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Lesion on the right testicle of 21-year-old patient

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ABSTRACT

Human dirofilariasis is an emerging disease that is rising and driven by increasing travel of both humans and their companion animals and climate change. We report a case of *Dirofilaria repens* in the scrotum of a 21-year-old patient, who experienced right testicular pain. Ultrasonography revealed a tubular, worm-like lesion extracted successfully and confirmed as an immature *D. repens* through parasitological and molecular analyses. Post-surgery, the patient underwent anthelmintic treatment and was discharged. Increased awareness of this parasitosis among healthcare professionals is crucial, given the expected rise in dirofilariasis cases. Climate change in Poland, characterized not so much by record high temperatures but by a systematic increase in the number of warm days, affects many aspects of life. Due to the presence of disease vectors, the introduction and reintroduction of exotic and parasitic disease, previously rare or absent in temperate climate zones, is possible.

1. Case presentation

In February 2023, a 21-year-old male presented himself at the urology clinic in Toruń, Central Poland. The patient reported a palpable mass in the scrotum that he had noticed two weeks earlier. He denied itching, pain, dysuric symptoms, or febrile states. He had been healthy previously and was not on any long-term medication. He lived in a rural area, had never travelled abroad, and had regular contact with animals, without noting insect bites. Laboratory tests performed by the family physician showed blood cell count within normal range, unremarkable white blood cell differential, including eosinophils at 0.27 G/l (0.04-0.4 G/l), creatinine level at 0.82 mg/dl (0.5-1.2 mg/dl), CRP at 0.8 mg/l (<5 mg/l). In the general urine examination, numerous strands of mucus and abundant oxalates were found. On physical examination, the scrotal skin showed no abnormalities. Both testicles were palpable and painless, elastic, and without focal changes. On the posterior surface of the right testicle, a soft, painless lesion with a diameter of approximately 10 mm was detected. No lymphadenopathy was observed. Ultrasound examination revealed a well-defined focal lesion measuring 0.97×0.58 mm, with a tubular structure moving within it, arranged in parallel hyperechoic bands (Fig. 1). The testicles had normal echogenicity and echostructure with preserved symmetric vascular flow, and the epididymides were regular, with normal fluid between their membranes. Focal changes were not detected.

The ultrasonographic image raised suspicion of nematode infection. After consultation with a parasitology specialist and obtaining the patient's consent, an excision under local anaesthetic was performed.

2. Discussion

The ultrasonographic image raised suspicion of dirofilariasis. A white, thread-like structure with a length of 80 mm exhibiting movement was extracted (Fig. 2). The material was preserved in 70% ethanol and subjected to molecular diagnostics. Whole-cell DNA was isolated, and a polymerase chain reaction specific to Filariidae was performed by amplifying the internal transcribed spacer 1 (ITS1) of the ribosomal DNA using pan-filarial primers. (Supplementary Fig. 1). The sequence was obtained using Next-Generation Sequencing, and BLAST analysis confirmed a 100% match with *D. repens* records. After the surgical procedure, the patient was discharged home, and during the outpatient follow-up, the wound healed well, and the sutures were removed. Treatment with doxycycline was initiated at a dose of 200 mg orally daily for 6 weeks [1].

In Poland, a country that is non-endemic for tropical diseases, diagnosing parasitic infections, including those of cosmopolitan nature, is rarely implemented. Consequently, there are only a few specialists in this field. Often, the approach adopted during the diagnostic and therapeutic process is based on recommendations from international

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Fig. 1. Ultrasonography image of a lesion present on patient's right testicle surface. The lesion measured 0.97×0.58 cm. A typical tubular structure was observed within the lesion. Picture by: Pawel Poblocki.



