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Case report

Human *Dirofilaria repens* infection of the zygomatico-temporal region

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ABSTRACT

A 40-year old patient developed a painless swelling in the left zygomatico-temporal region. Magnetic resonance images and computed tomograms showed a non-specific soft tissue mass in the tumour region, but no invasion of bone. After application of antibiotics, the tumour reduced in size but a firm mass of about 3 cm in maximum diameter persisted under therapy. Surgical exploration revealed a distinct firm mass adhering to the superficial layer of the temporal muscle. Histological and molecular biological investigations demonstrated fragments of *Dirofilaria repens* in the centre of the lesion. Clinical follow-up was uneventful and additional investigations excluded further manifestations of the parasite. *D. repens* infections are extremely rare in northern Europe, but recent reports about the increase of human dirofilariasis in northern parts of Europe should alert the clinician to include helminthoses in the differential diagnosis of atypical space-occupying lesions of the maxillofacial regions.

1. Introduction

Human dirofilariasis infection is a zoonotic infectious disease (Popescu et al., 2012). Dirofilariasis is caused by the canine filarial nematodes *Dirofilaria* (*D.*) *repens* and *Dirofilaria immitis* (Genchi et al., 2011; Pampiglione and Rivasi, 2000; Simón et al., 2012). Dirofilariae constitute a group of filarial nematodes infecting a number of carnivores as definitive hosts (Albanese et al., 2013). Adult dirofilariae are able to release microfilaria into the host's blood. The microfilariae are taken up by various mosquito species that serve as intermediate hosts and transmit the disease to final or aberrant hosts (Genchi et al., 2011). The classical hosts of *D. repens* and *D. immitis* are dogs, but the reservoir for dirofilariae has extended to other carnivores such as cats, wolves, bears and foxes (Genchi et al., 2011, Pampiglione and Rivasi, 2000; Simón et al., 2012; Albanese et al., 2013). Furthermore, other species of the dirofilariae can eventually infect humans. Humans may be infected as aberrant hosts, mainly by *D. repens* and *D. immitis* (Popescu et al., 2012). In human infections by dirofilariae usually one larva develops, which remains infertile (Genchi et al., 2011; Pampiglione and Rivasi, 2000; Robert et al., 2007). The larva migrates through the body and finally forms a nodule or firm mass. *D. immitis* usually infiltrates the lung, while *D. repens* resides in subcutaneous layers anywhere in the human body (Foissac et al., 2013; Leccia et al., 2012). In cases with dirofilariasis of the head and neck region the subcutaneous layers are predominantly affected by *D. repens* (Genchi et al., 2011), but *D. repens* may also be detected in the lungs (Pampiglione and Rivasi, 2000). These parasites usually cause only a few and non-specific symptoms. *D. immitis* infections are usually only detected incidentally, e.g. on X-rays of the thorax, and may initially be confused with a malignant process. However, *D. immitis* can also affect subcutaneous layers (Foissac et al., 2013). Thus, the definite diagnosis of this zoonosis relies on adequate microbiological or molecular biological investigations. Dirofilariasis of the head and neck region affects predominantly the orbital region (Pampiglione and Rivasi, 2000; Akst et al., 2004; Fuehrer et al., 2013).

Human *D. repens* infections are most often reported from various regions of the world with mild to moderate climate (Pampiglione and Rivasi, 2000; Fuehrer et al., 2013), but cases in Germany appear to be rare (Hempel et al., 2012). This is a report of a *D. repens* infection localized in the maxillofacial area detected in a patient living in the north of Germany. The infection was diagnosed only after excision of the space-occupying lesion.

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2. Case report

2.1. History and physical findings

The 40-year old male experienced a swelling of the left temporal region about 4 weeks prior to attending our outpatient clinic. The patient had visited his practitioner who had asked us to perform computed tomography and magnetic resonance imaging (MRI) of the head. Both imaging modalities confirmed the clinical finding of a left temporal space-occupying and ill-defined lesion. On MRI the high water content equivalent to the region of inflammation far exceeded the palpable tumour mass (Fig. 1). Neither investigations lead to a decisive diagnosis. The practitioner had prescribed an antibiotic the week before the patient's admission to the outpatient clinic. On admission, the patient was in excellent general health condition. He reported that the tumour volume had markedly decreased during the last few days. Furthermore, the lesion had never been painful nor had the patient experienced any kind of generalized symptoms like fever or arthralgia since the tumour had occurred.

The patient had visited Sri Lanka 8 months before the first symptoms were noted. Further overseas travels to the Far East and the Indian subcontinent dated back 5 and 20 years. He reported no continuous contact with dogs or other carnivores.

Physical inspection revealed a firm mass about 2 cm above the left pinna and 3 cm in maximum diameter. The skin of the hairy region showed neither erythema nor ulcer and appeared absolutely unaltered. Taking into consideration the history of the patient and the imprecise delineation of the tumour on the images, we decided to explore the region surgically.

