Commentary

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Health problems associated with international travel: A case of cutaneous myiasis in China due to *Cordylobia anthropophaga* imported from Uganda

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Summary **More affordable international travel, global trade and commerce, and the exporting of labor have all contributed to international population mobility. Furthermore, population migration leads to the incidence or recurrence of once-controlled diseases. Evidence shows that the popularity of travel can impact health through imported infections and illness. Imported cutaneous myiasis, a type of skin lesion, has attracted the attention of the current authors. This condition often occurs among travelers and it has been reported in several non-endemic countries. However, diagnosis of myiasis and identification of the larvae are difficult. Advances in molecular detection techniques could provide a new way to identify larvae. This study used sequencing of the 28S rRNA gene and morphology to identify the larva infesting the upper arm of a Chinese woman returning from Uganda. The larva was identified as *Cordylobia anthropophaga* (*C. anthropophaga*) and the sequences were submitted to GenBank (accession number: KM506761). As foreign interaction increases, imported health problems may become more common in China. Knowledge about various pathogens needs to be increased and molecular methods need to be used to accurately identify those pathogens.**

Keywords: Larva, imported, molecular identification, morphology

1. Introduction

More affordable international travel, the development of global trade and commerce, and the exporting of labor have all contributed to international population mobility. Migration is a major factor that has led to changes in infectious diseases, such as the reappearance of controlled malaria (*1*) and an increasing number of dengue outbreaks (*2*).

Every year, 20%-70% of travelers from the industrialized world to the developing world report travel-associated illness, including fever, diarrhea, dermatologic conditions (*3*). According to the China National Tourism Administration, more than 9.8 million Chinese traveled internationally in 2013, representing an increase of 18% from the figure in 2012. This indicates massive migration. The popularity of international travel is overshadowed by threats to travelers' health from imported infections and illness such as malaria, Chagas disease, African trypanosomiasis, leishmaniasis, toxoplasmosis, and babesiosis (*4*). According to the Canadian Travel Medicine Network, 90.3% of travelers in Canada acquired a travel-related arthropod bite, giardiasis, malaria, or strongyloidiasis from 2009 to 2011 (*5*). Herbinger *et al*. also reported that travelers in sub-Saharan Africa had the highest relative risk of acquiring skin disorders (*6*).

In recent years, cutaneous myiasis, a type of skin lesion, often occurring among travelers, has garnered attention. This condition has been reported in several countries, including Spain (*7*), Japan (*8*), the UK (*9*), and the US (*10*). Twenty-nine cases of cutaneous myiasis were reported in China from

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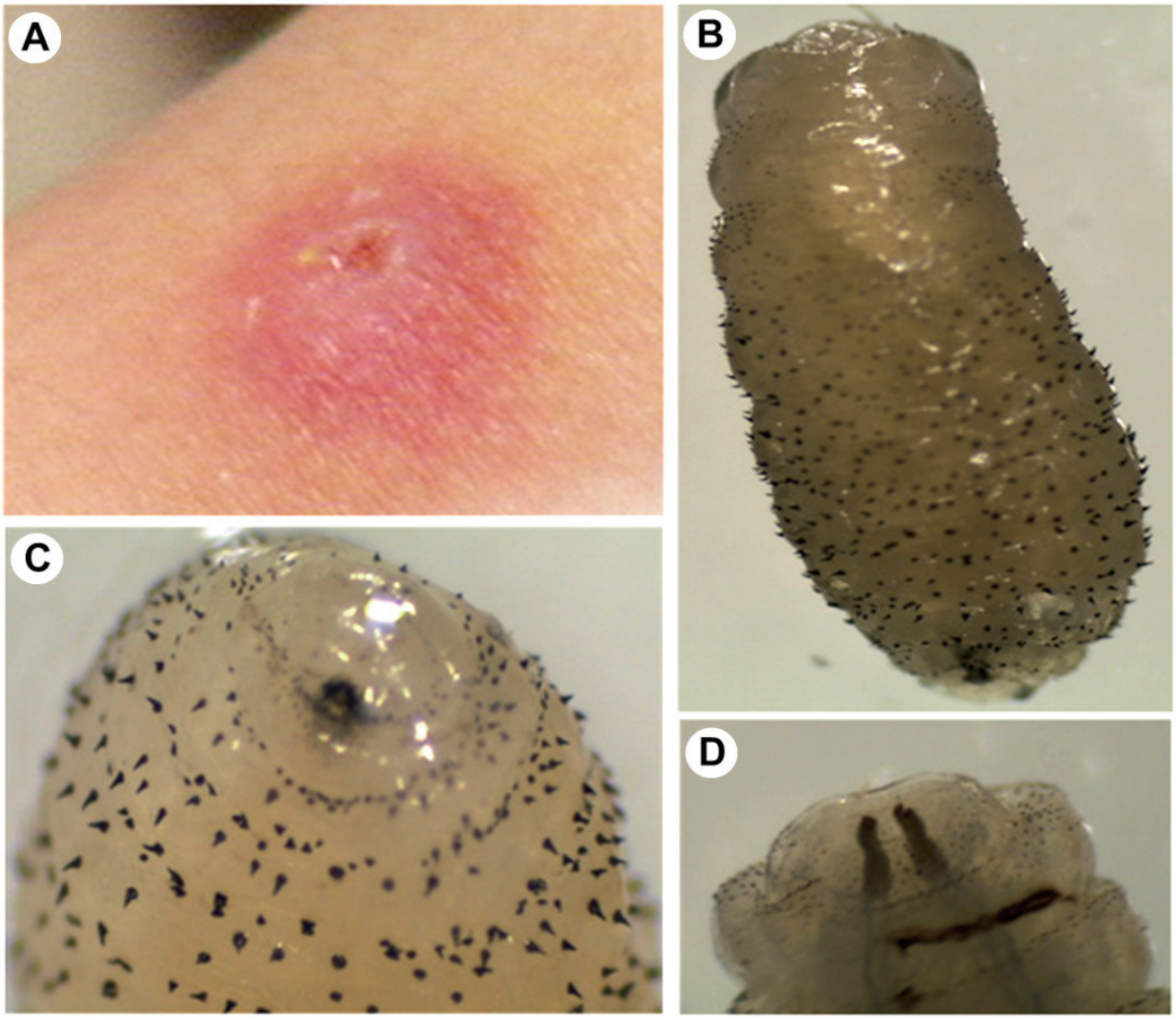

