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Case Report

Dirofilarial worms inside cutaneous nodules: a report with review of literature

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ABSTRACT

Dirofilaria is a filarial worm which affects humans as a zoonosis. The infection is carried by mosquito bite. In humans, the worm fails to achieve its full cycle and hence microfilaremia is absent. Apart from subcutaneous and subconjunctival locations, there are visceral and other presentations for the worm. Surgical removal and antihelminthic medications are the best options for treatment. We present a case of subcutaneous dirofilaria infection in a 13 year old boy from rural south India who presented with fever and a painless swelling on the leg. Detailed literature review is also enclosed.

Keywords: Cutaneous nodule, Dirofilaria, Microfilaria, Zoonosis

INTRODUCTION

Zoonosis is defined as a disease or infection that is naturally transmitted between vertebrate animals and humans. A zoonotic agent may be a bacterium, a virus, a fungus or other communicable disease agent. Cutaneous nodules are one of the commonest forms of manifestation of zoonotic infections. Of the various organisms producing cutaneous nodules, dirofilaria is a relatively common differential diagnosis.

CASE REPORT

A 13 year old boy hailing from rural area of South India presented to the local hospital with complaints of fever of short duration. While on treatment for the same, he developed a painless swelling on the antero-medial part of left thigh. Gradually, the swelling migrated downwards, towards the knee and subsequently localised over the medial aspect of lower leg Figure 1. On examination, there was a linear, painless, cutaneous swelling on the medial part of left leg of 3 centimeters length. The swelling was non tender, firm in consistency and had no features of inflammation. An ultrasound scan was taken and the report was given as inflammatory swelling. The patient was posted for surgical removal of the swelling for diagnostic purpose. On putting a skin incision over the swelling and reaching the deep sub-dermal tissue, there was a nodular swelling just over-lying the muscle fascia. Upon incising the nodule, a coiled, live, white worm was found inside, along with some inflammatory fluid Figure 2. The live worm was removed intact and was found to measure 10 cm in length and 1 mm in breadth. The worm was sent for microbiological examination for diagnosis. Final opinion was given by the microbiologist as *Dirofilaria repens* on the basis of morphological and histological features. Post-operative period was uneventful and the wound healed well. The patient was discharged home and remained asymptomatic at 1 year of follow up.

Figure 1: Photograph showing the cutaneous nodule in medial aspect of leg.

Figure 2: Intra-operative photograph of the live worm inside the nodule.

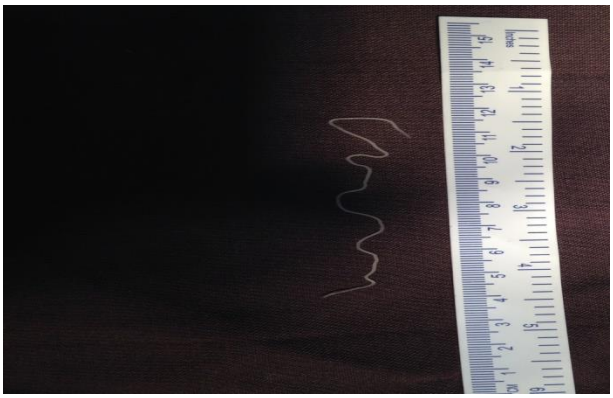

Figure 3: In-vitro specimen of the live worm.

DISCUSSION

Dirofilaria is a nematode of domestic and wild animals which sometimes infects humans as a zoonotic infection. Currently, human dirofilariasis is considered an emerging disease in some areas because of the dramatic increase in the number of reported human cases in the last 10 years. This contradicts the concept that human dirofilariasis is accidental and infrequent. Also referred to as the 'heartworm', the parasite was first observed by Birago in 1626 in a greyhound dog at autopsy.[1] Dirofilariae are spirurid nematodes, which localize, with a few exceptions, in subcutaneous tissues of mammalian hosts (e.g., foxes, coyotes, wolves, dogs, sea lions, harbour seals, ferrets, horses, bears, wolverines, muskrats, raccoons, bobcats, cats, monkeys, and red pandas) and are transmitted predominately by mosquitoes.[2] It is a genus under the family Onchocercidae in the subphylum Nematoda. The genus Dirofilaria has two subgenera : Dirofilaria with *D. immitis* as the type species and Nochtiella with *D. repens* as the type species. Six out of 40 species of dirofilaria are known to cause diseases in humans. *Dirofilaria immitis*, *Dirofilaria repens*, *Dirofilaria striata*, *Dirofilaria tenuis*, *Dirofilaria ursi* and *Dirofilaria spectans.* In addition, as a novel Dirofilaria species, Dirofilaria sp. ''*hongkongensis*'' has been reported from Hong Kong.[3]

