**Bone marrow leishmaniasis: a review of situation in Thailand**

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**ABSTRACT**

Leishmaniasis is an important tropical vector–borne disease. This infection can be seen in tropical area and it is considered to be one of the most important vector–borne infections at present. The general situation of the leishmaniasis in Thailand is hereby reviewed. Although Thailand is a tropical country, the leishmaniasis is not endemic but sporadic. The imported cases are documented in some literatures. The serious form of leishmaniasis, the visceral leishmaniasis is also detectable in Thailand. Also, the author performed an in depth literature review of the reports of bone marrow leishmaniasis, a specific kind of visceral leishmaniasis, in Thailand in order to summarize the characteristics of this infection among Thai patients. According to this review, there have been at least 5 reports in the literature of 6 cases of bone marrow leishmaniasis in the Thai population, of which no case was lethal. Concerning the clinical manifestations, all except had prolonged fever with unknown origin. From physical examination, all had hepatosplenomegaly. The striking findings were active hemophagocytosis with increased proliferation of lymphoidplasma cell line in the bone marrow and amastigotes of Leishmania donovani was demonstrated. Considering the treatment, pantavalent antimony compound was used and the excellent improvement and complete recovery. Finally, the author also discussed the importance of leishmaniasis in Thailand relating to the present globalization and good traveling system.

1. **Introduction**

Leishmaniasis is an important tropical vector–borne infectious disease. There are two common forms of leishmaniasis, cutaneous and visceral presentations. Visceral leishmaniasises (VL), with spreading epidemics in India and Africa, and some sporadic cases in Mediterranean countries, reveal various clinical and public health characteristics depending on the geographic underlyings[1–4]. VL is considered an important tropical blood infection. Palumbo et al noted that “Leishmaniasis is distributed worldwide and 13 million people are estimated to be infected, with about 1.8 million new cases each year”[5]. Hence, it is no doubt on the public health importance of this parasitic infection, WHO accepted for the public health importance of this infection and proposed for these strategies (a) training program on diagnosis and case management of leishmaniasis; (b) setting up a harmonized regional surveillance system; (c) creating a connecting network of experts and (d) promoting international commitment of disease management[6].

Although Thailand has high prevalence of vector–borne diseases malaria and dengue fever, the VL is a non endemic infectious disease and seldom mentioned in the literature. The first Thai case report of leishmaniasis infection was documented in the literature in 1981 by Puavilai et al[7]. After the first report, there have been many sporadic case reports of leishmaniasis in Thailand. However, most cases are cutaneous leishmaniasis. Nevertheless, the serious form of leishmaniasis can be detectable in Thailand. The infected cases seem to be the serious concern in the disease control since there has never been the vector of leishmanial parasite in Thailand and the existence of the disease seems to be the new emerging infectious disease and the root cause analysis has to be performed. The existence of the leishmaniasis in Thailand is an interesting situation. Indeed, the infection should not be existed due to two main reasons (a) there is no vector and (b) there is no pathogen. However, the disease finally occurred and this implies the importance of traveling medicine at present.

The general situation of the leishmaniasis in Thailand is hereby reviewed. Although Thailand is a tropical country, the leishmaniasis is not endemic but sporadic. The serious form of leishmaniasis, the visceral leishmaniasis is also detectable in Thailand. Here, the author performed a literature review of the reports of bone marrow leishmaniasis in Thailand and present the summation as a review. The main aim is to summarize the characteristics of this infection among Thai patients for further referencing database.
2. Retrospective review

