Reindeer Warble Fly–associated Human Myiasis, Scandinavia

To the Editor: We report migratory myiasis that occurred during 1991–2012 caused by the reindeer warble fly, Hypoderma tarandi (online Technical Appendix Figures 1, 2, wwwnc.cdc.gov/EID/article/19/5/13-0145-Techapp1.pdf), in 7 tourists to reindeer habitats of northern Scandinavia. We also report 2 additional women (patients 8 and 9), independent of each other, who were asymptomatic but sought medical care in August 2012 after finding 30–60 parasite eggs in scalp hair 3 days after hiking in Kebnekaise and Jämtland Mountains (northern Sweden), respectively.

Patients 1–7 (Table) had enlarged regional lymph nodes and migratory dermal swelling of the head and upper face. Rounded cutaneous swelling of 2–5 cm occurred 1 at a time, persisted for 1–3 days, and reappeared after 2–34 days.

In mid-January 2009, 4 months after initial symptoms, patient 1 felt a sudden pain in his left eye; 10 days later, an ophthalmologist discovered an intraocular larva (online Technical Appendix Figure 3). Patient 3 had a swelling on his forehead, which reappeared 2’ before his right eyelid swelled; the day after the eyelid swelling disappeared, vision decreased in his right eye. Patients 1, 3, and 7 underwent eye surgery; 1 living larva was extracted from each patient. Patients 3 and 7 lost vision in the affected eye.

For 5 patients, ivermectin was administered orally (≈200–350 µg/kg body weight), on 3–5 occasions in relation to the swellings. Patients 8 and 9 also each received 1 dose of ivermectin; they remained asymptomatic. Patient 3 received the first dose on day 5 after the living larva was extracted because of a new swelling. Swelling recurred on 3 occasions 2 weeks–1.5 months after surgery. In patient 7, swelling reappeared on several occasion 10–30 days after eye surgery, indicating that retrieval of 1 larva does not exclude concomitant occult infestations. This probably was also the case for patient 2, who had a swelling on his upper forehead when pain developed at the root of his nose, where a new swelling appeared 4 days later.

The 3 larvae removed from patients 1, 3, and 7 were identified as H. tarandi, 2 by morphology and 1 by molecular-specific amplification and sequencing (1). Antibodies against hypodermic C, an enzyme released by the larva during migration in host tissues, were detected in 5 of the symptomatic patients (2,3).

H. tarandi eggs take 4–7 days to hatch, depending on the temperature of the hair layer (4); thus, patients 8 and 9 were treated soon after oviposition and were seronegative. Newly hatched H. tarandi larvae can easily dry, so their chance of survival is higher when they are close to scalp skin. Eggs from patient 2 were initially misidentified as head lice eggs but were eventually identified as H. tarandi by T.G. Jaenson (Uppsala). Published photographs of the H. tarandi eggs alongside the eggs of head lice (5) helped identify H. tarandi eggs in patients 8 and 9. According to those patients, H. tarandi eggs could not be removed from the hair with a lice comb. The H. tarandi fly is well adapted to sub-Arctic climate; nearly all reindeer were found to be infested in some districts of northern Finland and Norway (6). Reindeer habitats attract tourists, mostly during summer. H. tarandi is mainly active on warm summer days; warm weather perhaps does not encourage persons to cover their heads, which may predispose for oviposition. Also, persons moving around probably attract more flies than do those staying still, and strong wind, rain, and temperatures <10°C–12°C are thought to inhibit the warble fly’s flight activity and oviposition (7). Awareness of human infestation by H. tarandi warble flies increased in Sweden and Norway after news media in Sweden described patient 2 (5; www.lakartidningen.se/engine.php?articleId=146443). This publication helped in the recognition of symptoms and in shortening diagnostic delay in patients 3–6, 8, and 9. Of the 3 cases for which diagnosis was not delayed, patients 4 and 5 were children of a physician who read our publication and recognized the symptoms; patient 6, herself a physician, also read the article (5). Increased awareness, rather than increased incidence, explains the emergence of new cases. Nine of 12 cases of proven H. tarandi myiasis found in the literature occurred in persons who had ophthalmomyiasis interna (3,8,9); migratory dermal swellings, the clinical signature of hypodermiosis, have been reported only in 1 case (10). Such swellings occurred in all the patients reported here, suggesting that clinicians overlooked this finding, possibly because of the overtaking severity of eye complications and the reporting of most previous cases by ophthalmologists (3,8,9). Persons who seek care for migratory dermal swellings during August–December should be asked about recent travel to reindeer habitats.

