CASE REPORT

Visceral leishmaniasis in an infant following a holiday trip to Spain

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SUMMARY

Imported leishmaniasis is rare in non-endemic countries such as the UK. Visceral leishmaniasis (VL) can be life-threatening and its recognition is imperative for successful clinical management. We present a case of VL in an 11-month-old infant several months after returning from a 1-week holiday trip to the South of Spain. The infant suffered from intermittent fever for 5 weeks, and hepatosplenomegaly and pancytopenia, and was successfully treated with a short course of liposomal amphotericin B. This case of VL is to highlight the possibility of transmission of unusual pathogens when travelling to the Mediterranean and therefore the importance of taking a detailed travel history. VL should be considered in the differential diagnosis in returning travellers presenting with prolonged fever, hepatosplenomegaly and/or pancytopenia.

BACKGROUND

Visceral leishmaniasis (VL) is a well-known entity in endemic countries but rarely imported to non-endemic countries and therefore often diagnosed late. VL can occur several months following travel to endemic countries such as the Mediterranean, and should therefore be considered in any child presenting with prolonged fever, hepatosplenomegaly and/or pancytopenia.

CASE PRESENTATION

An 11-month-old girl presented to a district general hospital with an isolated history of intermittent fever for 5 weeks. The girl was normally healthy, as were her Caucasian parents and 6-year-old sister. She was fully immunised. Seven months previously, the family spent 1 week on holiday in the Malaga region of Spain. Physical examination revealed only pallor and hepatosplenomegaly, without lymphadenopathy.

INVESTIGATIONS

On admission, blood results showed severe anaemia (haemoglobin concentration 5.4 g/dL), leucopenia and neutropenia (white cell count $3.5 \times 10^9/L$, neutrophils $0.8 \times 10^9/L$), and thrombocytopenia (platelets $77 \times 10^9/L$). C reactive protein was raised (93 mg/L) and other biochemical tests revealed mild hypernatraemia (131 mmol/L), hypoalbuminaemia (27 g/L) and hyperferritinaemia (1220 ng/mL). Blood film confirmed severe pancytopenia and was negative for malaria parasites and lymphoblasts. The infant was admitted and started on intravenous piperacillin/tazobactam. Two blood cultures taken before, and 3 days into

antibiotic treatment, did not grow any organisms. Over the course of the following week, the infant remained febrile and had progressive pancytopenia (haemoglobin concentration 4.7 g/dL, white cell count $2.0 \times 10^9/L$, neutrophils $0.3 \times 10^9/L$, platelets $53 \times 10^9/L$). Subsequently, she was given a red cell and platelet transfusion.

One week after the initial presentation the infant was transferred to a tertiary hospital. Blood tests performed at this stage showed increasing ferritin concentrations (7680 ng/mL), hypertriglyceridemia (4.74 mmol/L), hypofibrinogenaemia (1.4 g/L), a mildly elevated alanine aminotransferase level (60 IU/L) and pancytopenia. Careful examination of a bone marrow aspirate demonstrated activated macrophages with intracellular and extracellular amastigotes (figure 1A) in a normocellular but reactive marrow with some minor degree of erythrophagocytosis. The infant was subsequently started on empiric therapy with liposomal amphotericin B. PCR of bone marrow material confirmed presence of *Leishmania donovani* complex DNA, and antibody testing to K39 antigen and Leishmaniasis serology were both strongly positive.

DIFFERENTIAL DIAGNOSIS

This infant presented with prolonged fever of unknown origin, hepatosplenomegaly and pancytopenia. Paediatricians often see children with prolonged fever and there are many possible causes. The differential diagnoses can be narrowed down when organomegaly and pancytopenia are present and most likely include infectious causes (bacterial, parasitic or viral) and haematological diseases (acute leukaemia, haemophagocytic lymphohistiocytosis).¹

TREATMENT

Following confirmation of the diagnosis, the infant continued liposomal amphotericin B, the recommended treatment for VL, at 3 mg/kg, for five consecutive days followed by a single dose of 3 mg/kg 6 days later.²

OUTCOME AND FOLLOW-UP

The fever settled within 4 days of initiating therapy, and the infant's haematological and biochemical markers improved by the end of the treatment course. Long-term follow-up was unremarkable.

DISCUSSION

Leishmaniasis is an infection caused by the parasite *Leishmania*, which is transmitted to humans by the bite of phlebotomine sand flies. Leishmaniasis is considered a neglected tropical disease found in

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Figure 1 (A) Stained bone marrow aspirate smear. Amastigotes are seen inside of macrophages (black arrow) but also in the extracellular matrix (white arrow). In addition to a nucleus, each amastigote has a rod-shaped kinetoplast (red arrow). (B) Map showing the estimated annual incidence of VL in Europe.³

many parts of the tropics, subtropics and the Mediterranean (figure 1B).³ Imported Leishmaniasis is rare despite increasing numbers of international travellers to endemic areas.¹ VL (or 'kala-azar') is the most severe form of the disease and can be life-threatening. The incubation period is usually 2–6 months but may be years. Diagnosis is made by detecting *Leishmania* amastigotes (or DNA) from infected tissue (bone marrow or spleen), and is supported by serology. Once diagnosed, it is relatively easy to treat with few side effects of the currently used medication and with good long-term outcome.

Learning points

- ▶ Imported leishmaniasis is rare in non-endemic countries such as the UK.
- ▶ Transmission of unusual pathogens is possible when travelling for a short holiday to the Mediterranean and therefore taking a detailed travel history is very important.
- ▶ Visceral leishmaniasis should be considered in the differential diagnosis in any travellers returning from endemic countries presenting with prolonged fever, hepatosplenomegaly and/or pancytopenia.

Between 1999 and 2008, only 59 cases of VL were reported in England, Wales and Northern Ireland.⁴ In non-endemic countries, such as the UK, the management of leishmaniasis is challenging mainly because of delayed diagnosis and inappropriate treatment.¹

Contributors All authors cared for the patient. JT drafted the initial manuscript, which was subsequently revised by the other authors. All authors approved the final version of the manuscript.

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