Here, the author performed an in depth literature review of the reports of bone marrow leishmaniasis, a specific kind of visceral leishmaniasis, in Thailand in order to summarize the characteristics of this infection among Thai patients. Adding to the previous knowledge, an updating literature review of the papers concerning bone marrow leishmaniasis in Thailand was done. The two international database of published works, Index Medicus and Science Citation Index were using in searching of documents. Additionally, the author also reviewed the published works in all 256 local Thai journals, which are not included in the international citation index but available in local searching engine namely Thai Index Medicus. The literature review focused on the years 1981–2011. The key word for searching is “lesismaniasis” and “Thailand”. According to review, there were 24 reports on leishmaniasis but only 5 reports were dealing with bone marrow leishmaniasis and were further recruited for further study. The details of clinical presentations of the patients (such as demographical data; sex and age, clinical manifestation, diagnosis, treatment, and discharge status) of all indexed case in all included reports were studied. Descriptive statistics using SPSS 7.0 for Windows were used in analyzing the patient characteristics. There have been at least 5 reports[7–9] in the literature of 6 cases (5 males and 1 female) of bone marrow leishmaniasis in the Thai population without any death case. Average age of the indexed cases is 25.6±17.1 years old. All except 1 cases of published works, Index Medicus and Science sero-positive case, Concerning the clinical manifestation and physical examination, all had hepatosplenomegaly and all except two cases had prolonged increased body temperature. At the time of diagnosis, there was no detectable leishmanial parasite in examined peripheral blood smear however anaemia and thrombocytopenia could be seen in all cases (pancytopenia can be seen in 5 cases). The bone marrow study showed revealed increased bone marrow cellularity, adequate production of magakaryocytes, erythroid and myeloid precursors with the important findings “active hemophagocytosis with increased proliferation of lymphoidplasma cell line in the bone marrow with detected amastigotes of Leishmania donovani.” Considering the treatment, pentavalent antimony compound was prescribed for all except 1 indexed cases (the left case was treated by amphotericin B[10]) and the excellent improvement and complete recovery of the clinical and hematologic abnormalities were observed promptly after the administration.

3. Discussion

Leishmanioses are a group of parasitic infections that affect human beings and other mammals. They are caused by different species of trypanosomatids of the genus *Leishmania*[11–12]. The distribution of this specific infectious disease, which is found throughout the world, is determined by various factors linked to both human activity as well as climatic change. The heteroeccious life cycle of the *Leishmania* is mentioned. It includes an invertebrate host, the specific sandflies in the Phlebotomidae family. The dog is also a main reservoir host and it can present both cutaneous and visceral clinical signs[12].

Considering VL, the typical symptomatic triad, anemia–fever–enlarged spleen, may be not completely fulfilled in all cases. The diagnosis of visceral form is generally derived by the demonstration of amastigotes of the leishmanial parasite(s) in the aspirated fluid from the bone marrow, the spleen, and rarely from the lymph nodes, or the liver[13]. Berentsen et al said that the identification of the parasites in bone marrow biopsy should be performed in all pancytopenic patients with levers of unknown origin and had the previous history of visiting to the Mediterranean, the endemic area of VL[13]. In Thailand, it can be seen that all bone marrow leishmaniasis cases had the history of visiting to the Middle East for working or working in the oil fields[12]. Some had the classical triad but negative smear[7]. Indeed, in Thailand, many other tropical infectious diseases such as malaria and dengue can result in the mentioned triad characteristics as well. However, the bone marrow aspiration to find the cause of unexplained pancytopenia can be the final tool that brings the final confirmations of infections in all cases[2,14].

In this series, the bone marrow appearance is concordant with the classical findings according to the bone marrow leishmaniasis definition[2]. Detection of amastigote is the key point of diagnosis[2]. However, rare appearances such as myelofibrosis could be observed[15]. Concerning the treatment, the pentavalent antimony is very effective. Complete curative outcome can be derived in all cases in this series. For treating VL, pentavalent antimonial compounds are still the first–line antiinfective agents[16]. However, owing to increasing resistance to this agent, many patients at present require other drugs including amphotericin B and pentamidine[19]. Toxic effects of these second–line agents have led to development of new drug delivery systems, especially for the liposomal amphotericin B, which has shown uniform efficacy in clinical trials[15]. In summary, the clinical characteristics of the bone marrow leishmaniasis in Thai cases are not different from the classical cases in the original site. Focusing on the treatment, the adopted therapeutic protocol was effective and there is no problem of the drug resistance.

