Pulmonary Dirofilariasis in a Patient with Multisystem Langerhans Cell Histiocytosis - The First Reported Case in Thailand

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Abstract

Despite a high prevalence of canine dirofilariasis, there is no case of pulmonary dirofilariasis reported from Thailand. We herein report a case of multisystem Langerhans cell histiocytosis who had an incidental pulmonary dirofilariasis found at the time of autopsy as a solitary nodule at the periphery of the right lower lobe. This is the first reported case in Thailand. Association between pulmonary dirofilariasis and Langerhans cell histiocytosis has not been described before in the literature.

Pulmonary dirofilariasis (PD), an uncommon zoonosis caused by accidental infestation of immature larva of *Dirofilaria immitis* (dog heartworm), can produce problems in daily clinical practice mainly as a solitary pulmonary nodule. At least 93 cases have been reported; most of which were from the United States (U.S.) and a few were scattered in other countries[1-5]. The reason for a higher incidence of PD in the U.S. than in other countries is not known[3]. The frequency of dirofilariasis in animals is high in the eastern, southeastern, and southern coastal states in the U.S.[5]. Although the frequency of canine dirofilariasis was found to be high in stray dogs in Chiang Mai[6,7], the second largest city in Thailand, it is surprising that there has been no case of PD reported in Thailand.

We report herein a case of multisystem Langerhans cell histiocytosis (LCH) who had an incidental PD found at the time of autopsy as a solitary nodule at the periphery of the right lower lobe. The pathologic findings confirmed a diagno-

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sis of PD and multisystem LCH in this patient. To the best of our knowledge, this is the first case of PD reported in Thailand. The association between PD and LCH in this particular case has not been described before in the literature.

CASE REPORT

A 20-year-old Thai man, who was previously healthy, developed relapsing papillo-squamous lesions progressively for four years. These skin lesions were first described as acne-like papules in the face and scalp. They were increased in number and spread to the neck, trunk, and inguinal areas over time. Only a few papules were noted on the extremities. At times, these lesions turned into pustules, broke out and healed, leaving more or less scars. The patient had not received any investigation or specific treatment during the past four years until this hospitalization at Siriraj Hospital on June 13, 1996. About one year prior to this admission, he noticed some changes in the figure of his face. The maxilla and mandible were decreased in size; teeth were easily pulled out. He also developed jaundice six months prior to this admission. Anorexia and loss of 12 kg body weight were also noted during the time of illness. The patient used to work in a furniture factory, and had a previous history of drug abuse (volatile oil, thinner, etc.) There was no family history of any disease recorded.

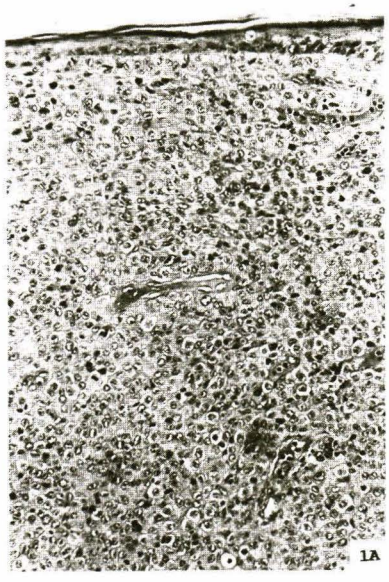
Physical examination revealed an emaciated young Thai man who showed an overwhelming number of skin lesions. The scalp was covered with thick scales and scattered desquamative areas with erythematous appearance along with alopecia. Numerous discrete erythematous papules and plaques were noted throughout the face, trunk, both inguinal regions, and proximal parts of all extremities. Pustules were frequently seen. No mucosal lesions were found. Slight anemia and moderate jaundice were observed. Deformity of facial bones was observed due to decrease in size of maxilla and mandible. Loosening of teeth was also observed. Neurological deficit included lower motor neuron type of left cranial nerves XI, XII and absence of gag reflex indicating involvement of cranial nerves IX and X. Cardiovascular and respiratory systems were within normal limits. No hepatosplenomegaly or lymphadenopathy was found.

