in the 89 appearance of a creamy-white colored worm measuring 13 mm long and 0.3 mm wide with both 90 ends tapered. The species was identified as *Thelazia callipaeda* based on the morphology of the 91 organism, particularly the width of the smooth and non-prominent cuticle striations, and the 92 posterior ventral curving indicated that the nematode was male (figure 2).

Following this intervention, the patient was given levamisole 250 mg single dose, natrium diclofenac 50mg bid., ciprofloxacin 500 mg bid., topical antibiotic, and topical steroid. The postoperative inflammation subsided in one week, remaining a minor lesion on the corneal endothelium and minimal lens opacity at the anterior capsule. During the follow-up a month after the surgery, the VA of the left eye slightly improved to 3/60. There was no recurrence or appearance of any other symptoms was reported in two months of follow-up.

4

99 Discussion/Conclusion

Ocular parasitosis in human is a prevalent disease in certain areas, which depends on the habitat of the causative organism, vector of transmission, the host's habits, and environmental factors. Meanwhile, thelaziasis is caused by nematodes of the genus Thelazia (known as "eyeworms"), which parasitize the orbital cavity and related structures in birds and mammals, including humans, rodents, dogs, monkeys, cattle, deer, cats, pigs, foxes, horses, and camels. Thelazia parasites feed on the tears or ocular secretions of their host and are common in regions with poor hygiene and sanitation where humans live near animals.(14)

107 Thelaziasis report is still rare especially in Asia, throughout our library search, this present case is 108 the second ocular thelaziasis occurrence in the country where the worm resided in the anterior 109 chamber, while Indonesia's first case occurred in North Sumatra reported in 1989 in a 10-month-110 old child.(15) In this study, the patient was living and working as a farmer in a rural area and had 111 a cat in his house, all of which may be related to this pathological finding. Several studies 112 suggested a relationship between human ocular thelaziasis and rural settings, improper personal 113 hygiene, low socio-economic status, and rearing livestock or parasitized animals, such as sheep, 114 dogs, pigs, and cats, in the same environment where humans reside.(16–18)

115 Thelazia is a member of nematode family and has a length of 7-20 mm. The adult worms are 116 creamy-white and thread-like with transversely striated cuticles. Their open mouth is hexagonally 117 shaped, with a well-developed buccal cavity and a slightly short esophagus. Generally, male 118 Thelazia species have lengths ranging between 5 - 12 mm and widths 0.3 - 0.4 mm, while the 119 female is slightly above 10 mm to nearly 20 mm long with widths between 0.4 - 0.5 mm. Male 120 nematodes can be distinguished macroscopically from females by the indentation on the 121 posterior area, as they possess 6-10 pairs of precloacal papillae and 3-5 pairs of postcloacal 122 papillae. Meanwhile, the female parasite is recognized by a genital opening known as the vulva, 123 which has a short flap and is located in the anterior region near the esophageal-intestinal junction. 124 The female's posterior end is rounded and blunt, with a pair of lateral papillae under the surface, 125 and the anal canal is close to the tail tip. Therefore, the number of male pre- and post-cloacal 126 papillae, as well as the position of the female vulva, are used to sex differentiation of Thelazia 127 species. In this study, the parasite species were identified as Thelazia callipaeda based on the 128 morphology of the worm. (11,19,20)

Thelazia worms parasitize the orbital cavity and related structures of the eye, such as theconjunctival sac, nictitating membrane, as well as nasal and lacrimal ducts. Although a few cases

131 of intraocular thelaziasis have been reported, this case discovered a worm in the anterior 132 chamber, and similar cases have been reported in Pakistan and Nepal.(14,21,22) However, the 133 process of the worm's entry into the anterior chamber is still unidentified, as the mouth of T. 134 callipaeda lacks hooks or sharp spines, making tissue penetration unlikely. Although the route of 135 entry into the eyes is still undetermined, some studies suggested the skin or the ingestion of 136 untreated drinking water containing the larvae or embryonated eggs as a plausible means.(23) 137 Despite various investigations, the ability of the larvae to penetrate human skin and travel along 138 the bloodstream or the larvae and embryonated eggs to survive in the human digestive tract is 139 still unexplained. However, previous studies proved that Thelazia parasites are transmitted by 140 intermediate hosts that land on the eye region and discharge larvae into the conjunctiva.(9,24)

