VIEWPOINT

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 protozoon, *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patients were reported in the literature, and the other 2 patients from Nakhon Si Thammarat and Chaing Rai were from unpublished

Keywords: *Leishmania siamensis*, *Leishmania infantum*, leishmaniasis, visceral leishmaniasis, autochthonous

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data (Sukmee T, personal communication). 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*[12] and *L. tropica*[13] 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.[12] 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.[1,2] 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.[1,2]

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.[14] 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.[1,2] In Thailand, there are 5 genera (*Sergentomyia*, *Phlebotomus*, *Chinius*, *Nemopalpus*, and *Idiophlebotomus*) and 26 species of sandflies documented in many regions of Thailand.[15-21] *Sergentomyia* is generally the most predominant genus in all parts of the country. *S. (Neophlebotomus) gemmea* was prevalent in Southern Thailand.[18] *P. argentipes* is

Table. Summary of 12 case reports of autochthonous leishmaniasis in Thailand.

Year, province	Age (years), sex	Occupation	Underlying disease	Clinical features; duration	Form of leishmaniasis, species of *Leishmania*	Investigations		Treatment	Outcome
						Sandfly vectors	Animal reservoirs (DAT)		
1996, Surat Thani[3]	3, female	No	No	Fever, hepatosplenomegaly, anemia thrombocytopenia; 2 months	VL, no species identified	No study	No study	Pentamidine isethionate for 15 doses	Remission
2005, Nan[4]	40, male	Construction worker in several provinces	Amphetamine and opium addiction	Fever, hepatosplenomegaly, pancytopenia, mediastinal mass; 31 months	VL, no species identified	No potential vectors	Positive in 3 cows and 1 cat	2 courses of ABd for 30 days	Remission
2006, Phangnga[5]	55, male	Rubber planter	No	Fever, hepatosplenomegaly, pancytopenia; 3 years	VL, *L. siamensis*	No potential vectors	Positive in 9 cats	ABd (100 mg) mixed with 1 mg lipid for 14 days	Relapse 2 months after treatment
2007, Bangkok[6]	66, male	Lumber truck driver	Diabetes, hypertension	Fever, weight loss, hepatosplenomegaly pancytopenia; 6 months	VL, *L. infantum*	Inability to obtain vectors due to raining	Negative in 9 dogs, 1 cat, 3 rats	ABd every other day for 30 days	Remission
2007, Nakhon Si Thammarat	44, male	Rubber planter	Diabetes	NA; 6 months	VL, *L. siamensis*	*P. argentipes* and other 4 non-potential vectors	Positive in 1 cow and 1 cat	NA	NA

NA: not applicable, ABd: amphotericin B deoxycholate, VL: visceral leishmaniasis, DAT: direct agglutination test for *Leishmania* antibody, HCV: hepatitis C virus

Table. Summary of 12 case reports of autochthonous leishmaniasis in Thailand (continued).

Year, province	Age (years), sex	Occupation	Underlying disease	Clinical features; duration	Form of leishmaniasis, species of *Leishmania*	Investigations		Treatment	Outcome
						Sandfly vectors	Animal reservoirs (DAT)		
2007, Chiang Rai	36, male	Employee	AIDS	Skin papules, nodules; 1 year	CL, *L. siamensis*	*P. argentipes* and other 3 non-potential vectors	Negative	NA	Remission
2009, Chantha-buri[7]	37, male	Fisherman, history of travel to North Indonesia	AIDS, chronic HCV infection	Fever, nephritonephrotic syndrome, hepatosplenomegaly, anemia, thrombo-cytopenia; 8 weeks	VL, *L. siamensis*	No potential vectors	Negative	ABd every other day for 14 days, and itraconazole (400 mg/day)	Remission
2012, Songkhla[8]	46, male	Rubber planter	AIDS	Knee ulcer, anemia, thrombocytopenia, hepatosplenomegaly; few months	VL & CL, *L. siamensis*	No study	No study	ABd for 14 days, and itraconazole (400 mg/day)	Relapse 2 months after treatment
2012, Trang[8]	30, male	Pet store owner	AIDS	Skin papules and ulcers, hepatosplenomegaly, pancytopenia; 4 years	VL & CL, *L. siamensis*	No study	No study	ABd for 14 days, and itraconazole (400 mg/day)	Remission

NA: not applicable, ABd: amphotericin B deoxycholate, VL: visceral leishmaniasis, CL: cutaneous leishmaniasis, DAT: direct agglutination test for *Leishmania* antibody, HCV: hepatitis C virus

Table. Summary of 12 case reports of autochthonous leishmaniasis in Thailand (continued).

Year, province	Age (years), sex	Occupation	Underlying disease	Clinical features; duration	Form of leishmaniasis, species of *Leishmania*	Investigations		Treatment	Outcome
						Sandfly vectors	Animal reservoirs (DAT)		
2012, Trang[9]	32, female	NA	AIDS	Skin nodules, plaques, hepatomegaly, anemia; 1 month	VL & CL, *L. siamensis*	No study	No study	ABd for 14 days	Death 2 weeks after treatment
2012, Lop Buri[10]	3, female	No	No	Check ulcer; 1 month	CL, *L. siamensis*	No study	No study	Itraconazole (5 mg/kg/day) for 2 months	Remission
2013, Satun[11]	5, female	No	No	Hepatosplenomegaly, anemia, thrombocytopenia; 2 years	VL, *L. siamensis*	No study	No study	ABd for 2 times: 3 and 5 weeks, and ABd 5 day/mg/month for 6 months	Remission

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.[21] A recent study in the Naresuan Cave, Phitsanulok, Northern Thailand reported that *Nemopalpus vietnamensis* was the most prevalent species.[16] 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.[1] It is considered the zoonotic sandfly since it does not bite humans.[21]

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.[22] *P. major major* is the known vector of visceral leishmaniasis in the Mediterranean.[23]

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[9] was reported.[20] 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[24] and *S. sintoni* in Iran[25], respectively. In addition, cutaneous autochthonous leishmaniasis caused by *L. siamensis* was recently described in horses of central Europe[26] and the United States[27] as well as a cow in Switzerland.[28] 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.

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