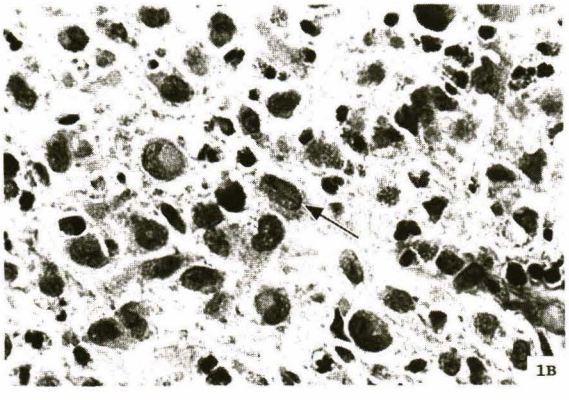
Hemoglobin was 10.6 g%, hematocrit 32.6 vol%, leukocyte count 11,700 cells/mm^3 with 89% neutrophils and 11% lymphocytes. Platelet count was 333,000 thrombocytes/mm^3. Urinalysis revealed pH 6.0, specific gravity 1.010, negative protein, sugar, and urine sediment. Gram positive cocci were demonstrated in the pus from pustules. Blood chemistry revealed BUN 6 mg%, creatinine 0.7 mg%, total bilirubin 10.1 mg%, direct bilirubin 7.9 mg%, SGOT 106 IU/L, SGPT 58 IU/L, alkaline phosphatase 644 IU/L, albumin 2.3 g%, and globulin 4.2 g%. A radiograph of the skull demonstrated bony destruction of maxilla and mandible as well as widening of alveolar sockets. A chest radiograph revealed no specific lesion. Ultrasonographic study revealed no definite lesions of the liver and spleen. Serologic test for anti-HIV antibody was non-reactive.

Skin biopsies taken from one papule at the chest wall and at the postauricular area showed histologic findings characteristic of LCH (see "pathologic examination"). Clinical staging indicated multisystem LCH (class D according to the Histiocytic Group in 1982)[8] including skin, skull, mandible, maxilla, liver, and left cranial nerves X, XI, XII. During hospitalization, the patient was found to have diabetes insipidus with positive water deprivation test, indicating involvement of sella or suprasellar area by LCH. He also developed malabsorption syndrome by presence of diarrhea, positive Oil Red O stool and D-xylose test, implying involvement of the small intestine. The patient was poorly nourished due to anorexia and depression. The multiorgan deterioration was progressive and the patient eventually expired after hospitalization for 23 days. Autopsy was performed after permission was granted.

Pathologic Examination

Skin biopsy demonstrated findings characteristic of LCH including accumulation of Langerhans cell histiocytes in the upper dermis admixed with eosinophils (Fig. 1A). These Langerhans cells had delicate nuclear membrane with irregular nuclear contours. Typical longitudinal nuclear groove was observed in many cells (Fig. 1B). These cells typically showed immunoreactivity with antibodies to CD68 (KP-1) and S-100 protein. Birbeck granules, a typical inclusion in LCH, were demonstrated by transmission electron microscopy (Fig. 1C). Besides skin involvement, LCH was demonstrated to involve skull and sella turcica, pituitary