Worm extraction is the definitive treatment for alleviating the symptoms of infestation. Furthermore, the effectiveness of levamisole and ivermectin for similar infestations in Asia and Europe has been reported.(6,25) Studies also recommend irrigation with lugol's iodine or 2% –3% boric acid after removing the worms or when the parasites are suspected to be in the lacrimal tract.(26) For this patient, 5 mg/kgBW of levamisole was used to eradicate the parasite after the thelaziasis diagnosis was confirmed by parasitologist. During two months observation, the patient did not complain of recurrence and any other related symptoms.

As a conclusion, this case of ocular thelaziasis caused by *Thelazia callipaeda*, a rare form of parasitosis in Indonesia, was discovered in South Sulawesi. The definitive treatments for this condition are worm extraction and the administration of an anti-helminthic drug. Consequently, this case highlights the importance of parasite identification based on clinical presentation and parasitologic confirmation.

153 Statements

154 Acknowledgement

- 155 The author would like to thank Professor Agnes Kurniawan from the Department of Parasitology,
- 156 University of Indonesia for the intensive discussion on parasite morphology. We also appreciate
- 157 the team of nurses and staff of Hasanuddin University Hospital for their kind support.

158 **Statement of Ethics**

- 159 All procedures performed in this study were in accordance with the ethical standards of the
- 160 institutional and national research committee with the 1964 Helsinki Declaration standards. The
- 161 study was reviewed and approved by The Ethics Committee of Medical Research, Faculty of
- 162 Medicine, Hasanuddin University (No.108/UN.4.6.4.5.31/PP36/2022). Written informed consent
- 163 was obtained from the patient for all medical examinations, treatments, and also publication of
- 164 this case report including any accompanying images.

165 **Conflict of Interest Statement**

166 The authors state that there was no conflict of interest in documenting this study.

167 Funding Sources

168 This manuscript did not receive any funding.

169 Author Contributions

170 LMKH: conception or design of the work, caring for the patient, performing follow-up after 171 surgery, analysis, interpretation of data, and drafting the work. SW: parasite identification and 172 laboratory analysis. AR: performing the surgical. JS, HBE: revising the work critically for important 173 intellectual content. ICI: project administrator, drafting and revising the work critically for 174 important intellectual content. AMI: conception or design of the work, perform surgical, revising 175 the work critically for important intellectual content.

