93

A 35-Year-Old Male Logger from Peru With Fever, Jaundice and Bleeding

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Clinical Presentation

History

A 35-year-old Peruvian man is referred to a hospital in Lima. Eight days prior, he developed fever and retro-orbital headache. Two days into the illness he was admitted to a local hospital in the jungle after he had developed jaundice, coffee-ground vomiting, gross haematuria and increasing mental obtundation. During the transfer to the referral hospital in Lima the patient had a generalized seizure. His past medical history included hepatitis of unknown aetiology 20 years before.

The patient was born in Lima, but for the past 5 years has been working as a logging supervisor in a remote jungle area near Pucallpa on the shores of the Ucayali River (which joins the Marañón to form the Amazon river). He has not taken any malaria prophylaxis and has not received any vaccinations since his early childhood.

Clinical Findings

Temperature 38.8°C (101.8°C), blood pressure 110/70 mmHg, heart rate 110 beats per minute, respiratory rate 24 breaths per minute. He is agitated, unresponsive to verbal commands and intermittently stuporous. There is marked flapping of hands, no focal neurological signs and no meningeal signs. He is jaundiced, and there is spontaneous bleeding of his oral mucosa and at venipuncture and IV sites. There are multiple large ecchymoses on the face, the trunk and all limbs (Fig. 93.1). On auscultation of the lungs there are crepitant rales in both bases. The heart sounds are normal. The liver is felt 3 cm below the right costal margin; the spleen is not palpable and there is no lymphadenopathy.

Laboratory Results

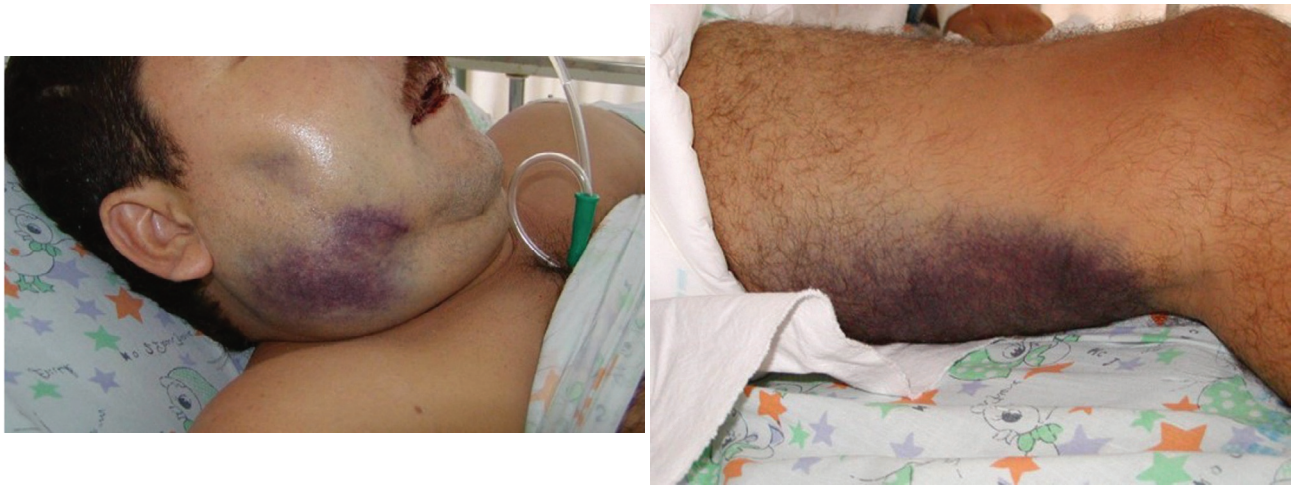
His routine laboratory results on admission are shown in Table 93.1. His malaria thick film is three times negative. Blood cultures are negative. Brucella serology is negative. Hepatitis B IgM anti-Hbc are negative.