Finally, the author hereby also would like to discuss on the importance of leishmaniasis in Thailand relating to the present globalization and good traveling system. Of interest, almost all indexed cases in this report are the Thai labors who had the history of working in the endemic areas[2]. The left one case is a fisherman who also had history of long term visiting to the endemic area. It is no doubt that the disease was carried from those endemic countries to Thailand. The new emerging infectious disease can be diagnosed in these cases. Luckily, there is no specific vector for leishmanial parasite in Thailand hence there is no continuous propagation of infection into the community. In addition, there has been only 1 new case report on bone marrow leishmaniasis since 1990’s. This might be due to the concern of this disease and improvement of disease control system in Thailand. However, this does not mean that there is no possibility. It is no doubt that the vector might be carried into Thailand via airplane in the future and this is the totally unwanted situation.

The present situation of leishmaniasis in Thailand is under control[2]. It is only the disease under surveillance among the labors who go working at the Middle East. This is due to the basic social factor that the Thai labors would like to go working in the Middle East where the salary is better than Thailand. Each year, thousands of Thai labors emigrate to the Middle East. Nevertheless, it should be further noted that there is no reported case in tourist. Indeed, the Middle East is not the favorable target of the Thai tourists to go in the long vacation and this is the reason that there is no reported case in the tourist. On the other hand, it should be noted that Thailand is also reported as the original site.
of many infections such as malaria and dengue among the Western tourists who go back to their hometown after a visit to Thailand[17]. It is no doubt that the present globalization makes the disease easily wanders around the world.

A concern on leishmaniasis among the traveler is therefore an important topic to be discussed. It is no doubt that leishmaniasis is accepted as an important disease to be focused among traveler at present[18-19]. Pavli et al[18] noted that “Leishmaniasis should be considered in patients presenting with a compatible clinical syndrome and a history of travel to an endemic area, even if this occurred several months or years ago[18]”. The emergence of leishmaniasis in other settings, not only Thailand, was also reported. In USA and Europe, leishmaniasis becomes a focused travel-borne disease among the tourists[20] (which is different from Thailand that leishmaniasis is a focused disease among the labors.) It is no doubt that leishmaniasis becomes the disease under surveillance program of the Western[21]. For the Southeast Asia, the emergence of leishmaniasis can be seen in many countries adding to the Thai case. For example, the case in Vietnam is still controversial for its origin and it is implies for the possible new zoonosis from rural dogs[22]. Hence, the disease control program must be designed.

Focusing on how to control the leishmaniasis in Thailand, these recommendations can be set.

1 The disease control program for any labors going back to Thailand from the long period of working in the endemic area in the Middle East; 2 The health educations on the dissecting to any working as labors in the Middle East before their emigration; 3 The promotion of the knowledge of this new emerging disease to the general practitioner in Thailand who might have to deal with this new emerging infection; 4 The concern should also be given on the animal leishmaniasis since the emergence of zoonosis leishmaniasis is also possible[23] although it has never been existed in Thailand; 5 Finally, the note on the effect of the climate change on the pattern of vector that might result in the coming of new vector is very important[24-25]. Entomological surveillance is also important.

These recommendations can be applied to other settings where the problem of imported leishmaniasis can be detectable.

Although Thailand is not an endemic area of leishmaniasis, the infection can be detected in Thailand. There are many reported cases on the serious form of leishmaniasis, the bone marrow leishmaniasis. The Thai cases are all imported infection in the labors that went working in the endemic area and carried the infection back to their hometown, Thailand. The importance of traveling medicine in this case can be shown. Due to the present globalization, the migration, into and out of a country, is easily and this can be the root cause of the emerging of the new infection in the new setting. The summarized cases of bone marrow leishmaniasis in Thailand can be the good example.

Conflict of interest statement

We declare that we have no conflict of interest.

References
