ACTA FACULTATIS MEDICAE NAISSENSIS

UDC: 616.995.132-07

Scientific Journal of the Faculty of Medicine in Niš 2010;27(2):81-84

Professionl article ■

Diagnosis and Clinical Importance of Human Dirofilariosis

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SUMMARY

The dog parasites *Dirofilaria immitis* (*D. immitis*) and *Dirofilaria repens* (*D. repens)*, well known as zoonotic agents, can infect humans with immature forms.

Human dirofilarioses in many asymptomatic patients are undiagnosed because physicians do not consider this etiology, and because it is impossible to apply non-invasive diagnostic procedures.

So far, in Serbia, about 28 cases with parasite determination of human dirofilariosis have been reported. It is possible that the majority of cases are undiagnosed, considering the fact that systemic investigation, at the territory of our country, shows that there are endemic zones for dirofilarioses in dogs.

Clinical spectrum of human dirofilariosis includes superficial infections (subcutaneous, subconjuntival), which are easy to detect, and pulmonary nodules. Most pulmonary cases are asymptomatic infections, especially in cases of transitory or residual small calcified nodules.

In humans, parasites do not usually reach the adult stage and microfilariae are absent. The scheme that *D. repens* enables subcutaneous infections and *D. immitis* pulmonary infections is an oversimplification.

***Key words: Dirofilaria repens, Dirofilaria immitis,* human dirofilariosis**

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INTRODUCTION

Species Dirofilaria immitis (D. immitis) and Dirofilaria repens (D. repens) most frequently cause filarioses in dogs in Europe. Permanent habitats of these nematodes are, besides dogs, many domestic and wild animals. Cases of human dirofilarioses caused by these species have been more and more noted lately (1-6). Human dirofilariosis is most frequently manifested as subcutaneous and subconjunctival infection; lung infec tions have been described as well (2, 3, 7-9). Human infections caused by these filaria can, in the majority of cases, be asymptomatic, whether they are manifested as subcutaneous nodules or affect the lung' parenchyma. In nature, the human is just an accidental carrier of dirofilaria.

In case of human infection, the life cycle of nematodes finishes, because these species cannot mature in the human body. Generally, human dirofilariosis is an infection, during which there is no production of microfilaria because they are created by sexual intercourse between male and female adult form of these nematodes. A human is an accidental carrier of immature larva or adult forms. So far, only one case of microfilaria detection in human dirofilarioses was described by Nozais in 1994 (10).

Epidemiologically viewed, the prevalence of human dirofilariosis is in correlation with the prevalence of canine filariosis, with the presence of mosquitoes as vectors and a human action which causes exposure to these vectors (5). The retrospective study of previously published human cases, documents the emergence of infection by D. immitis and D. repens. More than 300 cases in the European Union have been reported. Most of them have been attributed to D. repens. The country where most cases have been diagnosed is Italy, followed by France, Greece and Spain (5). Women are affected more often than men. Age-group distribution shows a higher incidence of these cases after 40 years of age, in both sexes, for both parasites. A number of cases have been diagnosed in the Northern Europe, but they have been attributed to infections acquired while travelling to the Southern countries (5, 6).

The most frequent parasite that causes dirofilariosis in humans is D. repens. This species is considered to be a parasite of the old world. Endemic areas for D. repens on our continent are in the Eastern Europe (3, 12).

Contrary to the aforementioned, lung dirofilariosis caused by D. immitis has been detected on almost all continents (5, 6).

Up to now, 28 cases of human dirofilarioses have been reported in Serbia. Considering the fact that endemic areas for dirofilariosis in dogs exist in our country, probably a large number of cases remain undiagnosed. However, in 1930s, Southern Serbia was a hyperendemic area for dirofilariosis in dogs. In the last few years, Vojvodina has been established as hyperendemic area for D. repens, and endemic area for D. immitis infections in dogs. There have not been registered cases of infected dogs in the City of Niš (11-15).

Other species of Dirofilaria spp. that can cause a human dirofilariosis have not been reported in Europe (5).

MORTALITY/MORBIDITY

D. immitis lung dirofilariosis is a symptomatic infection in 38-45% of cases. This parasitosis is rarely diagnosed in children, despite the fact that initially in 1887 a case of dirofilariosis in one child was described in Brazil (3). It is difficult to define the prevalence of exposure to *D. imittis,* because the infection of the dogs is spread all over the world. The prevalence of human *D. immitis* infection is still undetermined, because in the majority of cases it is an asymptomatic infection with the appearance of transitory nodules or calcified nodules in the lungs of the infected.

A *D. immitis* infection in human has, most frequently, a pulmonary form. In sporadic cases it can be found that *D. immitis* - like species can cause nodules, skin infections, conjunctival infections and abdominal infections (16-19).

D. repens species is the most common cause of dirofilariosis in humans around the world. The most frequent localisation of this infection is the submucosis, where nodules can be formed (5). The eye infections have been described as well. Then, it is possible to extirpate the adult filaria from the bulbar conjunctiva (5). The thoracal nodules caused by *D. repens* infection are diagnosed mainly in the hyperendemic regions. Diagnostically, these forms of infection are mistaken for potential tumours. Until today, this clinical entity of dirofilariosis has been registered in Italy and Sri Lanka, and the imported cases have been registered in the USA, Canada, Japan and Australia. *D. repens* infection can cause a lesion in the lung tissue and abdominal lesions, and such forms have been registered in endemic regions of Italy, France, Greece (2, 5, 6).

