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Unveiling the surge of subcutaneous dirofilariasis in lithuania: A comprehensive exploration of a zoonotic parasite's emergence, clinical manifestations, and management strategies. Brief literature review and three reports of cases

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SUMMARY

Introduction. This article comprehensively explores Dirofilariasis, focusing on Dirofilaria repens and Dirofilaria immitis as rare zoonotic ailments. Emphasis is placed on their prevalence, life cycle intricacies, and symptoms, particularly the rising incidence of Dirofilaria repens in Europe, notably Lithuania. The report details three cases of oral dirofilariasis, presenting clinical histories, diagnostics, interventions, and species identification. The discussion highlights the rarity of maxillo-mandibular dirofilariasis, addressing diagnostic challenges and diverse treatment options.

Objective. The objective is to investigate the emergence, clinical aspects, and management of Dirofilariasis, with a focus on Dirofilaria repens, emphasizing its prevalence in Europe, particularly Lithuania.

Materials and methods. The article presents three cases of oral dirofilariasis, providing detailed clinical histories, diagnostic procedures, interventions, and species identification. A thorough examination of Dirofilaria repens prevalence and characteristics in Europe, especially Lithuania, is conducted.

Results. The discussion reveals insights into the rarity of maxillo-mandibular dirofilariasis, highlighting diagnostic challenges and diverse treatment options. The cases contribute valuable information on clinical and diagnostic aspects, enhancing the understanding of this unusual condition.

Conclusion. The conclusion emphasizes the critical need for heightened awareness and a comprehensive diagnostic approach in managing oral dirofilariasis. It serves as a reminder to healthcare professionals about the importance of increased awareness for effective management in medical practice.

Keywords: dirofilariasis, zoonosis, parasitism, helminthiasis, mosquito-borne.

INTRODUCTION

Dirofilariasis is an uncommon zoonotic illness caused by a minimum of 40 different species, with only a handful having the potential to infect humans. Primarily, two species stand out: *Dirofilaria repens* and *Dirofilaria immitis* (1). Dirofilariasis is transmitted by vectors, and humans become infected through the bites of susceptible mosquito vectors (2). The typical presentation of human dirofilariasis includes pulmonary, ocular, or subcutaneous lesions (3). In Europe, *Dirofilaria repens* is the primary cause of human dirofilariasis, as evidenced by the increasing reported cases (1). Dirofilariasis is an uncommon condition in Lithuania that may be inaccurately identified as a subcutaneous tumor (5). It is imperative to enhance

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awareness about this newly emerged zoonotic parasite among medical practitioners, veterinarians, and the general public (6). In this context, we present a rare instance of oral dirofilariasis and provide insights into the differential diagnosis, clinical, radiologic, and histopathological features, as well as the management (2).

LITERATURE REVIEW

Definiton

Dirofilariasis is the most prevalent mosquito-borne nematode infection in Europe, with two primary causative agents: *Dirofilaria immitis and Dirofilaria (Nochtiella) repens* (7). *Dirofilaria repens* typically induces a relatively mild subcutaneous infection in dogs, wild predators, and occasionally in cats, emerging as the primary culprit behind dirofilariasis in humans (8). Morphologically, the *Dirofilaria repens* parasite features a robust external cuticle marked by longitudinal ridges, resulting in a distinctive cogwheel-like appearance in transverse sections. These parasites exhibit large lateral chords, a tall and slender coelomian muscle layer, and a single gut tube. In humans, nodules may develop in various body parts, particularly in areas prone to mosquito bites (2). The complete life cycle of *D. repens* involves five larval stages with an incubation period of around 6–9 months (9). The etiopathogenesis study reveals that adult nematodes inhabit the subcutaneous tissues of their natural hosts, reaching full size and depositing microfilariae into the blood. Vector arthropods acquire the first-stage larvae while feeding on an infected host, and the microfilariae develop into infective third-stage larvae, migrating to the proboscis. Transmission occurs when a mosquito vector carrying the infective third-stage larva penetrates a new host, which can be either a human or a natural host. Since humans are a dead-end host, the nematode in humans does not reach sexual maturity, remaining nonfertile. Consequently, microfilariae are not released into the peripheral blood in humans. The presence of an adult nematode in subcutaneous tissue can lead to chronic inflammatory infiltration in the surrounding tissue, forming a parasitic granuloma (2).