176 Data availability statement

177 All data that support the findings of this study are included in this article.

References

179	1.	Nimir AR, Saliem A, Ibrahim IAA. Ophthalmic parasitosis: A review article. Interdiscip Perspect
180		Infect Dis. 2012;2012(September 2012):1–10.
181	2.	Bradbury RS, Gustafson DT, Sapp SGH, Fox M, De Almeida M, Boyce M, et al. A second case of
182		human conjunctival infestation with thelazia gulosa and a review of T. gulosa in North America.
183		Clin Infect Dis. 2020;70(3):518–20.
184	3.	Yang YJ, Liag TH, Lin SH, Chen HC, Lai SC. Human thelaziasis occurrence in Taiwan. Clin Exp Optom.
185		2006;89(1):40–4.
186	4.	Chanie M, Bogale B. Thelaziasis: Biology, Species Affected and Pathology (Conjunctivitis): A
187		Review. Acta Parasitol Glob. 2014;5(1):65–8.
188	5.	Otranto D, Cantacessi C, Testini G, Lia RP. Phortica variegata as an intermediate host of Thelazia
189		callipaeda under natural conditions: Evidence for pathogen transmission by a male arthropod
190		vector. Int J Parasitol. 2006 Sep;36(10–11):1167–73.
191	6.	Otranto D, Dutto M. Human Thelaziasis, Europe. Emerg Infect Dis. 2008;14(4):647–9.
192	7.	Sah R, Khadka S, Adhikari M, Niraula R, Shah A, Khatri A, et al. Human thelaziasis: Emerging ocular
193		pathogen in Nepal. Open Forum Infect Dis. 2018;5(10).
194	8.	Liu SN, Xu FF, Chen WQ, Jiang P, Cui J, Wang ZQ, et al. A Case of Human Thelaziasis and Review of
195		Chinese Cases. Acta Parasitol. 2020;65(3):783–6.
196	9.	Sohn WM, Na BK, Yoo JM. Two cases of human thelaziasis and brief review of Korean cases.
197		Korean J Parasitol. 2011;49(3):265–71.
198	10.	Do Vale B, Lopes AP, Da Conceição Fontes M, Silvestre M, Cardoso L, Coelho AC. Systematic
199		review on infection and disease caused by Thelazia callipaeda in Europe: 2001-2020. Parasite.
200		2020;27.
201	11.	Viriyavejakul P, Krudsood S, Monkhonmu S, Punsawad C, Riganti M, Radomyos P. Thelazia
202		callipaeda: a human case report. Southeast Asian J Trop Med Public Health. 2012 Jul;43(4):851-6.
203	12.	De N Van, Le TH, Chai J-Y. The First Human Case of Thelazia callipaeda Infection in Vietnam.
204		Korean J Parasitol. 2012 Aug;50(3):221–3.
205	13.	Agha RA, Borrelli MR, Farwana R, Koshy K, Fowler AJ, Orgill DP, et al. The SCARE 2018 statement:
206		Updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg [Internet].
207		2018;60(October):132–6. Available from: https://doi.org/10.1016/j.ijsu.2018.10.028
208	14.	Singh K, Khindria A. First case of Human Ocular Thelaziasis from India caused by Thelazia
209		californiensis : A case report . J Dent Med Sci. 2018;17(01):24–7.
210	15.	Kosin E, Kosman ML, Depary AA. First case of human Thelaziasis in Indonesia. Southeast Asian J
211		Trop Med Public Health. 1989 Jun;20(2):233–6.
212	16.	Purnima B, Parveez U, Angshurekha D, Uttara B. Thelaziasis: an emerging ocular parasite in

213		Northeast of India. Int J Heal Res Med Leg Pract. 2019;5(1):20.
214	17.	Otranto D, Lia RP, Buono V, Traversa D, Giangaspero A. Biology of Thelazia callipaeda (spirurida,
215		thelaziidae) eyeworms in naturally infected definitive hosts. Parasitology. 2004;129(5):627–33.
216	18.	Rolbiecki L, Izdebska JN, Franke M, Iliszko L, Fryderyk S. The vector-borne zoonotic nematode
217		thelazia callipaeda in the eastern part of europe, with a clinical case report in a dog in poland.
218		Pathogens. 2021;10(1):1–7.
219	19.	Prasertsilpa S, Bhaibulaya M, Vajrasthira S. Thelazia Callipaeda (Railliet and Henry, 1910) in Man
220		and Dog in Thailand. Am J Trop Med Hyg. 1970 May;19(3):476–9.
221	20.	Eser M, Miman Ö, Acar A. Thelazia callipaeda (Railliet and Henry, 1910) case in a dog: First record
222		in Turkey. Kafkas Univ Vet Fak Derg. 2019;25(1):129–32.
223	21.	Pal A, Atreya A, Maharjan N, Mahat M, Bom R. Human ocular Thelaziasis: A case report. J Nepal
224		Med Assoc. 2021;59(242):1060–2.
225	22.	Luo B, Xiang N, Liu R, Wang W, Li Y, Qi X. Phthiriasis palpebrarum, thelaziasis, and
226		ophthalmomyiasis. Int J Infect Dis. 2020;96:511–6.
227	23.	Otranto D, Dantas-Torres F. Transmission of the eyeworm Thelazia callipaeda: Between fantasy
228		and reality. Parasites and Vectors. 2015;8(1):7–9.
229	24.	Krishnachary PS, Shankarappa VG, Rajarathnam R, Shanthappa M. Human ocular thelaziasis in
230		Karnataka. Indian J Ophthalmol. 2014;62(7):822–4.
231	25.	Chai JY, Jung BK, Hong SJ. Albendazole and mebendazole as anti-parasitic and anti-cancer agents:
232		An update. Korean J Parasitol. 2021;59(3):189–225.
233	26.	Naem S. Thelazia Species and Conjunctivitis. In: Pelikan Z, editor. A Complex and Multifaceted
234		Disorder. InTech; 2011. p. 201–20.
235		

