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Human and animal sarcocystosis in Malaysia: A review

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ABSTRACT

Sarcocystosis is a zoonotic disease caused by a coccidian intracellular protozoan parasite of the genus *Sarcocystis*. More than 200 *Sarcocystis* species have been recorded and the parasites are found in mammals, birds and reptiles. They require two hosts to complete their life cycle. In Malaysia, sarcocystosis was reported as a potential emerging food and water-borne disease after a series of large outbreak of human infections. There was not enough attention given before even though it was reported in both humans and animals. The first human case of invasive muscular sarcocystosis among local Malaysian was reported in 1975. Besides, a retrospective autopsy examination on 100 tongues revealed 21% positive cases. On top of that, a sero-epidemiological survey conducted in 243 subjects in West Malaysia showed that 19.7% had *Sarcocystis* antibodies. The clinical symptoms of muscular sarcocystosis were first described comprehensively in 1999. Meanwhile, many types of animals including livestock were found harbor the sarcocysts in their tissue. The first case of human intestinal sarcocystosis was reported in 2014. This review indicates that human sarcocystosis is currently endemic in Malaysia and parallel to that reported in animals. However, more studies and investigations need to be conducted since the source of human infection remains unknown.

1. Introduction

Sarcocystosis is a zoonotic disease caused by a coccidian intracellular protozoan of the genus *Sarcocystis*. *Sarcocystis* spp. requires two hosts to complete its life cycle; with sexual reproduction in the intestine of carnivores or omnivores (definitive host) and asexual reproduction in the tissues of herbivores (intermediate hosts) [1]. It was first observed in 1843 by Miescher as white threadlike cysts and simply known as Miescher's tubule for 20 years [1]. To date, there are more than 200 *Sarcocystis* species recorded in the world and the parasites can be found in the tissues of mammals, humans, birds, reptiles and probably in fish [1,2].

There are two forms of sarcocystosis inflicting in man; intestinal and muscular. Intestinal sarcocystosis is acquired when

humans eat raw or undercooked meat which harbors the cystic stage of the parasite. Man becomes the definitive host after the ingestion of raw beef or pork infected with *Sarcocystis hominis* (*S. hominis*) and *Sarcocystis suihominis* (*S. suihominis*), respectively [2]. If acquired, it can cause gastroenteritis. However, in most people, the infections are asymptomatic and self-limiting [1,2]. Muscular sarcocystosis infection is acquired by the ingestion of contaminated food and water with sporocysts [3]. In this case, the parasite forms the muscular type in which consequently cause clinical signs such as fever, myalgia and arthralgia. Generally, based on early reports, the prevalence of human extra intestinal sarcocystosis was considered low with only less than 100 cases reported worldwide [1].

In Malaysia, muscular sarcocystosis was reported as a potential emerging food-borne zoonosis after a series of large outbreak of human infections. However, there was not enough attention given before even though it was reported in both humans and animals. Therefore, the aim of this review is to provide the latest updates regarding sarcocystosis in humans and animals in Malaysia.

2. Human muscular sarcocystosis

Historically, the first case of muscular sarcocystosis in Malaysia recorded involving an English man who had returned

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to England from Sarawak, East Malaysia [4]. Second case was reported by Jeffrey in 1974, in patient who also had returned to U.K from Malaysia [5]. However, the first human case of extra-intestinal sarcocystosis among local Malaysian was reported in 1975 which involved a Malay man [6] followed by an incidental finding of sarcocyst in nasopharyngeal/oropharyngeal tissues of an Orang Asli girl with malignancy [7] within the same year. Since that, a total of ~13 cases of invasive muscular sarcocystosis have been reported sporadically until 1992 [8–10]. However, most of the findings were incidentally taken from autopsied/biopsied specimens with no symptoms described. In addition, most of the cases were associated with malignancies. Nevertheless, seroprevalence study conducted in 1978 showed that 20% out of 243 respondents from four main ethnic groups in Malaysia had antibodies for *Sarcocystis*, indicating the endemicity of the disease [11]. On top of that, examination of human tongue tissue in 100 routine autopsies revealed a prevalence rate of 21% [12].

