Fourth case of louse-borne relapsing fever in Young Migrant, Sicily, Italy, December 2015. Mini Review Article


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ABSTRACT

Objectives: Currently louse-borne relapsing fever (LBRF) is primarily found in limited endemic foci in Ethiopia, Somalia and Sudan; no case of imported LBRF has been reported in Europe in the 9 years prior to 2015. The aim of our paper is to describe a new case of imported LBRF detected in Sicily, Italy, and to review all cases reported in migrants arrived in Europe in the last 10 years.

Study design: Mini review of all published cases of louse-borne relapsing fever in Europe in the last 10 years.

Methods: A computerized search without language restriction was conducted using PubMed combining the terms ‘(louse-borne relapsing fever or LBRF or recurrentis) and (refugee or Europe or migrant)’ without limits. Furthermore, the ‘Ahead-of-Print Articles’ of the top 10 journals (ranked by Impact factor – Web of Science) of Infectious diseases and of Epidemiology were checked.

Results: Our search identified 26 cases of LBRF between July and October 2015 in migrants recently arrived in Europe: 8 had been described in Italy; 1 in Switzerland; 2 in the Netherlands; 15 in Germany. We describe data regarding the clinical characteristics, diagnostic methods, therapy and outcome of these patients and of the new case.

Conclusions: LBRF by Borrelia recurrentis should be considered among the clinical hypotheses in migrants presenting with fever, headache, chills, sweating, arthralgia, myalgia, dizziness, nausea and vomiting.

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Introduction

Louse-borne relapsing fever (LBRF) is a vector-borne disease caused by infection with Borrelia recurrentis, a human-restricted spirochaeta transmitted by the body louse Pediculus humanus humanus.1 Transmission of infection occurs when a louse is accidentally squished and the patient then rubs the spirochaetes into his eyes or mouth. LBRF must be
distinguished from tick-borne relapsing fever (TBRF) that is caused by several Borrelia species transmitted to humans by the bite of soft ticks of the genus Ornithodoros. TBRF is characterized by recurrent bouts of fever, headache, and malaise. B. recurrentis is closely related to Borrelia duttonii, one of the 23 species of Borrelia currently implicated in TBRF, both are human specific unlike the other Borrelia which have an animal host.

In the first half of the twentieth century, major outbreaks of LBRF occurred in Eastern Europe, the Balkans, former Soviet Union and Africa, linked with periods of war and famine. The geographical distribution of LBRF has reduced due to improvements in living standards. Currently, the disease is primarily found in limited endemic foci in Ethiopia, but also in Somalia and Sudan where, according to recent studies, LBRF is among the top 10 causes of hospital admission nowadays.4,12 LBRF can be severe and death occurs in 10%–40% of cases in the absence of appropriate treatment, and in 2%–5% of treated patients.13 The aim of our paper was to describe a case of imported LBRF detected in Sicily, Italy, and to review all published cases of LBRF by B. recurrentis reported in migrants arrived in Europe in the last 10 years. We underline the epidemiology of this potentially re-emerging and serious disease in the context of a recent increase in refugees from East Africa travelling to Europe.

Methods

To review all cases of LBRF by B. recurrentis reported in migrants arrived in Europe in the last ten years a computerized search without language restriction was conducted using PubMed combining the terms ‘louse-borne relapsing fever or LBRF or recurrentis’ and ‘refugee or Europe or migrant’ without limits. Furthermore, the ‘Ahead-of-Print Articles’ of the top 10 journals (ranked by Impact factor – Web of Science) of Infectious diseases and of Epidemiology were checked.

Results

A 26-year-old man from Somalia who arrived in Lampedusa, Sicily, Italy, on December 24, 2015 was admitted to the University Hospital of Palermo 2 days later because of high fever, headache, and general malaise, which developed 2 days after his arrival. Blood analyses showed increased aspartate aminotransferase and alanine aminotransferase levels (263 U/l and 115 U/l), mild anaemia (haemoglobin level 10.8 g/l), elevated C-reactive protein (74.9 mg/dl), elevated creatinine (4.72 mg/dl) and blood urea nitrogen levels (132 mg/dl). Antigen-based malaria rapid diagnostic tests were negative, blood cultures were performed, and doxycycline 100 mg twice a day and intravenous hydration for 10 days. The patient recovered after treatment with doxycycline (100 mg/twice a day) and intravenous hydration for 10 days.

