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Short Report

Transnational exchange of surveillance data reveals previously unrecognized TBEV microfocus

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 Tick-borne encephalitis (TBE) is a tick-borne infection with an increasing presence in many European countries. It is caused by the TBE virus (TBEV), a flavivirus transmitted by the *Ixodes ricinus* tick in northern Europe. In Denmark, the virus exists endemically on the island of Bornholm. However, a large proportion of Danish cases are also imported from Sweden, where the incidence of TBE has steadily been increasing during the last few decades. With the prospect of expanding risk areas due to climate change, TBE surveillance data exchange between countries could facilitate the identification of new TBEV microfoci and thereby aid healthcare workers in the issuing of vaccination recommendations. We present data from a collaborative effort between Denmark and Sweden on the surveillance of TBEV that resulted in the uncovering of a previously unrecognized possible TBEV microfocus in central Sweden.

Introduction

Tick-borne encephalitis virus (TBEV), spread by *Ixodes* ticks, is an emerging pathogen that, during the last few decades, has increased its presence in many European countries.¹ Every single case of TBEV infection can contribute to define new risk areas for tick-borne encephalitis (TBE). This information is important for the establishment of vaccination guidelines to the general public, as vaccination is recommended in people at particular risk of tick exposure in these areas.²

Meningoencephalitis caused by TBEV has been known in Sweden since 1953 and was for decades restricted to the Stockholm archipelago area.³ Since 1990 the annual number of cases has steadily increased and the disease has appeared in other parts of the country.⁴ In Denmark, there are usually 1–5 cases of TBE per year, mostly imported cases and cases acquired on the island of Bornholm.⁵ TBE was until 2008 restricted to Bornholm but in the years 2008 and 2009, two cases of meningoencephalitis following tick bites north of Copenhagen (Tokkekøb Hegn) were reported.⁶ TBEV was, subsequently, detected, using PCR, in field-collected ticks from the same area in 2009 and, again, in 2011.⁷ Following the two cases, no new cases of TBE acquired outside Bornholm, have been reported in Denmark and no TBEV has since been detected in the previous microfocus.⁵

TBE has since July 2004 been a notifiable disease in Sweden. Prior to that, it was thoroughly monitored as all TBE analyses were performed at the same microbiological laboratory belonging to the Swedish Public Health Agency.

In Denmark, it is not yet notifiable but has been monitored since the year 2000.⁵ As many of the TBE cases in Denmark are imported from Sweden,⁵ we hypothesize that an exchange of surveillance data between

the two countries could help reveal new TBEV microfoci and could potentially be extrapolated to other European countries. The aim of this study was to investigate the possibility of such collaboration facilitating the identification of new TBEV risk areas, thus aiding in the issuing of vaccination recommendations to the general public.

Methods

Our knowledge of TBEV risk areas is mainly based on thorough patient interviews. An estimate of the most probable location for an infectious tick bite can often be made by inquiring patients of any recent stay in TBEV risk areas or other locations of potential tick activity. A witnessed tick bite can further increase the accuracy of the estimated geographic location for contracting an infection caused by TBEV.

In Denmark, TBEV infection is monitored at Statens Serum Institut (SSI) where the serological analysis for TBEV is centralized. In the period 2010–15, 73 sera or blood samples displayed IgM antibodies against TBEV. Following the exclusion of duplicate samples and samples displaying weak IgM reactivity, a total of 39 patients could be identified. Thirty-one of these patients displayed both IgM and IgG antibodies, indicative of TBEV exposure. Of these, fourteen (45%) had a travel history to Sweden noted in their laboratory records. Four of these patients could be reached and agreed to a telephone interview. The patients were inquired about prior vaccination, tick exposure, prior consumption of unpasteurized dairy products and clinical manifestations at the time of the disease. They were also asked to plot, as accurately as possible, the presumed locations at which they could have been bitten by the culprit tick.