236 Figure Legends

- Fig. 1.a. Surgical removal of the worm (arrow) from the anterior chamber.
- 238 Fig. 1.b. A clear corneal incision was made using keratome
- 239 Fig. 1.c. A small amount of lidocaine and viscoelastic material were inserted into the anterior
- chamber.
- Fig. 1.d. The worm was extracted using microsurgery tweezers.
- Fig. 1.e. Aspiration and irrigation to remove the ophthalmic viscosurgical devices.
- 243 Fig. 1.f. Device was extracted from the anterior chamber.
- 244
- Fig. 2.a. The anterior part of the nematode has a tapered end, though the lips and buccal cavity
- 246 were not visible. Cuticle stylization appeared smooth with narrow spaces.
- Fig. 2.b. Posterior area of the adult male showing spicules (arrows), and the anal canal appears at
- 248 the end of the tail. The curved posterior sections and long spicules are characteristic of adult male
- 249 nematodes.
- Fig. 2.c. Mid-section of the nematode with intestinal tube and transversally striated smooth cuticle.
- 252 Fig. 2.d. The appearance of adjacent stria in the cuticle is characteristic of *Thelazia callipaeda*.

RESPONSE TO REVIEWER

Dear editor,

Thank you very much for your kind information. Here is our point-by-point response to the reviewers' comments:

Reviewer 1:

It look interesting. Cases with this parasite are limited in literature and in some area clinician must be careful. The paper is well structured. The authors have followed the journal rules and I suggest to accept this paper.

Response:

Thank you very much for your kind comment and support. It means a lot to us.

<mark>Reviewer 2:</mark>

I suggest reviewing the grammar. I suggest not using figure 1. Figure 2 and 3 are sufficient. **Response:**

Thank you very much for your kind suggestions. We have made some improvements to the grammar errors through the "Goodlingua English editing service". Furthermore, according to your suggestion, we have removed figure 1 in the revised version of the manuscript. Some of the changes contained in the manuscript include:

- 1. We removed the "figure 1" legend from manuscript line 77 (page 4)
- 2. We changed the legend "figure 2" to "figure 1" on the line 86 (page 4)
- 3. We changed the legend "figure 3" to "figure 2" on the line 92 (page 4)
- 4. We change the figure legends on line 237-253 (page 10):
 - Fig. 1.a. Surgical removal of the worm (arrow) from the anterior chamber.
 - Fig. 1.b. A clear corneal incision was made using keratome
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COVER LETTER

Date: 10th April 2022

To The Editor, **Case Reports in Ophthalmology**

I am enclosing herewith a **revised version** of manuscript entitled:

Case Report

Human Ocular Thelaziasis: A Case Report from Indonesia

For publication in Case Reports in Ophthalmology for possible evaluation. The aim of this paper is to report an uncommon occurrence of ocular thelaziasis in human. Throughout our library search, this present case is the second ocular thelaziasis occurrence in the country where the worm resided in the anterior chamber, while Indonesia's first case occurred in North Sumatra reported in 1989 in a 10-month-old child. Consequently, this case also highlights the importance of parasite identification based on clinical presentation and parasitologic confirmation.

Submitted manuscript is Case Report.

