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CASE REPORT

Pseudo-Tumor of the Epididymis, a Rare Clinical Presentation of Human *Dirofilaria repens* Infection: a Report of Autochthonous Case of *Dirofilariasis* in Southwestern Slovakia

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Abstract

Purpose Dirofilariasis caused by the filarial nematode *Dirofilaria repens* is mainly a disease of dogs and other carnivores. Also, humans can be accidentally infected with this parasite. The infective third-stage filariform larvae are transmitted by various species of mosquitoes. Until this day, a total of 17 human cases caused by *D. repens* have been diagnosed in Slovakia, 11 subcutaneous, 4 ocular, 1 pulmonary and 1 in the epididymis. The aim of this report was to describe an unusual clinical case of dirofilariasis of the scrotum.

Methods Extirpated worm was subjected to the molecular and histological identification. PCR for the amplification of cytochrome oxidase subunit 1 (CO1) was performed using specific *D. repens* primer pair.

Results Here we document the 13th case of human dirofilariasis in a 46-year-old man from southwestern Slovakia. Very rare in humans, genital involvement manifests itself as pseudotumor nodule affecting the epididymis. The patient consulted a general practitioner due to a palpable subcutaneous lump in the scrotum. Routine laboratory analysis revealed blood eosinophilia (16.6%). The ultrasound examination was indicated, and subsequently, surgical excision of the right epididymal nodule was performed. On the basis of histological microscopic examination and PCR-based detection, the helminth was identified as *Dirofilaria repens*. This represents the ninth case of autochthonous dirofilariasis in Slovakia.

Conclusions The majority of *D. repens* infections were recorded in southwestern regions of Slovak Republic, which are considered to be endemic areas for canine dirofilariasis. Our described patient also comes from southwestern part of Slovakia (Topoľníky, Dunajská Streda region).

Keywords *Dirofilaria repens* · Human dirofilariasis · Genital involvement

Introduction

Dirofilariasis is a helminthic zoonosis caused by filarial species of the genus *Dirofilaria* transmitted by hematophagous dipterans that primarily parasitize domestic dogs, cats, and other species of wild mammals. Vector-borne zoonotic transmitted diseases cause deaths and economic losses in human and domestic animal populations around the world [8, 11]. The infective larval stage is transmitted by blood-sucking mosquitoes of genera *Aedes*, *Culex*, and *Anopheles* [28]. Rarely, humans represent an accidental host for this parasitic species and human´s tissues are not a suitable environment for the nematode to live. Pets, such as dogs, cats, ferrets and a wide range of wild carnivorous species are definitive hosts and also reservoirs of dirofilariasis [18, 21, 31]. The fertilized female worm gives birth to live microfilariae in the

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blood of the host. Mosquitoes ingest the first-stage larvae with a blood meal from the infected host, which develop into the infective third-stage filariform larvae. When the third-stage larvae have matured and are found in the salivary glands of the mosquito, the infection can be transmitted to the next animal including humans from which the mosquito takes the next blood meal [10]. The multicellular filiform roundworm (50–170 mm in length) is responsible for dirofilariasis of the definitive hosts, including humans [20]. The epidemiological profile of canine dirofilariasis in Europe is characterized by the presence of *D. immitis* and *D. repens* [3]. All diagnosed human cases of dirofilariasis in Slovakia were caused by *D. repens* [22]. Infection presents itself clinically as subcutaneous nodules (measuring up to 3 cm in diameter), subcutaneous migration of parasite in tissues, pruritus, erythema, and conjunctival nodules. In rare cases, the helminth can penetrate deeper into the internal organs. Lesions involving the scrotum, epididymis or spermatic cord may mimic malignant tumors and the diagnosis is based on histological examination. Genital localization of dirofilariasis is extremely rare, only few cases were reported in the literature [12, 19, 28]. *D. immitis* is responsible for canine cardiopulmonary dirofilariasis in Slovakia [24].

The only known treatment is surgical removal of the worm [32]. Preventive measures are similar to other mosquito-transmitted pathogens, which include the wearing of protective clothing, the use of repellents and bed nets [27].

