IDCases 2 (2015) 49–52

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case Report

Unusual cause of recurrent fever after travel in South America

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ARTICLE INFO

Article history:
Received 28 February 2015
Received in revised form 23 March 2015
Accepted 23 March 2015

Keywords:
Recurrent fever
Travel
South America
Aroma oils

ABSTRACT

Fever in returning travelers is a common problem and usually the diagnosis is made within a few days or the traveler recovers.

We present two travelers who presented with fever two weeks after returning from a six week vacation in South America. Over the following 18 months they presented with short attacks of fever, elevated CRP and leukocytosis and the program for investigation became more and more elaborate. A curious and key feature was, that they were completely synchronous both developing symptoms within an hour and presentation with the same laboratory findings of leukocytosis and elevated CRP. Extensive and repeated tests were performed, at our facility and abroad. After a year it was discovered that the uses of aroma oils were associated with the symptoms. No similar case has been found to be reported previously.

These cases emphasize that natural products are not inherently safe. The investigational program was build up over time as new attacks continued to occur and suggestions from different centers which were consulted were followed up. The number of tests performed at different laboratories took an extensive amount of time. These cases emphasize that a panel of analysis in returning travelers in which no clear diagnosis is found should be developed.

Introduction

Fever in returning travelers is a common problem and usually the diagnosis is made within a few days or the traveler recovers [1,2].

We report here two travelers who presented with fever two weeks after returning from a six week vacation in South America. Over the following 18 months they presented with short attacks of fever, elevated CRP and leukocytosis and the program for investigation became more and more elaborate. A curious and key feature was, that they were completely synchronous both developing symptoms within an hour and presentation with the same laboratory findings of leukocytosis and elevated CRP.

Extensive and repeated tests were performed. After about a year it turned out that the couple used aroma oils (Nature and Decouvertes – Fig. 1) in the home applied by a nebulizer placed in the middle of a table. The use of the oil matched perfectly with the fever attacks. The oils were not used during summer, also explaining the absence of symptoms during the summer months.

Aromatic oils have been used for centuries as healing and soothing scents.

Since the use of the oils ended there has been no relapse in any symptoms. It has not been possible to test them with exposure for ethical reasons.

We are not aware of or have found any previous reports, in English or other languages, reporting similar events after the use of similar products.

Case presentation

After traveling to South America for a six weeks tourist holiday the two patients returned home to Denmark. Ten days after returning they were both admitted to hospital with fever, muscle and joint pains and vomiting. From the 8 September 2012 to the 22 October 2012 they spent 3 weeks in Peru, half a week in Bolivia, half a week in Chile and 2 weeks in Brazil. They traveled by local busses, stayed at medium level hotels and were not ill at any time during their travels.

Prior to their travels they had received vaccines against hepatitis A and B, yellow fever and tetanus/diphtheria. Table 1 shows the patients' history and Table 2 lists CRP, white blood cell count and recorded rectal temperatures. Day 0 is defined as the first day the couple was admitted to hospital, 10 days after the

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http://dx.doi.org/10.1016/j.idcr.2015.03.002

Fig. 1. Aroma oils used by the patients.

return from South America. There was no eosinophilia at any given time and the total IgE remained normal throughout.

Approximately nine episodes occurred within the following 18 months, all attacks being identical in symptoms, duration and paraclinical results for both patients (Table 2).

Initially the patients were tested negative for malaria and dengue fever. Under the suspicion of a rickettsial infection they were treated with doxycycline 100 mg two times daily initially for one week [3]. This was immediately afterwards repeated again for one week. After the third relapse, Day 20, the patients received 3 months Doxycycline 100 mg two times daily plus moxifloxacin 400 mg × 1, as it was believed they previously had had a good effect.

The patients went through an elaborate program of serological tests and test for nucleic acids of different pathogens, which is summarized in Table 3. Through the whole course a wide range of tests were performed including heart echocardiography, PET-CT and an MRI which were all normal.

Discussion

Definition of travel associated disease "is a patient who has crossed an international boarder within the past 10 years and presents for a presumed travel-related disease" [4]. It is not uncommon for travelers to report an illness associated with their travels (20–70%), but only a small portion of these actually seek medical attention [2,5,6]. A detailed medical history is a very important tool in correct diagnosis, including destinations, risk factors, previous medical history. Incubation time is also important to keep in mind through the process (Table 5) [2,5,7].

Table 1
Symptom history.

Day	Symptoms
0	Fever, joint and muscle pain
10	Vomiting, headache, muscle pain, fever
20	Night sweats, shivering, headache, light respiratory pain
112	Fever, night sweats, shivering, muscle and joint pain, slight non-productive cough
127	Muscle and joint pain
136	Fever, night sweats, shivering, headache
139	Fever, muscle and joint pain
412	Fever, muscle and joint pain
434	Fever, chest pain, dyspnea, tiredness

The GeoSentinel surveillance program has found that the most common causes of fever after traveling is malaria, dengue fever, enteric fever (*Salmonella typhi*) and rickettsioses [2]. Initially malaria and dengue fever were excluded and the patients were treated with doxycycline under the presumption of a rickettsia or bartonella infection. When the fever attacks continued we excluded endocarditis due to *Coxiella burnetii* (Q fever) and looked for South American trypanosomiasis due to *Trypanosoma cruzi* (Chagas disease), which can be transmitted orally through fresh fruit juice. We speculated that *Toxoplasma gondii* was a possibility as *T. gondii* genotypes in South America are more pathogenic compared to Europe [8], but only one of the subjects had antibodies at a low titer, not compatible with an acute infection. Leptospirosis was also a diagnostic option, especially with a second phase of fever shortly after the first; this was however also excluded by a negative serology. Acute schistosomiasis and other parasites were ruled out as there was no eosinophilia or elevated total-IgE in either patient.

Different centers were asked to assist with this case, including Unité Des Rickettsies, France, Porton Down, UK and Center for Disease Control and Prevention (CDC), United States. See Tables 3 and 4 for list of all the test and results found on the patients. Everything that was tested for came out negative, including blood and urine cultures.

Table 2
Biochemical infectious markers.

Day	Patient A			Patient B		
	Temperature (°C)	CRP (mg/l)	WBC (10*9/l)	Temperature (°C)	CRP (mg/l)	WBC (10*9/l)
0	37.5	58	32.2	37.7	67.2	34.9
3		19.9	6.5		26.1	6.7
10	37.1	36.6	25	37.2	40.6	24.8
12					26.8	8.2
13		11	5.3			
24		1	4.6		0.9	6.2
40		4.4	6.3		<0.6	5.9
112		26.3	18.2		59	22.7
119		6.8	5		24.4	5.5
127		5.7	15.8		22.4	18.5
129		24.3	6.4		48.3	5.5
153		<0.6	8.1			
166		<0.6	7.7			
194					1.2	4.8
196		17	5			
395		44.5	17		60.2	18.5
412		0.6	7.6			
434	37.1	20.5	24		15.9	18.6
435		38.1	10.8			