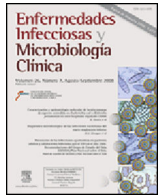




Enfermedades Infecciosas y Microbiología Clínica

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Scientific letters

A case of human ocular dirofilariasis in a patient with multiple endocrine neoplasia in Northwest Spain



Un caso de dirofilariasis ocular humana en el Noroeste de España en un paciente con neoplasia endocrina múltiple

Subcutaneous/ocular dirofilariasis caused by *Dirofilaria repens* is a vector-borne zoonosis affecting dogs and humans in the Old World. While dogs are the natural reservoirs, humans can be accidentally infected when they are bitten by mosquitoes that previously fed on infected dogs. Human subcutaneous/ocular dirofilariasis is characterized by the appearance of benign subcutaneous nodules that can be mistaken by cutaneous carcinomas and by the location of immature or fully developed worms free or encapsulated in the ocular area.¹ Most cases have been reported in Europe, where a geographical spreading from the Southern endemic countries to previously non-endemic central and Northern countries has been observed in the last ten years. These spreading is attributed both to global warming and the lack of preventive measures in canine populations, given the usually asymptomatic character of this parasitosis in the animal reservoirs.² To the present, in Spain *D. repens* has been detected exclusively in the canine populations of the Mediterranean coastal provinces and Balearic Islands and only 8 human cases have been reported in the same areas.³ In the present work a clinical case of human subconjunctival dirofilariasis, reported in an area of Northwestern Spain where canine infections by *D. repens* have not been previously observed, is described in a patient with Multiple Endocrine Neoplasia type 2 (MEN2).

Case presentation

A 39-year-old man attends medical consultation in the Ophthalmology Service of the Healthcare Complex of Zamora (Northwestern Spain) for the follow-up of a chronic keratoconjunctivitis related to MEN2. During consultation the patient refers only a slight conjunctival irritation. Ophthalmological exploration evidenced hyperemia and the presence of a subconjunctival nodule in each eye, compatible with filarial parasites. Surgical removal of the 2 worms with topical anesthesia was difficult as a consequence of the adherence of the parasites to the conjunctiva and their friability. Several fragments of both worms with different sizes were obtained (Fig. 1A). Parasitological identification was not possible on the basis of the morphology and morphometry in our laboratory because the nematode was significantly damaged. It was sent to Laboratory of Parasitology of the University of Salamanca for identification by polymerase chain reaction (PCR) technique.

DNA was extracted, amplified by PCR⁴ and visualized in agarose gel electrophoresis (Fig. 1B) showing a pattern of bands compatible

with *D. repens*. This confirms that both subconjunctival nodules were due to a dirofilariasis caused by this species. Subsequent exploration did not evidenced residues of the parasites. Blood tests showed a number of eosinophils within normal range ($0.1 \times 10^3/\text{mm}^3$) and characteristic alterations of MEN: high calcitonin (11,220 ng/L), parathormone (92 ng/L) and cromogranine A (>2445 ng/L) levels. The patient has not farming, hunting or fishing activities and he had not traveled outside the residence area in the last years and ever has had dogs. He lives in a humid area with 3 rivers and extensive irrigated crops, typical environmental characteristics of endemic areas of dirofilariasis in Spain.⁵

Discussion

To our knowledge this is the first time that conjunctival dirofilariasis is described in a patient suffering from MEN. This is characterized by the appearance of multiple malignant or benign tumors in endocrine gland. The basic treatment of this condition is the surgical removal of the tumors associated, when necessary, to pharmacological treatment of the hormonal hypersecretion and/or substitutive hormonal therapy.⁶ Nevertheless, not immunosuppressive therapy that could facilitate the establishment of pathogens is employed and consequently we cannot establish the relationship of cause/effect between MEN syndrome and dirofilariasis. However, MEN especially variant 2, is associated with chronic keratoconjunctivitis. Probably this fact has been a local risk factor to make it susceptible to infection. Human dirofilariasis caused by *D. repens* presents as subcutaneous nodules/subconjunctival location. Thus it is necessary to consider this condition in the differential diagnosis of other pathological processes affecting subcutaneous or subconjunctival tissues. Canine and human subcutaneous/ocular dirofilariasis is considered currently an emergent parasitosis in Europe, attributing this fact to the introduction of infected asymptomatic dogs from Southern endemic areas into non endemic central and Northern areas of the continent in which adequate environmental conditions for the transmission have appeared as a consequence of global warming.² In Spain human and animal dirofilariasis caused by *D. repens* has been reported exclusively in the Eastern Mediterranean area³. The variety and abundance of vector species and the number of larvae that complete the development are factors that determine the efficiency of transmission in this area. Although in this patient there was no epidemiological suspicion, since there are no previous cases described in the area, it must be considered that there is a risk of infection if there are infected dogs in the environment. The fact that this case has been detected in the West of the Iberian Peninsula suggests that, like in the rest of Europe, *D. repens* could be spreading stealthily in canine populations living in other parts of Spain and consequently becoming a risk factor for the human populations of these areas. In conclusion, this case should take attention about the possibility to find

