Neoehrlichia – a new tick-borne bacterium

In the course of a review of archival data from an earlier publication we discovered that the bacterium *Candidatus* Neoehrlichia mikurensis (CNM) is present in Norwegian *Ixodes ricinus* ticks. Human disease caused by this bacterium has recently been described in other countries. It seems likely that this disease also occurs in Norwegian patients.

At present, five tick-borne diseases of humans are recognised in Norway: borreliosis (1), tularaemia (2), human granulocytic anaplasmosis (3), tick-borne encephalitis (TBE) (4) and babesiosis (5). It is known that the tick *Ixodes ricinus* can also transmit other diseases. In Sweden, *Rickettsia helvetica* has been found in ticks (6, 7). The list of diseases that ticks can transmit will probably be extended further in years to come.

Neoehrlichia – the newest of the new

In 1999–2001, AS Telelab (now Unilabs Telelab AS), and colleagues from the Netherlands conducted a PCR-based study of *Borrelia* and *Ehrlichia* (now *Anaplasma phagocytophilum*) in ticks from Telemark (8). The first PCR tests revealed several members of the *Ehrlichia/Anaplasma* group that did not belong to any of the species recognized at that time.

The most prevalent of these was an *Ehrlichia*-like organism (ELO), which had previously been found in ticks from the Netherlands (9). ELO was present in 6–7 % of the Norwegian ticks. We were curious as to the organism's identity and whether it might be pathogenic, but at that time ELO was little more than an anonymous DNA sequence and its identity remained a mystery for many years.

Brought to light

In the course of reorganising archival sequence files in 2011–12, we decided to reinvestigate the ELO sequence. A search of the GENBANK sequence database showed that the sequence was virtually identical to that of *Candidatus* Neoehrlichia mikurensis (CNM). CNM is a tick-borne member of the *Rickettsia* group that was found in rats (*Rattus norvegicus*) and ticks (*Ixodes ovatus*) in Japan and characterized by Kawahara et al. in 2004 (10).

Widespread

CNM appears to be widespread in Europe, with varying prevalence. It is reported to be the next most prevalent tick-borne pathogen in central Europe after *Borrelia afzelii* (11) and has also been found in Sweden, Denmark, the Netherlands, the Baltic states, Italy, Slovakia, Asiatic Russia and Japan.

In Norway, we found CNM (ELO) in ticks from two localities in Telemark: the island of Langøya in the municipality of Bamble (prevalence 7 %) and Marka in the municipality of Siljan (prevalence 6 %). The prevalence on Langøya was highest in May (12.5 %), declining to 2–3 % in June and July. We therefore conclude that *Candidatus* Neoehrlichia mikurensis is present in ticks in Norway and – if the results from 1999–2000 still apply – that its prevalence is considerable. The possibility has been raised that CNM infection can exacerbate, or be exacerbated by, co-infection with other tick-borne agents (12). In this context, it is interesting to note that we found a statistically significant excess of ticks co-infected with CNM and *Borrelia afzelii* (8).

Human CNM infections

CNM is a human pathogen (13–15). Cases of febrile illness caused by CNM have been described in several European countries, including Sweden (16). CNM infection appears to principally affect immunocompromised individuals. One fatality has been reported (15). Persistent or recurring fever is a common feature of all cases, while joint pain, oedema, erysipelas and acute diarrhoea may also occur. Successful treatment with doxycycline (200 mg/d for three weeks) is reported in several publications (13, 15, 17). Beta-lactams and cephalosporins are without effect since CNM, in common with other *Rickettsiae*, has no cell wall.

«The list of known tick-borne diseases is likely to be extended further in years to come.»

CNM-infection has not been found in Norway, but as far as we are aware no attempt has yet been made to detect it. However, it seems likely that such infections do occur. It may be worth considering whether CNM or other under-investigated tick-borne pathogens may be involved in the aetiology of so-called «chronic seronegative borreliosis».

CMN should therefore be considered as a possible aetiology in cases of febrile illness in immunocompromised individuals who are exposed to ticks. At present, the only definitive diagnostic test is PCR on whole blood. Various PCR methods have been employed, including generic 16s rRNA PCR followed by DNA sequencing. This is a methodology that is in use at a number of Norwegian laboratories. A specific real time PCR test has been developed at Telemark University College and is currently under evaluation.

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