Dirofilaria repens nematodes generally exhibit smaller dimensions in comparison to *D. immitis*. Female *D. repens* nematodes measure approximately 100–170 mm in length and 4.6–6.3 mm in diameter, while female *D. immitis* nematodes have dimensions of around 250–300 mm in length and 1–1.3 mm in diameter. Male *D. repens* nematodes are approximately 50–70 mm in length and 3.7–4.5 mm in diameter, whereas male *D. immitis* nematodes measure about 120–200 mm in length and 0.7–0.9 mm in diameter. Distinct differences in their cuticle characteristics can be observed under microscopic examination. *D. repens* features a thick cuticle, measuring approximately 8–40 μm, whereas *D. immitis* has a thin cuticle, measuring around 9–12 μm in males and 5–25 μm in females. Microscopically, *D. repens* displays prominent rounded longitudinal ridges and fine transverse striations in the cuticle, while the cuticle of *D. immitis* appears relatively smooth (20). These nematodes are known to have a slow growth rate, and literature suggests that the manifestation of the first clinical symptoms typically requires a minimum of 6 months (21).

Frequency

Dirofilaria repens, originally found predominantly in dogs in Africa, southeastern Asia, and the Mediterranean region, has experienced a notable increase in prevalence in 1previously reported areas over recent decades. Moreover, its distribution has extended to new European regions, leading to a rise in clinical cases observed in both dogs and humans (10). Presently, dirofilariasis induced by *D. repens* is acknowledged as the most rapidly spreading zoonotic disease in Europe. The reported human cases surged from approximately 1200 cumulative cases until 2009 to over 4000 cases, with recent occurrences documented in Ukraine and southern Russia. The northward expansion of *D. repens* continues, as the parasite establishes itself in countries such as Austria, Germany, Netherlands, Poland, Latvia, Lithuania, Estonia, and Finland, generating newly endemic regions. Poland, specifically, witnessed several indigenous cases of dirofilariasis in humans between 2009 and 2018 (11). Lithuania reported its first diagnosis of human dirofilariasis in September 2011, followed by three ocular and six subcutaneous cases between 2011 and 2018 (4). The primary motive for this overarching northward expansion in Europe is deemed to be climate changes associated with global warming, enabling the development and survival of larval stages within the mosquito vector in central and northern European regions (11).

Symptoms

The mature worms and microfilariae of *Dirofilaria repens* exhibit an extended lifespan of around four years within their natural hosts. Similar to other filarioids, this parasite hosts an endosymbiotic bacterium called Wolbachia, which

plays a crucial role in dampening the innate immune response of the host, ensuring the prolonged survival of the worms. Notably, there is an absence of an inflammatory reaction or connective tissue capsule around the active, moving parasite, situated under the connective serous layers. In a majority of cases, including experimental infections, the presence of the infection goes unnoticed, with no apparent clinical signs. On occasion, individuals may experience cutaneous disorders such as itching, dermal swelling, subcutaneous nodules containing the parasite, and ocular conjunctivitis (12). In very rare instances, there may be satellite lymphadenopathies accompanied by high fever. The migration of the parasite beneath the skin in the head tissues can lead to trigeminal neuralgia (2). Allergic reactions, likely stemming from sensitization to microfilaria and Wolbachia-mediated inflammatory responses in severe infections, have been documented (12). Typically, there is no observation of peripheral blood eosinophilia or elevated IgE levels in affected individuals (13).

Prevention and treatment

Combination therapy using ivermectin and doxycycline can effectively eliminate Dirofilaria infection in dogs, serving as a preventive measure against potential public health issues (12). The most effective strategy to avoid dirofilariasis involves preventing mosquito bites. For human subcutaneous dirofilariasis, the definitive treatment is surgical excision of the lesion (14). Surgical removal of subcutaneous worms may face challenges due to difficulties in precisely locating the parasite (15). Alternatively, chemotherapy with ivermectin and diethylcarbamazine is a viable option (14). Medical treatment using anthelminthic drugs like albendazole, in combination with doxycycline, has been shown to halt worm migration and promote the formation of a fixed nodule, facilitating removal. The efficacy of this treatment suggests a potential role for doxycycline in targeting endosymbiont Wolbachia, as observed in dogs. Additionally, human immune responses to Wolbachia can be utilized to confirm exposure to the parasite. Once *D. repens* is removed, further medical treatment is generally unnecessary, unless the patient is immunosuppressed or in the extremely rare case of a suspected second nematode. Due to the rarity of the disease in humans, there are no established guidelines or treatment studies, necessitating physicians to rely on their experience. However, with or without treatment, there have been no reports of fatalities or permanent body damage (15).

CASE REPORTS

Case I

Patient Information

Age: 38 years. Female.

