Autochthonous Leishmaniasis: an Emerging Zoonosis in Thailand

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ABSTRACT
There have been increasing reports of autochthonous leishmaniasis in Thailand during the past 5 years. All cases, excluding one, were caused by the novel *Leishmania siamensis* which have been reported only in Thailand. However, cutaneous autochthonous leishmaniasis caused by *L. siamensis* was recently described in horses of central Europe and the United States as well as a cow in Switzerland. It is believed that this is an emerging vector-borne zoonotic disease of potential public health concern in Thailand. The clinical manifestations can be visceral, cutaneous, as well as mixed visceral and cutaneous forms. Surprisingly, of 3 patients with mixed visceral and cutaneous leishmaniasis, 2 initially presented with cutaneous leishmaniasis for few months and 4 years, respectively, before a development of visceral leishmaniasis. Regarding diagnostic investigations, the PCR test is practical and available in most university hospitals in Bangkok. The saliva specimen for PCR testing seems to be the most sensitive method, in comparison with other clinical specimens. To date, there are 3 potential sandfly vectors including *Phlebotomus argentipes*, *P. major major*, and *Sergentomyia (Neophlebotomus) gemmea*. There is an urgent need for comprehensive studies regarding potential sandfly vectors, reservoir animals, and case finding for both symptomatic and asymptomatic patients of leishmaniasis in Thailand. (*J Infect Dis Antimicrob Agents* 2014;31:1-8.)

INTRODUCTION
Leishmaniasis is a tropical infectious disease caused by an obligate intracellular protozoan, *Leishmania* sp. which is transmitted by phlebotomine sandflies.1-2 There are 3 clinical presentations of leishmaniasis including visceral, cutaneous, and mucocutaneous forms. There had been no reports of autochthonous leishmaniasis in Thailand until 1996. This article reviews autochthonous leishmaniasis in Thailand regarding clinical manifestations, epidemiology, microbiologic investigations, and potential sandfly vectors, in comparison with leishmaniasis in other regions.

CASE REPORT
To the best of our knowledge, there have been 12 autochthonous cases of leishmaniasis in Thailand (Table).3-11 Ten patients were reported in the literature, and the other 2 patients from Nakhon Si Thammarat and Chaing Rai were from unpublished...
All patients lived in all parts of the country except Northeastern Thailand. There were 8 males and 4 females aged from 3 to 66 years, respectively. There were 5 AIDS patients. There were 7, 3, and 2 patients with visceral, mixed visceral and cutaneous, as well as cutaneous leishmaniasis, respectively. Surprisingly, of 3 patients with mixed visceral and cutaneous leishmaniasis, 2 patients initially presented with cutaneous leishmaniasis for few months and 4 years, respectively, before developing visceral leishmaniasis. The other patient had concomitant cutaneous and visceral leishmaniasis. Generally, a particular species of *Leishmania* can cause only one form of leishmaniasis, either visceral or cutaneous form. However, some species including *L. infantum* and *L. tropica* can cause both cutaneous and visceral leishmaniasis. However, based on sequential manifestations (cutaneous followed by visceral manifestations) in these 2 HIV-infected patients with autochthonous leishmaniasis, the altered host adaptive immune status may play a pivotal role in the diverse spectrum of these patients with AIDS. Of 12 patients, the species of *Leishmania* could be identified in 10 patients, 9 with *L. siamensis* and 1 with *L. infantum* (the patient living in Bangkok), respectively. The nucleotide sequence of the internal transcribed spacer1 (ITS1) region of ribosomal DNA gene of *L. siamensis* is novel. The phylogenetic tree shows that it is located as a sister taxon of the clade of *L. brasiliensis* and *L. guyanensis* which are the causative agents of New World visceral and cutaneous leishmaniasis, respectively. Of 12 patients, only 1 patient with mixed visceral and cutaneous leishmaniasis died 2 weeks after treatment with amphotericin B. Two patients with visceral (without underlying disease) and mixed visceral and cutaneous (with HIV infection) leishmaniasis relapsed 2 months after treatment.

**Diagnostic investigations**

There are several kinds of diagnostic tests generally including serologic tests, identifying amastigotes in clinical specimens, cultures, and molecular microbiologic methods. Serologic tests are not helpful in the diagnosis of leishmaniasis. They are mostly used in epidemiologic studies. A definite diagnosis of leishmaniasis is made by identifying amastigotes or promastigotes in clinical specimens or cell cultures, respectively. However, the PCR method using *Leishmania*-specific nucleotide sequence is practical and regarded as the most sensitive and specific test.

Regarding *L. siamensis* in Thailand, Phumee and colleagues recently reported that the saliva specimen for PCR testing seems to be the most sensitive method, in comparison with other clinical specimens. In addition, the monitoring of the levels of PCR product could be used as a marker for the successful response and relapse after the treatment.

