





Review Article

Dirofilariasis and related traumas in Greek patients: Mini Review

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Abstract

Dirofilariasis is a rare vector-borne parasitic human disease. The culprit pathogens belong to the nematode's family Filaridae. In humans most commonly species related to disease are *Dirofilaria repens*, *D. tenuis*, and *D. immitis* (the dog heartworm). Of those, *D. immitis* is related to pulmonary infection, whilst the other species are related to subcutaneous dirofilariasis. The vector is mosquitoes of the genera *Aedes*, *Culex*, *Anopheles*, and *Mansonia*. The natural transmission of *Dirofilaria* species from animals to humans occurs during the blood meals of the arthropods, where the worm is injected via the bite. Herein we describe case reports related to autochthonous dirofilariasis in Greek patients. All data have been retrieved from PubMed and Google Scholar. Many autochthonous cases of pulmonary, ocular and subcutaneous disease have been described in Greek patients from 1996 till 2020. Climate change and global warming is affecting the vectors and dirofilariasis should be considered as an emerging parasitic disease. All forms of dirofilariasis, although rare, should be included in the differential diagnosis of subcutaneous or ocular nodules or coin like formations in the lungs in Greek patients.

Keywords: *Dirofilaria*, Dirofilariasis, Subcutaneous Nodule, Nematoda

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Introduction

Dirofilariasis is a zoonotic vector-borne parasitic disease. The culprit pathogens belong to the nematode's family Filaridae. The family includes the genera *Dirofilaria*, *Brugia*, *Wuchereria*, *Onchocerca*, *Dipetalonema*, *Loa*, and *Meningonema* (1). In humans most commonly species related to disease are *D. repens*, *D. tenuis*, and *D. immitis* (the dog heartworm) (2). Of those, *D. immitis* is related to pulmonary infection, whilst the other species are related to subcutaneous and ocular dirofilariasis (2). The vector are mosquitos of the genera *Aedes*, *Culex*, *Anopheles*, and *Mansonia* (2). The natural transmission of *Dirofilaria* species from animals to humans occurs during the blood meals of the arthropods, where the worm is injected via the mosquito's bite (3). For *D. immitis*, the most typical hosts are canids: domestic dogs, coyotes, jackals, and wolves. Aberrant hosts of

adult worms are domestic cats, bobcats, ferrets, and foxes. For *D. repens* definitive hosts are canids, and occasionally felids. For *D. tenuis* the only definitive host is the raccoon. *D. immitis* is cosmopolitan in dogs in America, Australia, Japan and Europe. *D. repens* infects dogs and cats in Europe (especially the Mediterranean region), Asia, and Africa. *D. tenuis* seems prevalent in raccoons in Florida (2). When a mosquito has a blood meal, the circulating microfilariae of the infected host get to the insect's midgut. From there, they migrate from the mosquito's Malpighian tubules in the abdomen, where they evolve initially into first-stage larvae (L1) and finally into the L3 stage. L3 are the infective forms and migrate to the mosquito's proboscis to be injected to another definitive host (2). Pulmonary infection (most commonly *D. immitis*): The third-stage filarial larvae (L3 larvae) of the nematode are ingested by the blood meal of a mosquito to the skin of the definite host (canids), where they evolve to L4 and adult worms. Adult forms are female and male and have a lifespan of 5 – 10 years. Females are longer (230-310 mm) than the male (120-190 mm). Adults reside in pulmonary arteries. In the right heart ventricle, the female worms produce microfilariae which circulate in the peripheral blood (2). Subcutaneous infections (most commonly *D. repens* and *D. tenuis*) and ocular infections (most commonly *D. repens*): The third-stage filarial larvae (L3 larvae) of the nematode are ingested by the blood meal of a mosquito to the skin of the definite host (canids and sometimes felids for *D. repens*, raccoons for *D. tenuis*), where they evolve into L4 and adults. The adult forms reside in subcutaneous tissues. Adult females of *D. repens* are usually 100—170 mm long whilst males are usually 50—70 mm long. Adult females of *D. tenuis* are usually 80-130 mm long, whilst males are usually 40—50 mm long. In humans, the nematode is either a wandering worm in the subcutaneous tissue or forms a granulomatous nodule (2-4).

In humans, *D. immitis* that migrate to the heart do not usually survive. In pulmonary vessels, those dead worms cause infarcts known as “coin lesions” in chest x-rays. The patient has the typical symptoms of

pulmonary embolization. Subcutaneous nodules may be fixed or migratory and are usually located in the exposed sites of the body, where usually the mosquito bites. In this area they may form cyst, abscess, nodule, granuloma, or swelling (5-7). Humans are suboptimal hosts and the nematode does not usually evolve to the adult form. Thus, microfilariae are not usually detectable in the blood and the lesions typically contain an immature worm (2). The purpose of this review was to describe case reports related to autochthonous dirofilariasis in Greek patients.