TABLE 93.1 Laboratory Results on Admission

Parameter	Result (Reference Range)
Haematocrit	30% (41–53)
White cell count	8700/μL (4500–11000) Bands: 4% (0–10) Neutrophils: 62% (40–70) Eosinophils: 0% (0–8) Basophils: 0% (0–3) Monocytes: 6% (4–11) Lymphocytes: 28% (22–44)
Platelets	110000/μL (150000–450000)
AST (GOT) ALT (GPT)	2890 U/L (0–35) 2676 U/L (0–35)
AP	496 U/L (38–126)
Total Bilirubin Direct Bilirubin	11.6 mg/dL (0.3–1.2) 9.2 mg/dL (0–0.4)
Urea Creatinine	89 mg/dL (17–49) 1.2 mg/dL (0.6–1.2)
Glucose	80 mg/dL (70–110)
Serum Protein Albumin	4.2 g/L (5.5–8.0) 2.8 g/L (3.5–5.5)
Prothrombin Time INR aPTT	17 s (11.1–13.1) 2.6 (0.9–1.3) 80 s (22.1–35.1)
Fibrinogen	250 mg/dL (150–400)
CK	6200 U/L (52–336)
Urine	Proteins 3+, RBC: 50–60/f, WBC: 4–6/f

Questions

1. What is your differential diagnosis?
2. What tests will you do to confirm the diagnosis?



• **Fig. 93.1** Extended ecchymoses in a febrile Peruvian logger with fever and jaundice

Discussion

A young male Peruvian logger working in the South American jungle presents with fever, jaundice, bleeding, encephalopathy and seizures. Laboratory results indicate liver failure.

Answer to Question 1

What is your differential diagnosis?

This patient presents with an acute febrile illness that produces liver failure. Severe malaria is a possibility, although transaminases are usually not so high. The differential diagnosis includes viral hepatitis (A, B, C, D, and E) and toxin-mediated hepatitis.

Leptospirosis seems possible, but the transaminases in leptospirosis are usually only mildly elevated (less than 200 U/L) and jaundice is caused by cholestasis rather than hepatocellular damage. Typhoid fever and brucellosis are other bacterial infections to be taken into account.

Severe dengue has to be considered, although 8 days of fever appears long for dengue and usually jaundice is not so prominent. Also, haematocrit would be increased rather than low, as in this case.

Other viral haemorrhagic fevers (VHFs) with jaundice are possible, particularly given his occupation as a logger in the Peruvian jungle with possible contact to sylvatic mosquitoes and animals. The most prominent VHF in Peru is yellow fever and he does not appear to be vaccinated against this disease.

Answer to Question 2

What Tests Will You Do to Confirm the Diagnosis?

Serial thick blood smears for malaria should be ordered.

Dengue NS1 and dengue IgM should be performed (because NS1 might have turned negative after more than 1 week of illness).

Blood cultures should be done to look for *Brucella* species, as well as *S.* Typhi and *S.* Paratyphi. If brucellosis is suspected, microbiologists must be informed because specimens have to be handled under special biosafety precautions to prevent laboratory infections.

If available, PCR of urine and blood should be done to look for leptospirosis; microscopic agglutination test is an alternative if PCR is not available.

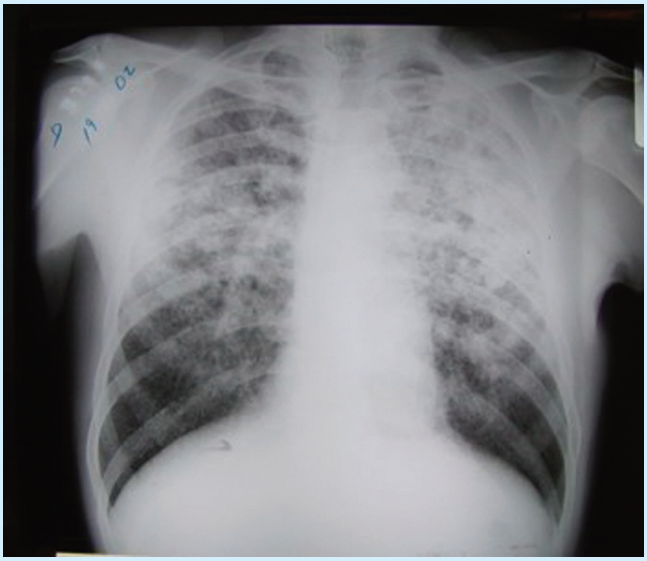
Laboratory tests should include IgM antibodies for the different viral hepatitis viruses (except for acute hepatitis D because of delayed antibody production).