Case Report

A 46-year-old man working as a truck driver (business trips to Germany and Denmark) who lived in the village of Topoľníky (Dunajská Streda region, southern Slovakia) consulted a general practitioner on August 2017 due to a nodule in the right epididymis. The patient did not remember being bit by a mosquito, but he did not exclude it either. Also, subcutaneous migration of the parasite was not observed. The doctor presumed a cyst that should be absorbed after a few months. Routine laboratory analysis revealed blood eosinophilia (16.6%) and a decreased neutrophil count (38.9%). Even after 9 months (April 2018), the lump (probable cyst) was not absorbed. The patient was forced to visit the urology department at St. Lukas's hospital in Galanta, where the ultrasound examination was indicated. The conclusion of this examination was a local finding of probable pseudotumor with free fluid at the right epididymis. Ultrasound analysis showed a nodule measuring 13 × 18 mm, with calcification and no vascularity. The amounts of eosinophils had dropped to normal levels (3.2%) just before surgical resection. In April 2018, surgical excision of the right epididymal nodule was performed. After surgery, the patient was discharged to outpatient care. The man had a postoperative course without complication. The biopsy samples were sent for histological examination. They were processed by a routine procedure and tissue sections were stained with hematoxylin–eosin. After examinations, an oval whitish smooth excision with a diameter of 15 mm was observed, in which a 5-mm cyst was located indicating a suspected fibroma. Microscopic examination of extirpated worm revealed morphological signs (longitudinal ridges, multilayered cuticle, and sex organs) typical for an adult non-gravid female of *Dirofilaria repens* (Fig. 1). The parasite's cuticle was approximately 10 µm thick with spikes on the entire outer surface with crests measuring 3 µm in height (Fig. 2). Internal structures like a double uterus containing oocytes and a digestive tract were located in a pseudocoelomic cavity and clearly visible (Fig. 3). DNA from embedded paraffin tissue was isolated using DNeasy Blood and Tissue Kit (Quiagen, Hilden Germany). PCR for the amplification of cytochrome oxidase subunit 1 (CO1) was performed using specific *D. repens* primer pair [29] and PCR conditions according to



Fig. 1 Cross section of *Dirofilaria repens* with typical longitudinal cuticular ridges (LCR)

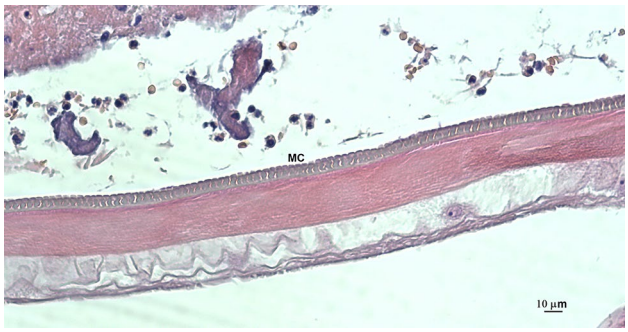


Fig. 2 Longitudinal section of the worm with a characteristic multilayered outer cuticle (MC)

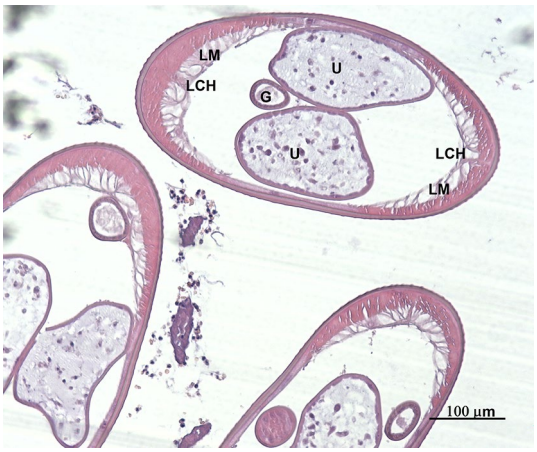


Fig. 3 Transversal section of the nematode showing double uterus (U), one central gut section (G), longitudinal muscles (LM) and lateral chords (LCH)

Antolová et al. [2]. The presence of 209-bp long band of nematode-specific mitochondrial DNA (CO1) on 1.5% agarose gel confirmed that our helminth belongs to *D. repens* species. The serological examination was not performed.