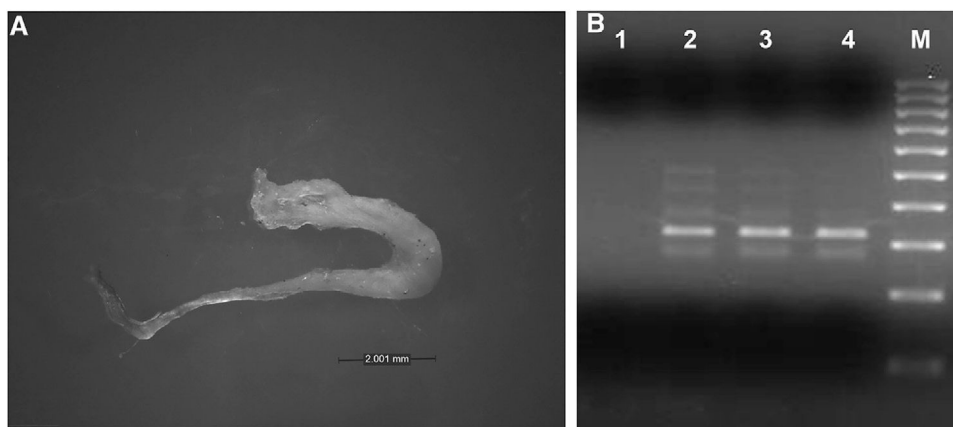


Fig. 1. (A) One of the fragments of the worms removed from the subconjunctival tissue of the patient. (B) Multiplex PCR amplification of the DNA extracted from the worms removed from the patient. Lane 1: negative control; lane 2: *D. repens* positive control; lanes 3 and 4: samples obtained from the worms surgically removed from the patient; M: molecular marker, 100–1000 pb.

cases of subcutaneous/ocular dirofilariasis associated to MEN and the spreading of *D. repens* into previously non-endemic areas in Spain.

Unfortunately, we do not have images of the nodules prior to excision, which would have allowed a differential diagnosis, however the initial suspicion was ocular dirofilariasis since the worm was appreciated with the naked eye.

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Inmaculada Ramírez de Ocáriz Landaberea^{a,*},
María F. Brezmes Valdivieso^a, Sara C. García Sanz^b,
Fernando Simón Martín^c

^a Microbiology Unit, Healthcare Complex of Zamora, Zamora, Spain

^b Ophthalmology Service, Healthcare Complex of Zamora, Zamora, Spain

^c Laboratory of Parasitology, Faculty of Pharmacy and IBSAL, University of Salamanca, Salamanca, Spain

* Corresponding author.

E-mail address: iramirez@saludcastillayleon.es
(I. Ramírez de Ocáriz Landaberea).

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Neonatal epididymo-orchitis with pyoceles caused by *Escherichia coli*: Successful treatment with antimicrobial therapy alone



Orquiepididimitis neonatal asociada a piocelos por *Escherichia coli*: tratamiento efectivo con antibioterapia exclusiva

Evaluation of acute scrotum in neonates is a surgical emergency since the most common diagnosis is testicular torsion. Other causes, such as epididymo-orchitis (EO), are very uncommon during neonatal age.¹ We present a neonatal EO and review all similar cases reported in the literature.

A 19-day-old male was brought to the Emergency Department with an erythematous and firm swelling of his left scrotum associated with irritability and fever that had begun five hours before. He had been born healthy at 38 weeks of gestational age and prenatal ultrasounds were normal. Clinical examination revealed a firm and erythematous left hemiscrotum. Doppler ultrasound findings were compatible with bilateral EO, mainly in the left hemiscrotum with a right hydrocele and a left pyocel. Laboratory examinations showed a white blood cell count of $13,700 \text{ mm}^{-3}$ (neutrophils 55%), C-reactive protein 132 mg/L and procalcitonin 4.5 ng/mL. Urine and

cerebrospinal fluid (CSF) analysis were normal. He was admitted and empirical treatment with intravenous ampicillin and cefotaxime was started. After *Escherichia coli* was isolated in urine and blood cultures, ampicillin was discontinued. CSF culture was sterile. Renal ultrasound was normal. Fever resolved within 24 h. A new scrotal ultrasound after nine days of treatment showed improvement in inflammatory changes and pyocel resolution. He was discharged after ten days of intravenous cefotaxime with an almost full recovery of scrotal inflammatory signs.

In neonates presenting with acute scrotum it is mandatory to distinguish between testicular torsion and other conditions using Doppler ultrasound. Compared with testicular torsion, the majority of cases of EO present with fever, increased acute phase reactants and increased blood flow.²

Only 11 cases of EO with a microbiological isolation in patients below 1 month of age have been reported in the literature in the last 30 years (1987–2016; Table 1).^{2–4} Hematogenous spread appears to be the causative mechanism in eight cases. Direct extension from a urinary tract infection has been described in one patient.

Although uropathy can predispose to EO,⁵ only three cases were associated with genitourinary malformations. The pathogenesis