In Serbia, the majority of described cases have been detected in patients from Belgrade (the city on the rivers Sava and Danube), Vojvodina (the cities of Zrenjanin, Sombor, Pančevo, Sivac, Vršac). Besides, there have been sporadic cases in the cities of Varvarin, Šabac, Pirot, Jagodina, Zaječar, Vranje. All identified dirofilarias in these patients were *D. repens* species (11, 14, 15).

DIAGNOSIS OF HUMAN DIROFILARIOSIS

The correct diagnosis is usually histological, based on the identification of nematode using morpho-

logical characteristics of the species to differentiate it from other dirofilariae or other nematodes. It is possible that dirofilariosis in humans is more frequent than presented by literature; however, many cases have not been diagnosed, or not published, other recover spontaneously without medical intervention (1, 5, 6).

In the diagnosis of human dirofilariosis, the most significant principle is clinicians' and practitioners' awareness of the possibility that this parasitosis can be the cause of patient symptoms. The significant anamnestic data is travelling or staying in the areas that are habitats for mosquito species which are dirofilaria careers. Patients usually do not remember or make a connection between a mosquito byte and the symptom appearance, so these data are usually absent in anamnesis.

The detection and diagnosis of *D. repens* in human causes different problems. In case of subcutaneous nodules, it is usually the patient who seeks medical attention, while most pulmonary nodules are detected accidentally, by a thoracic radiography. Taking into consideration that both subcutaneous and pulmonary nodules can cause suspicion of malignant tumour and other pathological conditions (tuberculosis, fungal infection), surgery is usually recommended (5). The lack of diagnostic tests for determination of dirofilaria which causes human infection, results in unreliability of facts about the dirofilarioses prevalence caused by either *D. repens,* or *D. immitis* species (3, 4). Histological identification of worms in the nodules removed by surgery may cause problems because of the similarity in morphological features between species, and also because of the disruption of normal anatomy by the host tissue response. As alternatives, molecular biological techniques could be applied (20, 21). However, traditional morphology and innovative DNA analysis both have limitations as diagnostic tools for dirofilariosis (8).In order to convey parasitological examinations to determine morphological and morphometrical characteristics, it is necessary for helmint to be in the adult form, to stay intact during the extirpation, and not to be significantly destroyed by the tissue reaction. Amplification tests can be used only in highly specialised laboratories. Samples kept in formalin (usually extirpated samples for histopathological analyses are transported and conserved in formalin) can not be examined by using this methodology since formalin affects inhibitory DNA polymerase (8). Both also require previous application of invasive techniques to remove the worms, but surgical removal is a particular problem with pulmonary infection.

Serology could be an advantageous alternative to invasive diagnosis because it avoids surgical intervention; hidden infections can be detected, facilitating therapeutic and epidemiological investigation (5, 7, 8).

However, serology has its lacks, first of all it is impossible to define the distinct level of the positive and negative predictive value of the taken test; these tests are still in the experimental area, and they are still not available for commercial use. A problem is in an existence of higher seroincidence in people, exposed to mosquitoes-possible vectors, in the endemic zones. This should always be considered before immunodiagnosis (22-24).

In conclusion, we can say that in the European Union, the geographical distribution of human dirofilariosis coincides with that observed in dogs, and the most reported cases have been reported in the southern countries. Considering the geographical and climatic characteristics of our country and that it has been confirmed that we are a hyperendemic area for canine dirofilariasis, we should give a high priority to the prevalence of the human dirofilariosis in our country, mainly in Vojvodina.

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DIJAGNOZA I KLINIČKI ZNAČAJ HUMANE DIROFILARIOZE

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Sažetak

Vrste *Dirofilaria repens (D. repens)* i *Dirofilaria immitis (D. immitis)* paraziti pasa, dugo poznati uzročnici zoonoza, mogu kao nezrele jedinke da parazitiraju i u organizmu čoveka.

Humana dirofilarioza kod mnogih asimptomatskih bolesnika ostaje neverifikovana, jer, najčešće, većina lekara praktičara ne razmatra ovu etiologiju. Razlog više su još uvek nedostupni komercijalni testovi koji bi omogućili neinvazivnu dijagnostiku ove parazitske infekcije.

Na području naše zemlje do sada je dijagnostikovano 28 autohtonih slučajeva humane dirofilarioze. To ukazuje da je najveći broj slučajeva najverovatnije ostao nedijagnostifikovan, s obzirom na činjenicu da je u sistemskim istraživanjima utvrđeno postojanje endemskih zona za dirofilarioze pasa u našoj zemlji.

Sa kliničkog aspekta, humana dirofilarioza uključuje superficijale infekcije (subkutane, subkonjuktivalne) koje je lakše detektovati i takođe razvoj plućnih infekcija (nastanak nodula). Veći broj infekcija pluća ovim parazitima biva asimptomatsko bilo zbog razvoja tranzitornih plućnih nodula ili kalcifikacije manjih rezidualnih nodula u plućnom tkivu.

U čovekovom organizmu, kao slučajnom nosiocu, paraziti najčešće ne dostižu zrelu formu i mikrofilarije se ne detektuju.

Stav da vrsta *D. repens* najčešće izaziva superficijalnu formu, a vrsta *D. immitis* plućnu formu dirofilarioza, još uvek se razmatra.

***Ključne reči: Dirofilaria repens, Dirofilaria immitis,* humana dirofilarioza**