The corresponding author of this manuscript is Andi Muhammad Ichsan (am_ichsan@med.unhas.ac.id) and contribution of the authors as mentioned below:

- 1. Liem Meysie Kristi Harlimton^a
- 2. Sitti Wahyuni^b
- 3. Alif Reza^a
- 4. Junaedi Sirajuddin^a
- 5. Hasnah B. Eka^a
- 6. Itzar Chaidir Islam^a
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With the submission of this manuscript, I would like to undertake that:

- 1. All authors of this paper have directly participated in the planning, execution, or analysis of this study;
- 2. All authors of this paper have read and approved the final version submitted;
- 3. The contents of this manuscript have not been copyrighted or published previously;
- 4. The contents of this manuscript are not now under consideration for publication elsewhere;
- 5. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere, while acceptance by the Journal is under consideration;
- 6. There are no directly related manuscripts or abstracts, published or unpublished, by any authors of this paper;
- 7. My Institute's Department of Ophthalmology, Hasanuddin University, Makassar, Indonesia representative is fully aware of this submission.

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A 49-year-old man with the complaint of a moving worm in the left eye was referred to Hasanuddin University Hospital. The initial symptom was blurred vision, followed by redness and an itchy feeling in the left eye that began about 2 weeks later. A history of trauma, systemic disease, and previous ocular symptoms were denied. According to the information obtained, the patient was a farmer who resided in a district about 500 km from the capital city, where humans and animals coexisted, and no similar history had been reported in his neighbourhood.

75 Subsequently, the visual acuity (VA) of the right and left eyes were 20/20 and 1/60, while the 76 intraocular pressure measured with non-contact tonometry obtained 11 and 10 mmHg, 77 respectively. The slit-lamp examination, as shown in figure 1, revealed conjunctival hyperaemia, 78 corneal and palpebral oedema, minimal lens opacification at the anterior capsule, and a living 79 worm in the anterior chamber of the left eye. In addition, the assessment indicated that the right 80 eye was normal, the funduscopic examination showed a normal posterior segment, and routine 81 investigations, including chest X-rays and blood tests, were conducted to rule out systemic 82 disorders.

83 The surgical was performed under topical and intracameral anesthesia of lidocaine, the worm 84 then extracted from the patient's eye via a clear corneal incision made at the superior with a 85 keratome blade. The injection of Ophthalmic Viscosurgery Devices (OVD) rouse positive pressure 86 in the anterior chamber resulting the worm moved out through the main incision as shown in 87 figure 2 figure 1. The worm transferred immediately into the tissue container then identified in 88 the Parasitology Laboratory of The Faculty of Medicine of Hasanuddin University and The 89 University of Indonesia. This involved submerging the organism in a formalin solution, resulting in 90 the appearance of a creamy-white colored worm measuring 13 mm long and 0.3 mm wide with 91 both ends tapered. The species was identified as Thelazia callipaeda based on the morphology of 92 the organism, particularly the width of the smooth and non-prominent cuticle striations, and the 93 posterior ventral curving indicated that the nematode was male (figure 3) (figure 2).

Following this intervention, the patient was given levamisole 250 mg single dose, natrium diclofenac 50mg bid., ciprofloxacin 500 mg bid., topical antibiotic, and topical steroid. The postoperative inflammation subsided in one week, remaining a minor lesion on the corneal endothelium and minimal lens opacity at the anterior capsule. During the follow-up a month after 98 the surgery, the VA of the left eye slightly improved to 3/60. There was no recurrence or 99 appearance of any other symptoms was reported in two months of follow-up.

100 Discussion/Conclusion

Ocular parasitosis in human is a prevalent disease in certain areas, which depends on the habitat of the causative organism, vector of transmission, the host's habits, and environmental factors. Meanwhile, thelaziasis is caused by nematodes of the genus Thelazia (known as "eyeworms"), which parasitize the orbital cavity and related structures in birds and mammals, including humans, rodents, dogs, monkeys, cattle, deer, cats, pigs, foxes, horses, and camels. Thelazia parasites feed on the tears or ocular secretions of their host and are common in regions with poor hygiene and sanitation where humans live near animals.(14)

