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Velev V.

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Several Cases of Ocular Dirofilariasis in Bulgaria

¹Valeri Velev

¹Department of Infectious Diseases, Parasitology and Tropical Medicine, Medical University of Sofia, University Hospital “Prof. Iv. Kirov”, Sofia, Bulgaria

Short Title: Ophthalmic Dirofilariasis

Corresponding author:
Valeri Velev
Department of Infectious Diseases, Parasitology and Tropical Medicine
Medical University of Sofia, Blvd. “Iv. Geshov” 17
Sofia, Bulgaria,
E-mail: velev_md@abv.bg

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Highlights of the Study

- One of the most common insect-borne nematodiasis in the world is dirofilariasis. *Dirofilaria repens* typically causes subcutaneous infection in dogs, rarely in humans.

- Data in this report were collected by observation and study of 7 patients with subconjunctival or periorbital dirofilariasis.

- The most common location of *D. repens* larvae is subcutaneous. Ocular location is most commonly subconjunctival, followed by eyelid and orbital.

- The diagnosis is made by the histological assessment of the larvae.
Abstract

Objectives: In this study we describe ocular dirofilariasis in Bulgaria. Materials and Methods: We studied 7 patients with subconjunctival or periorbital form of *Dirofilaria repens* infection during 2010 - 2019. Morphological, serological and paraclinical diagnostic methods were used. Results: The patients (6 females, 1 male) were aged between 23 and 72. In 3 patients, subcutaneous nodules were detected in the area of the upper eyelid, in one patient the location was suborbital. In 3 other patients, subconjunctival location was found. All patients were cured definitively by removal of the larva, without etiologic treatment. Conclusion: The most reliable and easily accessible diagnostic method is morphological analysis by microscopy of histological preparations of the parasite. In dirofilariasis, ocular location is the most common in humans, and it deserves special attention of clinicians.
Introduction

Dirofilariasis is a widespread zoonosis caused by nematodes of the genus *Dirofilaria*. It includes species that are natural parasites in dogs and other wild animals. They are all transmitted by mosquitoes; *Dirofilaria repens* and *Dirofilaria immitis* have the most zoonotic potential. Both nematode species are common among wild animals on the Eurasia, and the Mediterranean countries are considered to be endemic areas [1,2]. In Bulgaria, all reported cases of infected people are of *D. repens*. Harizanov et al. summarized 47 cases in different centers during 1973 – 2011 [3]. Velev et al. describe the first case of a child with epididymal dirofilariasis caused by *D. repens* [4].

*D. immitis* can cause severe heart disease by locating in the pulmonary artery of dogs and other carnivores. *D. immitis* is less common in humans [5]. *Dirofilaria repens* is a major cause of non-pathogenic subcutaneous infections in dogs, more rarely in other carnivores, and is a major cause of human dirofilariasis in Europe. In final hosts, adult parasites are most commonly located in the skin or the subcutaneous tissue, and microfilariae circulate in the bloodstream. Microfilariemic dogs are the major reservoir from which infection is spread by vectors from the order Diptera [5,6].

Material and Methods

Data were collected by observation and study of 7 patients with subconjunctival or periorbital dirofilariasis, from different regions of Bulgaria, treated at the University Hospital “Prof. Iv. Kirov”, Sofia, during 2010 - 2019. The patients were from 7 out of 28 regions in Bulgaria. Patients were classified by demographic, clinical, and laboratory parameters. Morphological methods were used for species determination of the parasite in all patients; the macroscopic method in the case of a preserved worm, and microscopic examination of the histological
preparation of the parasite in all cases. In one case, we also applied a serological method using a commercial ELISA kit for the detection of Dirofilaria-specific antibodies based on purified somatic antigen of immature female *D. repens* (Bordier Affinity Products SA, Crissier, Switzerland). Complete blood counts were done in all patients for determination of eosinophil numbers. The study was conducted in accordance with the Declaration of Helsinki 2000.