Discussion

This is the first reported case of scrotal infection with *D. repens* in Slovakian patient. Here we document probably the ninth case of autochthonous dirofilariasis in Slovakia despite the fact that the patient as a truck driver travelled abroad. The patient was driving from Slovakia to Germany and Denmark. In both of those foreign countries, only two cases of human dirofilariasis have been documented. Even the case of human infection with *D. repens* in Denmark was probably imported from Crete (Greece) [17, 33]. Our patient lives in the village of Topoľníky (Dunajská Streda region, southern Slovakia), southwestern Slovakia. Until this day, a total of 17 human cases caused by *D. repens* have been diagnosed in Slovakia, 11 subcutaneous, 4 ocular, 1 pulmonary [22] and 1 in the epididymis. The majority of patients (12/17) infected with *D. repens* came from southwestern regions of Slovak Republic, which are considered to be endemic areas for canine dirofilariasis as had been confirmed during the previous large-scale epidemiological studies in dogs (prevalence to 25%) [23]. Investigation of mosquito material from southwest Slovakia revealed 4.26% relative prevalence of *Dirofilaria* spp.[7]. Of the infected patients, 11 were males and 6 were females, and their age varied between 15 and 72 years.

Emergence of autochthonous human dirofilariasis caused by *D. repens* was recorded in Hungary [9], Austria [14], and Poland [6], i.e. countries neighboring Slovak Republic. From several to 30 cases of human dirofilariasis were diagnosed in these countries. In the Europe, the highest incidence of human cases occurs in traditional endemic areas of southern countries (Italy, France, and Greece) and Ukraine [25]. In the Ukraine, bordering Slovakia in the east, an extensive epidemiological study revealed more than 1400 cases of human *D. repens* infection [30].

Approximately 25% of all epididymal tumors are malignant including fibrosarcomas, rhabdomyosarcomas, squamous cell carcinomas, teratomas, and other neoplasms of germ cell origin, carcinomas, adenocarcinomas, lymphomas, and undifferentiated carcinomas [4]. Benign lesion is distinguishable by their clinical presentation and ultrasound appearance. In some region of the world, nematodes infection as dirofilariasis should be considered in the differential diagnosis of the asymptomatic scrotal mass [34]. Dirofilariasis of the male genitalia remains a rare event with only 22 cases reported in the literature [5, 19, 34] involving the epididymis, scrotum or spermatic cord, and can be mistaken for scrotal malignancy or malignant neoplasm, resulting in unnecessary extensive operation [1]. Absent vascularization inside the mass and the absent of a vascular pole allowed differential diagnosis with a neoplastic mass as a para-testicular rhabdomyosarcoma, in which a more aggressive treatment is mandatory [12]. The long-lasting incubation period of dirofilariasis in the vertebrate host is 6–8 months [17]. The rare localization in the epididymis likely occurs after subcutaneous migration of the worm from the bite side. The common sites of the lesions are face and eyelids, chest wall, and upper arms [15, 22]. Treatment of nodule consists of complete excision [34]. In our case, the surgery was also applicable.

In humans, the worms are usually single and immature, and so the microfilariae are not present in peripheral blood [34]. However, one report of circulating microfilaria in a human exists in medical literature, and a case report showing the present of microfilaria in a nodule examinated by fine needle aspiration [13]. In dirofilariasis, no reliable signs, symptoms or laboratory parameters are available. Elevated IgE level and eosinophilia are almost always absent, although increased IgE level could confirm the diagnostic suspicion [34]. Nevertheless, the increased level of eosinophils was observed in our case in the beginning of infection. Filariasis serologies are not very specific, and are mostly negative [26]. Diagnosis is primarily based on histopathological characteristics of the helminth. In most cases (similarly in our patient), a female worm is found, presenting a double uterus, usually without microfilariae. The male worm is characterized by a single sex organ [16, 19]. Precise identification of *Dirofilaria* species may be achieved at the molecular level with DNA analysis using the polymerase chain reaction [2, 29].