108 Thelaziasis report is still rare especially in Asia, throughout our library search, this present case is 109 the second ocular thelaziasis occurrence in the country where the worm resided in the anterior 110 chamber, while Indonesia's first case occurred in North Sumatra reported in 1989 in a 10-month-111 old child.(15) In this study, the patient was living and working as a farmer in a rural area and had 112 a cat in his house, all of which may be related to this pathological finding. Several studies 113 suggested a relationship between human ocular thelaziasis and rural settings, improper personal 114 hygiene, low socio-economic status, and rearing livestock or parasitized animals, such as sheep, 115 dogs, pigs, and cats, in the same environment where humans reside.(16–18)

116 Thelazia is a member of nematode family and has a length of 7-20 mm. The adult worms are 117 creamy-white and thread-like with transversely striated cuticles. Their open mouth is hexagonally 118 shaped, with a well-developed buccal cavity and a slightly short esophagus. Generally, male 119 Thelazia species have lengths ranging between 5 - 12 mm and widths 0.3 - 0.4 mm, while the 120 female is slightly above 10 mm to nearly 20 mm long with widths between 0.4 - 0.5 mm. Male 121 nematodes can be distinguished macroscopically from females by the indentation on the 122 posterior area, as they possess 6-10 pairs of precloacal papillae and 3-5 pairs of postcloacal 123 papillae. Meanwhile, the female parasite is recognized by a genital opening known as the vulva, 124 which has a short flap and is located in the anterior region near the esophageal-intestinal junction. 125 The female's posterior end is rounded and blunt, with a pair of lateral papillae under the surface, 126 and the anal canal is close to the tail tip. Therefore, the number of male pre- and post-cloacal 127 papillae, as well as the position of the female vulva, are used to sex differentiation of Thelazia species. In this study, the parasite species were identified as *Thelazia callipaeda* based on themorphology of the worm. (11,19,20)

130 Thelazia worms parasitize the orbital cavity and related structures of the eye, such as the 131 conjunctival sac, nictitating membrane, as well as nasal and lacrimal ducts. Although a few cases 132 of intraocular thelaziasis have been reported, this case discovered a worm in the anterior 133 chamber, and similar cases have been reported in Pakistan and Nepal.(14,21,22) However, the 134 process of the worm's entry into the anterior chamber is still unidentified, as the mouth of T. 135 callipaeda lacks hooks or sharp spines, making tissue penetration unlikely. Although the route of 136 entry into the eyes is still undetermined, some studies suggested the skin or the ingestion of 137 untreated drinking water containing the larvae or embryonated eggs as a plausible means.(23) 138 Despite various investigations, the ability of the larvae to penetrate human skin and travel along 139 the bloodstream or the larvae and embryonated eggs to survive in the human digestive tract is 140 still unexplained. However, previous studies proved that Thelazia parasites are transmitted by 141 intermediate hosts that land on the eye region and discharge larvae into the conjunctiva.(9,24)

Worm extraction is the definitive treatment for alleviating the symptoms of infestation. Furthermore, the effectiveness of levamisole and ivermectin for similar infestations in Asia and Europe has been reported.(6,25) Studies also recommend irrigation with lugol's iodine or 2% –3% boric acid after removing the worms or when the parasites are suspected to be in the lacrimal tract.(26) For this patient, 5 mg/kgBW of levamisole was used to eradicate the parasite after the thelaziasis diagnosis was confirmed by parasitologist. During two months observation, the patient did not complain of recurrence and any other related symptoms.

As a conclusion, this case of ocular thelaziasis caused by *Thelazia callipaeda*, a rare form of parasitosis in Indonesia, was discovered in South Sulawesi. The definitive treatments for this condition are worm extraction and the administration of an anti-helminthic drug. Consequently, this case highlights the importance of parasite identification based on clinical presentation and parasitologic confirmation.