Life cycle of this parasite is the same as that of other filarial worms. It is mediated by two hosts, a definitive vertebrate host and an intermediate arthropod host, which also holds the role of a vector. Microfilariae which are in the blood of wild animals such as the raccoon and domestic animals such as dog or cat are transmitted to humans when they are bitten by infected mosquitoes. Both *D. immitis* and *D. repens* demonstrate poor vertebrate host specificity given that they can infect numerous mammalian species.[4] Culex, Aedes, and Anopheles are the genera of mosquitoes which form the vectors. These mosquitoes take up the microfilaria while feeding on the blood of an infected host and transmit it. Microfilaria develops in the malpighian tubules into the third stage larva and then migrates to the proboscis through the body cavity.[5]

In dogs, the infection may be asymptomatic although cutaneous signs of varying severity, such as dermatitis, (sub)-cutaneous nodules and lesions, itching and various allergic reactions could be caused by both adult stages and/or circulating microfilariae.[6] *D. immitis* is a very common filaria of stray dogs and sheep dogs in the right ventricle of the heart and causes disabilities in dogs. Infected dogs are unable to follow the sheep kept in the yards. Microfilariae in the blood of sick dogs are transmitted through mosquito biting.[7] Canine cardiopulmonary dirofilariasis (heartworm disease) is a serious and potentially fatal disease caused primarily by adult *D. immitis* worms and their antigenic products, including Wolbachia symbiotic bacteria.[8]

Humans contract the disease when they are bitten by an infested mosquito. In humans, the parasites do not reach the adult stage and microfilaraemia is absent, as has been proven by direct visualisation after surgical removal of the nodules.[9] However, a study from France did report the presence of microfilariae in the blood of one patient.[10] Microfilaraemia is possible, especially when the causative organism is *D. immitis*. Immature *D. immitis* worms can reach a branch of the human pulmonary artery, triggering an inflammatory response that destroys the worms, occasionally resulting in pulmonary nodules which cause radio-opaque lesions.[11]

The endemic foci for this zoonosis appear to be Southern and Eastern Europe, Southern and Central Asia. The countries most affected are Italy, Srilanka and some republics of the previous Soviet Union. In the Old World, most cases refer to subcutaneous infestations by *Dirofilaria repens*, whereas in the New World pulmonary dirofilariosis by *D. immitis* predominates.[12] In fact, the evident increase in the number of cases in the last few years has prompted the discussion that it is an emergent zoonosis.[13] Also, most of the cases reported in Europe and Americas have a history of travel to the Mediterranean region.[14] The state of Kerala in India is considered as endemic for dirofilariasis due to the climatic conditions and the presence of suitable vectors species as well as proximity to Srilanka.[15] *D. repens* is the most common causative agent of human dirofilariasis in India, however few cases caused by *D. immitis* have been reported.[16] The patients vary in age group from as young as 4 months to as old as 100 years, the majority being middle aged adults. Of the various forms of human dirofliariasis, that due to *dirofilaria repens* is the most significant due to the higher number of patients affected and the wide geographical distribution and also the wider variety of organs involved.