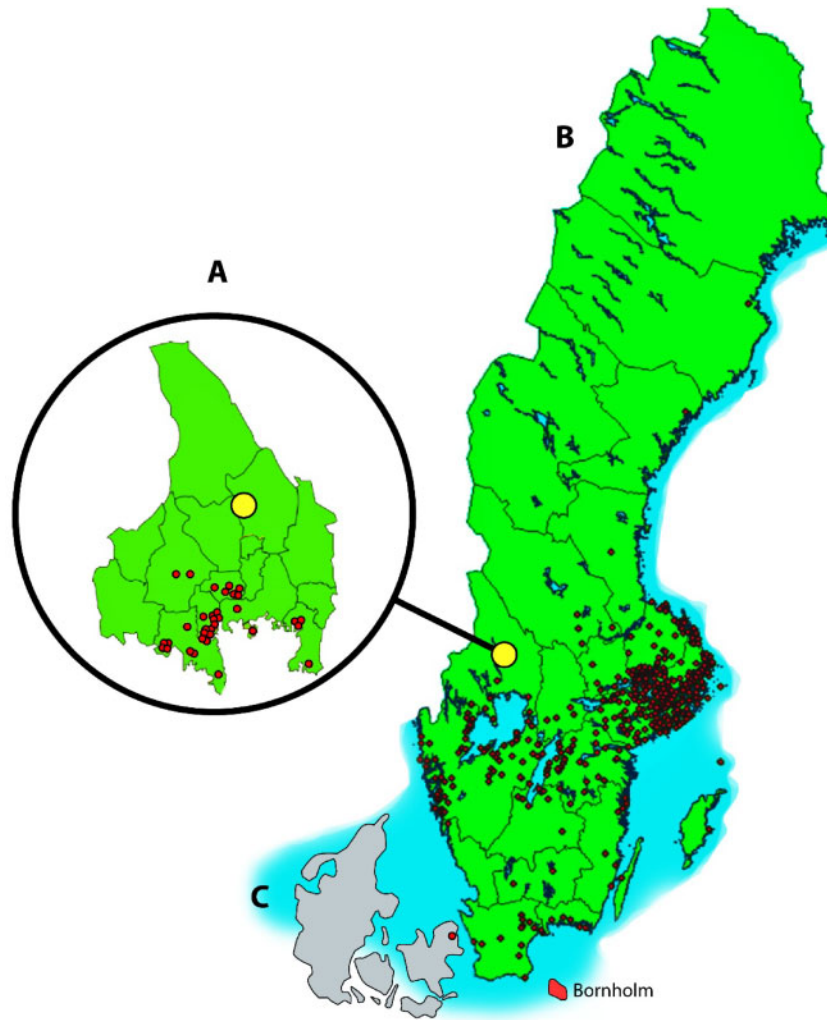


Figure 1 Map showing the geographical distribution of (A) TBE cases in the county of Värmland in the period 2007–17 and (B) Swedish TBE cases in the years 2007–12. The new TBEV microfocus south of Gunnerud revealed by the Danish patient from 2010 is represented by a large dot on both maps. (C) Map of Denmark displaying the location of Tokkekøb Hegn in northern Zealand, where the only endemic cases of TBE, outside of Bornholm, had contracted the virus and where the virus was later detected in field-collected ticks in 2009 and 2011

Results

Two of the patients interviewed experienced neurological symptoms indicative of TBE. The remaining two had experienced non-specific flu-like symptoms consistent with the initial viremic phase of TBEV infection in the weeks prior to being tested. None of the patients was immunized against TBEV or had consumed unpasteurized dairy products in the months prior to diagnosis. Three of the patients were assessed to have contracted the virus in already recognized Swedish TBEV microfoci, namely Ryr Nature Reserve at the west side of lake Vänern, Ekerö at the east side of lake Mälaren and Rejmyre in Östergötland county. However, one patient, a 42-year-old man, had most likely contracted the virus in a previously unrecognized microfocus, south of the village of Gunnerud in the county of Värmland, in the Midwest of Sweden, in July 2010 (figure 1).

The Danish patient, who had most likely contracted the infection south of Gunnerud, had participated in a 50-km long rafting tour along Klarälven, a river flowing from Norway into the lake of Vänern. The tour, which lasted for 5 days, went along Klarälven from the village of Osebol to Gunnerud with three stops along the way for overnight sleeping on the raft. The tour-participants rallied south of Gunnerud on a grass area where they camped overnight and drove to Osebol the next morning to board the rafts. The rest of the

tour was spent rafting and the tick, which was discovered and removed on the first day of the tour, must thus have attached at the grass area in Gunnerud. A few days after his return home, the patient developed headache, fever, myalgia and fatigue but recovered with no sequelae 14 days later. No neurological symptoms were present at any point during the infection. He had not camped or travelled in any known TBEV risk areas and had not witnessed any other tick bites in the month leading up to this event.

Discussion

The Danish patient had most likely experienced the initial viremic phase of TBEV infection, which is not notifiable in many countries. It does, however, constitute an important marker for the presence of TBEV. During the last 10 years, and especially during the last 3 years, Värmland has experienced an increase in the number of TBE infections. In 2017, 13 patients had contracted TBEV within the county, most of whom had contracted the virus near Vänern with a major risk area being the northwestern part of the lake in the area between Segmon and Grums. This is a considerable increase compared with 2010, with only four cases of TBE reported to the Regional Office of Communicable Disease Control in Värmland.

In Denmark, almost all new reported cases of TBE are imported or contracted on the island of Bornholm.⁵ Despite this, sentinel studies on Danish deer could indicate that the virus is more widespread than previously believed, with infections likely underdiagnosed among humans.⁸

In the EU Interreg project ScandTick Innovation, Scandinavian countries implemented routines for sharing surveillance data between health authorities regarding cases of TBEV infection. This approach aims at facilitating the identification of new TBEV microfoci, allowing such areas to be discovered earlier, and can also provide additional data on the TBE burden in already established risk areas. On a European level, such collaboration between countries could further improve the surveillance of this infection. This is an important task considering the recent spread of TBEV to new areas in Europe and the prospect of additional spread in the coming decades driven by climate change and possibly resulting in both latitudinal and longitudinal expansion of risk areas.^{9,10}

Conclusion

Exchange of surveillance data on TBEV could prove to be a viable strategy in the identification of new possible TBEV microfoci in Scandinavia. Adaptation of a similar approach has the potential to facilitate the surveillance of this virus in the rest of Europe. This is important considering the recent emergence of TBEV in previously non-endemic countries and its increased presence in already endemic ones.

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Conflicts of interest: None declared.

Key points

- All cases of TBEV infection can contribute to the establishment of new risk areas for contracting the virus.
- Identification of new TBEV risk areas is important for the issuing of vaccination recommendations to the general public.
- Exchange of TBEV surveillance data could prove to be a viable strategy for identifying new TBEV risk areas in Scandinavia and potentially other European countries.

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