



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

Vojtech Boldiš¹ · František Ondriska^{1,2} · Vladimír Bošák² · Ondrej Hajdúk³ · Daniela Antolová⁴ · Martina Miterpáková⁴

Received: 13 August 2019 / Accepted: 9 January 2020 / Published online: 20 January 2020
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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

✉ Vojtech Boldiš
vojtech.boldis@medirex.sk

¹ Department of Parasitology, Medirex Ltd., Galvaniho 17/C, 82016 Bratislava, Slovakia

² School of Health Sciences and Social Work Trnava, University Trnava, Univerzitné námestie 1, 91843 Trnava, Slovakia

³ Hospital With St. Lukas Polyclinic in Galanta, Hodská 373/38, 924 22 Galanta, Slovakia

⁴ Institute of Parasitology, Slovak Academy of Sciences, Hlinkova 3, 040 01 Košice, Slovakia

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

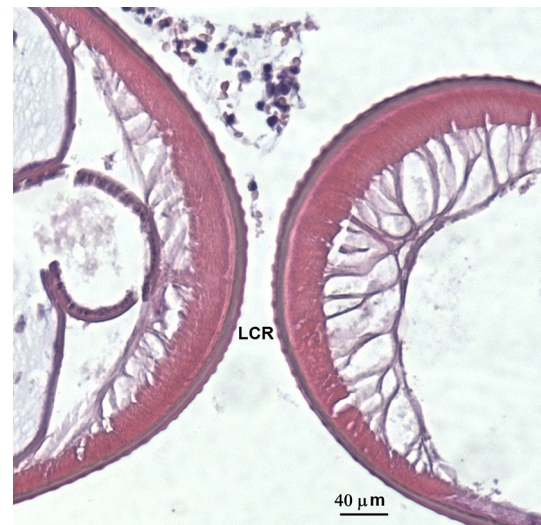


Fig. 1 Cross section of *Dirofilaria repens* with typical longitudinal cuticular ridges (LCR)

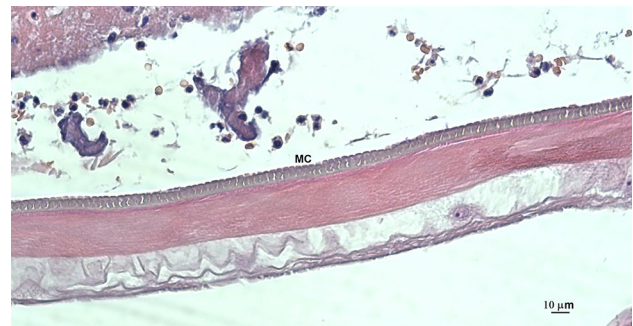


Fig. 2 Longitudinal section of the worm with a characteristic multi-layered outer cuticle (MC)

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

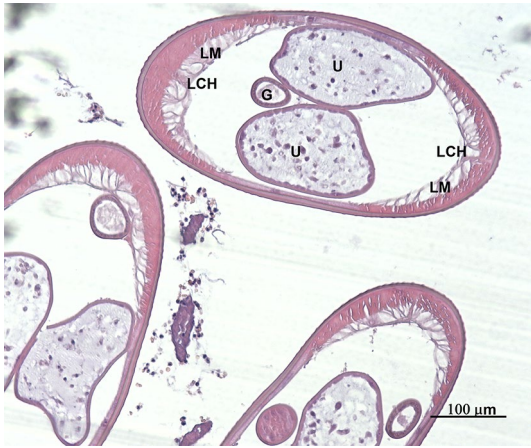


Fig. 3 Transversal section of the nematode showing double uterus (U), one central gut section (G), longitudinal muscles (LM) and lateral chords (LCH)

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 examined 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.

Acknowledgements This study was supported by the KEGA 013TTU-4/2019.

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