Cutaneous Manifestations of a Zoonotic Onchocerca Species in an Adult Male, Acquired in Nova Scotia, Canada

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A 65-year-old male with known hypertension and hypercholesterolemia sought medical attention because of a 3-month history of skin swelling on his upper back. Histopathology and molecular techniques were employed and identified an organism in the Onchocerca genus. This represents a very uncommon example of cutaneous infection by a zoonotic Onchocerca species.

CASE REPORT

A 65-year-old Caucasian man from rural Nova Scotia sought medical attention because of a sudden onset of localized swelling of the skin in the inferior left scapular area. He had noted a small, mildly tender pruritic papule one morning, measuring less than 1 cm, which he regarded as a possible insect bite. Over the course of 1 day, the lesion enlarged to form a nodule measuring approximately 4 cm in diameter. Medical attention was sought. The patient was given a 10-day course of antibiotics which caused the swelling to decrease in size, but the nodule did not resolve completely. Elective surgical excision was undertaken.

Within the previous 5 years, the patient had traveled to Florida in April 2009 and had been working in Ontario until 31 May 2010. While in Ontario, he had been in charge of maintaining a high-rise apartment block in Windsor for 12 years. Prior to this, he had worked in the automotive industry. There was no history of foreign travel. During the previous 3 years, the patient had resided in rural Nova Scotia, where he had a pet dog with a free range in an open hayfield where contact with wild animals was minimal. The dog showed no symptoms of infection during this period and remains healthy to the present day. The patient’s medications included 12.5 mg hydrochlorothiazide once daily for hypertension and 20 mg simvastatin once daily for hypercholesterolemia. He was otherwise healthy. There was no history of immunosuppression.

On examination, an erythematous nodule was evident on the left upper back just inferior to the scapula. This area had been covered by clothing, and the patient could not recall any history of an arthropod bite. No other skin lesions were detected. Preliminary blood work was not performed. Following excision, the specimen was submitted to the laboratory for processing. Clinically interpreted as a cyst, the submitted sample consisted of an ellipse of skin and subcutaneous adipose tissue measuring 1.4 by 0.3 by 1.3 cm. It was serially sectioned and submitted in total. Histopathologic examination revealed a dense, nodular, superficial and deep, perivascular lymphocytic infiltrate with abundant eosinophils in the dermis and superficial panniculus. Small foci of interstitial granulomatous inflammation were noted (Fig. 1A and B). Close to the edge of the biopsy specimen, in association with the inflammatory infiltrate, cross sections of a nematode were noted (Fig. 1C).

A microbiological consultation confirmed the presence of a nematode measuring 60 by 68 μm. There were no lateral alae, and the cuticle was smooth, with a 3-μm thickness. The lateral cords had 2 cells with prominent nuclei, but the dorsal and ventral lines were not prominent. A muscular layer was present internal to the cuticle. An esophagus and possibly a reproductive system were present, although a double uterus was not observed. No ovum or larvae were seen within the organism. Based on the microbiologist’s evaluation, certain organisms were excluded, including Strongyloides stercoralis, hookworm, Toxocara canis or Toxocara cati, Gnathostoma spp., and Baylisascaris procyonis. Candidate organisms included Brugia spp., Mansonella spp., and Acanthocheilonema delicata. A trichrome stain was not performed, and unstained slides were not available for examination.

Because the nematode could not be further identified by conventional microscopic examination, the specimen was referred in consultation to the Mayo Clinic in Rochester, MN. There, a molecular approach to identification of the organisms was undertaken. PCR using primers for the mitochondrial NADH dehydrogenase subunit 5 gene of Onchocerca species was employed (1). Sequence analysis of the amplified product (174 b) in conjunction with a query in the public NCBI (National Center for Biotechnology Information) Nucleotide database enabled identification of the nematode as an Onchocerca species, with the closest (96%) homology to O. volvulus, O. duiei, and O. linealis.

The localized clinical lesion was considered to be a result of accidental inoculation by a zoonotic species, without further implications for the patient’s health. Excision was regarded as curative, and the patient remains well 10 months after excision of the lesion.