Fig. 2. Picture of removed lesion with a nematode measuring approximately 8 cm.

experts. In this instance, the urologist who recognized the pathological condition showed commendable vigilance. Together with radiologists, he arrived at an accurate diagnostic hypothesis. He then sought a specialist in parasitic diseases, across several healthcare facilities, to guide the subsequent therapy. The decision to recommend oral doxycycline treatment after surgery drew inspiration from the publication by Lechner et al [2]. Microfilaremia was not observed in this patient, and it is generally rarely encountered in humans. However, there are reports confirming its occurrence in some cases [3,4]. Definitive hosts for D. repens primarily include wild and domestic canids, with occasional infections reported in felids [5]. D. repens-associated lesions can manifest in various anatomical locations, predominantly in exposed areas such as the scalp, arms, legs, eyelids, and chest. However, lesions have also been identified in deeper tissues including the breast, epididymis, spermatic cord and subconjunctiva [6–8]. Up until 2012, approximately 2000 cases of human dirofilariasis caused by D. repens have been diagnosed and documented across Europe [9]. The highest number of cases was reported in Ukraine, followed by Mediterranean regions (e.g., Italy), and countries such as Hungary, Austria, Serbia, and Slovakia [10]. The first documented human case of D. repens infection occurred in Poland in 2007 [9].

Climatic changes leading to warmer temperatures that favor survival of *Dirofilaria*- susceptible mosquito species, together with rise in the movement of dogs with their owners across Europe, have caused an increase in the geographical range of *Dirofilaria* infections [11]. Human dirofilariasis has emerged as a global concern with which physicians increasingly grapple [12]. The surge in international travel poses added challenges to European Health Units, which often face rare pathologies, making diagnosis difficult for health professionals unfamiliar with these conditions [13]. Despite dirofilariasis being easily manageable when correctly identified, it frequently remains undiagnosed because of the challenges stemming from accurate parasite identification.

For the described patient, the decision was made to surgically remove the parasitic lesion, which is considered a widely accepted and radical therapeutic approach. The inclusion of doxycycline was prompted by case reports of the extremely rare, but not impossible, occurrence of microfilaremia in humans infected with *D. repens*. Due to the lack of international treatment guidelines for dirofilariasis, therapeutic decisions were based on medical literature and involved an individualized, cautious approach for this patient and it is not recommended as generally approved approach.

An increase in the number of *Dirofilaria* infections in both humans and animals is anticipated in coming years in Poland and other Central and Eastern European countries, because of a significant influx of refugees, together with their companion animals, into the European Union from regions in the east that are hyperendemic for dirofilariasis [14]. Based on our experience, we consider that current terminology lacks clarity in capturing the disease's multifaceted presentations. Emphasizing the exact lesion location and ensuring species identification can minimize any confusion and uncertainty about the etiology of suspected cases. There is also an urging need for comprehensive epidemiological data on human dirofilariasis, encompassing the environment where cases emerge, patient habits, and parasitological findings [15]. As clinical cases remain a primary source of information about the disease, routinely capturing such data becomes indispensable [16].

Climate change is occurring globally, accompanied by intensified human migration. This significantly impacts the epidemiology of tropical diseases. In previous studies, it has been proven that climate change influences the spread of *D. repens* in Europe [17–19]. This is attributed to an increased number of warm days per year, the migration of humans and dogs, and the stable or expanding populations of vector species (e.g. *Aedes, Culex, Anopheles*) [20]. For instance, dengue fever, known a few decades ago in only a few countries, is now spread in tropical regions and Europe. It is anticipated that diseases previously confined to the tropics will increasingly appear in cooler climate regions.

The One Health concept emphasizes that the health of humans, animals, and plants is interdependent and connected to the state of the ecosystems in which they live. This approach is based on the collaboration of societies and governments, aiming to understand, predict, and eliminate global health threats [21,22]. Both medical services and travelers, as well as residents of non-endemic countries, should be aware of the presence of tropical or parasitic diseases and have access to their diagnostics and effective treatments.

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Anna Kuna: Writing - review & editing, Writing - original draft,

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Declaration of competing interest

Authors declare no conflict of interests.

Data availability

All relevant data are included in the article. Dirofilaria repens sequence has been deposited in BioProject under accession number SUB13879323.