154 Statements

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159 **Statement of Ethics**

- 160 $\,$ All procedures performed in this study were in accordance with the ethical standards of the
- 161 institutional and national research committee with the 1964 Helsinki Declaration standards. The
- 162 study was reviewed and approved by The Ethics Committee of Medical Research, Faculty of
- 163 Medicine, Hasanuddin University (No.108/UN.4.6.4.5.31/PP36/2022). Written informed consent
- 164 was obtained from the patient for all medical examinations, treatments, and also publication of
- 165 this case report including any accompanying images.

166 **Conflict of Interest Statement**

167 The authors state that there was no conflict of interest in documenting this study.

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170 Author Contributions

171 LMKH: conception or design of the work, caring for the patient, performing follow-up after 172 surgery, analysis, interpretation of data, and drafting the work. SW: parasite identification and 173 laboratory analysis. AR: performing the surgical. JS, HBE: revising the work critically for important 174 intellectual content. ICI: project administrator, drafting and revising the work critically for 175 important intellectual content. AMI: conception or design of the work, perform surgical, revising 176 the work critically for important intellectual content.

177 Data availability statement

178 All data that support the findings of this study are included in this article.

References

180	1.	Nimir AR, Saliem A, Ibrahim IAA. Ophthalmic parasitosis: A review article. Interdiscip Perspect
181		Infect Dis. 2012;2012(September 2012):1–10.
182	2.	Bradbury RS, Gustafson DT, Sapp SGH, Fox M, De Almeida M, Boyce M, et al. A second case of
183		human conjunctival infestation with thelazia gulosa and a review of T. gulosa in North America.
184		Clin Infect Dis. 2020;70(3):518–20.
185	3.	Yang YJ, Liag TH, Lin SH, Chen HC, Lai SC. Human thelaziasis occurrence in Taiwan. Clin Exp Optom.
186		2006;89(1):40–4.
187	4.	Chanie M, Bogale B. Thelaziasis: Biology, Species Affected and Pathology (Conjunctivitis): A
188		Review. Acta Parasitol Glob. 2014;5(1):65–8.
189	5.	Otranto D, Cantacessi C, Testini G, Lia RP. Phortica variegata as an intermediate host of Thelazia
190		callipaeda under natural conditions: Evidence for pathogen transmission by a male arthropod
191		vector. Int J Parasitol. 2006 Sep;36(10–11):1167–73.
192	6.	Otranto D, Dutto M. Human Thelaziasis, Europe. Emerg Infect Dis. 2008;14(4):647–9.
193	7.	Sah R, Khadka S, Adhikari M, Niraula R, Shah A, Khatri A, et al. Human thelaziasis: Emerging ocular
194		pathogen in Nepal. Open Forum Infect Dis. 2018;5(10).
195	8.	Liu SN, Xu FF, Chen WQ, Jiang P, Cui J, Wang ZQ, et al. A Case of Human Thelaziasis and Review of
196		Chinese Cases. Acta Parasitol. 2020;65(3):783–6.
197	9.	Sohn WM, Na BK, Yoo JM. Two cases of human thelaziasis and brief review of Korean cases.
198		Korean J Parasitol. 2011;49(3):265–71.
199	10.	Do Vale B, Lopes AP, Da Conceição Fontes M, Silvestre M, Cardoso L, Coelho AC. Systematic
200		review on infection and disease caused by Thelazia callipaeda in Europe: 2001-2020. Parasite.
201		2020;27.
202	11.	Viriyavejakul P, Krudsood S, Monkhonmu S, Punsawad C, Riganti M, Radomyos P. Thelazia
203		callipaeda: a human case report. Southeast Asian J Trop Med Public Health. 2012 Jul;43(4):851-6.
204	12.	De N Van, Le TH, Chai J-Y. The First Human Case of Thelazia callipaeda Infection in Vietnam.
205		Korean J Parasitol. 2012 Aug;50(3):221–3.
206	13.	Agha RA, Borrelli MR, Farwana R, Koshy K, Fowler AJ, Orgill DP, et al. The SCARE 2018 statement:
207		Updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg [Internet].
208		2018;60(October):132–6. Available from: https://doi.org/10.1016/j.ijsu.2018.10.028
209	14.	Singh K, Khindria A. First case of Human Ocular Thelaziasis from India caused by Thelazia
210		californiensis : A case report . J Dent Med Sci. 2018;17(01):24-7.
211	15.	Kosin E, Kosman ML, Depary AA. First case of human Thelaziasis in Indonesia. Southeast Asian J
212		Trop Med Public Health. 1989 Jun;20(2):233–6.
213	16.	Purnima B, Parveez U, Angshurekha D, Uttara B. Thelaziasis: an emerging ocular parasite in

