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# Katayama's Syndrome Related to *Schistosoma intercalatum* in Two Travellers Returning from Mali

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## ABSTRACT

Katayama syndrome associated with *Schistosoma intercalatum* has been reported in few cases in the literature. In this study we indicate the clinical characteristics, the diagnostic methods (parasitological and serological) and the therapeutic management in two patients with this syndrome after a trip to Mali.

**Keywords:** *Schistosoma Intercalatum*, Katayama's Syndrome

## 1. INTRODUCTION

Schistosomiasis is a parasitic disease widespread in tropical and subtropical regions of the world. Africa, South America, the Caribbean and Asia are endemic areas which morbidity and mortality are common.

Katayama syndrome and cercarial dermatitis are the two main forms of acute schistosomiasis in non-immune individuals. Katayama syndrome (also known as Katayama fever) is characterized by nocturnal fever, cough, myalgia, headache and abdominal tenderness (Ross *et al*., 2007). This clinical picture is usually associated with pulmonary infiltrates and eosinophilia (Ross *et al*., 2007).

Pathogenesis of acute schistosomiasis is due to the immune response against cercariae and schistosomula antigens (migratory phases). In this period of time eggs are not yet eliminated by faeces or urine and immunological or molecular detection may be used.

In this study we report two cases of Katayama syndrome in a couple returning from Mali. Although no causal agent could be demonstrated in the male, probably due to early treatment, his wife presented a milder clinical picture being *S. intercalatum* detected in faeces.

### 1.1. Case Report 1

A 30-years old male living in Las Palmas de Gran Canaria (Spain) was referred to the Emergency Unit of Hospital Insular (Gran Canaria, Spain) without relevant medical history or pathological habits. He complained of diarrhea with visible mucus in number of 3-4 stools/day, without blood and low-grade fever (38°C) after 4 days of returning from Mali, where he had traveled as a tourist for 15 days (**Fig. 1**).

The patient had been vaccinated properly and had made adequate malaria chemoprophylaxis. The main epidemiological history was non-potable water consumption and bathing in fresh water 17 days before the medical attention. In addition, the patient reported

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cough and wheeze in two days earlier. Complementary tests performed at baseline (blood count, coagulation, blood chemistry, including liver function tests and urinalysis) were normal. *Giardia intestinalis* were detected in stool analysis and the patient was treated with tinidazole. He came back a week later with stopping diarrhea and starting paroxysmal cough. At this point, blood tests showed eosinophilia (1.100 $\mu L^{-1}$) and stool examination (Kato and Ritchie), urine sediment and serological studies of *Schistosoma* spp. (indirect hemagglutination) were negatives. Katayama syndrome was suspected and praziquantel was prescribed at conventional doses, attending the patient three days later due to the onset of abdominal pain, fever of 38-39°, malaise and myalgia. At this moment, his blood samples showed intense eosinophilia (4.100 $\mu L^{-1}$) and elevated serum alanine aminotransferase and aspartate aminotransferase levels (80 and 199 U/L respectively). Treatment was started with prednisone at tapered doses, with the disappearance of clinical symptoms and a decrease in eosinophilia in the following months.

## 1.2. Case Report 2

A 34-years old, living in Las Palmas de Gran Canaria (Spain) which had made the same trip and the same activities (bathing in fresh water and consumption of untreated water) than your partner (case report n° 1) came to the emergency room in the same time (**Fig. 1**).

The initial clinical picture was characterized by diarrhea and fever being treated empirically with ciprofloxacin. Subsequently the patient made a new trip to Morocco presenting a febrile syndrome with diarrhea and intermittent pruritic and erythematous skin lesions. When the patient returned from the trip, asymptomatic, came to our unit and eosinophilia (4.030 $\mu L^{-1}$) were found in analytical study. Moreover, Kato technique showed showed large eggs with terminal spur, positive Ziehl-Neelsen, suggesting *S. intercalatum* infection (**Fig. 2**). Specific antibodies to *Schistosoma* spp. detection were confirmed using two techniques: Indirect hemagglutination (IAH Fumouze) and ELISA (Scimedx corporation). Although no antibodies were detected by IHA, ELISA was positive. Conventional treatment was initiated with praziquantel and corticosteroids, which was well tolerated. In later revisions, the patient was asymptomatic, blood tests showed mild eosinophilia (800 $\mu L^{-1}$) *Blastocystis hominis* were observed in fecal analysis. In a new study also IHA detected antibodies to *Schistosoma* spp.