Figure 1. Characteristics of a larva. (A) A furuncular lesion on the upper arm after the larva was removed; **(B)** Intact larva under the anatomical lens; **(C)** The larva's two black-toothed hooks; **(D)** Posterior spiracles under a light microscope.

1995-2001, occurring frequently in nomadic areas and most involved *Hypoderma bovis*, *H. lineatum*, or *Gastrophilus nigricornis* (*11*). Cutaneous myiasis caused by other species has seldom been reported in China.

Currently, methods for diagnosis of myiasis and identification of the larvae are limited to clinical manifestations, an epidemiological history, and morphology of the larvae or identification of the adult fly when the larvae mature. Nevertheless, identification could be indeterminate if a clear picture is unavailable. Advances in molecular detection techniques may provide a new way to identify larvae, particularly when the larvae are dead or only partially intact. The 28S rRNA gene has been used as a genetic marker for molecular identification of larvae in Japan and Nigeria (*8,12*) but its use in China has never been reported. The current study used a new method of molecular identification to identify an ivory white worm from the upper arm of a Chinese woman who returned from Uganda.

2. Case presentation

2.1. *General information*

A 26-year old woman from Zhejiang Province, China travelled to Uganda for 10 days at the end of July 2014. During her time in Uganda, the woman claimed to have suffered mosquito bites. When she returned to China, she noted swelling, slight itching, and pain from a bite on her left upper arm. A lesion appeared and then developed into a nodule approximately 2-3 cm in diameter. In order to drain the nodule, the patient pressed hard on the lesion and she removed an ivory white worm. Swelling partially subsided the next day and the woman sent the worm to the Provincial Center for Disease Control and Prevention. A physical examination of the woman revealed a hard red nodule covered with a thin scab on the left upper arm (Figure 1A). The woman was in good condition overall with no fever or lymphadenectasis. The patient was advised to dab iodine and erythromycin ointment onto the skin

A

Primer	Sequence
28S rRNA F1	GGGAGGAAAAGAAACTAACAAGGA
28S rRNA R1	CTGTTTCGGTCTTCCATCAGGG
28S rRNA F2	CTTAGTAGCGGCGAGCGAAAA
28S rRNA R2	TTCCCCTGACTTCAACCTGATC

B

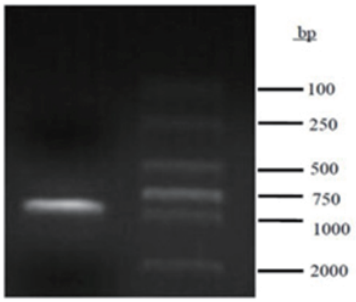

Figure 2. PCR amplification of the 28S rRNA gene. (A) Primers for PCR identification; **(B)** Agarose gel electrophoresis of the PCR product.

lesion. Three days later, the lesion scabbed and the swelling subsided. Ten days later, the nodule gradually disappeared. The patient developed no additional skin lesions.