**Sandfly vector and potential reservoir host**

In general, there are 2 genera of phlebotomine sandflies including *Phlebotomus* and *Lutzomyia* which are the agents of the old and new world leishmaniasis, respectively. In Thailand, there are 5 genera (*Sergentomyia*, *Phlebotomus*, *Chinius*, *Nemopalpus*, and *Idiophlebotomus*) and 26 species of sandflies documented in many regions of Thailand. *Sergentomyia* is generally the most predominant genus in all parts of the country. *S. (Neophlebotomus) gemmea* was prevalent in Southern Thailand. *P. argentipes* is
### Table. Summary of 12 case reports of autochthonous leishmaniasis in Thailand.

<table>
<thead>
<tr>
<th>Year, province</th>
<th>Age (years), sex</th>
<th>Occupation</th>
<th>Underlying disease</th>
<th>Clinical features; duration</th>
<th>Form of leishmaniasis, species of <em>Leishmania</em></th>
<th>Investigations</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996, Surat Thani</td>
<td>3, female</td>
<td>No</td>
<td>No</td>
<td>Fever, hepatosplenomegaly, anemia, thrombocytopenia; 2 months</td>
<td>VL, no species identified</td>
<td>No study No study</td>
<td>Pentamidine isethionate for 15 doses</td>
<td>Remission</td>
</tr>
<tr>
<td>2005, Nan</td>
<td>40, male construction worker in several provinces</td>
<td>Amphetamine and opium addiction</td>
<td>No</td>
<td>Fever, hepatosplenomegaly, pancytopenia, mediastinal mass; 31 months</td>
<td>VL, no species identified</td>
<td>No potential vectors Positive in 3 cows and 1 cat</td>
<td>2 courses of ABd for 30 days</td>
<td>Remission</td>
</tr>
<tr>
<td>2006, Phangnga</td>
<td>55, male rubber planter</td>
<td>No</td>
<td>Rubber</td>
<td>Fever, hepatosplenomegaly, pancytopenia; 3 years</td>
<td>VL, <em>L. siamensis</em></td>
<td>No potential vectors Positive in 9 cats</td>
<td>ABd (100 mg) mixed with 1 mg lipid for 14 days Relapse 2 months after treatment</td>
<td></td>
</tr>
<tr>
<td>2007, Bangkok</td>
<td>66, male truck driver</td>
<td>Diabetes, hypertension</td>
<td>No</td>
<td>Fever, weight loss, hepatosplenomegaly, pancytopenia; 6 months</td>
<td>VL, <em>L. infantum</em></td>
<td>Inability to obtain Negative in 9 cats, 1 cat, 3 rats vectors due to raining</td>
<td>ABd every other day for 30 days Remission</td>
<td></td>
</tr>
<tr>
<td>2007, Nakhon Si Thammarat</td>
<td>44, male rubber planter</td>
<td>Diabetes</td>
<td>NA; 6 months</td>
<td>VL, <em>L. siamensis</em></td>
<td><em>P. argentine</em> and other 4 non-potential vectors</td>
<td>Positive in 1 cow and 1 cat NA</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

NA: not applicable, ABd: amphotericin B deoxycholate, VL: visceral leishmaniasis, DAT: direct agglutination test for *Leishmania* antibody, HCV: hepatitis C virus
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<th>Outcome</th>
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<tr>
<td>2007, Chiang Rai</td>
<td>36, male</td>
<td>Employee</td>
<td>AIDS</td>
<td>Skin papules, nodules; 1 year</td>
<td>CL, <em>L. siamensis</em></td>
<td><em>P. argentipes</em> and other 3 non-potential vectors</td>
<td>NA</td>
<td>Remission</td>
</tr>
<tr>
<td>2009, Chanthaburi</td>
<td>37, male</td>
<td>Fisherman, history of travel to North Indonesia</td>
<td>AIDS, chronic HCV infection</td>
<td>Fever, nephrotic syndrome, hepatosplenomegaly, anemia, thrombocytopenia; 8 weeks</td>
<td>VL, <em>L. siamensis</em></td>
<td>No potential vectors</td>
<td>Negative</td>
<td>ABd every other day for 14 days, and itraconazole (400 mg/day)</td>
</tr>
<tr>
<td>2012, Songkhla</td>
<td>46, male</td>
<td>Rubber planter</td>
<td>AIDS</td>
<td>Knee ulcer, anemia, thrombocytopenia, hepatosplenomegaly; few months</td>
<td>VL &amp; CL, <em>L. siamensis</em></td>
<td>No study</td>
<td>No study</td>
<td>ABd for 14 days, and itraconazole (400 mg/day)</td>
</tr>
<tr>
<td>2012, Trang</td>
<td>30, male</td>
<td>Pet store owner</td>
<td>AIDS</td>
<td>Skin papules and ulcers, hepatosplenomegaly, pancytopenia; 4 years</td>
<td>VL &amp; CL, <em>L. siamensis</em></td>
<td>No study</td>
<td>No study</td>
<td>ABd for 14 days, and itraconazole (400 mg/day)</td>
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NA: not applicable, ABd: amphotericin B deoxycholate, VL: visceral leishmaniasis, CL: cutaneous leishmaniasis, DAT: direct agglutination test for *Leishmania* antibody, HCV: hepatitis C virus
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<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012, Trang 70</td>
<td>32, female</td>
<td>NA</td>
<td>AIDS</td>
<td>Skin nodules, plaques, hepatomegaly, anemia; 1 month</td>
<td>VL &amp; CL, <em>L. siamensis</em></td>
<td>No study</td>
<td>No study</td>
<td>ABd for 14 days</td>
</tr>
<tr>
<td>2012, Lop Buri</td>
<td>3, female</td>
<td>No</td>
<td>No</td>
<td>Check ulcer, 1 month</td>
<td>CL, <em>L. siamensis</em></td>
<td>No study</td>
<td>No study</td>
<td>Itraconazole (5 mg/kg/day)</td>
</tr>
<tr>
<td>2013, Satun 11</td>
<td>5, female</td>
<td>No</td>
<td>No</td>
<td>Hepatosplenomegaly, anemia, thrombocytopenia; 2 years</td>
<td>VL, <em>L. siamensis</em></td>
<td>No study</td>
<td>No study</td>
<td>ABd for 2 times: 3 and 5 weeks, and ABd</td>
</tr>
</tbody>
</table>