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References

- [1] G. Capelli, C. Genchi, G. Baneth, P. Bourdeau, E. Brianti, L. Cardoso, P. Danesi, H.-P. Fuehrer, A. Giannelli, A.M. Ionică, C. Maia, D. Modrý, F. Montarsi, J. Krücken, E. Papadopulos, D. Petrić, M. Pfeffer, S. Savić, D. Otranto, S. Poppert, C. Silaghi, Recent advances on Dirofilaria repens in dogs and humans in Europe, Parasit. Vectors 11 (2018) 663, https://doi.org/10.1186/s13071-018-3205-x.
- [2] A.M. Lechner, H. Gastager, J.M. Kern, B. Wagner, D. Tappe, Case report: successful treatment of a patient with Microfilaremic dirofilariasis using doxycycline, Am. J. Trop. Med. Hyg. 102 (2020) 844–846, https://doi.org/10.4269/ajtmh.19-0744.
- [3] A. Pupić-Bakrač, J. Pupić-Bakrač, A. Beck, D. Jurković, A. Polkinghorne, R. Beck, Dirofilaria repens microfilaremia in humans: case description and literature review, One Health 13 (2021) 100306, https://doi.org/10.1016/j. onehlt.2021.100306.
- [4] M. Kłudkowska, Ł. Pielok, K. Frąckowiak, A. Masny, E. Gołąb, M. Paul, Dirofilaria repens infection as a cause of intensive peripheral microfilariemia in a polish patient: process description and cases review, Acta Parasitol. 63 (2018) 657–663, https://doi.org/10.1515/ap-2018-0077.
- [5] M. Alsarraf, D. Dwużnik-Szarek, J. Hildebrand, E.J. Mierzejewska, A. Kloch, K. Kot, K. Kurek, S. Nowak, R.W. Mysłajek, I. Myśliwy, M. Popiołek, A. Rodo, M. Alsarraf, K. Tołkacz, M. Topolnytska, D. Wężyk, A. Bajer, Occurrence of Dirofilaria repens in wild carnivores in Poland, Parasitol. Res. 122 (2023) 1229–1237, https://doi.org/10.1007/s00436-023-07823-5.
- [6] M. Joseph, M.M. Krishna, A. Vijayan, Human Subcutaneous Dirofilariasis, Cureus (2023), https://doi.org/10.7759/cureus.35879.
- [7] B.K. Saha, A. Bonnier, W.H. Chong, H. Chieng, A. Austin, K. Hu, B. Shkolnik, Human pulmonary dirofilariasis: a review for the clinicians, Am J Med Sci 363 (2022) 11–17, https://doi.org/10.1016/j.amjms.2021.07.017.