Date of Presentation: November 29, 2022

Clinic: Lithuanian University of Health Sciences Kaunas clinics, department of Maxillofacial surgery

Clinical History

The patient sought medical attention at the Lithuanian University of Health Sciences Kaunas Clinics with a chief complaint of persistent edema in the buccal region, extending to the temple area for the past two months. At the time of the appointment, the edema was less pronounced. The patient, a 38-year-old individual, reported no history of recent travel and had no known systemic or genetic diseases

Diagnostic Investigations

An ultrasound examination was performed on the same day, revealing a well-defined structure measuring approximately 2.2×1.2 cm with an associated cavity measuring 1.0×0.5 cm in the left buccal region. The radiological findings were consistent with an abscess.

Intervention

Prompt surgical intervention was carried out on the same day to address the abscess. Intraoral infiltration anesthesia with 4% articaine (1.7 ml) was administered in the buccal region. An incision was made slightly below the parotid gland duct, and the soft tissue was separated with mosquito forceps. During the procedure, a structure resembling a helminth was discovered within the tissue.

The incision site was thoroughly irrigated with a 0.02% chlorhexidine solution, and closure was achieved using Vicryl 4-0 sutures.

Postoperative Management

The patient was prescribed a seven-day course of Amoxicillini 1000 mg, one tablet twice daily.

Histopathological Examination

The excised tissue, including the unidentified structure, was sent for histopathological examination. The findings indicated adipose and fibrous tissues with prominent mixed inflammatory infiltration, predominantly composed of eosinophilic granulocytes, which confirms the clinical

Case II

Patient Information

Age: 43 years. Male

Date of Presentation: October 25, 2023

Clinic: Lithuanian University of Health Sci-

ences Kaunas clinics, department of Maxillofacial surgery

Clinical History

A 43-year-old male presented to the clinic with the chief complaint of a painless bump in the right buccal area. The patient reported the appearance of the bump approximately two weeks before the visit. The patient, a 43-year-old individual, reported no history of recent travel and had no known systemic or genetic diseases.

Clinical Examination

Both intraoral and extraoral examinations revealed a 1×2 cm, mobile, and firm bump in the right buccal area. Despite being non-painful, the clinical appearance raised suspicion of a glandular stone or tumor.

Diagnostic Investigations

An ultrasound examination was performed, revealing a well-defined, anechoic zone measuring about 1 cm in diameter at a depth of approximately 0.5 cm in the right cheek. Within this zone, multiple linear hyperechoic structures were observed, showing movement during the examination. The ultrasound findings were suggestive of dirofilariasis or other parasitic origins.

Intervention

The patient returned the next day for surgery. Local infiltration anesthesia with 4% Articaine (3.4 ml) was administered. A 1 cm incision above the parotid gland duct was made, and the soft tissue was separated with mosquito forceps. During the procedure, the capsule of the helminth ruptured, and the intact helminth was extracted. The wound was irrigated with 0.02% chlorhexidine solution, and closure was achieved using Vicryl 4-0 sutures.

Postoperative Management

The patient was prescribed a seven-day course of amoxicillin 1000 mg, one tablet twice a day.

Species Identification

The extracted helminth was sent to the National Lithuanian Health Bureau laboratory for species determination. The laboratory identified the helminth as *Dirofilaria repens*.

Case III

Patient Information

Age: 55 years. Female

Date of Presentation: November 17, 2023

Clinic: Lithuanian University of Health Sciences Kaunas clinics, department of Maxillofacial surgery

Clinical History

A 55-year-old female presented to the Lithuanian University of Health Sciences Kaunas clinics, Maxillofacial Surgery department on November 17, 2023, complaining of a bump in the left cheek. The non-painful bump had appeared in August and remained unchanged in size. The patient denied any recent travel history and had no known systemic or genetic diseases.

Clinical Examination

Both extraoral and intraoral examinations revealed a firm, mobile, and unpainful bump in the buccal area, unrelated to the teeth.

Diagnostic Investigations

The initial diagnostic test was an ultrasound, which revealed a cystic structure measuring approximately 1.1×0.9 cm in the left cheek. Within the cyst, multiple hyperechoic linear structures were observed, showing movement during the examination. These findings were highly suggestive of dirofilariasis or another parasitic origin. Additionally, a 0.5 cm hypoechoic structure adjacent to the cyst was identified, possibly representing a reactive lymph node.

Treatment Decision

The patient opted to undergo removal of the helminth under general anesthesia, declining local anesthesia.

Operative Procedure (December 04, 2023)

Under general anesthesia, supplemented with local anesthesia using 2% lidocaine (2 ml), a 2 cm width incision above the parotid glandular duct was made. The soft tissue was separated with mosquito forceps, leading to the eruption of the helminth nodule, which was subsequently removed. The wound was irrigated with 0.02% chlorhexidine solution, and closure was achieved using Vicryl 4-0 sutures.

Postoperative Management

The patient was prescribed a seven-day course of amoxicillin 1000 mg, one tablet twice a day.