For 3 patients with ophthalmomyiasis reported here, ophthalmologists initially had difficulty establishing a diagnosis, raising the possibility that some cases of “idiopathic” uveitis from H. tarandi–endemic areas may be caused by H. tarandi. Ophthalmomyiasis should be considered in cases of unilateral uveitis, lens subluxation, and suspicion of intraocular foreign body (3,8,9). Eosinophilia might be absent and should not be used to guide treatment.

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Table. Myiasis caused by warble reindeer fly (*Hypoderma tarandi*), Scandinavia, 1991–2012*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case-patient no.</th>
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<tbody>
<tr>
<td>Age, y/sex</td>
<td>1/2/3/4†/5/6/7††</td>
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<tr>
<td>Signs and symptoms</td>
<td>Enlarged occipital and retroauricular lymph nodes/Eggs in scalp; enlarged occipital and cervical lymph nodes/Forehead swelling/Enlarged occipital and cervical lymph nodes/Forehead and eyebrow swelling/Occipital swelling/Occipital swelling</td>
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<tr>
<td>Travel Dates</td>
<td>2008 late Jul–early Aug/Norway; extreme northeast: patient resides in Troms County where reindeer are occasionally seen/2009 Jul 20–Aug 7/Sweden: Lapland/2010 Jul 7–16/Sweden: Kiruna, Riksgränsen, Abisko (several short hiking tours)/Norway: Bodø/Sweden: family undertook a 5-d hiking tour in Lunndörsfjällen, a mountain area in Jämtland County/Norway: Lapland/Norway; short trips to Arvidsjaur (Lapland) and Jämtland Mountains</td>
</tr>
<tr>
<td>Observed reindeer</td>
<td>Yes/Yes§/No/Yes; at close range/Yes/Yes</td>
</tr>
<tr>
<td>Migratory swellings, no.</td>
<td>Temple, 1/Head; forehead, 5/Forehead; 4; eyelid; 1; behind ear, 1/Forehead and eyelid, 5/Forehead and eyelid, 2/Head, temple, eyelid, &gt;5/Head, &gt;5</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes/Yes (1.0)/No/Yes (0.6)/No/Yes (0.8)/No/Yes (3.8)/No/No/No/Unknown</td>
</tr>
<tr>
<td>Eosinophilia (highest value)¶¶</td>
<td>Yes/Yes/No/Yes/Fever, headache, nausea/No/Enlarged nuchal lymph nodes/Uveitis, glaucoma, retinal hemorrhage</td>
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<tr>
<td>Other signs and symptoms</td>
<td>Yes/Yes/No/Yes/Localized exanthema/Itching of scalp, enlarged retroauricular lymph nodes, headache, uveitis/Uveitis, failure to gain weight</td>
</tr>
<tr>
<td>Diagonal delay, d#</td>
<td>74/25/14/0/0/1/60</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Positive serology, morphologic identification of larva/Positive serology, identification of eggs/Positive serology, molecular identification of larva/Positive serology/Positive serology/Negative serology**/Negative. serology in 2011 and 2012, morphologic identification of larva in 1991</td>
</tr>
<tr>
<td>Drugs received</td>
<td>Ivermectin/No/No/5 doses/5 doses†/5 doses/3 doses/2 doses/No/No/No</td>
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<tr>
<td>Antihistamines</td>
<td>No/No/Yes/Yes/No/Yes/Yes/Yes/No/Unknown</td>
</tr>
<tr>
<td>Oral steroids</td>
<td>Yes/Yes/Yes/Yes/Yes/No/Yes/Yes/No/Unknown</td>
</tr>
<tr>
<td>Outcome</td>
<td>After eye surgery/Good/Eye surgery; visual loss, right eye/Good/Good/Good/Good/Eye surgery; visual loss, right eye</td>
</tr>
<tr>
<td>Exner®</td>
<td>Temporalis, 9/Good/Good/Good/Good/Good/Good/Good/Good/Good/Good/Good/Good/Good</td>
</tr>
</tbody>
</table>

*Patients 8 and 9 are not included in the table because myiasis did not develop in them.
†Patients 4 and 5 are siblings.
‡Patient 7 was discovered by the father of patients 4 and 5 among his acquaintances, suggesting the possibility of additional unreported cases in the population.
§In Jukkasjärvi (Sweden), the child had visited an enclosure where the reindeer were agitated because of swarms of flies.
¶Referent: 0–0.5 × 10²/L.
†Interval between date of first visit for myiasis-associated symptoms and date when treatment began.
**The diagnosis could not be confirmed, but her clinical picture and response to treatment were similar to those of other patients.
††Ivermectin was given first after eye surgery.

