



Case Report

Fever in a traveler returning from the Amazon. Do not forget hepatitis A

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ABSTRACT

Travelers returning from the tropics with fever remain a diagnostic challenge. Fever and chills suggest malaria, but may be present in dengue, chikungunya and influenza, and splenomegaly favors malaria or typhoid fever. In terms of laboratory tests, leukopenia suggests dengue fever, chikungunya fever or influenza. Atypical lymphocytes are present in malaria, dengue fever, chikungunya fever and influenza HAV, but not typhoid fever. Thrombocytopenia is profound in dengue fever, is also present in influenza and malaria. Mildly increased serum transaminases are common in malaria, typhoid fever, dengue fever, chikungunya fever and influenza while very high serum transaminases point to HAV. We present a case of a young woman traveler returning from the Amazon with splenomegaly, leukopenia, atypical lymphocytes, elevated LDH and minimally elevated serum transaminases who was found to have acute hepatitis A infection.

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Introduction

Travelers returning from the tropics with acute fevers remain a diagnostic challenge. Differential diagnosis (DDx) includes malaria, typhoid fever, dengue fever, chikungunya fever, influenza and hepatitis A (HAV) [1–3]. Fever and chills suggest malaria, but may be present in dengue, chikungunya and influenza. Splenomegaly favors malaria or typhoid fever. Leukopenia suggests dengue fever, chikungunya fever or influenza. Atypical lymphocytosis may be present in malaria, dengue fever, chikungunya fever and influenza, but not typhoid [4–7]. Thrombocytopenia can be profound in dengue fever, but is also present in influenza and malaria. Mildly increased serum transaminases are common in malaria, typhoid fever, dengue fever, chikungunya fever and influenza. While very high serum transaminases point to hepatitis A or hepatitis E [8–10] (Table 1). We present a young woman after returning from the Amazon with atypical lymphocytosis, splenomegaly, and leukopenia who was diagnosed with hepatitis A.

Case report

Two weeks after returning from the Amazon (Manaus, Brazil), a 40-year-old female developed fever, chills, headache, and myalgias with temperatures to 103.5 °F, and saw a physician. She was not anorexic and had no abdominal complaints. She had been vaccinated for yellow fever and took atovaquone/proguanil for malaria prophylaxis. Her white blood cell (WBC) count was 6.9 K/ μ L ($n = 3.9$ – 11.0 K/ μ L), hemoglobin 9.8 g/dL ($n = 11.6$ – 16.3 g/dL), hematocrit 33.1% ($n = 36$ – 48%), and platelet count 411 K/ μ L ($n = 160$ – 320 K/ μ L). Her AST was 37 IU/L ($n = 13$ – 39 IU/L), and ALT was 50 IU/L ($n = 4$ – 36 IU/L).

Headache and chills continued which prompted hospitalization. On admission, her review of systems was negative except for myalgias and left upper quadrant pain. Past medical history and physical examination were unremarkable. Her WBC count was 3.6 K/ μ L (atypical lymphocytes = 5%), hemoglobin 10.4 g/dL, hematocrit 33.5%, and platelet count 172 K/ μ L. Her erythrocyte sedimentation rate (ESR) was 26 mm/h. Serum ferritin was unelevated, and her lactate dehydrogenase (LDH) was 1167 IU/L ($n = 100$ – 250 IU/L). The left upper quadrant pain prompted an abdominal CT scan which showed mild splenomegaly [2,6]. Blood smears for malaria and babesiosis were negative. Blood and stool cultures were negative. Dengue and chikungunya titers were negative. Her aminotransferases became prominently elevated with a rise in AST to 1757 IU/L and ALT to 1375 IU/L prompting serological

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Table 1
Differential diagnosis of acute fevers in returning travelers from Latin America.

	Malaria	Typhoid fever	Dengue fever	Chikungunya fever [‡]	Influenza	Hepatitis A (HAV)
Symptoms						
Feverish	+++	++	++	+++	+	+
Chills	+++	–	±	±	+	–
Headache	+	+	++	++	++	–
Polyarthralgias	–	–	+	+++	+	–
Myalgias	+	–	+++	+	+++	–
Dry Cough	±	±	–	–	+++	–
Malaise/fatigue	+	+	–	–	+++	+
N/V/D	±	±	±	±	±	±
Generalized pruritus ^{††}	–	–	–	+++	–	–
Signs						
Fever > 102 °F	+	+	+	+	±	–
Relative bradycardia	+	+	+	–	±	–
Conjunctivitis	–	–	±	–	±	–
Bilateral posterior cervical adenopathy	–	–	±	+	–	±
Truncal Rash	–	± ^{**}	+++	+++	–	–
Hepatomegaly	±	+ [†]	–	–	–	±
Splenomegaly	+	+	–	–	–	±
Arthritis	–	–	–	+++	–	–
Laboratory tests						
Leukopenia	–	–	+++	+	±	±
Relative lymphopenia	+	+	++	+++	++	–
Atypical lymphocytes	+	–	+	±	±	±
Thrombocytopenia	+	–	+++	–	+	–
Highly elevated ESR	+++	–	–	–	–	–
Mild/moderately elevated LDH	+++	–	±	±	±	–
Mild/moderately elevated AST/ALT	+	+	+	+	+	+++ ^{‡‡}

* During malarial paroxysm, but not between attacks.

** Rose spots.

† Tender hepatomegaly.

†† Intense pruritis with late desquamation of palms/soles.

‡ Often marked lymphocytosis.

‡‡ Early, but highly elevated later.

testing for acute viral hepatitis. Her IgM anti-HAV was markedly elevated, confirming the diagnosis of acute hepatitis A infection.

Discussion

This case presented a diagnostic dilemma as a febrile traveler with leukopenia, atypical lymphocytosis, elevated LDH and splenomegaly as hepatitis A is often neglected in the differential diagnosis of returned torpical travelers. The presentation is interesting for several reasons as the serum aminotransferases were not substantially elevated at the time of presentation, atypical lymphocytosis in HAV infection is not usual and splenomegaly is not generally a feature of acute hepatitis A infection. In this case, unless a combination of infections were present simultaneously, the presentation of acute HAV infection was particularly atypical. HAV infection should always be in the differential diagnosis of travelers returning from high risk areas even with initially minimally elevated aminotransferases. Later during hospitalization her serum transaminases became highly elevated, i.e., AST was 1757 IU/L and ALT was 1375 IU/L prompting testing for hepatitis. Her HAV IgM titer was >400 mg/dl ($n = <300$ mg/dl), confirming the diagnosis of acute HAV. This case is interesting for several reasons. Firstly, HAV is often forgotten in the DDx of returning travelers. Secondly, serum transaminases are usually highly elevated early, which was not the case here. Thirdly, she had splenomegaly which is not usually a feature of HAV. Furthermore, atypical lymphocytes are unusual in HAV. HAV may mimic other infections if unusual clinical laboratory findings are present as was the case here, e.g., splenomegaly, atypical lymphocytes, decreased hemoglobin/hematocrit and elevated LDH [3,5]. If the diagnosis remains unclear, serial non-specific tests may, during hospitalization, suggest the correct diagnosis and prompt specific testing [1,8]. We conclude

that HAV should always be in the DDx of febrile returning travelers even with initially minimally elevated transaminases.

Author contributions

All authors were involved equally in the editing and writing

Conflicts of interest

None of the authors have conflicts of interest to declare.

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