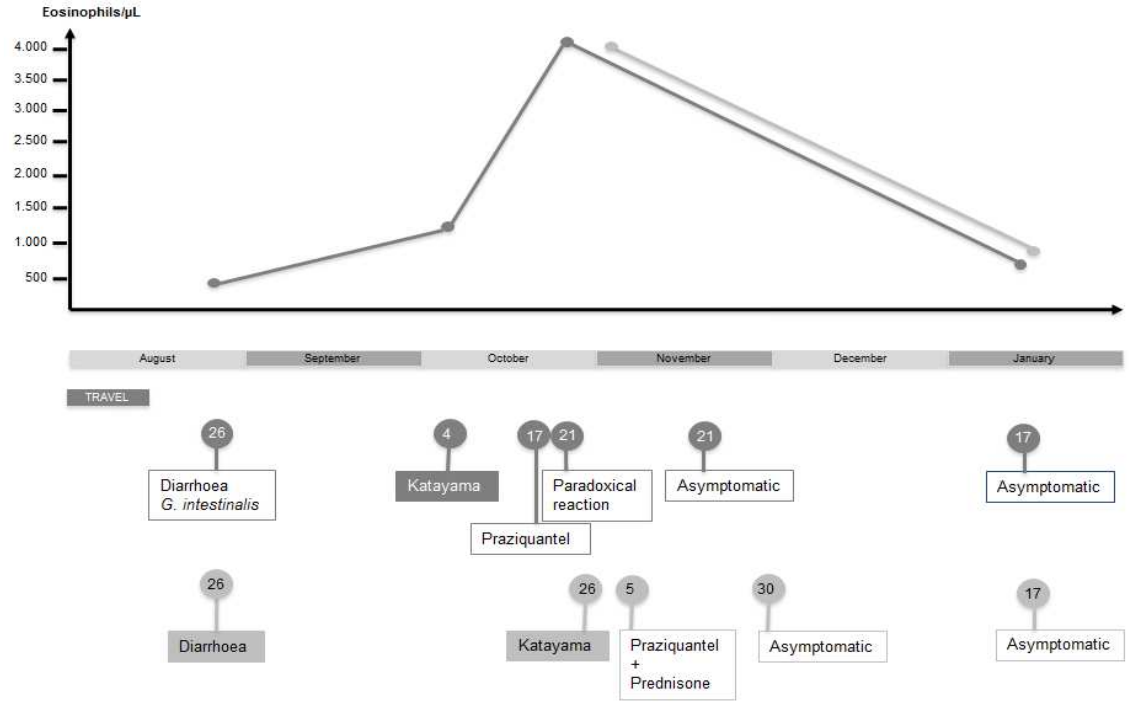
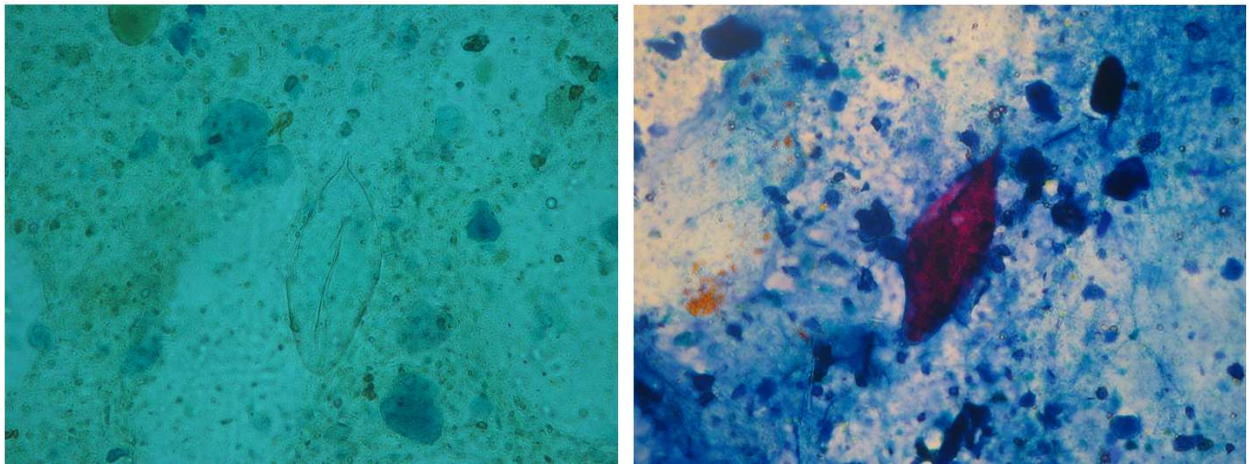