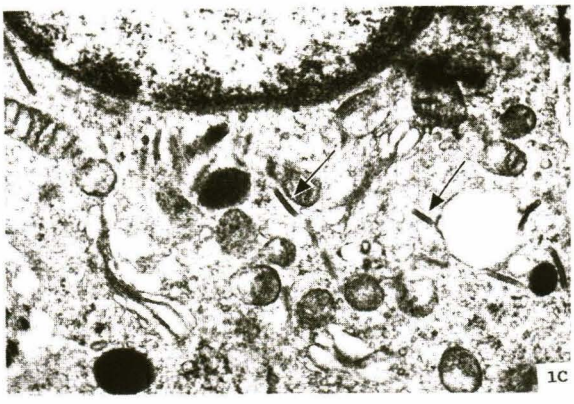


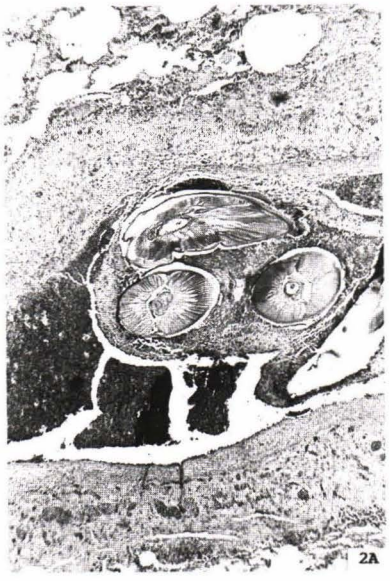
Fig. 1. Langerhans cell histiocytosis, skin biopsy.
A. The epidermis is atrophied by dense accumulation of large pale Langerhans cell histiocytes and variable number of eosinophils in the upper dermis. H&E, x100.
B. Typical nuclear features of Langerhans cell histiocytes with delicate irregular nuclear membrane and characteristic longitudinal groove (arrow). H&E, x400.
C. Characteristic Birbeck granules (arrow), showing rod-shaped structures with a central striated line, are evident in the cytoplasm. Transmission electron micrograph, x31,500.

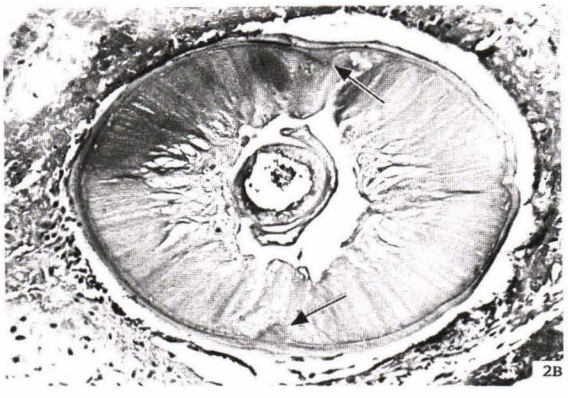
stalk and infundibulum, liver, lymph nodes, thyroid gland, pancreas, and lungs at autopsy.

A solitary pulmonary nodule, approximately 1.5 cm in diameter, located at the periphery of the right lower lobe demonstrated thrombosis of a branch of pulmonary arteriole caused by a *Dirofilaria immitis* larva, which was approximately 180 μm in cross-sectional diameter (Fig. 2A). Multiple cross-and longitudinal sections of the larva included faintly eosinophilic smooth thick cuticle with distinct inner lateral ridges, abundant muscle masses, portions of alimentary and genital tracts (Fig. 2B and 2C). Many portions of the larva began to degenerate. Infarct as well as acute and chronic granulomatous inflammation was noted in the surrounding lung tissue.

DISCUSSION

In this present report, we describe a case of multisystem LCH who had an incidental PD at the time of autopsy as a solitary nodule at the periphery of right lower lobe. Despite the high prevalence of canine dirofilariasis in stray dogs observed by Choochote et al in Chiang Mai[6,7], there has been no PD reported in Thailand. To the best of our knowledge, this case is the first reported case of PD in Thailand. Two cases of orbit infection by *Dirofilaria rapens* have been reported in Thailand [9,10]. However, they are different from *D. immitis* infection. *D. rapens* produces subcutaneous lesions and the parasites have longitudinal ridges on the outer surface of the cuticle with fine transverse striations, whereas, *D. immitis* produces pulmonary nodule and the parasites have smooth cuticle[5,10].





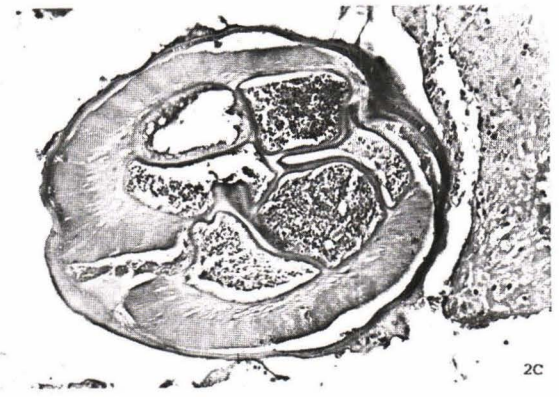


Fig. 2. Pulmonary dirofilariasis.

A. Cross and oblique sections of a *Dirofilaria immitis* larva in a branch of pulmonary arteriole producing thrombosis. H&E, x20.

B. Cross section of *D. immitis* larva showing smooth thick cuticle. Note the inner lateral ridges (arrows), abundant muscle masses and a central alimentary tract. H&E, x100.

