RAPID COMMUNICATIONS

Louse-borne relapsing fever (*Borrelia recurrentis*) diagnosed in 15 refugees from northeast Africa: epidemiology and preventive control measures, Bavaria, Germany, July to October 2015

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We report 15 imported louse-borne relapsing fever (LBRF) cases in refugees in Bavaria, Germany. One patient died. Epidemiological findings confirmed that all were young males from the Horn of Africa (12 from Somalia), who had similar migration routes converging in Sudan continuing through Libya and Italy. The majority likely acquired their infection during migration. Healthcare workers should be aware of LBRF in refugees passing through north Africa to ensure correct treatment and preventive measures.

From July 2015 until October 2015, Louse-borne relapsing fever (LBRF) was diagnosed in 15 refugees originating from the Horn of Africa and arriving in Bavaria, southern Germany, presenting with fever. The main travel route included Sudan, Libya and Italy. In this rapid communication, microbiological confirmation, simple first-line epidemiologic assessment and preventive control measures in relation to these cases are described.

Case investigation

In all cases, a preliminary diagnosis was established by clinicians based on clinical symptoms and visible spirochetes in Giemsa stained blood films The German National Reference Centre (NRC) for Borrelia in Oberschleißheim was contacted directly by clinicians for confirmation. Microbiological confirmation of LBRF from EDTA blood included: Dark field microscopy (Leitz Dialux 20 microscope, Leitz, Germany, objective 40, occular 10) and PCR targeting 16S rRNA, *flab*, and *glpQ* followed by sequencing [1-3].

Blood samples were used for in vitro cultures in modified Kelly-Pettenkofer (MKP) medium [4]. A case was regarded as confirmed when sequencing revealed *B. recurrentis*.

Because of a potentially high public health relevance, i.e. establishment of local foci of louse-borne transmission in refugee facilities, treating hospitals and spill over to the local population, epidemiological data to establish preventive measures are of utmost importance. Therefore a standardised questionnaire for case investigations and interviews was developed, distributed and evaluated by the Bavarian Task-Force Infectiology and International Health Regulations. Interviews were performed by public health physicians of local public health agencies as part of the official investigation of infectious diseases of public health concern according to the German federal law, and with the help of an interpreter. The interviews were performed in a hospital setting and by taking into consideration potential emotional and psychological trauma of refugees. Anonymised data were used for further analysis. When interviewing was not possible, information was retrieved from medical records, if available. A leaflet informing about clinical presentation, epidemiology, diagnostics as well as preventive control measures, was developed and sent to clinicians and public health authorities to raise general awareness.

FIGURE 1

Travel routes of cases of imported louse-borne relapsing fever in refugees from northeast Africa to Bavaria, Germany, July–September 2015 (n=7ª)



Map obtained from d-maps (http://www.d-maps.com/carte. php?num_car=18215&lang=en).

^a Comprehensive information on migration routes was available for seven of the 15 cases.

ER: Eritrea; ET: Ethiopia; IT: Italy; KE: Kenya; LY: Libya; SD: Sudan; SO: Somalia; SS: South Sudan.

Results of the investigations

Of the 15 suspected LBRF cases submitted to the NRC, 14 were confirmed as being caused by *B. recurrentis*. In one case, spirochetes were visible on Giemsa stained blood films, but insufficient material was provided for molecular diagnosis. However, the epidemiological data suggest LBRF. Details of diagnostic results are shown in Table 1.

Table 2 gives an overview of basic epidemiological information including disease onset and travel history.

All 15 cases were males with a median age of 20 years (range 15 to 33 years) and all originated from northeast

FIGURE 2

Duration from onset of symptoms to and since arrival in Bavaria for cases of imported louse-borne relapsing fever in refugees from northeast Africa to Bavaria, Germany, July–October 2015 (n=15)



Negative numbers represent an onset of symptoms before arrival in Bavaria whereas positive numbers represent an onset of symptoms after arrival in Bavaria.

NR: not reported.

Africa: 12 from Somalia, two from Eritrea and one from Ethiopia.

Information about migration route was available from 12 patients (Table 2). A comprehensive migration route was indicated by seven patients, all from Somalia: From Somalia via Ethiopia to Sudan (n=4) or via Kenya, South Sudan to Sudan (n=3), all went further to Libya and then via Italy and transit through Austria to Bavaria (Figure 1).