IgM antibodies against the yellow fever virus persist for several weeks and can be detected by various methods, e.g. IgM capture ELISA. Detection of viral RNA by RT-PCR could also be attempted.

The Case Continued…

The patient received presumptive treatment for malaria, broad-spectrum antibiotics, and supportive care. Over the next 3 days, he developed increasing hepatic encephalopathy, renal failure, coma, and DIC with increasing spontaneous bleeding. The chest x-ray showed bilateral pulmonary infiltrates compatible with ARDS (Fig. 93.2). Repeat laboratory results on day 3 showed deterioration of his kidney function (creatinine 6.5 mg/dL, urea 120 mg/dL) and a sudden drop in his liver transaminases (AST 100 U/L, ALT 200 U/L), most likely indicating acute hepatic disintegration. Sadly, the patient passed away 1 day later.

IgM capture ELISA for yellow fever came back highly positive at 1:10 000. Anti-dengue IgM was negative. Direct viral isolation in culture was negative on a blood specimen drawn on admission (8 days into the illness), which is not surprising because viraemia in yellow fever is short (4–5 days). Permission for autopsy was refused, therefore liver histology was not available.



• **Fig. 93.2** Chest x-ray of the patient showing bilateral patchy infiltrates.

SUMMARY BOX

Yellow Fever

Yellow fever is and arboviral infection caused by a flavivirus and transmitted by Aedes and Haemagogus mosquitoes. It is endemic in South and Central America and in Africa. There is no yellow fever in Asia.

The incubation period of yellow fever is usually 3 to 6 days. Most cases are subclinical or show mild and non-specific symptoms. After an acute febrile illness with headache and myalgia without a rash that likely represents the peak viraemia, there may be a period of remission, as seen in other flaviviral infections. Fever may then resume joined by back pain, nausea, vomiting and altered mental status progressing to the severe clinical syndrome described above. Haematemesis is commonly described. In fatal cases, death usually occurs 7 to 10 days into the illness.

Yellow fever causes an infection of hepatocytes and Kupffer cells. There is mid-zonal hepatocellular necrosis with a minimal inflammatory response. Councilman bodies and microvesicular fatty changes are seen. The sudden and marked decrease of hepatic transaminases in our patient just before death likely represented near total destruction of functioning hepatocytes and acute hepatic disintegration.

As with other flaviviruses there is no specific treatment for yellow fever, making prevention by use of the 17D live yellow fever vaccine imperative. Vaccine efficacy in immunocompetent persons is at nearly 100%. While most individuals in endemic areas (Amazon basin and sub-Saharan Africa) have poor access to vaccines and there are regular shortages during yellow fever epidemics there is dramatic under-use of the vaccination by travellers and expatriates. Data indicates that the number of unvaccinated travellers visiting risk areas is substantial. Each year, deaths in unvaccinated travellers to yellow fever endemic areas are reported.

Further Reading

1. Blumberg L, Enria D, Bausch DG. Viral haemorrhagic fevers. In: Farrar J, editor. Manson's Tropical Diseases. 23rd ed London: Elsevier; 2013 [chapter 16].
2. Monath TP, Vasconcelos PFC. Yellow fever. J Clin Virol 2015; 64:160–73.
3. Quaresma JAS, Pagliari C, Medeiros DBA, et al. Immunity and immune response, pathology and pathologic changes: progress and challenges in the immunopathology of yellow fever. Rev Med Virol 2013;23(5):305–18.
4. Visser LG. Fractional-dose yellow fever vaccination: how much can we do less? Curr Opin Infect Dis 2019;32(5):390–93.
5. Reno E, Quan NG, Franco-Paredes C, et al. Prevention of Yellow Fever in travellers: an update. Lancet Infect Dis 2020;20(6): e129–37.