- [8] K. Riebenbauer, P.B. Weber, J. Walochnik, F. Karlhofer, S. Winkler, S. Dorfer, H. Auer, J. Valencak, M. Laimer, A. Handisurya, Human dirofilariosis in Austria: the past, the present, the future, Parasit. Vectors 14 (2021) 227, https://doi.org/ 10.1186/s13071-021-04696-4.
- [9] J. Czyżewska, J. Zajkowska, R. Sałamatin, J. Kamińska, O.M. Koper-Lenkiewicz, J. Matowicka-Karna, Multiple subcutaneous Dirofilaria repens; infection in a patient from Poland with a rheumatic history, Pol. Arch. Intern. Med. (2023), https://doi.org/10.20452/pamw.16557.
- [10] M. Alsarraf, V. Levytska, E.J. Mierzejewska, V. Poliukhovych, A. Rodo, M. Alsarraf, D. Kavalevich, D. Dwużnik-Szarek, J.M. Behnke, A. Bajer, Emerging risk of Dirofilaria spp. infection in Northeastern Europe: high prevalence of Dirofilaria repens in sled dog kennels from the Baltic countries, Sci. Rep. 11 (2021) 1068, https://doi.org/10.1038/s41598-020-80208-1.
- [11] C. Genchi, M. Mortarino, L. Rinaldi, G. Cringoli, G. Traldi, M. Genchi, Changing climate and changing vector-borne disease distribution: the example of Dirofilaria in Europe, Vet. Parasitol. 176 (2011) 295–299, https://doi.org/10.1016/j. vetpar.2011.01.012.
- [12] C. Genchi, L. Rinaldi, M. Mortarino, M. Genchi, G. Cringoli, Climate and Dirofilaria infection in Europe, Vet. Parasitol. 163 (2009) 286–292, https://doi.org/10.1016/ i.vetnar.2009.03.026.
- [13] C. Genchi, L.H. Kramer, F. Rivasi, Dirofilarial infections in Europe, Vector-Borne and Zoonot. Diseas. 11 (2011) 1307–1317, https://doi.org/10.1089/ vbz/2010.0247
- [14] R. Sałamatin, T. Pavlikovska, O. Sagach, S. Nikolayenko, V. Kornyushin, V. Kharchenko, A. Masny, D. Cielecka, J. Konieczna-Sałamatin, D. Conn, E. Golab, Human dirofilariasis due to Dirofilaria repens in Ukraine, an emergent zoonosis: epidemiological report of 1465 cases, Acta Parasitol. 58 (2013), https://doi.org/ 10.2478/s11686-013-0187-x.
- [15] F. Simón, M. Siles-Lucas, R. Morchón, J. González-Miguel, I. Mellado, E. Carretón, J.A. Montoya-Alonso, Human and animal dirofilariasis: the emergence of a zoonotic mosaic, Clin. Microbiol. Rev. 25 (2012) 507–544, https://doi.org/ 10.1128/CMR.00012-12.
- [16] K. Riebenbauer, P.B. Weber, J. Walochnik, F. Karlhofer, S. Winkler, S. Dorfer, H. Auer, J. Valencak, M. Laimer, A. Handisurya, Human dirofilariosis in Austria: the past, the present, the future, Parasit. Vectors 14 (2021) 227, https://doi.org/ 10.1186/s13071-021-04696-4.
- [17] J.P. Gutiérrez-Jara, M. Salazar-Viedma, C.R. González, B. Cancino-Faure, The emergence of Dirofilaria repens in a non-endemic area influenced by climate change: dynamics of transmission using a mathematical model, Acta Trop. 226 (2022) 106230, https://doi.org/10.1016/j.actatropica.2021.106230.
- [18] D.D. Colwell, F. Dantas-Torres, D. Otranto, Vector-borne parasitic zoonoses: emerging scenarios and new perspectives, Vet. Parasitol. 182 (2011) 14–21, https://doi.org/10.1016/j.vetpar.2011.07.012.
- [19] C. Genchi, L. Rinaldi, M. Mortarino, M. Genchi, G. Cringoli, Climate and Dirofilaria infection in Europe, Vet. Parasitol. 163 (2009) 286–292, https://doi.org/10.1016/ j.vetpar.2009.03.026.
- [20] E. Shaikevich, A. Bogacheva, L. Ganushkina, Dirofilaria and Wolbachia in mosquitoes (Diptera: Culicidae) in central European Russia and on the Black Sea coast, Parasite 26 (2019) 2, https://doi.org/10.1051/parasite/2019002.
- [21] B.H. Bird, J.A.K. Mazet, Detection of emerging zoonotic pathogens: an integrated one health approach, Annu. Rev. Anim. Biosci. 6 (2018) 121–139, https://doi.org/ 10.1146/annurey-animal-030117-014628.
- [22] R.R. Ghai, R.M. Wallace, J.C. Kile, T.R. Shoemaker, A.R. Vieira, M.E. Negron, S. V. Shadomy, J.R. Sinclair, G.W. Goryoka, S.J. Salyer, C. Barton Behravesh, A generalizable one health framework for the control of zoonotic diseases, Sci. Rep. 12 (2022) 8588, https://doi.org/10.1038/s41598-022-12619-1.