The clinical symptoms of the infection were first described in Malaysia after the first outbreak reported in 1999 involving 7 out of 15 US servicemen [13]. Acute manifestations including fever, myalgia and bronchospasm were noted and extensive investigation showed transient lymphadenopathy and subcutaneous nodules associated with eosinophilia, raised erythrocyte sedimentation rate, and elevated levels of muscle creatinine kinase. Muscle biopsy examination from one patient revealed microscopic sarcocysts. No more case of human sarcocystosis has been reported since 1999 until two large outbreaks of probable acute symptomatic muscular sarcocystosis which happened recently among travelers in two Malaysian islands (Figure 1), Tioman Island is located 32 km off the East Coast of Peninsular Malaysia, while Pangkor Island is located in Perak, 3.5 km off the West Coast of Peninsular Malaysia.

The outbreak were known to start during the late summer of July–August 2011 after Geo Sentinel (The surveillance program of the International Society of Travel Medicine and Centers for Disease Control) reported at least 32 acute cases of extra-intestinal sarcocystosis suspected among travelers upon returning home from Tioman Island [14]. Most of them were from Germany while the others were from Europe, North America and Asia. The clinical symptoms of fever and severe muscle pain were recorded within days and weeks in addition to the laboratory findings which had shown peripheral eosinophilia and the rise of serum creatinine phosphokinase level. Further results from muscle biopsy taken from two patients had revealed the possibility of sarcocystosis in the patients [15,16].



Figure 1. Location of the reported cases of human muscular sarcocystosis in Malaysia.

Following that, a survey for sarcocystosis was conducted soon after the outbreak in Tioman Island by Malaysian authorities but no trace of *Sarcocystis* parasites were found in humans, animals or in the water samples during that time [14]. A small number of samples was the limitation of the study. Moreover, no wild life was included for the screening of the study.

Approximately few months to one year later (July–August 2012), another wave of outbreak involving 65 people from various nationalities and with the history of travelling to Tioman Island were identified [17] with having almost similar symptoms as reported before. This second group of patients formed a total of 100 cases suspected with muscular sarcocystosis. Muscle biopsy taken from eight patients revealed that six of them had myositis and intramuscular cysts were identified in two patients [17]. Slesak and his colleagues in their further investigations involving 26 patients in German reported that the incubation period was approximately 2 weeks with biphasic development [18]. The third wave of extra intestinal sarcocystosis-like illness was suspected in May 2014 comprising 6 German patients [19]. All patients suffered from fever, myalgia and headache. No muscle biopsies were taken. However, the history, clinical symptoms and laboratory findings had shown the possibility of sarcocystosis.

Another concurrent outbreak of symptomatic sarcocystosis was reported within the same time frame (January 2012) but from different vicinity. From 92 college students and teachers, 89 of them were identified with symptoms including fever, myalgia, headache and cough after visiting Pangkor Island [20]. Molecular detection from biopsied specimens of 4 patients had revealed that the infection was caused by *Sarcocystis nesbitti* (*S. nesbitti*) [20–22]. Non-Malaysians were noticed to experience the symptoms longer and severe than the Malaysians [21]. Phylogenetic analysis suggested the source of infection was probably from snakes [22], but until now, the findings are still uncertain.

Therefore, following the latest outbreaks, it is now postulated that the possible source of infection of human muscular sarcocystosis in Malaysia is the contamination of food and water with sporocysts of *S. nesbitti* excreted with snakes (definitive hosts). Historically, the species was first discovered in the skeletal muscle of a rhesus monkey in China [23]. Through intensive research conducted in Malaysia in search for the clue and source of infection, *S. nesbitti* have been identified in the fecal sample of *Naja khaoutia* (cobra) and in reticulated python by molecular analysis [24]. The latter findings suggested the possibility of snake as the source of infection with rhesus monkey or rats probably serve as intermediate host (Figure 2). The summary of human muscular sarcocystosis in Malaysia is shown in Table 1.

The spectrum of clinical symptoms is broad and varies among individual ranging from asymptomatic to chronic and prolonged form of infection in which can also cause relapse [32]. Myalgia with or without fever, > 5% eosinophilia, elevated serum creatinine phosphokinase levels, myositis and negative trichinellosis and toxoplasmosis by serology are considered as the most important parameters for acute muscular sarcocystosis [32]. It was noted that the elevated level of blood eosinophils and serum creatinine phosphokinase were prominent during the late phase (~4 weeks post-departure) of period [19,32].

Generally, there is no definite treatment for human muscular sarcocystosis. The infection is usually mild and self-limiting in

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