Our search identified five publications reporting 26 cases of LBRF between July and October 2015 in migrants recently arrived in Europe: eight had been described in Italy (three in Sicily and five in Piedmont); one in Switzerland; two in the Netherlands; 15 in Germany (Bavaria).3,4,10,11,12 Data regarding the clinical characteristics, diagnostic methods, therapy and outcome of these patients and of the new case we report, are analytically listed in Table 1.

The majority of cases (21) involved Somali people, five cases Eritrean people, one case an Ethiopian patient. The most frequent migration route chosen by migrants was that from East Africa, through Sudan and Libya, to North Africa and eventually Europe. Travel duration ranged from a few weeks to 1 year and all migrants reported to have been exposed to very poor and overcrowded living conditions during travel. Two patients, among those described in Italy, were long-term residents in Italy, and they denied recent travel to Africa, so they probably acquired the infection sharing the same house of the newly arrived refugees. In 12 of the 17 patients with available information, onset of symptoms was after arrival in the country of destination. All the patients were young and male.

Infestation with lice was present in seven cases and two patients had head lice. All the cases had similar clinical presentation characterized by malaise, fever, headache, myalgia; five had vomiting and three abdominal pain; only one patient was afebrile. The outcome was good in all but one case who died of multi-organ failure after initiation of antibiotic therapy despite intensive care treatment.

In all cases found in the literature the diagnosis was based on clinical symptoms and visible spirochaetes on Giemsa stained blood films. PCR targeting 16S rRNA, flab, and glpQ followed by sequencing confirmed cases as being caused by B. recurrentis. All patients except one received antibiotic treatment with doxycycline and 12 cases doxycycline plus ceftriaxone. Jarisch-Herxheimer reaction (JHR) occurred in 15 (58%) patients.

Discussion

LBRF by B. recurrentis is a recurrent febrile illness with variable periods of apyrexia between the febrile episodes, accompanied by non-specific symptoms as headache, arthralgias and myalgias. Hence, presentation of LBRF may resemble many other serious infections as malaria, leptospirosis, tick-borne recurrentis fever, typhoid fever.

Our research shows that cases of imported LBRF have only been reported since July 2015. This can be explained by the massive increase of refugees from LBRF-endemic areas since 2014.