Filariasis is a parasitic infection caused by nematodes (roundworms) belonging to the family Filarioidea. When filariae that
normally infect animals infect humans, the condition is termed zoonotic filariasis. These are often transmitted by bloodsucking arthropod vectors, such as black flies and mosquitoes. Zoonotic filariasis has been reported worldwide, with variable clinical presentations ranging from an asymptomatic state to a serious illness with widespread dissemination of the organism. Zoonotic filariasis of the skin is most commonly caused by filariae of the Dirofilaria, Onchocerca, and Brugia genera. In this report, we have described an inflammatory skin lesion in an adult male which was caused by a zoonotic Onchocerca species acquired in Nova Scotia, Canada.

Zoonotic filariae are occasionally identified in biopsy specimens or removed intact from superficial sites, such as the orbit or conjunctiva (2). The site of human infection is often analogous to the site of infection in the native mammalian host (2). In humans, zoonotic nematodes have typically been found in the subcutaneous tissue, heart, lungs, eyes, lymphatic system, brain, and spinal cord (2). Zoonotic filariae that have been isolated in humans include Dirofilaria, Brugia, Onchocerca, Dipetalonema, Loa, and Meningonema (2). While many filariae species can cause infections in birds, reptiles, and amphibians, only filariae with natural mammalian hosts cause zoonotic filariasis in humans (2).

Human infection occurs by way of an arthropod vector which had previously ingested a blood meal from an animal with an active filarial infection. During their development, filarial larvae elicit a minimal host response, with the exception of colonization of sensitive areas like conjunctiva (2). However, due to the incompatibility of the host, the larvae inevitably die and generate an intense host inflammatory response to the organism (2). Why humans mount a host response only when the larvae die is unclear. It is known that larvae live for an extended period of time within their natural hosts without generating a host response (2). Rarely, filariaemia is seen in zoonotic filariasis (2). Removal of the parasite is therapeutic.

Onchocerca are natural parasites of animals, often cows and horses (2). Many species of Onchocerca can be found within connective tissues of wild and domestic animals worldwide (3). In tropical areas where Onchocerca volvulus is endemic, human infection is quite common. Human onchocerciasis, also known as river blindness, manifests as intense pruritis, skin depigmentation, and ocular scarring due to migration of the microfilariae (3). The adult filariae are stationary in the human host and are found within a subcutaneous nodule. In our case, it is unclear what the vector might have been. Certainly, the pet dog could be suspected, although this is unlikely given that the dog showed no symptoms of infection and remains healthy to this day. Previous reports suggest that Simulium spp. (blackflies) are often implicated as vectors in zoonotic onchocerciasis (4, 5).

To date, 16 cases of zoonotic filaria by Onchocerca spp. whose natural hosts are animals have been reported outside their areas of endemcity (Table 1). All cases but one were infected by a single female worm. The remaining patient, who had systemic lupus erythematosus and was on immunosuppressive therapy, had multiple lesions and multiple worms on the face and neck (1). The adult forms of Onchocerca spp. have a marked predilection for connective tissues and often assume a coiled nodular appearance, a characteristic seen also in their natural hosts (2). Histomorphologic assessment of the parasite may allow accurate identification to the genus level. Features of relevance include cuticle thickness, musculature development, hypodermis development, lateral

FIG 1 (A) Elliptical excision of skin and panniculus, at scanning magnification, shows a superficial and deep perivascular inflammatory infiltrate extending to the panniculus. There are no epidermal changes. Hematoxylin and eosin (H&E) staining and ×5 magnification were used. (B) Higher-power view of the infiltrate reveals a predominantly lymphohistiocytic population with numerous eosinophils, along with a focal interstitial histiocytic component. H&E, ×72. (C) Adjacent to the interstitial histiocytic inflammatory infiltrate, cross sections of a larval nematode are seen (H&E, ×400). Note the unevenly thick cuticle, the small number of weak muscle cells, and the absence of reproductive tubes, consistent with diagnosis of an Onchocerca sp. larva.
TABLE 1 Previously reported zoonotic filariasis by *Onchocerca* species outside areas of endemicity