Four patients reported a stay in Italy between two and 14 days, respectively. Six patients reported changing of clothes upon arrival in a refugee camp in Italy. Five patients reported a longer stay in Libya (ranging from 17 days to nine months). Three of them reported to have been exposed to very poor, overcrowded living conditions during transit in Libya. They also reported of fellow refugees with pruritus and infestation with lice. Travel duration of individuals ranged from eight weeks to one year. In eight of the 10 patients with available information, onset of symptoms was before arrival in Munich. Only two reported onset of symptoms after arrival (Figure 2). Nine refugees reported that they had already been accommodated in a refugee facility in Bavaria, four were directly hospitalised upon arrival in Munich, and for two patients information was not specified. Duration of stay in a refugee

Table 3 gives an overview over reported symptoms. All patients were hospitalised and received antibiotic treatment with doxycyline. One of the 15 patients died of multi-organ failure after initiation of antibiotic therapy despite intensive care treatment. Although Jarisch-Herxheimer reaction was not systematically

TABLE 1

Diagnostic results of cases of imported louse-borne relapsing fever in refugees from northeast Africa to Bavaria, Germany, July–October 2015 (n=15)

Caso	Micros	бсору	Sequencing				
Case	Darkfield	Giemsa	16S rDNA	glpQ	flab		
1 ^a	Positive	Positive	Positive	Positive	Positive		
2	Negative	Positive	Positive	Positive	Positive		
3ª	Positive	Positive	Positive	Positive	Positive		
4 ^a	Positive	Positive	Positive	Positive	Positive		
5ª	Positive	Positive	Positive	Positive	Negative		
6	NA	Positive	NP	NP	NP		
7 ^a	Positive	Positive	Positive	Positive	Positive		
8	Negative	Positive	Positive	Negative	Positive		
9	Negative	Positive	Positive	Positive	Negative		
10	Negative	Positive	Positive	IP	Positive		
11	Positive	Positive	Positive	Positive	Positive		
12	Positive	Positive	Positive	Positive	Positive		
13 ^a	Positive	Positive	Positive	Positive	Positive		
14	Positive	Positive	Positive	IP	Positive		
15	Positive	Positive	Positive	Positive	Positive		

^a Successful cultivation.

IP: in process; NA: not available; NP: no material provided.

investigated, all 10 patients with available information were reported to have had Jarisch-Herxheimer reaction to antibiotic treatment.

Discussion

Historically, LBRF was observed as large outbreaks affecting millions of people during wars, civil unrest or under extreme poverty [5,6]. Notably, mortality can still be high, above 30% for untreated cases and 2% to 6% for those receiving appropriate treatment [7]. Endemic areas of LBRF were known to exist in northeast Africa in Ethiopia and in neighbouring countries, including Eritrea, Somalia and Southern Sudan, and are suspected in the Peruvian Andes and the Himalayas [5,8-10]. However, according to recent research, it is believed that endemic LBRF hot spots only persist in Ethiopia, occasionally spilling to neighbouring countries [7,11,12].

In Germany, only three cases of imported LBRF were reported since 1999 [13-15]. Imported LBRF among refugees from endemic areas entering the European Union (EU) is not unexpected considering the massive increase in migration of refugees from northeast Africa [16,17]. According to official data, Eritrea is one of the main countries of origin of refugees in Bavaria (652 in January–June 2015) [18]. In Germany, 3,284 refugees from Somalia were seeking asylum in 2015 until the month of August [19].

Our data suggest that young male refugees originating from the Horn of Africa may be at particular risk of acquiring LBRF. Accordingly, imported LBRF was found

TABLE 2

Descriptive epidemiological information on cases of imported louse-borne relapsing fever in refugees from northeast Africa to Bavaria, Germany, July–October 2015 (n=15)

Characteristic	Number of cases						
Sex							
Male	15						
Age (years)							
15-20	8						
20-25	4						
25-33	3						
Country of origin							
Somalia	12						
Eritrea	2						
Ethiopia	1						
Migration route							
SO-KE-SS-SD-LY-IT	3						
SO-ET-SD-LY-IT	4						
SO-unknown-SD-LY-IT	1						
From SO via LY	3						
From ER via LY and IT	1						
NR	3						
Travel duration							
1–2 months	1						
2–5 months	6						
5 months-1 year	1						
NR	7						
Onset of symptoms							
Before arrival in Bavaria	8						
After arrival in Bavaria	2						
NR	5						
Stay in a refugee facility in Bavaria							
Yes	9						
No	4						
NR	2						

ER: Eritrea; ET: Ethiopia; IT: Italy; KE: Kenya; LY: Libya; NR: not reported; SD: Sudan; SO: Somalia; SS: South Sudan.

in three young male refugees from Eritrea only recently in Switzerland and the Netherlands [20,21].