2.2. Surgery

An incision of about 4 cm was made in the left temporal region above the firm, flat and ovoid, non-moveable mass. Below the skin a flat tumour of whitish-grey colour covering an area of about $2 \times 2\ cm^2$ became apparent, sharply demarcated to the lateral sides but firmly adhering at the base. The tumour was excised with adhering superficial parts of the temporal muscle. After excision, the deep layers of the muscle appeared to be unaffected by the space-occupying lesion. The wound was closed by primary intention and the healing was uneventful. The temporal swelling disappeared within a week.

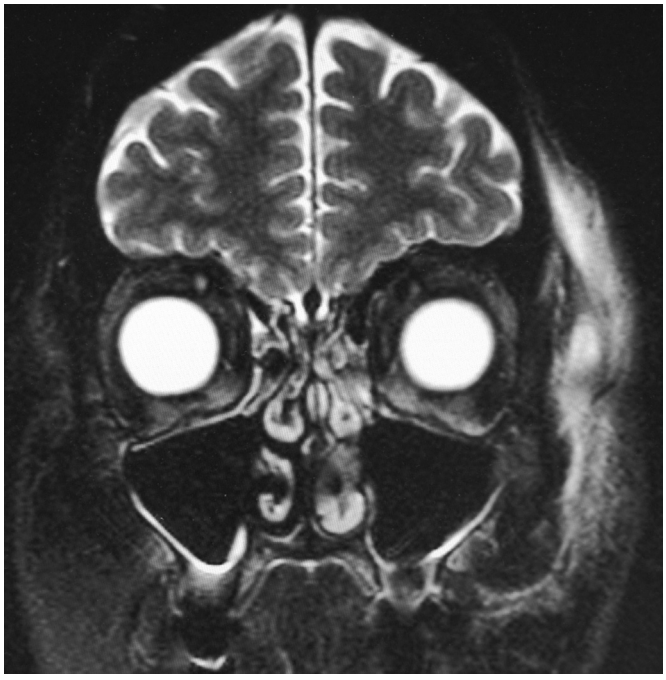

Fig. 1. On magnetic resonance image the widespread infiltration of the left temporozygomatic region becomes visible.

2.3. Histology

A resection specimen of $3 \times 2 \times 1\ cm^3$ volume, firm elasticity, and red–brown colour was prepared for standard investigation. Histologically the connective tissue and adjacent muscle showed an intense, partially follicular lympho-monocytic infiltration surrounding a central suppurative focus. Numerous multinuclear giant cells surrounded the focus that contained several organoid oblong structures. Tentative diagnosis was a chronic inflammation, partially purulent infection with foreign bodies of oblong organoid structure, suggestive for parasites. Further histological investigation revealed that the subcutaneous nodule contained a tangential and several oblique sections of worms (Fig. 2A). They were located 2.4 mm to each other as measured by an Axio Imager M1 microscope equipped by an Axiovision Rel 4.6 (Carl Zeiss Microscopy, Jena, Germany). Inflammatory reaction surrounding the parasites consisted of macrophages, epithelioid cells, lymphocytes, some multinucleated giant cells and abundant eosinophil leukocytes (Fig. 2B). The parasite showed a thick multilayered cuticle with longitudinal ridges and well-developed musculature (Fig. 2B). The traverse sections revealed a dying worm (Fig. 2C and D). The cuticle was recognizable. Eosinophil granulocytes were attached to the surface of the cuticle and were also infiltrating the parasite (Fig. 2D). The findings suggest that eosinophils could mediate parasite damage in context of antibody-mediated cellular cytotoxicity (Robert et al., 2007). The adjacent muscle also exhibited the same lympho-monocytic infiltrate (Fig. 2). The diagnosis of dirofilaria infection was raised.

2.4. Immunohistochemistry

The inflammation infiltrates were composed of various cell types including T-cells (CD3-positive) and B-cells (CD79a-positive), both also identified by LCA antibody. Further, monocytes and multinuclear giant cells (CD68-positive) were present. The proliferation-index as demonstrated by labelling of the Ki67 antigen was low (Fig. 3).

2.5. Molecular biology

The specimen was further processed for polymerase chain reaction to detect the species. The analysis performed with ^{12}Sr-RNA sequences revealed *D. repens* in the specimen. The probe has homologies to sequences of *D. repens* from India/Sri Lanka by 99%, Vietnam by 98% and Europe by 95–97%.

2.6. Follow-up

After final diagnosis the patient's blood was investigated for changes related to infection with nematodes. No eosinophilia or other alterations were detected. However, the IgG4 ELISA for *D. repens* was positive indicating a contamination with this parasite. An X-ray of the thorax revealed unremarkable cardiothoracic findings, in particular no suspicious solitary pulmonary nodules.