20

A 43-Year-Old Male Traveller Returning from Mozambique With Fever and Eosinophilia

GERD-DIETER BURCHARD

Clinical Presentation

History

A 43-year-old German man presents to a local travel clinic on 21 May because of fever. He had been in Mozambique from 16 April to 30 April, and travelled to Chile afterwards from 30 April to 17 May. He did not take any malaria chemoprophylaxis in Mozambique and reports self-treatment for malaria with atovaquone/proguanil because of fever (27 April to 29 April). He is now complaining of recurrent fever for the past 3 days. The day before presentation his temperature was as high as 39.8°C (103.6°F). He also has some headache and diarrhoea.

He reports freshwater contact in a small lake near Maputo. His past medical history is unremarkable.

Clinical Findings

43-year-old male, febrile, with a temperature of 39.2°C (102.6°F). The rest of the physical examination is normal and there is no rash, no hepatomegaly, no splenomegaly and no lymphadenopathy.

Laboratory Results

The relevant laboratory results on admission are shown in Table 20.1.

Further Investigations

Electrocardiogram is normal. Chest radiography reveals some nodular lesions ranging in size from 2 to 5 mm in the periphery of the lower lung zones bilaterally (Fig. 20.1); this finding is confirmed by a CT scan of his chest.

TABLE 20.1 Laboratory Results on Admission

Parameter	Patient	Reference
WBC ($\times 10^9$/L)	9.0	4–11.3
Eosinophils ($\times 10^9$/L)	2.1	<0.5
LDH (U/L)	422	135–225
Creatinine (µmol/L)	88.4	53–106
AST/GOT (U/L)	106	10–50
ALT/GPT (U/L)	179	10–50
GGT (U/L)	186	<65
C-reactive protein (mg/L)	57.9	<5

• **Fig. 20.1** Chest radiograph showing nodular changes in the periphery of both lungs.

Questions

1. What are your differential diagnoses and which investigations would you like to do?
2. What is the significance of eosinophilia in returning travellers?

Discussion

A 43-year-old man presents with of a 3-day history of high fever. He has recently returned from a 5-week trip to Mozambique and Chile. He did not take any malarial chemoprophylaxis, but he took standby emergency treatment for presumed malaria when feeling febrile about 3 weeks ago. He reports freshwater contact in Mozambique. On examination he is febrile. His FBC shows eosinophilia with a normal total white cell count. His liver enzymes, lactate dehydrogenase (LDH) and C-reactive protein (CRP) are slightly raised. Chest radiography and CT show small, nodular changes in the periphery of both lungs.

Answer to Question 1

What Are Your Differential Diagnoses and Which Investigations Would You Like to Do?

The patient has travelled in Mozambique without taking any antimalarial chemoprophylaxis. Thus first of all malaria has to be excluded – irrespective of any other symptoms or laboratory results.

The differential diagnosis of pyrexia in a returned traveller is long, but typhoid fever and amoebic liver abscess should always be excluded because they are common and potentially life-threatening diseases. Therefore blood cultures should be taken and an abdominal ultrasound should be done. In contrast to what was seen in this patient though, typhoid fever usually causes eosinopaenia.

The further differential diagnosis of fever after a stay in tropical areas relies on the precise itinerary, the activities indulged in during travel, the presence of focal symptoms, signs and laboratory results.

The patient has slightly elevated liver enzymes. The differential diagnosis of acute infections involving the liver includes viral hepatitis, including hepatitis E.

EBV and CMV infections may also cause fever, elevated liver enzymes and a rise in LDH. They are important differentials of fever in returned travellers. However, EBV and CMV cause lymphocytosis with atypical lymphocytes, rather than eosinophilia. Splenomegaly is usually part of the clinical picture of mononucleosis and lymphadenopathy, even though the latter can be less prominent in acute CMV infection.

Leptospirosis, rickettsioses and Q-fever are bacterial infections to consider, as well as brucellosis, secondary syphilis and relapsing fever. Yet none of these infections as such would explain the patient's pronounced eosinophilia.

Answer to Question 2

What is the Significance of Eosinophilia in Returning Travellers?

In any patient returning from the tropics with eosinophilia, a helminth infection should be ruled out. The most relevant differential diagnosis in this patient who presents with eosinophilia and fever reporting freshwater contact is acute schistosomiasis, also known as Katayama syndrome. Another rare cause of fever, eosinophilia and elevated liver transaminases is acute fascioliasis.

The Case Continued…

Thick films for *Plasmodium* species were negative. Microscopy of stool and urine samples for *Schistosoma* eggs were three times negative.

The patient was tested for antischistosomal antibodies using an enzyme-immunoassay and an immunofluorescence assay (IFA); both came back negative.

Four weeks later antischistosomal antibodies could be detected (IFA 1:1280, cercarial- and egg-ELISA positive). *S. mansoni* ova were found in the stool and a diagnosis of schistosomiasis was established. The patient was treated with praziquantel.

• **Fig. 20.2** Schistosoma mansoni egg.

SUMMARY BOX

Acute Schistosomiasis (Katayama Syndrome)

Acute schistosomiasis (Katayama syndrome) is an acute hypersensitivity reaction caused by newly expressed antigens on developing worms. It is named after the Katayama region in Japan, where it was first described.

Katayama syndrome usually occurs 2 to 12 weeks after *Schistosoma* infection. It is characterized by fever, urticaria and a dry cough sometimes accompanied by a wheeze. Patchy pulmonary infiltrates or micronodular changes in the lower lung zones may be present on chest radiograph. Full blood count in the majority of cases shows eosinophilia, but of note, eosinophilia can occur with a delay of several weeks after the onset of

symptoms and may be missed. Most patients recover spontaneously after 2 to 10 weeks. Rarely, neurological complications can occur, e.g. transverse myelitis, conus medullaris or cauda equina syndrome.

Diagnosis of acute schistosomiasis can be challenging. *Schistosoma* ova (Fig. 20.2) may still be absent from urine or stool at this early stage and serological tests can take up to 3 months to become positive. As a consequence, these investigations have to be repeated several times after the diagnosis has been clinically suspected. PCR-based methods are promising for the diagnosis of acute *Schistosoma* infection in recently primarily exposed populations such as travellers.

Praziquantel has a lack of activity against immature flukes and severe reactions have been reported after praziquantel treatment during the acute phase. Therefore antiparasitic treatment should be delayed until the flukes are adult, i.e. until eggs can be detected in stool or urine.

Under certain circumstances, such as severe symptoms and in particular neurological complications, supportive steroid therapy may be useful in Katayama syndrome.

Of note, different stages of the parasite life cycle may overlap in a patient who is infected with many schistosomules. Therefore control examinations after several months are necessary and treatment with praziquantel may have to be repeated.

Further Reading

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