2.2. *Identification of the larva*

2.2.1. *Morphological identification*

The larva was kept in normal saline so that it would remain alive when placed on a glass slide for morphological identification. The larva had a cylindrical body about 5 mm in length that was ivory white in color. Light microscopy revealed that the body of the larva had 10 segments and each segment had a number of black mucrones arranged uniformly in transverse rows (Figure 1B). In addition, a pair of black-toothed hooks was noted near the mouth (Figure 1C). Distinctive posterior spiracles with two linear slits on each side were noted on the caudal region of the larva (Figure 1D).

2.2.2. *Molecular identification*

DNA was gradually extracted from the larva with a QlAamp DNA Mini kit (Qiagen, Germany) in accordance with the manufacturer's instructions. Nested PCR amplification of the 28S rRNA gene was performed with uniquely designed primers (Figure 2A). Two successive runs of nested PCR were both carried out under the following conditions: initial denaturation at 94°C for 5 min, 30 cycles of denaturation at 94°C for 30 sec, annealing at 60°C for 30 sec, and elongation at 72°C for 2 min, followed by a final elongation step at 72°C for 5 min. Amplified target fragments were verified using 1.5% agarose gel electrophoresis (Figure 2B). The PCR product was purified and bi-directionally sequenced by BGI, China. The sequences had 99% (918/919) similarity to partial 28S rRNA gene sequences from *C. anthropophaga* in the GenBank database (isolated by Yaounde in 1999, accession number: AJ551432) according to the Basic Local Alignment Search Tool (BLAST). The current sequences were subsequently submitted to GenBank and given the accession number KM506761.

3. How does infestation with *C. anthropophaga* happen?

Myiasis was first described by Hope in 1840 and refers to the infestation of human and vertebrate animal tissue by the larvae of *Diptera* (adult flies with two wings). Myiasis usually occurs in tropical and subtropical areas including Central America, South America, Africa, and the Caribbean Islands (*13,14*). Based on the site of infestation, myiasis is classified as cutaneous, enteric, ophthalmic, nasopharyngeal, auricular, oral, or urogenital (*15*).

Depending on the species of larvae responsible, cutaneous myiasis presents clinically in three main forms: furuncular, migratory, and wound myiasis (*16*). Furuncular myiasis is commonly caused by the larvae of *Dermatobia hominis*, *Cordylobia anthropophaga* (*C. anthropophaga*), *Cuterebra* spp., *Wohlfahrtia vigil*, and *W. opaca* (*14*). The geographic location of these larvae varies. As an example, *Dermatobia hominis* is common in Central and South America while *C. anthropophaga* is common in Tropical Africa (*14,17*).

The *Cordylobia* genus, which falls under the family *Calliphoridae*, includes three species: *C. anthropophaga*, *C. ruandae*, and *C. rhodhaini*. All three of these species can cause furuncular myiasis but *C. anthropophaga* is the most common cause. *C. anthropophaga* is commonly known as the tumbu fly (*14*) and it infests a variety of different hosts but particularly rodents and dogs (*17*). The adult female *C. anthropophaga* lays batches of 100-300 eggs in sandy soil and damp clothing that are often contaminated with urine or feces. Humans are readily susceptible to the tumbu fly during the rainy season (*17*). When the host lays in sand or comes in contact with contaminated clothing, the larvae can approach and penetrate the skin unnoticed in 60 sec (*17*). In the current case, the larva may have penetrated the tissue via a lesion caused by a

mosquito bite. The larval infestation causes a protruding lesion below the skin and the host may feel pain of varying degrees. If the host is not treated, the mature larva will emerge from the skin, fall to the ground, and pupate in 8-12 days (*18*).

4. Challenges in identification

Outside endemic regions, diagnosis of imported illness is challenging and requires experienced specialists. Identification of larvae is also demanding and requires specialists in parasitology and entomology. When travelers with symptoms seek care after they return from endemic areas, their travel history can easily be overlooked by both doctors and patients. Moreover, a lack of knowledge and experience on diagnosing imported illness of part of doctors often results in failure to identify the parasite responsible. However, molecular identification requires few specific skills related to morphology and can easily be performed by most hospitals in China.

This study described a typical case of furuncular myiasis caused by *C. anthropophaga*. To the extent known, few studies in China have described the identification of myiasis based on molecular methods and morphology. Sequencing of the 28S rRNA gene of the larva provides a simpler method of diagnosis and provides better evidence than morphology.

Given the potential for an increase in imported health problems in China, both doctors and CDC personnel should pay more attention to these rare microorganisms and parasites. Knowledge about various pathogens needs to be increased and accurate methods of molecular identification need to be used to identify these pathogens. These steps should help patients receive adequate and timely treatment and result in a good prognosis.

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