C. Cross section of *D. immitis* larva at the level of genital tract. H&E, x100.

Pulmonary dirofilariasis is an uncommon zoonosis caused by *D. immitis* larva[1-3]. Humans are an accidental host since the larvae cannot turn to mature forms or reproduce. *D. immitis* is a filarial nematode with worldwide distribution. The adult worms reside in the right ventricle and pulmonary arteries. Dog is a main definitive host and a reservoir of the parasite, hence the so-called "dog heartworm" for this parasite. The *D. immitis* microfilariae are carried by mosquitoes of *Aedes, Anopheles, Culex,* and *Myzorhynehus* species. In Thailand, many species of the aforementioned mosquitoes, including *Mansonia uniformis, Culex pipiens quinquefasciatus, Aedes albopictus,* and *Aedes aegypti*, were found to be vectors of *D. immitis in vitro*, but interestingly only a few of them in nature were found to have parasitemia. *M. uniformis* is an important natural vector of *D. immitis* in Chiang Mai[6,7].

Once penetrating the blood vessel in the subcutaneous tissue after being released from the infected mosquitoes, only *D. immitis* larvae surviving from host immune system reach the right atrium *via* the venous return. They will stay in the right atrium, a usual habitat for the parasite, until they die and are thrown into pulmonary vasculature. Most frequently, the dead larvae are lodged in the periphery of the lung, producing infarction and granulomatous reaction leading to a solitary nodule or sometimes multiple nodules. These nodules ranged from 1 to 4.5 cm in diameter on chest radiographs. Most of the reported cases of PD in humans

are mainly solitary nodules, indicating the meager chance of larvae reaching the right atrium[1-5].

The reason for a higher incidence of PD in the U.S. is not clear[3]. Similarly, the reason for the absence of PD in Thailand except for the present case is not known, despite the high prevalence of *D. immitis* infestation in stray dogs in Chiang Mai reported by Choochote et al[6,7]. The discrepancy between the detection rate of *D. immitis* microfilariae in mosquitoes in the laboratory and in the nature is observed, but the reason for this discrepancy is not known[6,7]. Whether this evidence contributes to the rare incidence of PD in most countries except the U.S. remains to be investigated.

Most cases of PD described in the literature, at least 93 cases at the time of this report, presented with incidental pulmonary nodule found at the time of annual check-up or work-up for other diseases[1-5]. This coin lesion mostly led to the surgeons' attention. At present, there are no distinguishing clinical, roentgenographic, or laboratory features allowing the preoperative diagnosis. However, a serological approach for a preoperative diagnosis has been attempted[11,12]. In the U.S., the geographic distribution has followed that of canine dirofilariasis[3]. Infections occurred in males twice as often as in females and most of the cases were adults. It predominantly occurred in whites. Most of the cases (approximately 90% of cases) had a single nodule, mainly containing a single worm. Peripheral eosinophilia was present in 20 per cent of cases. Interestingly, approximately 12 per cent of cases were potentially immunocompromised[3]. However, no case of LCH was described in any previous reports.

Due to the high prevalence of canine dirofilariasis, we believe that pulmonary dirofilariasis might be overlooked due to the small size of the nodule and location at the periphery of the lung. The possibility of pulmonary dirofilariasis should be kept in mind when a subpleural coin-like pulmonary nodule is encountered.

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ไดโรฟิลาริเอลิสของปอดในผู้ป่วยโรคฮิสติโอซัยโตสิสของเซลล์แลงเกอร์ฮานส์ในหลายระบบ – รายงานผู้ป่วยรายแรกในประเทศไทย

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แม้ว่าไดโรฟิลาริเอลิสในสุนัขพบได้บ่อย แต่ไม่มีรายงานผู้ป่วยที่เป็นไดโรฟิลาริเอลิสของปอดในประเทศไทยเลย คณะผู้รายงานจึงได้รายงานผู้ป่วยหนึ่งรายที่เป็นโรคฮิสติโอซัยโตสิสของเซลล์แลงเกอร์ฮานส์ในหลายระบบ ซึ่งมีไดโรฟิลาริเอลิสของปอดเป็นก้อนเดี่ยวที่ชายปอดขวากลีบล่างจากการตรวจศพ นับเป็นรายงานผู้ป่วยโรคนี้รายแรกในประเทศไทย ความสัมพันธ์ระหว่างโรคทั้งสองนี้ไม่พบว่ามีบันทึกไว้ในเอกสารทางการแพทย์มาก่อน

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