EVALUATION OF TICKBORNE ENCEPHALITIS CASE CLASSIFICATION IN POLAND

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Central European tickborne encephalitis (TBE) is a viral disease of the central nervous system. Despite a surveillance system for TBE existing in Poland since 1970, there are no standardised case definitions and different diagnostic tests are used in various regions. The purpose of this study was to summarise four years of surveillance data using standardised case definitions. From 1999 to 2002, 607 cases of TBE were reported to Poland's national surveillance system: 386 (63.6%) were males, 331 (54.5%) lived in rural areas, and 186 (30.6%) were between 30 and 50 years old. Of 606 diagnosed cases, 453 (74.7%) had aseptic meningitis, 109 (18.0%) had meningoencephalitis, and 44 (7.3%) had meningoencephalomyelitis. Of the 607 reported cases, 602 (99.2%) could be classified: 153 (25.4%) as confirmed, 343 (57.0%) as probable, and 106 (17.6%) as possible cases. There was a significant difference in classified cases by gender: 28.6% of male cases were classified as confirmed, compared with 19.7% of female cases ($\chi 2$= 10.48, p=0.0053). There was a significant difference in case classification by clinical diagnosis: 32.4% of cases with meningoencephalitis were classified as confirmed cases, compared with 24.7% of cases with aseptic meningitis ($\chi 2$=11.79, p=0.019). There were also significant differences in the distribution by case definition group across geographical regions. For appropriate monitoring of TBE, a uniform and valid case definition should be used in European countries. With only 25% of reported cases meeting the definition for confirmed cases, there is a need for more complete follow-up and standardised testing of suspect cases.

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Introduction

Central European tickborne encephalitis (TBE) is a viral disease of the central nervous system [1,2]. This infection due to the central European subtype of TBE virus usually progresses biphasically (viraemic phase, then neurological phase). Often, the infection is asymptomatic or influenza-like,. It develops to the second phase only a third of cases. Patients are hospitalised mainly during the neurological phase.

Symptomatic syndromes of TBE include aseptic meningitis, meningoencephalitis, and meningoencephalomyelitis. To confirm the diagnosis of TBE, serological testing and demonstration of specific IgM in the acute phase, or a significant rise in antibody titre is required. All serological IgG tests show cross-reaction with other flaviviruses [3]. In Poland only enzyme-linked immunosorbent assay (ELISA) tests are used. Diagnostic procedures to confirm TBE infection based on available tests were Published by the National Institute of Hygiene [4]. Because of the lack of a commonly accepted case definition, regional health providers use different diagnostic protocols to confirm the diagnosis of TBE.

In Poland, serologic surveys of more then 20 000 foresters and 17 000 blood donors were done in the 1960s and 1970s [5]. Antibodies against the TBE virus were found in 0.5-6.5% of population in different regions and in 7.0-27.0% of foresters. Serologic data has enabled the identification of regions with particularly high infection rates.

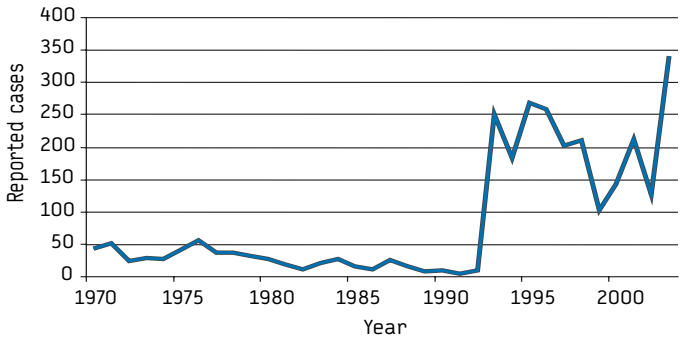
Reporting of TBE cases is mandatory in all central European countries. Thus, cases have been reported in Austria, Byelorussia, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Norway, Poland, Russia, Romania, Slovenia, Slovakia, Sweden and Switzerland [6,7]. The largest number of cases are reported from countries in central Europe. Increasing reports from areas that were previously disease-free (Norway, northern Russia, the Netherlands) have been attributed to global warming and increases in rodent and tick populations [8].

Most of the previous descriptive TBE studies were of hospitalised TBE patients with a neurological presentation [9,10]. Asymptomatic or forms with few symptoms are probably not diagnosed and/or taken into account during consultation. There is a notion of tick bite in 56% to 90% of cases [2]. Patients had often been involved in professional forest activity (56%) or occasional forest activity (48%) [8]. There were also several prospective follow-up studies gathering information about long-term prognosis and possible risk factors [11,12]. The primary weakness of these follow-up studies was the lack of control groups needed to assess risk factors.