214		Northeast of India. Int J Heal Res Med Leg Pract. 2019;5(1):20.
215	17.	Otranto D, Lia RP, Buono V, Traversa D, Giangaspero A. Biology of Thelazia callipaeda (spirurida,
216		thelaziidae) eyeworms in naturally infected definitive hosts. Parasitology. 2004;129(5):627–33.
217	18.	Rolbiecki L, Izdebska JN, Franke M, Iliszko L, Fryderyk S. The vector-borne zoonotic nematode
218		thelazia callipaeda in the eastern part of europe, with a clinical case report in a dog in poland.
219		Pathogens. 2021;10(1):1–7.
220	19.	Prasertsilpa S, Bhaibulaya M, Vajrasthira S. Thelazia Callipaeda (Railliet and Henry, 1910) in Man
221		and Dog in Thailand. Am J Trop Med Hyg. 1970 May;19(3):476–9.
222	20.	Eser M, Miman Ö, Acar A. Thelazia callipaeda (Railliet and Henry, 1910) case in a dog: First record
223		in Turkey. Kafkas Univ Vet Fak Derg. 2019;25(1):129–32.
224	21.	Pal A, Atreya A, Maharjan N, Mahat M, Bom R. Human ocular Thelaziasis: A case report. J Nepal
225		Med Assoc. 2021;59(242):1060–2.
226	22.	Luo B, Xiang N, Liu R, Wang W, Li Y, Qi X. Phthiriasis palpebrarum, thelaziasis, and
227		ophthalmomyiasis. Int J Infect Dis. 2020;96:511–6.
228	23.	Otranto D, Dantas-Torres F. Transmission of the eyeworm Thelazia callipaeda: Between fantasy
229		and reality. Parasites and Vectors. 2015;8(1):7–9.
230	24.	Krishnachary PS, Shankarappa VG, Rajarathnam R, Shanthappa M. Human ocular thelaziasis in
231		Karnataka. Indian J Ophthalmol. 2014;62(7):822–4.
232	25.	Chai JY, Jung BK, Hong SJ. Albendazole and mebendazole as anti-parasitic and anti-cancer agents:
233		An update. Korean J Parasitol. 2021;59(3):189–225.
234	26.	Naem S. Thelazia Species and Conjunctivitis. In: Pelikan Z, editor. A Complex and Multifaceted
235		Disorder. InTech; 2011. p. 201–20.
236		

237 **Figure Legends**

- 238 Fig. 1.a. Surgical removal of the worm (arrow) from the anterior chamber.
- 239 Fig. 1.b. A clear corneal incision was made using keratome
- 240 Fig. 1.c. A small amount of lidocaine and viscoelastic material were inserted into the anterior
- chamber.
- 242 Fig. 1.d. The worm was extracted using microsurgery tweezers.
- Fig. 1.e. Aspiration and irrigation to remove the ophthalmic viscosurgical devices.
- Fig. 1.f. Device was extracted from the anterior chamber.
- 245
- Fig. 2.a. The anterior part of the nematode has a tapered end, though the lips and buccal cavity
- 247 were not visible. Cuticle stylization appeared smooth with narrow spaces.
- Fig. 2.b. Posterior area of the adult male showing spicules (arrows), and the anal canal appears at
- the end of the tail. The curved posterior sections and long spicules are characteristic of adult male
- 250 nematodes.
- Fig. 2.c. Mid-section of the nematode with intestinal tube and transversally striated smooth cuticle.
- 253 Fig. 2.d. The appearance of adjacent stria in the cuticle is characteristic of *Thelazia callipaeda*.