It is possible that the incidence of this zoonosis in man is more frequent than shown by the literature: many cases are not diagnosed, some not published, while others recover spontaneously without medical intervention. The most common sites of infection are the cutaneous, sub-cutaneous and the sub-mucosal areas. The commonly affected areas are the head, inguinal area, buttocks, thoracic wall, arms and legs.[17] Human ocular dirofilarial infections were reported from Kerala as early as 1976 and 1978.[18] However, some cases with internal localisations are recorded most of them being situated in the pulmonary region. Almost all of these internal swellings are initially diagnosed erroneously as malignant swellings. Most cases of pulmonary dirofilariasis are caused by *dirofilaria immitis* and present radiologically as single non-calcified coin lesions. These lesions usually require thoracotomy and biopsy for definite diagnosis. Clinical diagnoses for almost all the locations are generally erroneous initially, with the exception of the subconjunctival lesions, where it is possible to visualize the parasite directly under the bulbar conjunctiva using slit - lamp examination.[19] Some reports have found the nematode to be located in atypical sites in humans like the epididymis, spermatic cord, breast, omentum, sub-tenon, testes and even the pancreas.[10,20]

The best option for diagnosis is usually histological, based on the identification of the nematode using the specific morphological characters to differentiate it from other dirofilariae and other nematodes. This requires surgical removal of adult worms from the lesions and macroscopic examination. The diameter is almost same, through-out the length of the worm, except at the two ends where it is comparatively thin. The cuticle is multilayered with distinct longitudinal ridging. At the lateral cord, a thickening of the innermost layer forms an inwardly directed ridge on either side of the body. The spaces between the ridges are equal to the length of the ridges themselves. The muscle cells are well developed specially at the level of the lateral cords. The genus Dirofilaria is identified by its thick, multilayered cuticle with ridging and striations, large muscle cells, prominent lateral cord. The paired uteri and the intestinal tube are also seen characteristically.[21] *D. immitis* can be differentiated from *D. repens* by the absence of longitudinal ridges and transverse striations.

In order to confirm the diagnosis of *D. repens* infection, DNA extraction followed by pan-filarial polymerase chain reaction (PCR) may be performed.[22] The DNA barcoding of cox 1 and 12S mitochondrial markers has been shown to be useful for taxonomic identification of many filarioid species.[23] Finally, there is a good correlation between PCR-based and serology based results, as evidenced by a study of some cases with subcutaneous nodules or ocular localization that were analyzed in parallel by using molecular techniques, ELISA, and Western blotting.[24] Immuno-histo-chemical staining to confirm the existence of Wolbachia or its molecules in nodules can also be helpful, because a positive reaction indicates the prior presence of dirofilaria.[25]

Histologically, the inflammatory response is characterized by accumulation of eosinophilic material or eosinophilic pus adjacent to the parasite with surrounding granulomatous inflammation associated with extensive eosinophilic infiltration of the surrounding tissue. Also, unlike with fungal lesions, fat necrosis is conspicuously absent.[26] Eosinophilia in the blood is usually absent in most patients. The serum immunoglobulin E (IgE) levels are normal and signs of a specific humoral response to antigens of dirofilaria species are absent.

Pharmacological treatment is rarely indicated in dirofilariasis as microfilaraemia is extremely rare. Oral administration of di-ethyl carbamazine citrate (2 mg per kg thrice daily) over a period of 4 weeks may be added to the surgical treatment. For additional benefit, this can be preceded by oral ivermectine given as single dose (150 mg per kg).[27] The few reported cases of meningo-encephalitis secondary to *D. repens* microfilaraemia, were treated with the anti-helminthic drug albendazole plus methylprednisolone and subsequently showed good response.[22] Though there were some reports about development of vaccines, no definite evidence has been published.

CONCLUSION

Dirofilariasis should be considered in the differential diagnosis of a single migratory or non-migratory cutaneous or sub-cutaneous swelling, especially if the patient is coming from an endemic area. From an epidemiological perspective, dirofilariasis is considered

an emergent parasitic disease of humans and animals. Rapid and significant changes in the distribution and prevalence of canine reservoirs are being reported around the world, and these changes in turn change the epidemiological parameters for human dirofilariasis. Global warming and other climatic factors have been found to influence the stages of the parasite life cycle that take place in vectors. This, together with pet management and human intervention in the environment that affect vector and vertebrate hosts, could account for substantial increases in numbers of dirofilarial infections, making this a major public health hazard in the near future.

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