<table>
<thead>
<tr>
<th>Age (yr)/gender</th>
<th>Anatomical site</th>
<th>Geographic location</th>
<th>Species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>15/female</td>
<td>Tendon of oculomotor muscle</td>
<td>Russia</td>
<td><em>Onchocerca</em> species</td>
<td>6</td>
</tr>
<tr>
<td>25/male</td>
<td>Knee</td>
<td>Switzerland</td>
<td><em>Onchocerca</em> species</td>
<td>7</td>
</tr>
<tr>
<td>48/female</td>
<td>Wrist</td>
<td>Illinois</td>
<td><em>Onchocerca</em> species, most likely <em>O. cervicalis</em></td>
<td>8</td>
</tr>
<tr>
<td>43/female</td>
<td>Wrist</td>
<td>Ontario, Canada</td>
<td><em>Onchocerca</em> species</td>
<td>9</td>
</tr>
<tr>
<td>2/female</td>
<td>Left foot (plantar aspect)</td>
<td>Oita, Japan</td>
<td><em>Onchocerca</em> species</td>
<td>10</td>
</tr>
<tr>
<td>57/female</td>
<td>Wrist</td>
<td>Oita, Japan</td>
<td><em>Onchocerca</em> species, most likely <em>O. gutturosa</em></td>
<td>11</td>
</tr>
<tr>
<td>52/female</td>
<td>Right cornea</td>
<td>Colorado</td>
<td><em>Onchocerca</em> species, most likely <em>O. cervicalis</em></td>
<td>12</td>
</tr>
<tr>
<td>16/male</td>
<td>Subconjunctival area</td>
<td>Albania</td>
<td><em>Onchocerca</em> species</td>
<td>13</td>
</tr>
<tr>
<td>50/female</td>
<td>Left subdeltoid mass</td>
<td>Minnesota</td>
<td>O. gutturosa</td>
<td>14</td>
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<tr>
<td>69/female</td>
<td>Right infraocular region</td>
<td>Oita, Japan</td>
<td>O. dewittii japonica</td>
<td>15</td>
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<tr>
<td>65/male</td>
<td>Anterior vitreous cavity</td>
<td>Hungary</td>
<td><em>Onchocerca</em> species</td>
<td>16</td>
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<tr>
<td>59/female</td>
<td>Multiple nodules on face and neck</td>
<td>USA</td>
<td>O. jakutensis</td>
<td>1</td>
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<tr>
<td>12/female</td>
<td>Suprapubic skin nodule</td>
<td>Kuwait</td>
<td><em>Onchocerca</em> species</td>
<td>17</td>
</tr>
<tr>
<td>70/male</td>
<td>Subcutaneous nodule left knee</td>
<td>Hiroshima, Japan</td>
<td>O. dewittii japonica</td>
<td>18</td>
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<tr>
<td>18/female</td>
<td>Left subconjunctival area</td>
<td>Edirne, Turkey</td>
<td>O. lupi</td>
<td>5</td>
</tr>
<tr>
<td>56/female</td>
<td>Left anterior chamber of eye</td>
<td>Oregon</td>
<td><em>Onchocerca</em> species</td>
<td>19</td>
</tr>
</tbody>
</table>

chords, and a vestigial digestive system. Determining the species of zoonotic *Onchocerca* organisms, however, is often difficult and requires molecular ancillary techniques, namely, DNA sequencing. In our case, histomorphology was inconclusive and PCR and sequence analysis were required for identification. By utilizing primers for the mitochondrial NADH dehydrogenase subunit 5 gene, we were able to determine that this organism was of the *Onchocerca* genus. However, an attempt at species determination utilizing primers for the 18S gene provided by the Centers for Disease Control and Prevention was unsuccessful. We surmise that this may have been due to the fragmented nature of DNA in formalin-fixed, paraffin-embedded tissue.

**Conclusion.** Although it is rare, pathologists and dermatopathologists should be aware of zoonotic filariasis. Usually, a thorough clinical history with a focus on recent exposure to animals and/or arthropod bites is helpful in establishing the correct diagnosis. Immunosuppression may lead to more severe infections, although this needs to be further investigated. Consultation with a microbiologist is particularly valuable in this type of setting. Specific identification to the genus and species level may require ancillary molecular techniques.

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**REFERENCES**