**Fig. 1.** Clinical evolution in case 1 (dark gray) and case 2 (gray)



(a) (b)

**Fig. 2.** *Schistosoma intercalatum* (a) Kato technique (b) Ziehl-Neelsen stain

## 2. DISCUSSION

Penetration through the intact skin of free-living cercariae is the main mode of transmission of *Schistosoma* infection (Ross *et al*., 2007). Thus, all cases of Katayama syndrome among travelers appear with a history of bathing in rivers or lakes contaminated (i.e., Dogon Country, Lake Malawi, Omo River) (Ross *et al*., 2007; Grobusch *et al*., 2003). *S. mansoni* and *S. haematobium* are the main species involved of the imported cases in Europe (Grobusch *et al*., 2003). However, Katayama syndrome caused by *S. intercalatum* has been reported in few cases (Grobusch *et al*., 2003; Visser *et al*., 1995; Croft *et al*., 2005). Although *S. intercalatum* is endemic in several African regions (i.e., Cameroon, Congo, Nigeria and Mali), coexistence with *S. haematobium* and/or *S. mansoni* by interspecific sexual interactions between human schistosomes could have a role in limiting the distribution of *S. intercalatum*. Thus, the competitive sexual processes acting among human schistosomes show that *S. haematobium* and *S. mansoni* are always competitively dominant over *S. intercalatum* (Jourdane *et al*., 2001).

The cases described in this study also illustrate two important aspects of Katayama syndrome. Firstly, after a single exposure, both patients presented some different clinical manifestations (respiratory in case 1, cutaneous in case 2) and a different incubation period (56 days in case 1, 79 days in case 2). Secondly, as was observed in both cases, it is not uncommon coexistence of schistosomiasis with other parasites.

Diagnosis of Acute Schistosomiasis (AS) is based on clinical data and detection of antibodies against *Schistosoma* spp. Symptomatic AS was defined as a raised eosinophil count associated with at least one of the following symptoms appearing within 3 months from primary exposure to schistosomiasis: Urticaria, angio-edema, fever, diarrhea, abdominal pain and cough. Several types of serological techniques are useful in the diagnosis of Katayama syndrome, although some isolated techniques (i.e., IHA) have low sensitivity, especially in early stages (Gool *et al*., 2002). Additionally, this study checks the value of commercial techniques used in cases of infection with *S. intercalatum*.

The diagnosis of the species involved is based on various data: The geographic area of infection, the biological sample which eggs of *Schistosoma* are detected (*S. mansoni* and *S. intercalatum* in the faeces, *S. haematobium* in urine), the egg size and the location of the spike of the eggs (lateral in *S. mansoni*, terminal in *S. haematobium* and *S. intercalatum*). However, both fecal contamination of the patient's urine as the variable size of the eggs of *S. intercalatum* limit the accurate diagnosis (Croft *et al*., 2005; Almeda *et al*., 1996). In this sense, the Ziehl-Neelsen (positive in *S. intercalatum*, negative in the other species) has a clear diagnostic utility (Muller and Taylor, 1972). Clearly, PCR techniques are more specific, although they are not easily accessible in clinical practice (Gomes *et al*., 2010).

The treatment of Katayama syndrome is controversial (Jaureguiberry and Caumes, 2011). Randomised controlled trials have also shown that the effective praziquantel dosage regimen is 40 mg $kg^{-1}$ orally in divided doses over one day (2×20 mg $kg^{-1}$ doses 4-hourly) for *S. mansoni*, *S. haematobium* and *S.*

*intercalatum*. However, young schistosomulae (7-28 días) are not sensitive to praziquantel. Moreover, treatment with praziquantel frequently (40-60%) results in a paradoxical reaction (Jarisch-Herxheimer-like), as described in Case 1. Therefore, some authors add corticosteroids to minimize this reaction. However, two types of data arguing against this combination: (i) corticosteroids decrease plasma concentrations by 50% and (ii) concomitant ocult strongyloidosis may be present and corticosteroid treatment could trigger hyperinfection. Taking into account that the incubation period of acute schistosomiasis is very variable (18-84 days) (1), it seems reasonable to use artesunate in early cases (this drug is effective against the schistosomula) and praziquantel associated with corticosteroids in late or complicated cases (neurological or cardiac).

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