**Results**

In the period 2010-2019, we examined and described 7 patients with subconjunctival or periorbital form of dirofilariasis. The patients (6 females and 1 male) were aged between 23 and 72. Four patients lived in rural areas, and three in urban areas.

In 3 patients, subcutaneous nodules were detected in the area of the upper eyelid, in one patient the location was suborbital, immediately below the left eyelid, and in 3 other patients, subconjunctival location was found (Fig. 1). None of the patients had an orbital location of the parasite. The patients sought medical attention when they noticed a moving parasite or less often calcified subcutaneous larva. This was the case with our patients as well. However, all three patients with subconjunctival larvae had sought medical attention early because of unpleasant sensations in their eyes and noticing an intact, moving worm. Complaints included eye irritation, blurred vision, photophobia, conjunctival reddening. In all patients, microscopic examination of histological preparations prepared from the extirpated larvae was performed. In one of the patients, with a subconjunctival larva, a native living worm was removed. All patients with subconjunctival larvae were examined by an ophthalmologist using a slit-lamp, and their eye fundi and eye vision were examined (using Snellen's optotypes). No pathologic abnormalities were observed in the eye fundi and vision. Histologically, attention must be paid to the longitudinal ridges of the cuticle, which is a typical morphological characteristic of *D. repens* [8].
In one of the cases with subcutaneous dirofilariasis of the eyelid, we also applied a serological method using a commercial ELISA kit, but it was negative. No abnormalities were observed in the complete blood counts including eosinophil levels in any of the patients.

All 7 patients underwent surgical extirpation of the larva or parts of it. None of the patients was treated with antihelmintic medications, and there is no evidence of relapse of the disease. The three patients with subconjunctival larvae received topical treatment with tobramycin/dexamethasone eye drops for 3 days postoperatively.

**Discussion**

The increasing trend of dirofilariasis worldwide is usually explained by the warming of the climate and the increased activity of the parasite vectors and faster development of larvae in mosquitoes [9]. The most common locations of *D. repens* larvae are subcutaneous location in the upper body, including the eyelid, predominantly the upper eyelid, and, at the second place, the subconjunctival location [3, 10]. Ocular location is most commonly subconjunctival (about 60%), followed by eyelid and orbital (each about 25%) [10]. Patients with subconjunctival location seek medical attention most early, possibly due to subjective symptoms and easily visible larvae. Subjective symptoms or local inflammatory reactions have not been reported in patients with subcutaneous location. Initial diagnoses sometimes can be different, lipomas, lymphadenopathy, allergic conjunctivitis etc. Serological testing was negative, and this is consistent with other reports [10,11]. The absence of eosinophilia can be explained by the fact that patients had only larva each, and thus antigenic stimulation was insufficient. However, slightly elevated eosinophil levels has been reported rarely [10]. For us, this diagnostic method is non-specific and uncertain. For extracted larvae not placed in formalin, molecular analysis by conventional PCR and pan-filarial primers is recommended for the identification of the filarioid species [12].
As far as treatment is concerned, we suggest that surgical removal of the larva is sufficient; if necessary, subsequent antiinflammatory and antibacterial treatment may be administered in subconjunctival and orbital dirofilariosis. Although the larva is perfectly visible in most cases, after the removal of a subconjunctival larva, we consider that instrumental examination of eye fundi is obligatory [6,10].

**Conclusion**

Dirofilariosis has become endemic in many countries of Europe. Although a common disease in dogs it is still a rare and poorly known disease in humans. Here we describe 7 cases of ocular (periorbital and subconjunctival) location, which are particularly frightening for patients, as opposed to subcutaneous locations in other parts of the body. Such clinical case reports, are useful in order to draw the attention of clinicians in Europe.

**Disclosure Statement:** The authors report no conflict of interests.

**References**


Figure Legends

Figure 1. Larva within the upper eyelid (a), subconjunctival larva with conjunctival reddening (b) and histological preparation of cross-section of the extirpated larva. (HES, x20) (c).
Fig 1