DIAGNOSIS: Subcutaneous breast nodule due to *Dirofilaria repens* infestation

Joško Bezić,* Branka Vrbičić,† Paško Guberina,‡ Vinko Alfier,§ Petar Projić,* Zlatko Marović ||

The histological slides (Figures 1, 2) show transverse sections of a female filarial nematode of the genus *Dirofilaria*, enclosed in an inflammatory nodule. The number and organization of the ridges, which are neatly separated by a space between them, are highly characteristic of *Dirofilaria repens*. The worm was female, 436 µm in length, with a digestive tract and two oviducts in a coelomic cavity, a muscle layer and outer multilayered cuticle with external longitudinal ridges (Figure 2).

Figure 1. Transverse sections of *Dirofilaria repens* within a subcutaneous suppurative centre, surrounded by a granulomatous inflammatory reaction (H&E section, x 40).

Figure 2. Transverse section of *Dirofilaria repens* showing cuticle (C) with longitudinal ridges, muscular layer (M) and oviducts (O) in the coelomic cavity (H&E section, x 200).

From the *Department of Pathology, Clinical Hospital Split, Croatia; †Department of Pathology, Regional Hospital Šibenik, Croatia; ‡Department of Radiology, Regional Hospital Šibenik, Croatia; §Department of Surgery, Regional Hospital Šibenik, Croatia; ||Medical School, University of Split, Croatia

Correspondence and reprint requests:

Joško Bezić, MD
Institute of Pathology,
Cytology and Forensic Medicine
Clinical Hospital Split
Spincičeva 1; 21 000
Split, Croatia
jb@mefst.hr

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Filariasis is infestation caused by infection with the threadlike nematode of the superfamily Filarioidea. These zoonotic filariae in humans are found most commonly in the subcutaneous tissue, and the vast majority of them belong to the genus *Dirofilaria*. The main dirofilariids found in humans are *D. immitis*, *D. tenuis*, *D. ursi*, and mostly in Europe *D. repens*.¹ Filarial infestation due to *D. repens* is a zoonosis habitually parasitizing dogs, cats, and wild carnivores, transmitted by several species of mosquitoes. The viviparous female discharge microfilariae into the host's blood or subcutaneous tissue where they live for weeks or months, until they are taken up by hematophagous arthropods—mosquitoes. Within these vectors they are transformed into filariform larvae during a period of two weeks. When an arthropod takes another blood meal, the nematode penetrates the body of the new host in the form of infecting filariform larvae. The bite of the infected mosquito is the only mode of transmission. The adult worm in humans never causes microfilaremia since humans are dead-end hosts. In the human tissues microfilariae die before maturation probably due to immunological rejection, producing an inflammatory nodule at the site of arthropod's bite.¹ The life cycle of *D. repens* in human cases finishes inside the nodule.

In the majority of the human cases the nodules occur singly in the subcutaneous tissue of the upper half of the body, or subconjunctivally. In rare instances nodules occur in the lung, the omentum, the epididymis, the spermatic cord and the breast.²

A breast location for the *Dirofilaria* nodule is unusual, because this part of the body is usually covered with clothes, preventing the mosquito bite.³ Except in rare cases the parasite in the breast was located subcutaneously, mimicking a benign lesion, particularly an inflamed epidermoid cyst, as it was in the case presented here, or an abscess.^{4,5} A deeper breast location of the parasitic nodule combined with a mammographic finding of an ill-defined nodule raises the suspicion of malignancy, even necessitating frozen section analysis to rule out incipient carcinoma.^{6,7}

New cases of human dirofilariasis due to *D. repens* have been increasingly reported in the past few years, and this zoonosis has become the new emerging zoonosis in Mediterranean parts of Europe, Asia and Africa.^{2,8} The prevalence of subcutaneous dirofilariasis is probably even higher because of its innocuous clinical presentation that does not require excision and histopathologic examination. The main reason

for the increasing number of reported cases is probably the change in climatic conditions (temperature, relative humidity, rainfall) in the Mediterranean region in recent times, which favors both the development of the carrier mosquitoes and that of the larval phase of the nematode inside the carrier itself.² After the first two reported cases in 2003, this represents an additional case from the southern part of Croatia.⁹ There is no epidemiological relationship between our case and those previously reported in our country.

The diagnosis of parasites in tissue sections rests on the recognition of their microscopic anatomy. Without this knowledge, the dermatopathologist may regard the parasite in a biopsy as an artefact or wrongly identify the species. Microscopic analysis should put emphasis on the thickness and the organization of the cuticle, especially on the number and organization of longitudinal ridges. Gutierrez considers a number of the ridges between 95 and 105 as specific features of *D. repens*, with the spaces between them being wider than the thickness of the ridge.¹⁰ Upon host reaction, four categories of morphological features can be observed: abscess formation surrounded with reactive granulation tissue; granuloma formation; a regressed appearance of the nematode with scarring and occasional acute and chronic inflammatory cells; and surrounding of the nematode by a dense chronic inflammatory infiltrate forming lymphoid nodules with germinative centres. The first morphological category, abscess formation, is the commonest.² Surgically excised tissue biopsy is not only a diagnostic but also a therapeutic procedure. There is no need for whole body screening for other hidden infestation by advanced imaging techniques, because unrecognised foci are usually clinically indolent with no complications expected.

Serological identification of the parasite is also possible using the somatic antigenic complex of *D. repens*, as well as molecular biology techniques such as PCR.^{11,12} Serology is used to estimate the seroprevalence among dirofilarial natural hosts, particularly among dogs, giving information on the true extent of this zoonosis. Possible measures to control this infestation are information campaigns aimed at dog owners with free prophylactic treatment of this reservoir animal, as well as intensification of the battle against mosquitoes.² It is important that histopathologists familiarize themselves with the histological aspects of *D. repens* infestation, considering it in differential diagnosis during examination of solitary nodules of uncertain nature in the subcutaneous tissue.

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