A probable case of tick-borne encephalitis (TBE) acquired in England, July 2019

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The United Kingdom (UK) has thus far been considered to be free from tick-borne encephalitis (TBE), yet in July 2019, a German infant developed serologically diagnosed TBE following a tick bite in southern England. This first report of a probable human case together with recent findings of TBE virus in ticks in foci in England suggest that TBE may be acquired in parts of England and should be considered in patients with aetiologically-unexplained neurological manifestations.

End-July 2019, a case of tick-borne encephalitis (TBE) in a 3-month-old infant was notified to the German mandatory surveillance system for infectious diseases. The patient’s family, resident in a TBE-non-endemic region in Germany, had holidayed in England during the incubation time. We present the case report based on German surveillance data, information provided by the family, laboratory reports and two hospital discharge summaries, and describe the public health response.

Case report

A German family including a 3-month-old infant spent their holiday in southern England from 1 to 15 July 2019 (Figure 1). The mother was not vaccinated against nor reported past TBE infection. On 6 July, the family picnicked near Woodgreen in the New Forest National Park (Figure 2), where the child laid on a blanket on the grass. An unengorged tick, attached to the infant’s neck, was discovered on 7 July. The tick was removed incompletely, using tweezers, and the wound was disinfected. The remaining tick fragments detached 2 days later.

The previously healthy infant developed fever on 17 July, 11 days after the tick bite. Medical history was unremarkable; the infant had thus far received one hexavalent routine childhood vaccination. Subtracting the maximum incubation period of 28 days [1] from symptom onset, renders 19 June as the earliest possible infection date. The infant reportedly did not visit any other location where a tick bite could have occurred except their home area in Hesse, Germany which is non-endemic for TBE. Each bout of fever was accompanied by focal seizures, lasting ca 1 min. Hospitalisation occurred on 17 July, prompting a series of diagnostic tests (Table). Based on elevated cerebrospinal fluid markers (Table), meningitis was diagnosed and the infant was treated with intravenous cefotaxime, ampicillin and aciclovir. The focal seizures became generalised lasting up to 5 min and were treated with anticonvulsants (clonazepam, midazolam, levetiracetam). The infant was transferred to a specialised hospital on 20 July. Magnetic resonance imaging and repeated electroencephalograms revealed pathological results (Table). Having excluded numerous neurotropic pathogens, TBEV-specific serology tested positive for IgM and IgG (Table) and meningoencephalitis because of TBEV infection was diagnosed by the treating physicians. The infant was discharged 15 days after admission with mild remaining neurological symptoms, which had subsided by the check-up 6 weeks later.

Public health response

Upon receiving the notification on 25 July, the Robert Koch Institute asked the patient’s family for their detailed travel history in England. One week later, the event was reported through the European Commission Early Warning and Response System (EWRS) selective exchange to inform United Kingdom (UK) colleagues.

Following TBEV detection in ticks in Thetford Forest in 2019, from samples collected February 2018 to January 2019 [2], enhanced clinical surveillance activities were
**Figure 1**
Timeline of infection, disease progression and public health response to the probable tick-borne encephalitis case in an infant, Germany, July–August 2019

- **25 Jul** - Case notification
- **23 Jul** - Positive TBE test
- **25 Jul** - Hospitalisation 17 Jul to 01 Aug
- **02 Aug** - EWRS message
- **17 Jul** - Symptom onset
- **07 Jul** - Tick bite noticed
- **06 Jul** - Picnic
- **Holiday in England 01 to 15 Jul**
- **Maximum incubation time 19 Jun to 15 Jul**

EWRS: Early Warning and Response System; TBE: tick-borne encephalitis.

**Figure 2**
Map of the likely place of infection of tick-borne encephalitis case in a German infant, Woodgreen, New Forest National Park, England, 2019

TBEV: tick-borne encephalitis virus; UA: unitary authority.