Materials and Methods

All relative articles have been retrieved from PubMed and Google Scholar, using as keywords *Dirofilaria*, dirofilariasis, ocular, subcutaneous, pulmonary, Greece. Articles not referred to Greek patients with autochthonous disease have not been included in the present study. We included all relevant accepted articles without publication year limitation. The main language of publication research was English. We grouped the articles by year of publication, location of Dirofilariasis, culpable parasite, and implemented therapy.

Results

Several cases of pulmonary dirofilariasis in Greece have been described. Pampiglione et al (2000) reported the first case of human pulmonary dirofilariasis in a 31-year-old Greek man. Chest x-ray revealed a coin lesion in the left lung that proved to be *D. repens* (8). Foroulis et al (2005) presented a 55-year-old male patient with a peripheral pulmonary lesion which invaded the anterior chest wall and mediastinum and did not have the usual coin shaped form. The man proved to suffer from *D. immitis* infection (9). Miliaras et al. (2010) described a case of a 52-year-old Greek male patient with a coin lesion in the right lung, caused by *D. immitis* (10). Sileli et al (2016) described a 45-year-old Greek female with influenza-like symptoms and chest pain that proved to suffer from a solitary pulmonary nodule in the right upper lobe due to *D. immitis* (11). Ocular involvement may be periorbital, subconjunctival or intraocular. The common symptoms and signs if the worm enters the

subconjunctiva are redness, pain, swelling of the eyelids and blurred vision. Symptoms appear mostly weeks or months after infection (12). In Greece many cases of eye infection have been reported. Kalogeropoulos et al (2014) reported eight cases of unilateral ocular dirofilariasis: five subconjunctival, two intravitreal and one intraorbital (13). Subcutaneous lesions that proved to be dirofilariasis have been described. Pampiglione et al (1996) described the case of a subcutaneous nodule due to *D. repens* in a 45-year-old Greek male patient (14). Maltezos et al (2002) described the cases of two women and one man, (aged between 32 and 67 years) with breast axillary nodules respectively. From the lesions *D. repens* was isolated (15). Tzanetou et al (2009) described the case of a patient with subcutaneous inflammation of the groin by *D. repens*. (16). Falidas et al (2016) reported a 45-year-old immunocompromised woman patient with a subcutaneous nodule at the right hypochondrium due to *D. immitis* (17). Xaplanteri et al (2017) reported a 24-year-old Greek male patient who presented with a painless swelling in the right groin with duration of one month. The patient proved to suffer from subcutaneous dirofilariasis due to *D. repens* (18). An exceedingly rare case of microfilaremia was described by Petrocheilou et al (1998) probably due *D. repens* in a 70-year-old Greek man patient with marked eosinophilia in the peripheral blood and no subcutaneous lesions (19).

Discussion

In this study, most patients with pulmonary dirofilariasis presented with a lesion or nodule resembling a tumor. In all patients partial lobectomy and excision of the nodule were performed. Diagnosis was based on histopathologic examination. In one case the lesion appeared as an upper lobe mass, infiltrating the mediastinum, and chest wall. The posterior surface of the sternum and the third and fourth cartilages were invaded. In this patient anterior mediastinotomy with resection of the third costal cartilage was initially performed in order to obtain biopsy, followed by anterior thoracotomy and complete resection of the mass (9). All patients

reported in this review with subcutaneous dirofilariasis were successfully treated by complete surgical excision of the lesion, which is the treatment of choice (14,18). Subconjunctival dirofilariasis was treated by incision in the conjunctiva and complete removal of the worm (13). Intravitreal disease was treated via vitrectomy (13). Patients suffering from subcutaneous dirofilariasis have usually normal eosinophil count in the peripheral blood and normal Immunoglobulin E (IgE). Therefore, laboratory tests are of limited value in the differentiation of a subcutaneous mass (7-9). Subcutaneous lesions are often asymptomatic, but the usual signs and symptoms of inflammation may occur (7-16). In this study, elevated eosinophil count was reported in a case of breast dirofilariasis and in one case of ocular disease (13-15) Marked eosinophilia was reported in the unusual case of microfilaraemia reported by Petrocheilou et al (19). Eosinophil count returned to normal after the successful removal of the parasite (13-15). The infection is usually limited to the site of injection. Therefore, anthelmintic drugs are not routinely recommended (6-7).

Epidemiologic studies reveal that undiagnosed companion animals, especially canids, continue to facilitate the life cycle of the worm. In addition, climate change and global warming is affecting the vectors as the culpable mosquitoes move in previously non-endemic areas (20).

Thus, dirofilariasis should be considered as an emerging parasitic disease (20). There may be some possible limitations in this study. Data were retrieved from PubMed and Google Scholar databases in English language only. Also data presented in medical congresses were not included in this study. Therefore, the data represented in this study reflect the search findings in the aforementioned databases only.

Conclusion

All forms of dirofilariasis, although rare, should be included in the differential diagnosis of subcutaneous or ocular nodules or coin like formations in the lungs. Further epidemiologic studies are needed to provide more information about this emerging parasitic disease in Greece.

Conflict of Interest

The authors have no conflicts of interest to declare.

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