NA: not applicable, ABd: amphotericin B deoxycholate, VL: visceral leishmaniasis, CL: cutaneous leishmaniasis, DAT: direct agglutination test for *Leishmania* antibody, HCV: hepatitis C virus
the most common cave-dwelling sandfly in Northeast Thailand. A recent study in the Naresuan Cave, Phitsanulok, Northern Thailand reported that *Nemopalpus vietnamensis* was the most prevalent species. To date, there are 3 potential sandfly vectors for leishmaniasis including *P. argentipes*, *P. major major*, and *S. (Neophlebotomus) gemmea*. *P. argentipes*, a cavernicolous sandfly, is a vector of kala-azar in India. It is considered the zoonotic sandfly since it does not bite humans. *P. major major*, another cavernicolous sandfly like *P. argentipes*, is well known as the cow- and cat-biting sandfly. It can bite humans as well, and hence is considered as the zooanthroponotic sandfly. It was reported to be the vector of visceral leishmaniasis caused by *L. infantum* in Iran. *P. major major* is the known vector of visceral leishmaniasis in the Mediterranean. Kanjanopas and colleagues were the first group who recently demonstrated that DNA of *L. siamensis* was present in the pooled samples of sandfly *S. (Neophlebotomus) gemmea* captured in the affected area where the patient with visceral leishmaniasis was reported. So, *S. (Neophlebotomus) gemmea* might be the potential vector of leishmaniasis caused by *L. siamensis* in Thailand. Most *S. (Neophlebotomus) gemmea* captured were found at the cattle corral. *Sergentomyia* are generally considered as the carnivorous sandflies. They can be seen in association with several kinds of animals including reptiles (lizards and geckos) and mammals (cows, cats, and dogs). *L. donovani* and *L. major* DNA were identified in *S. babu* in India and *S. sintoni* in Iran, respectively. In addition, cutaneous autochthonous leishmaniasis caused by *L. siamensis* was recently described in horses of central Europe and the United States as well as a cow in Switzerland. So, it is believed that *S. (Neophlebotomus) gemmea*, the most predominant species of sandfly in Southern Thailand, might be the potential vector of *L. siamensis* in Thailand, and leishmaniasis caused by *L. siamensis* should be zoonotic leishmaniasis.

**CONCLUSIONS**

There have been increasing reports of autochthonous leishmaniasis in Thailand during the past 5 years. All except 1 patient were caused by the novel *L. siamensis* which have been reported only in Thailand. However, cutaneous autochthonous leishmaniasis caused by *L. siamensis* was recently described in horses of central Europe and the United States as well as a cow in Switzerland. It is believed that this is an emerging vector-borne zoonotic disease of potential public health concern in Thailand. The clinical manifestations can be visceral, cutaneous, and mixed visceral and cutaneous forms. Surprisingly, of 3 patients with mixed visceral and cutaneous leishmaniasis, 2 patients initially presented with cutaneous leishmaniasis for few months and 4 years, respectively, before a development of visceral leishmaniasis. Regarding diagnostic investigations, the PCR test is practical and available in most university hospitals in Bangkok. The saliva specimen for PCR testing seems to be the most sensitive method, in comparison with other clinical specimens. To date, there are 3 potential sandfly vectors including *P. argentipes*, *P. major major*, and *S. (Neophlebotomus) gemmea*. There is an urgent need for comprehensive studies regarding potential sandfly vectors, reservoir animals, and case finding for both symptomatic and asymptomatic patients of leishmaniasis in Thailand.
ACKNOWLEDGEMENTS

I would like to thank Dr. Padet Sriyasatien, Department of Parasitology, Chulalongkorn University, Bangkok; Dr. Theerayudh Sukmee, Department of Parasitology, Phramongkutklao College of Medicine, Bangkok; Bureau of Epidemiology, Department of Control Disease, Ministry of Public Health, Nonthaburi; and Bureau of Vector-borne Disease Control, Department of Control Disease, Ministry of Public Health, Bangkok, for providing information regarding the epidemiology and serology of some cases of leishmaniasis in Thailand.

References


