

Sarcocystis nesbitti related autoimmune diffuse alopecia

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Abstract

Background & Objective: Symptomatic sarcocystosis has been said to be rare until recent years, when there were reports of outbreaks of febrile myositis for travellers returning from the Malaysian island resorts. In 2012, an outbreak of *Sarcocystis nesbitti* infection involving 92 college students and staff occurred after returning from Pangkor Island, Malaysia. A few months after recovering from the febrile illness, some patients complained of hair loss. This study aimed to determine the prevalence, clinical features and outcome of this disorder. **Methods:** All patients who became sick in the outbreak were asked whether they had the hair loss. For those who had, they were interviewed with standard questionnaires, examined and investigated. Patients were followed-up via an online survey 2 years later. **Results:** Out of 89 patients who were ill, 19 patients (21.4%) complained of alopecia. The mean peak onset was 4 months after the initial illness. Eleven patients (57.9%) reported the hair fall of more than 100 per day. The other symptoms were itch 10 (52.6%), scaling 10 (52.6%), erythema 4 (21.1%), none had scarring. Eleven patients (57.8%) had positive antinuclear factor with high titre (speckled or nucleolar pattern). Two years after the event, 10 had complete or near complete spontaneous recovery, 1 had partial response and 1 had no improvement.

Conclusions: A delayed transient diffuse alopecia is seen in close to a fifth of patients with *Sarcocystis nesbitti* infection. The high frequency of positive ANF suggested an immune-mediated mechanism.

INTRODUCTION

Sarcocystis spp. infection is an emerging zoonosis in Southeast Asia. *Sarcocystis spp.* are intracellular protozoan parasites with 2-host life cycle based on a prey-predator relationship with carnivores as definitive hosts and herbivores as intermediate hosts.¹ Sarcocystosis is noted in a number of animals, but symptomatic human disease appears to be uncommon, with less than 200 cases of human infection reported in the literature.²⁻⁴ Symptomatic human infection were characterised by myalgia, fatigue, fever, headache, arthralgia, eosinophilia and raised muscle enzyme.⁴ There was recent increase in the number of cases reported, mainly among travellers. There was recent reports involving a total of 68 persons with sporadic acute muscular sarcocystis-like illness after returning from Tioman Island, off the east coast of Peninsular Malaysia, between 2011 and 2012.⁴ Sarcocysts were observed histologically in the muscles of 6 (40%) of patients. The muscles showed varying degrees of inflammation.⁴

In January 2012, an outbreak of *Sarcocystis* infection involving a group of college students

and staff after returning from a retreat in Pangkor Island, off the west coast of Peninsular Malaysia.⁶⁻⁸ Eighty nine of the visitors (97%) developed a febrile illness at an average of 10 days upon returning indicating a high infection rate. The main symptoms were fever, of which close to half were relapsing, and myalgia. Muscle biopsy was done in 4 patients, sarcocysts were seen in 3, and *Sarcocystis nesbitti* was identified in 3 patients. *Sarcocystis nesbitti* was first described in muscle tissues of *Macaca mulatta* monkeys in 1969.⁹ This is the first time that *Sarcocystis nesbitti* has been identified to cause symptomatic human illness.⁶⁻⁸ It is interesting to note that *Sarcocystis nesbitti* was also found in one patient in the sarcocystosis outbreak in Tioman Island.⁴ Phylogenetic analysis suggest that snakes could be a definitive host.¹⁰ More recently, *S. nesbitti* sequences have been detected from faeces of snakes from disparate parts of Malaysia, confirming that snakes may be the definite host.⁷ It is also of interest to note that about a month after the onset of initial illness, facial swelling from myositis of the jaw muscles occurred in 9 (10%) of patients, and 4

(4.5%) patients had swelling of the calf, and one at interossei muscle of the hand.⁸

A few months after recovering from the febrile illness, some patients complained of alopecia. Excessive hair shedding in *Sarcocystis* in cows has been observed but not in human.¹¹ This study aimed to determine the prevalence, clinical features and outcome of this disorder.

METHODS

All patients who became sick in the outbreak were asked whether they had hair loss. For those who had, they were asked to attend the Dermatology Clinic in the Medical Centre. They were interviewed with a standard questionnaire,

examined and investigated. Patients were followed-up via an online survey 2 years later.

RESULTS

Out of 89 patients who were ill, 19 patients complained of hair loss, giving a prevalence for alopecia of 21.4%. The demographic and clinical details of the patients are shown in Table 1. There were 9 males and 10 females with 13 Malaysian and 6 non-Malaysian (5 from China, 1 from Nepal). The mean age was 29.3±5.7 years. This was not significantly different from the overall patients who were ill, where the Male : Female ratio was 53 : 36, the mean age was 34 years, and Malaysians : non-Malaysians was 69 : 20.