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Azole-Resistant Aspergillus fumigatus, Iran

To the Editor: Aspergillus fumigatus causes a variety of diseases in humans. The drugs recommended for treatment of Aspergillus diseases are the mold-active azole antifungal drugs (1). However, a wide range of mutations in A. fumigatus confer azole resistance, which commonly involves modifications in the cyp51A gene (2), the target for azole antifungal drugs.

Azole resistance is thought to be selected for as a result of patient therapy or exposure toazole compounds in the environment; resistance in clinical A. fumigatus isolates has been increasingly reported in several European countries, Asia, and the United States (3–7). The most frequently reported resistance mechanism is a 34-bp tandem repeat (TR34) in combination with a substitution at codon 98 (TR34/L98H) (4); this mechanism is believed to have been selected for through environmental exposure toazole fungicides.

Because routine in vitro susceptibility testing of clinical Aspergillus isolates is not common in many centers worldwide, the prevalence of azole resistance might be underestimated. We investigated the prevalence of azole resistance in clinical A. fumigatus isolates stored for 6 years (2003–2009) at Tehran University Mycology Reference Centre and Islamic Azad University, Ardabil Branch, Iran.

We investigated 124 clinical A. fumigatus isolates obtained from patients with Aspergillus diseases (online Technical Appendix Table 1, wwwnc.cdc.gov/EID/article/19/5/13-0075-Techapp1.pdf). We conducted strain identification, in vitro antifungal susceptibility testing, and sequence-based analysis of the Cyp51A gene, as described (4). We performed microsatellite genotyping of all A. fumigatus isolates for which the MIC of itraconazole was $\geq 16$ mg/L (8) by using a short tandem repeat A. fumigatus assay, and we compared the results with those reported for the Netherlands (20 isolates) and other European countries (24 isolates) (online Technical Appendix Figure).

The distribution of azole-resistant and wild-type A. fumigatus isolates examined in this study, according to year of isolation, is shown in online Technical Appendix Table 1. Of 124 A. fumigatus isolates, 4 grew on the wells containing itraconazole and voriconazole, indicating a multidrug-resistant phenotype. Of these resistant isolates, 3 were from patients with chronic pulmonary aspergillosis and 1 was from a patient with allergic bronchopulmonary aspergillosis (Table).

Sequence analysis of the CYP51A gene indicated the presence of TR34/L98H in 3 isolates and no mutations in the other isolate (Table). The first TR34/L98H isolate had been recovered in 2005, which is relatively early compared with reported isolations in other countries (online Technical Appendix Table 2). Microsatellite typing of 6 short tandem repeat loci demonstrated identical patterns for 2 of the 3 azole-resistant isolates from Iran, but the TR34/L98H isolates from Iran did not cluster with those from the Netherlands and other European countries, indicating no close genetic relatedness (online Technical Appendix Figure). The TR34/L98H azole resistance mechanism was first described in 1998 in the Netherlands; since then, its presence in clinical and environmental A. fumigatus isolates in multiple European countries and recently in Asia has been increasingly reported (online Technical Appendix Table 2) (3–7). In the study reported here, prevalence of azole resistance in clinical A. fumigatus isolates obtained from patients in Iran was 3.2%; most isolates exhibited the resistant phenotype. Of the 3 TR34/L98H isolates recovered, 1 was from a patient with allergic bronchopulmonary aspergillosis (Table).

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Technical Appendix

Technical Appendix Figure 1. Female Hypoderma tarandi reindeer warble fly in flight. The parasite can fly for many hours and may cover 600–900 km during its lifetime. This flight capacity has evolved to find reindeers. They do not feed as adults. Photo by A. Nilssen.
Technical Appendix Figure 2. Eggs of Hypoderma tarandi stick to a reindeer hair with an attachment organ and a glue-like liquid. Upon hatching, the larvae borrow through the skin near the root of the hair shaft. Photo by K. Åsbakk.

Technical Appendix Figure 3. Intraocular larvae crawling on retinal surface of patient 1. Photo taken intraoperatively by K. Fossen.