In the future, an increasing number of infected patients in our country can be expected, which confirms that so far the highest number (four human dirofilariasis in 2018) of diagnosed cases within 1 year. Increasing prevalence of dirofilariasis in humans observed in the last decades throughout Europe (including Slovakia) connected with global climate changes points out the importance of proper diagnosis of this emerging parasitic disease.

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References

1. Annam A, Munden MM, Mehollin-Ray AR, Schady D, Browne LP (2015) Extratesticular masses in children taking ultrasound beyond paratesticular rhabdomyosarcoma. Pediatr Radiol 45:1382–1391
2. Antolová D, Miterpáková M, Paraličová Z (2018) Case of human *Dirofilaria repens* infection manifested by cutaneous larva migrans syndrome. Parasitol Res 114:2969–2973
3. Araujo AM (1996) Canine and human *Dirofilaria immitis* infections in Portugal. A review. Parassitologia 38:366
4. Aydin A, Aksoy HZ, Reis A, Özdemir F (2011) Undifferentiated carcinoma of the epididymis. Acta Clin Croat 50:415–418
5. Bertozzi M, Rinaldi VE, Perstipino M, Giovenali P, Appignani A (2015) Dirofilariasis mimicking an acute scrotum. Pediatr Emerg Care 31:715–716
6. Borkowski PK, Rymkiewicz G, Golebiewska J, Nestoros N, Romejko-Jarosinska J, Zarnowska-Prymek H, Masny A, Palucki J, Cielecka D (2015) The first case of human autochtonous subconjunctival dirofilariosis in Poland and MALT lymphoma as possible consequence of this parasitosis. Infect Agents Cancer 10:1–5
7. Čabanová V, Miterpáková M, Valentová D, Blažejová H, Rudolf I, Stloukal E, Hurníková Z, Dzidová M (2018) Urbanization impact on mosquito community and the transmission potential of filarial infection in Central Europe. Parasite Vectors 11:261
8. Day MJ (2011) One Health: the importance of companion animal vector-borne diseases. Parasit Vectors 4:49
9. Dóczi I, Bereczki L, Gyetvai T, Fejes I (2015) Description of five dirofilariasis cases in South Hungary and review epidemiology of this disease for the country. Wien Klin Wochenschr 127:696–702
10. Ermakova LA, Nagorny SA, Krivorotova EY, Pshenichnaya NY, Matina ON (2014) *Dirofilaria repens* in the Russian Federation: current epidemiology, diagnosis, and treatment from a federal reference center perspective. Int J Infect Dis 23:47–52
11. Faburay B (2015) The case for a 'one health' approach to combating vector-borne diseases. Infect Ecol Epidemiol 5:28132
12. Fleck R, Kurz W, Quade B, Geginat G, Hof H (2009) Human dirofilariasis due to Dirofilaria repens mimicking a scrotal tumor. Urology 73:209
13. Fontanelli SL, Gabrielli S, De Angelis M, Milardi GL, Magnani C, Di Marco B, Taliani G, Cancrini G (2016) *Dirofilaria repens* microfilariae from a human node fine-needle aspirate: a case report. BMC Infect Dis 16:248
14. Fuehrer HP, Auer H, Leschnik M, Silbermayr K, Duscher G, Joachim A (2016) Dirofilaria in humans, dogs, and vectors in Austria (1978–2014) from imported pathogens to the endemicity of *Dirofilaria repens*. Plos Negl Trop Dis 10:1–13
15. Gopinath TN, Lakshmi KP, Shaji PC, Rajalakshmi PC (2013) Periorbital dirofilariosis clinical and imaging findings: live worm on ultrasound. Indian J Ophtalmol 61:298–300
16. Guttierrez Y (2000) Diagnostic pathology of parasitic infections with clinical correlations, 2nd edn. Oxford University Press, London, pp 480–507