Table 1: Characteristics of patients with alopecia after *Sarcocystis nesbitti* infestation

Patient/ Nationality	Age/ Gender	Clinical symptoms	ANF titre
1/Malaysian	30/F	Itch, scaling	Speckled 1:80
2/Malaysian	24/F	Itch, scaling	Speckled 1:320
3/Malaysian	35/F	Itch, scaling	Negative
4/Malaysian	26/M	Nil	-
5/Malaysian	44/F	Nil	Speckled 1: 80
6/China	37/M	Itch	Speckled and nucleolar 1:80
7/Malaysian	30/F	Itch, scaling	Negative
8/Malaysian	26/M	Scaling	-
9/Malaysian	26/M	Nil	Nucleolar 1:160
10/Malaysian	32/M	Nil	Nucleolar 1:160
11/Nepalese	19/M	Itch, scaling, erythema	Speckled and nucleolar 1:40
12/Malaysian	25/M	Nil	-
13/Malaysian	33/M	Scaling	Speckled 1:40
14/China	31/F	Itch	Negative
15/China	28/F	Itch, scaling, erythema	Speckled and nucleolar 1:160
16/China	25/F	Itch, scaling, erythema	Speckled and nucleolar 1:320
17/China	24/F	Nil	Speckled 1:160
18/Malaysian	29/M	Itch, scaling, erythema	Negative
19/Malaysian	33/F	Nil	-

Out of 19 patients who complained of alopecia, 11 had self-reported hair fall with volume loss of more than 50%. Ten patients complained ofitch, 10 had scaling, 4 had erythema, and none had scarring. All of patients complained of diffuse alopecia, with peak onset 4 months after the initial illness. Pull test was positive for 3 patients.

As for the investigations performed, 11 patients had positive antinuclear factor (speckled or nucleolar pattern), 4 were negative, another 4 did not turn up for blood tests, giving an overall positive rate of 73% (11/15).

Only one patient had applied 5% topical minoxidil twice daily for 2 months and received intralesional steroid injection over central scalp once from a general practitioner, all other patients denied getting any form of hair treatment.

Two years after the event, 10 patients had complete or near complete recovery (including the patient who had been treated with intralesional steroids and 5% topical minoxidil application), one patient had partial response (self reported 50-75% recovery), patient reported no improvement, and 7 patients were lost to follow up. Duration to resolution of alopecia was a median of 6 months

(IQR 5-12).

As shown in Table 2, gender, nationality, previous personal and family history of alopecia and clinical symptoms were not significant risk factors of developing more severe alopecia, defined by a self reported hair loss of more than 50%.

DISCUSSION

We report here a group of subjects who developed alopecia about 4 months after the *Sarcocystis nesbitti* infection outbreak. The alopecia was diffuse and appeared to be largely transient with most patients experiencing spontaneous full or near full recovery at a median duration of 6 months. We believe the alopecia is related to the *Sarcocystis nesbitti* infection outbreak, as this is the common shared feature of the patients. There was no report of alopecia among the other college members and the family members who did not attend the retreat. The alopecia itself occurred as an “outbreak”, with onset and remission of the symptom related in time to the original *Sarcocystis nesbitti* infection outbreak.

Table 2: Risk factors of hair loss

Risk Factors	<50% hair loss, n (%)	50% or more hair loss, n (%)	p-value
Gender			
-Male	8 (50)	1 (33.3)	0.179
-Female	8 (50)	2 (66.7)	
Nationality			
-Malaysian	10 (62.5)	3 (100)	0.44
-China	5 (31.3)	0 (0)	
-Nepalese	1 (6.3)	0 (0)	
Personal history of alopecia			
-Yes	4 (25)	2 (66.7)	0.22
-No	12 (75)	1 (33.3)	
Family history of alopecia			
-Yes	4 (25)	2 (66.7)	0.22
-No	12 (75)	1 (33.3)	
Itch			
-Yes	9 (56.3)	1 (33.3)	0.582
-No	7 (43.8)	2 (66.7)	
Scaling			
-Yes	8 (50)	2 (66.7)	0.542
-No	8 (50)	1 (33.3)	
Erythema			
-Yes	4 (25)	0 (0)	0.47
-No	12 (75)	3 (100)	

The alopecia appeared to be common, occurring in about a fifth of patients with *Sarcocystis nesbitti* infection. Close to half of those affected were more severe, with hair loss of more than 50%. Half of the patients also had itch and scaling. The symptom was transient; with median duration of about 6 months.

ANF positivity in individuals of 12 years and older is reported to be seen in 13.8% of population.¹² There was a strong association with ANF among our patients with alopecia, with 73% reported positive. This strongly suggests an immune-mediated aetiology of the alopecia, and suggests that telogen effluvium is unlikely as cause of the alopecia. This is also supported by the low rate of positive hair pull test. Positive hair pull test is one of the diagnostic feature of telogen effluvium.¹³

Sarcocystosis manifest as a prolonged illness with multiple organ involvement and sometimes occurring in phases. In the *Sarcocystis nesbitti* outbreak seen earlier in these patients, relapsing fever was reported in 57.1% of patients, and 31.3% of those with relapsing fever had 3 or more cycles of fever. Between 34 and 38 days post-exposure, about 10% of patients developed visible facial swelling involving mainly the jaw muscle. There is also variation of blood parameter in the disease phase, with eosinophilia and raised creatinine kinase seen more commonly in the later phase of illness. The pathogenesis of these symptoms, whether they represent different phases of parasite life cycle, direct infection by the parasite, or immune-mediated reaction is uncertain. Our patients with alopecia show that immune-mediated response plays a role in the pathogenesis of the symptom.

As the onset of alopecia was only noticed a few months after the initial illness, and the outbreak involved both local Malaysians and foreign students, some may not have come forward for further examination. Hence the frequency of alopecia maybe an underestimation.

In conclusion, alopecia is a late complication of *Sarcocystis nesbitti* infection. The high frequency of associated positive ANF suggest an immune-mediated mechanism.

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