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A 28-Year-Old Woman from Sierra Leone With Fever and Conjunctivitis

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Clinical Presentation

History

A 28-year-old woman presents to a small rural hospital in eastern Sierra Leone with a 6-day history of fever, weakness, sore throat and retrosternal chest pain. She has had loose stools twice a day for the past 2 days. She was seen in a local health post the day before admission and given a course of artemether with amodiaquine and amoxicillin, but she had continued to get worse on this. Her examination was unremarkable except some mild pharyngitis. On arrival in hospital she was treated with IV ceftriaxone and she completed the course of her antimalarial medications. Her malaria slide was negative. She remained on this treatment for 2 days but continued to get worse.

On the second day after admission she develops conjunctivitis. By this stage she is very unwell and is unable to walk unaided. She has developed a cough and breathlessness.

Physical Examination

Axillary temperature 38.2°C (100.8°F), blood pressure 80/55 mmHg, pulse rate 100 bpm. On chest auscultation she has bilateral fine crepitations.

Investigations

Her chest radiograph reveals diffuse bilateral infiltrates. Blood chemistry shows mild renal impairment and raised transaminases (aspartate transaminase (AST/GOT) 514 U/L (<50 U/L)).

Questions

1. What is the differential diagnosis?
2. What tests would you do and how would you manage the patient?

Discussion

A young Sierra Leonean woman has a severe febrile illness with pharyngitis, conjunctivitis and chest involvement. She deteriorates on broad-spectrum antibiotics and antimalarials.

Answer to Question 1

What is the Differential Diagnosis?

Adenovirus infections can cause conjunctivitis and pharyngitis but these are normally mild. Also, measles presents with fever, cough, coryza and a striking conjunctivitis. It may also cause pneumonitis, but at this stage you would expect to see a rash.

Mycoplasma pneumoniae can cause a pharyngitis and pneumonia but is rarely severe. Other forms of pneumonia are possible but do not normally cause conjunctivitis.

Leptospirosis can start with a non-specific febrile illness. Pulmonary involvement including haemorrhages is common and it can cause renal impairment. Patients with severe leptospirosis tend to present with conjunctival suffusions rather than with conjunctivitis.

Typhoid can present as a non-specific febrile illness. You would expect the patient to eventually improve on ceftriaxone, but prolonged clinical courses in typhoid are not uncommon. Pharyngitis and conjunctivitis are usually not part of the clinical picture.

Lassa fever is quite common in Eastern Sierra Leone, accounting for 16–20% of hospital admissions in some studies. All the signs and symptoms the patient has are consistent with Lassa fever.

Answer to Question 2

What Tests Would You do and How Would You Manage the Patient?

Lassa fever is a serious disease. It has caused nosocomial outbreaks in which many medical staff have died. Therefore all procedures should be done with caution and the possibility

• **Fig. 74.1** Endemic areas for Old World arenaviruses. Only the two arenaviruses known to cause haemorrhagic fever, Lassa and Lujo, are shown. Countries where clinical cases of Lassa fever have been confirmed are depicted in green. Indirect evidence, such as anecdotal reports or seroprevalence data, exists for most of the other countries in West Africa, shown in red. Endemic countries for Lujo virus are shown in blue. Incidence and risk of disease may vary significantly within each country. (Adapted from Farrar, J., Hotez, P., Junghanss, T., et al., 2013. Manson's Tropical Diseases. In: Farrar, J. (Ed.) 23rd ed. Elsevier, London. Fig. 16.2. Pp. 177)

of Lassa fever should always be discussed with the laboratory. All specimens should be transported in sealed plastic containers.

Serological and PCR tests are available for the diagnosis of Lassa fever, and an antigen-based rapid point-of-care test has been licensed.

PCR tests are the most sensitive but are not available in most African countries. Antigen tests demonstrate the presence of the disease but may not detect low levels of the virus, especially if taken in the first days of illness. IgM antibody tests can show a high rate of false positive tests and may be hard to interpret.

The patient needs to be isolated until the results of the Lassa fever tests are known. Because the infection spreads through contact with blood or body fluids, the use of goggles, masks, double gloves and disposable (waterproof) surgical gowns is recommended when handling the patient until the diagnosis of a viral haemorrhagic fever has been ruled out. The patient should be isolated in a side room, which should ideally have an area outside for decontamination (i.e. removing potentially contaminated clothing). Needles and sharps should be handled with care by experienced staff. After significant occupational exposure to the bodily fluid of a patient with Lassa fever such as a needlestick injury, post-exposure prophylaxis with oral ribavirin should be considered.

The treatment for Lassa fever is with IV ribavirin, which is expensive and not commonly available. It seems to improve survival, particularly when given during the first 6 days of symptomatic disease, but the quality of studies on this are poor.

The Case Continued…

The diagnosis of Lassa fever was confirmed with antigen testing and the patient received IV ribavirin in a specialist isolation unit. Unfortunately, the patient was already very unwell by this stage and died 2 days later. All of the patient's family, close friends and medical staff were interviewed to determine whether they had had contact with the patient. All contacts were advised to monitor their temperature and seek medical help if they became unwell within 21 days of the contact.

SUMMARY BOX

Lassa Fever

Lassa fever is a severe systemic disease caused by infection with an arenavirus. It is a zoonosis of rats of the genus *Mastomys* and infections in humans are likely to result from contact with infected rat urine. Lassa fever is common in Liberia, Sierra Leone, Ghana and Nigeria, although it probably occurs in a much larger area of sub-Saharan West Africa (Fig. 74.1). Cases have been imported to Europe from other countries such as Mali, Côte d'Ivoire and Togo. There are up to 300 000 cases estimated a year with 5000 deaths, although the confidence limits of this estimate are likely to be very broad.

Most cases are thought to be mild and patients may not even present to a health facility; but in hospitalized patients, the case fatality rate may be as high as 20%. Lassa fever is more severe in pregnant women, with a higher case fatality rate in the third trimester. It frequently results in premature labour or spontaneous abortion and about 90% of fetuses of women infected with Lassa fever die.

The incubation period is 3 to 21 days. In individuals who are not pregnant the disease normally starts insidiously with fever, body aches and weakness. Sore throat and retrosternal chest pain are common, as are vague abdominal symptoms such as pain, diarrhoea and vomiting. Cough and breathlessness may occur in some patients. Conjunctivitis is common, especially late in the disease. Frank bleeding is rare. Raised liver transaminases are markers of severity and are associated with a higher case fatality rate.

Serological and PCR tests are available for the diagnosis of Lassa fever, and antigen-based rapid point-of-care tests have been licensed, although more testing on the sensitivity for different strains is needed.

Because Lassa fever is common, it should be considered in anyone with an unexplained febrile condition who has visited an endemic area within the past 21 days and appropriate infection control precautions should be implemented. It is more common in people from rural than urban areas, but it does occur in towns. Treatment with IV ribavirin is likely to be beneficial if given early in the disease, but it should also be considered in patients who are diagnosed late.

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].
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