17. Klintebjerg K, Petersen E, Pshenichnaya NY, Ermakova LA, Nagorny SA, Larsen CS (2015) Periorbital *Dirofilaria repens* imported to Denmark: a human case report. IDCases 2:25–26
18. Kravchenko V, Itin G, Kartashev V, Ermakov A, Kartashov S, Diosdado A, González-Miguel J, Simón F (2016) *Dirofilaria immitis* and *D. repens* in sylvatic reservoirs of Krasnodar Krai (Russian Federation). Vet Parasitol Reg Stud Rep 6:35–38
19. Leccia N, Patouraux S, Carpentier X, Boissy C, Del Giudice P, Parks S, Michiels JF, Ambrosetti D (2012) Pseudo-tumor of the scrotum, a rare clinical presentation of dirofilariasis: a report of two autochtonous cases due to *Dirofilaria repens*. Pathog Glob Health 106:370–372
20. Manfredi MT, Di Cerbo A, Genchi M (2007) Biology of filarial worms parasitizing dogs and cats. In: Genchi C, Rinaldi L, Cringoli G (eds) *Dirofilaria immitis* and *D. repens* in dog and cat and human infections. Mappe parassitologiche. Universita` degli Studi di Napoli Federico II, Naples, Italy, pp 39–47
21. McCall JW, Genchi C, Kramer LH, Guerrero J, Venco L (2008) Heartworm disease in animals and humans. Adv Parasit 66:193–285
22. Miterpáková M, Antolová D, Ondriska F, Gál V (2017) Human *Dirofilaria repens* infections diagnosed in Slovakia in the last 10 years (2007–2017). Wien Klin Wochenschr 129:634–641
23. Miterpáková M, Iglódyová A, Čabanová V, Stloukal E, Miklisová D (2016) Canine dirofilariosis endemic in Central Europe 10 years of epidemiological study in Slovakia. Parasitol Res 115:2389–2395
24. Miterpáková M, Valentová D, Čabanová V, Berešíková Ľ (2018) Heartworm on the rise new insights into *Dirofilaria immitis* epidemiology. Parasitol Res 117:2347–2350
25. Pampiglione S, Canestri-Trotti G, Rivasi F (1995) Human dirofilariasis due to *Dirofilaria repens*. Review of the world literature. Parassitologia 37:149–194
26. Pampiglione S, Rivasi F, Gustinelli A (2009) Dirofilarial human cases in the Old World, attributed to *Dirofilaria immitis*: a critical analysis. Histopathology 54:192–204
27. Patel SN, Brahmbhatt MN, Nayak JB, Desai ND, Kaje VS (2015) Human dirofilariasis: "An emerging zoonosis. J Foodborne Zoonotic Dis 3:39–41
28. Raccurt CP (2008) La dirofilariose, zone émergente et méconnue en France. Med Trop 59:389–400 **(In French)**
29. Rishniw M, Barr SC, Simpson KW, Frongillo M, Franz M, Dominquez Alpizar JL (2006) Discrimination between six species of canine microfilariae by a single polymerase chain reaction. Vet Parasitol 135:303–314
30. Sałamatin RV, Pavlikovska TM, Sagach OS, Nikolayenko SM (2013) Human dirofilariasis due to *Dirofilaria repens* in Ukraine, an emergent zoonosis: epidemiological report of 1465 cases. Acta Parasitol 58:592–598
31. Simón F, Siles-Lucas M, Morchón R, González-Miguel J, Mellado I, Carretón E, Montoya-Alonso JA (2012) Human and animal dirofilariasis: the emergence of a zoonotic mosaic. Clin Microbiol Rev 25:507–544
32. Smitha M, Rajendran VR, Devarajan E, Anitha PM (2008) Case report: orbital dirofilariasis. Indian J Radiol Imaging 18:60–62
33. Tappe D, Plauth M, Bauer T, Muntau B, Dießel L, Tannich E, Herrmann-Trost P (2014) A case of autochthonous human dirofilaria infection, Germany, March 2014. Euro Surveill 19:2–4
34. Tripi F, Scarlata F, Verde V, Voti GL, Chiaramonte C (2016) Human dirofilariasis presenting as scrotal mass. J Urol Nephrol 3:1–4

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