Onset of symptoms in the eight of 10 patients with available information in our series was just before or shortly after arrival in Bavaria. None of them reported recurring fever episodes. Hence, we assume an early stage of disease in them. Considering a mean incubation period of four to eight days (range 2 to 15 days) [22] and a duration of migration ranging from eight weeks to one year, infection in these eight patients has most likely been acquired towards the end of their journeys, hence in Libya or Italy. The patients could only provide rough estimates of the exact travel duration and accordingly very limited information on when they entered or left transit countries. Therefore, the exact place of infection remains unclear. However, especially

TABLE 3

Reported symptoms and outcome in louse-borne relapsing fever in refugees from northeast Africa to Bavaria, Germany, July– October 2015

Case	Symptoms at the beginning of the journey	Fever > 38 °C	Recurring fever	Severe malaise	Headache Myalgia	Other symptoms	Infestation with lice	Pruritus/ skin lesions	Hospitalisation	Recovery
1	No	No	No	NR	NR	No	No	NR	Yes	Yes
2	NR	Yes	NR	NR	NR	NR	NR	NR	Yes ^f	NR
3	NR	Yes	NR	NR	NR	NR	NR	NR	Yes ^f	NR
4	No	Yes	Several episodes	NR	No	Yes ^a	Yes⁵	No	ICU	Yes
5	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
6	No	Yes	No	Yes	Yes	No	No	No	Yes	Yes
7	No	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes
8	No	Yes	No	Yes	Yes	No	NR	No	Yes	Yes
9	NR	Yes	NR	NR	NR	NR	NR	NR	Yes ^f	NR
10	NR	Yes	NR	NR	NR	NR	NR	NR	Yes ^f	NR
11	NR	Yes	NR	Yes	NR	Yes c,d	Yes	Yes	Yes	Yes
12	NR	Yes	NR	Yes	NR	No	NR	Yes	Yes	Yes
13	NR	Yes	NR	NR	NR	NR	NR	NR	Yes	No ^e
14	NR	Yes	No	Yes	yes	No	Yes	No	Yes	Yes
15	NR	Yes	No	Yes	yes	Yes	No	Yes	Yes	Yes

ICU: intensive care unit; NR: not reported.

^a Abdominal pain.

^b Infestation was not reported, but seen at hospital admission.

^c Jaundice.

^d Vomiting.

^e Patient died.

^f Lost to follow-up.

for five cases who reported onset of symptoms within days before or shortly after arrival, an infection not only in Libya but also in Italy or while crossing the Mediterranean Sea is possible. Two patients reported an onset of symptoms 20 and 36 days, respectively, before arrival in Germany. The patient with the longer duration of symptoms reported that he had travelled through Ethiopia. For the two patients and those with insufficient information regarding the travel route, an infection while travelling through the known endemic hot spot Ethiopia or Sudan could not be ruled out. However, considering incubation time, onset of symptoms, travel duration and the fact that six patients did report no symptoms when leaving their country of origin, we assume that LBRF was acquired later, at places along migration routes with established endemic LBRF foci.

We are aware that the data retrieved during interviews are limited by recall bias and language problems. In particular, the lack of exact data on duration of the journeys remains problematic when estimating the probable place of infection. Indeed, we conclude that LBRF has already been introduced in places along migration routes, most likely in Libya, on refugee boats crossing the Mediterranean Sea and perhaps in Italy. Looking at specified migration routes, the introduction of LBRF to these places is possible by refugees who acquired the disease in Ethiopia.

Interestingly, not a single LBRF infection was found in refugees originating from other African regions though their migration routes partially overlap [23].

The current assessment provides no evidence that transmission occurred while the individuals were in Bavaria. However, public health measures were implemented to prevent further transmission, since nine of the 15 refugees already stayed in a refugee facility in Bavaria before they were diagnosed. As primary preventive public health measure, basic hygiene was recommended which includes changing, washing and drying of clothes and bedding at≥60 °C on a regular basis for infected individuals and close contacts [24]. Additionally, active contact tracing of cases in terms of symptoms, infestation with body lice and assessment of living conditions was recommended as a further precaution. Furthermore, it was recommended to actively offer washing of clothes upon arrival, especially, but not limited to refugees from endemic areas. As the detection of infestation with lice might generally not be very reliable (in our assessment only reported in four patients) these preventive measures have become pivotal [22,24].

To raise awareness in the medical and public health communities, public health authorities and physicians throughout Bavaria have been informed about clinical symptoms and general epidemiology of LBRF. Leaflets describing LBRF and recommended public health measures were distributed nationally. Public health institutions in Libya and Italy were already informed by the Robert-Koch-Institute (RKI) (personal communication, Dr H Wilking, RKI, September 2015) as well as further organisations such as the World Health Organization (WHO) and Médecins Sans Frontières (MSF).

Conclusions

Young male refugees originating from the Horn of Africa seem to be at major risk for acquiring LBRF. LBRF most likely was not acquired in their countries of origin but on migration routes, most likely in Libya or Italy. No evidence for transmission of LBRF infections in Bavaria was found. However meaningful preventive control measures were implemented. The findings of our investigation should be strengthened by further epidemiological studies and followed by a pan-European prevention strategy.

Conflict of interest

None declared.

Authors' contributions

Wrote the manuscript: MH, VF, AR; performed epidemiological analysis: MH, AR, FP; interviewed the patients: JZ; performed laboratory investigation: GM, VF, AW; revised the manuscript: KS, WH, TL, AS, GM; cared for the patients: MS, LB, UB, WG, KH.

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