From 2014 significant changes in migratory flows from Libyan coast to Sicily have been observed. In the past, most migrants came from Nigeria, Ghana, Senegal and other countries of West Africa, nowadays, migratory flow mostly come from East Africa (Ethiopia, Somalia, and Eritrea). Accordingly, LBRF by B. recurrentis should be considered among the clinical hypotheses in migrants
<table>
<thead>
<tr>
<th>Country (ref) (note)</th>
<th>Age/sex</th>
<th>Country of origin</th>
<th>Clinical picture</th>
<th>Infestation with lice</th>
<th>Onset of Symptoms</th>
<th>Microbial Diagnosis</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy (Ciervo et al. 2016) 3</td>
<td>17/M</td>
<td>Somalia</td>
<td>Fever Arthralgia Myalgia Confusion Thrombocytopenia Anaemia</td>
<td>Yes (head lice)</td>
<td>After arrival (2 days before hospital admission)</td>
<td>Microscopy, NAT</td>
<td>Doxycycline plus ceftriaxone</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>18/M</td>
<td>Somalia</td>
<td>Fever Arthralgia Myalgia Thrombocytopenia Anaemia Hypoponeraemia</td>
<td>Yes (head lice)</td>
<td>After arrival (3 days before hospital admission)</td>
<td>Microscopy, NAT</td>
<td>Doxycycline plus ceftriaxone</td>
<td>Good</td>
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<tr>
<td></td>
<td>13/M</td>
<td>Somalia</td>
<td>Fever Headache Skin lesions Thrombocytopenia Anaemia</td>
<td>ND</td>
<td>After arrival (5 days before hospital admission)</td>
<td>Microscopy, NAT</td>
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</tr>
<tr>
<td>Switzerland (Goldenberger et al. 2015) 3</td>
<td>NR/M</td>
<td>Eritrea</td>
<td>Fever Nausea Headache Bilateral flank pain Anaemia Thrombocytopenia Anaemia</td>
<td>ND</td>
<td>After arrival (12 days before hospital admission)</td>
<td>Microscopy, NAT</td>
<td>Doxycycline plus ceftriaxone</td>
<td>Good</td>
</tr>
<tr>
<td>Netherlands (Wilting et al. 2015) 2</td>
<td>NR/M</td>
<td>Eritrea</td>
<td>Headache Dizziness Right upper quadrant pain Myalgia Fever Anaemia Thrombocytopenia</td>
<td>Yes</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Ceftriaxone switched in doxycycline</td>
<td>JHR</td>
</tr>
<tr>
<td></td>
<td>NR/M</td>
<td>Eritrea</td>
<td>Headache Fever Cough Elevated transaminases</td>
<td>ND</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Doxycycline</td>
<td>JHR</td>
</tr>
<tr>
<td>Country of Residence</td>
<td>Age</td>
<td>Symptoms</td>
<td>Diagnosis</td>
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<td>Outcome</td>
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<tr>
<td>Italy (Lucchini et al. 2016)</td>
<td>20/M</td>
<td>Somalia</td>
<td>Fever, Vomiting, Headache, Thrombocytopenia</td>
<td>ND</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Doxycycline</td>
<td>JHR</td>
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<td></td>
<td>20/M</td>
<td>Somalia</td>
<td>Fever, Vomiting, Abdominal pain, Headache, Cough, Thrombocytopenia</td>
<td>ND</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Doxycycline plus ceftriaxone</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>26/M</td>
<td>Somalia</td>
<td>Fever, Headache, Myalgia, Chest pain, Itching, Thrombocytopenia</td>
<td>ND</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Doxycycline switched to ceftriaxone</td>
<td>JHR</td>
</tr>
<tr>
<td></td>
<td>27/M</td>
<td>Somalia</td>
<td>Fever, Vomiting, Headache, Myalgia, Lumbar pain, Severe thrombocytopenia</td>
<td>ND</td>
<td>In Italy since 2011</td>
<td>Microscopy, NAT</td>
<td>Doxycycline</td>
<td>Good</td>
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<tr>
<td></td>
<td>31/M</td>
<td>Somalia</td>
<td>Fever, Abdominal pain, Vomiting, Diarrhoea, Headache, Thrombocytopenia, Elevated transaminases, Elevated transaminases</td>
<td>ND</td>
<td>In Italy since 2012</td>
<td>Microscopy, NAT</td>
<td>Doxycycline</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>Present case</td>
<td>26/M</td>
<td>Somalia</td>
<td>Fever, Thrombocytopenia, Headache, Acute renal failure</td>
<td>ND</td>
<td>After arrival</td>
<td>Microscopy, NAT</td>
<td>Doxycycline</td>
</tr>
</tbody>
</table>

ND: not detected; NAT: nucleic acid test; JHR: Jarisch–Herxheimer reaction.
presenting with fever, headache, chills, sweating, arthralgia, myalgia, dizziness, nausea and vomiting.\(^5\)

Thin and thick blood smears are the gold standard diagnostic technique for relapsing fever as for malaria and should be performed at admission before starting antibiotic therapy. In our case the blood smear was negative for spirochaetes probably because the patient had received one dose of doxycycline.

Nucleic acid detection of Borrelia is carried out in research settings and can be used to support the clinical diagnosis.\(^2,6,7\) Regarding treatment, penicillins and tetracyclines, usually in a single dose, are the antibiotics of choice for LBRF. Outcome is usually good if prompt antibiotic treatment is administered. Anti-spirochaetes therapy is often associated with the potentially lethal JHR. JHR is a transient immunological phenomenon seen commonly in patients during treatment for infection by spirochaetes, and it manifests clinically with short-term constitutional symptoms such as fever, chills, headache and myalgias, besides exacerbation of existing cutaneous lesions. In our review 15 out of 27 (58\%) patients developed JHRs during treatment and most of them had been treated with doxycycline. Of note, a recent meta-analysis of five randomized controlled trials, performed in Ethiopia, comparing the rate of JHRs in patients with LBRF, treated with either penicillin or tetracycline, showed a significant benefit in favour of penicillin.\(^9\)

In consideration of the increasing number of refugees from LBRF-endemic areas observed in Europe since 2014, early detection, notification, and timely implementation of public health measures are needed in order to reduce the risk of outbreaks.

REFERENCES


Author statements

Ethical approval

Ethical approval was not required.

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There was not any financial support for this research.

Competing interests

Authors declare that they have no competing interest.