Species Identification

The extracted helminth was sent to the National Health Bureau laboratory for species determination. The laboratory identified the helminth as *Dirofilaria repens*, female, measuring 145 mm in length.

DISCUSSION

Dirofilaria repens infections affecting the maxillo-mandibular region are rare occurrences. The first documented instance of maxillo-mandibular dirofilariasis dates back to 1864 Italy, involving a 20-year-old male patient whose lip was affected. Only 100 cases of maxillo-mandibular dirofilariasis have been reported worldwide until 2018. Cases were scarce before 1980, but there was a notable

surge in reported instances during the following two decades, which gradually declined over the subsequent two decades. The peak period for reported cases was between 1991 and 2000, with 31 documented cases (16).

Diagnosing dirofilariasis can be challenging due to the diverse symptoms exhibited by patients (17). In the observed cases, patients presented with the chief complaint of a rapidly appearing nodule that demonstrated stability in terms of size without subsequent enlargement. Key diagnostic indicators include a comprehensive patient history and clinical examination (16). Hematological investigations, such as a full blood count (FBC), are valuable for excluding bacterial infections, with elevated eosinophil levels commonly associated with parasitic infections. In our cases, systemic blood analysis was not conducted on the patients. Nevertheless, in one instance, the exudate from the nodule was submitted for laboratory analysis, revealing the presence of eosinophilic granulocyte infiltration, indicative of a typical immune response observed in parasitic infections. Radiological studies like ultrasonography, computed tomography, and magnetic resonance imaging can provide useful insights, particularly in visualizing parasite movement within nodules. In all three cases, ultrasonography served as the principal diagnostic modality, playing a pivotal role in the diagnostic evaluation. Monitoring anti-*Dirofilaria repens* antibody levels aids in assessing treatment response in drug-treated cases (19).

Differential diagnoses for buccal or oral mucosa dirofilariasis encompass various conditions, including sialolithiasis, mucocele, granulomatous diseases, lymphadenopathy, epidermoid cysts, and salivary gland neoplasms. Malignancies, considering the patient's age, were meticulously ruled out through microscopic examination. The primary basis for dirofilariasis diagnosis lies in histology, where distinctive features of Dirofilaria nematodes, such as external longitudinal cuticular ridges, lateral hypodermal cords, and myoid tissue fibers, are observed. Longitudinal ridges aid in differentiation from Onchocerca, which possesses transverse ridges. Gravid worms and microfilariae are typically found in definitive hosts, but seldom in humans, usually with a single worm per nodule. Identifying the worm may be challenging due to degenerative changes and the host immune response. Peripheral blood hypereosinophilia may prompt further investigation for parasitic infection. Polymerase chain reaction, immunohistochemistry, and serology are additional diagnostic tools, though the availability of polymerase chain reaction tests is limited, and the efficacy of serology tests, according to the Centers for Disease Control and Prevention, is not well-established (18).

Numerous treatment options are available for managing subcutaneous dirofilariasis, with surgical removal of the parasite considered the most effective method. For all examined patients, a surgical procedure was performed for the removal of the helminth. Locating the live worm within the nodule can be challenging due to its movement. In such cases, complete removal of the nodule or immobilization of the parasite using a cryoprobe are viable approaches. Medical treatment is also successful in certain instances, with commonly employed drugs including diethylcarbamazine (DEC), ivermectin, and albendazole. DEC, known for its effectiveness, modifies the parasite's membrane, facilitating its phagocytosis by monocytes. Ivermectin, a broad-spectrum antiparasitic drug, is both a treatment and a preventive measure. Tetracycline and doxycycline have demonstrated some success as well. However in these cases, following surgical removal of the helminth, patients were prescribed antibiotics to prevent secondary infections. Prevention plays a crucial role in minimizing infection, emphasizing the importance of controlling mosquitoes and addressing issues related to stray dogs (19).

CONCLUSION

Dirofilariasis, caused by parasites like *Dirofilaria repens* and *Dirofilaria immitis*, is a growing zoonotic concern transmitted by mosquitoes. This report details three rare cases of oral dirofilariasis, emphasizing the importance of timely diagnosis.

Key findings include the prevalence of *D. repens* in Europe, particularly in Lithuania, driven by climate changes. The reported cases presented with rapidly appearing nodules, diagnosed through ultrasonography, and treated with surgical helminth removal.

Symptoms varied, with some cases being asymptomatic, while preventive measures focus on avoiding mosquito bites. Treatment involves surgical excision and, in some cases, anthelminthic drugs.

In summary, oral dirofilariasis requires a comprehensive approach for accurate diagnosis and timely intervention, highlighting the need for increased awareness among healthcare professionals.

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