Source: Ordnance Survey and National Statistics data for geographical and administrative boundaries.
| Date (2019) | Test (sample type/assay) | Result | Interpretation |
|-------------|--------------------------|--------|----------------|
| 17–19 Jul⁴  | CSF diagnostics          |        | Inflammation   |
|             | 1,000 cells (norm: 0–5)  |        |                |
|             | (40% granulocytes, 60% lymphocytes) |        |                |
|             | 1.5 g protein            |        |                |
|             | 59 mg/dL glucose level (norm: 40–80) |        |                |
| 17–19 Jul⁴  | Blood culture            | Negative| Normal         |
| 17–19 Jul⁴  | CSF culture              | Negative| Normal         |
| 17–19 Jul⁴  | Multiplex PCR (CSF) for: |        |                |
|             | -Escherichia coli,       |        |                |
|             | -Haemophilus influenzae, |        |                |
|             | -Listeria monocytogenes, |        |                |
|             | -Neisseria meningitidis, |        |                |
|             | -Streptococcus,          |        |                |
|             | -Cytomegalovirus,        |        |                |
|             | -Enterovirus,            |        |                |
|             | -Herpes Simplex Virus 1 and 2, |        |                |
|             | -Human herpesvirus 6,    |        |                |
|             | -Human parechovirus,     |        |                |
|             | -Varicella zoster virus, |        |                |
|             | -Cryptococcus            |        |                |
| 17–19 Jul⁴  | Enterovirus (stool)      | Negative| Normal         |
| 20 Jul      | MRSA and MRGN screening  | Negative| Normal         |
| 23 Jul      | TBEV-IgG (serum)         | 10.3 AE/mL| Positive (cut-off: 0.241) |
| 23 Jul      | TBEV-IgM (serum)         | 12.5 index| Positive (cut-off: 0.234) |
| 25 Jul      | Borrelia burgdorferi (IgG-ELISA) | < 5.2 U/mL| Negative (cut-off:< 7 U/mL) |
| 22 Jul and 25 Jul | Electroencephalography | Slowed activity in right hemisphere; Epileptic activity in right temporal/cen | Pathological |
|             |                          |        |                |
| 01 Aug      | Magnetic resonance imaging | Leptomeningeal enhancement. No sign of parenchymal defect or brain abscess. | Pathological |

CSF: cerebrospinal fluid; MDRGN: multidrug resistant Gram-negative bacteria; MRSA: methicillin-resistant *Staphylococcus aureus*; TBEV: tick-borne encephalitis virus.

⁴ Performed during the first hospital stay. Exact test dates were not given in discharge summary.

⁵ The test kit used was Enzygnost Anti-TBE virus (IgG, IgM) (Siemens, Marburg, Germany) which determines a specific cut-off for each run (alpha-method).
underway in the east of England, focusing on encephalitis cases without confirmed cause [3]. Following the EWRS message, these activities were extended to areas surrounding the New Forest National Park. TBEV seroprevalence studies in groups at high risk of tick bites and in the general population are also being implemented in both areas. Tick surveillance was already underway around the New Forest National Park following previous findings [2], but additional tick surveys were conducted around Woodgreen on 8 and 23 August 2019. Only 135 ticks (70 nymphs, 25 adult males, 40 adult females) were collected, likely because the peak tick questing season had already passed. Pools of 10 nymphs, five adult males or five adult females were homogenised for RNA extraction and RT-PCR analysis [4]. No TBEV or other TBEV-serocomplex RNA was detected.

Discussion

We report a human TBE case, believed to be the first acquired in the UK. Diagnosis was by serology only, which can be regarded as a limitation. No reserve sample was available for additional testing (TBE-specific PCR or neutralization assay [5]). Because of the lack of therapeutic consequences, no follow-up blood sample was drawn from the infant; therefore it was not possible to test for a rise in IgG titre in paired samples [5]. Several pieces of evidence support the likelihood that this is a true TBE case. First, the tick bite, the clinical symptoms and the incubation time of 11 days, close to the median of 8 days [5], fit the typical picture of TBEV-infection. This patient did not have the biphasic course of TBE, which is observed in 72–87% of TBE cases [5]. Second, as the infant resides in a TBE-non-endemic area in Germany it is highly unlikely that a second tick bite occurred there within the incubation time, went unnoticed and caused the infection. The likelihood of the infection having occurred near Woodgreen is far higher given the known tick bite. Third, the extensive array of differential diagnostics ruled out numerous other neurotrophic pathogens. Fourth, the TBE serological results were far above the cut-offs. Finally, as the infection having occurred near Woodgreen is far unnoticed and caused the infection. The likelihood of this interpretation has to be considered in light of the natural endemiity of Louping ill virus (LIV) in the UK.

In 2019, TBEV was reported for the first time in ticks in Thetford Forest, England [2], but the pathogenicity is unknown and no other human cases have yet been identified in the UK. Tick surveys around Woodgreen did not detect any TBEV, however, it must be noted that only a small tick sample was collected. Yet, a pool of questing ticks sampled previously, on the Hampshire/Dorset border in June 2019, tested TBEV-positive, suggesting that TBEV has established itself in the UK [6]. Follow-up tick surveys will be conducted during spring 2020.

Although the clinical presentation and serology are consistent with the European TBE case definition [7], this interpretation has to be considered in light of the

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Semper are based at Public Health England. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health and Social Care or Public Health England.

Conflict of interest

None declared.

Authors’ contributions

Teresa Kreusch, Thomas Harder and Ole Wichmann were involved in the public health response in Germany, collated and reviewed the relevant data from the case, and wrote the first draft. Tim Brooks, Amanda Semper, Amanda Walsh, and Katherine Russell were involved in the public health response in the UK. Maya Holding, Roger Hewson, Stuart Dowall, Kayleigh Hansford and Jolyon Medlock were involved in the tick collection and testing near Woodgreen. All authors discussed the article’s content and approved of the final version.

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