TBE surveillance in Poland is integrated into the ongoing communicable disease reporting system. Reporting of TBE cases as a separate syndrome began in 1970, but no uniform case definition was used. Typically, after a medical provider reports a clinically suspected case of TBE-related encephalitis, an epidemiologist from the District Health Department completes the standardised TBE surveillance report. The forms are sent to the National Institute of Hygiene (NIH) in Warsaw, where they are processed. The incidence information is Published in bi-weekly surveillance reports sent to all local health departments and subscribed healthcare providers. Annual reports on tickborne encephalitis are prepared in the Department of Epidemiology of the National Institute of Hygiene. The annual number of reported cases changed dramatically with the introduction of new serologic tests and a countrywide educational campaign in 1993 [FIGURE 1]. Between 1970-1992, only 5 to 50 cases were reported each year. From 1993, 100-350 cases have been reported annually. More than 80% of cases were reported from two northeastern provinces of Poland: Podlaskie and Warminsko-mazurskie. These two provinces are mostly rural and have more tourist traffic, compared with country average. Their forestation rate is similar to country average.

FIGURE 1

Reported cases of tickborne encephalitis in Poland, 1970-2001



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The aim of the study was to assess the usefulness of the newly introduced case definitions for differentiation of confirmed, probable and possible cases within the Polish communicable disease reporting system. A descriptive analysis of data was performed, with a comparison of cases by case definition groups.

Methods

The TBE reports from the years 1999-2002 were analysed using a new case definition, developed by a working group at national level [Table 1]. These case definitions will be implemented in 2005. The forms for years 1999-2002 were used in this study because there were administration reforms in 1998, which affect geographical comparisons of data before and after 1998. Based on data obtained, TBE cases were classified as confirmed, probable and possible cases. Newly defined case groupings were compared by year, season of onset, gender, age group, residential area type, occupation, clinical course and geographic location. Geographic comparisons were performed only for provinces where more than 10 cases were reported during the period 1999-2002.

Table 1

Tickborne encephalitis case definitions, Poland, 1999-2002

Possible case	a. clinically compatible disease (febrile illness with diverse neurological symptoms of aseptic meningitis or encephalitis), AND b. onset of illness during a period of increased tick activity (between April and November).
Probable case	Possible case AND a. visit of ill person to endemic area during previous 6 weeks, OR b. detection of specific IgM antibodies in serum, with no history of vaccination against any flaviviral disease during previous 3 months
Confirmed case	Possible case AND a. detection of specific IgM or IgG antibodies in cerebro-spinal fluid, OR b. fourfold or greater rise in serum antibody titre, with no history of vaccination against any flaviviral disease during previous 3 months, OR c. viral isolation from tissue, blood, or cerebrospinal fluid (CSF).

Source: Working group for communicable disease surveillance case definitions, Warsaw, Poland

Data was analysed using SAS software (version 8.2, SAS Institute, Carey, NC, USA). All variables were categorised. Cases were compared using case definition groups with the chi-square test. A logistic model was used to detect factors predicting the probability of being classified as a confirmed case.

Results

From 1999 to 2002, 607 cases of TBE were reported to Poland's national surveillance system. A total of 386 (63.6%) patients were males and 221 (36.4%) were females. Three hundred thirty one (54.5%) cases lived in rural areas and 276 (45.5%) in urban areas. There were no large differences in the number of cases by age group. By occupation, the largest groups were unemployed (108 cases; 17.8%), retired (106 cases; 17.5%), students (95 cases; 15.7%) and farmers (74 cases; 12.2%). All patients with TBE were hospitalised. The most common signs and symptoms in TBE cases were fever (581 cases, 95.7%), headache (580 cases, 95.6%), meningeal symptoms (479 cases, 78.9%), vomiting (385 cases, 63.4%), muscle pain (151 cases, 24.9%), and respiratory infection (105 cases, 17.3%).

More severe signs and symptoms were less common, including loss of consciousness (85 cases, 14.0%), cerebellar symptoms (38 cases, 6.3%), pyramidal symptoms (22 cases, 3.6%), limb paresis (22 cases, 3.6%), and cranial nerve palsy (12 cases, 2.0%). Based on these clinical signs and symptoms, 606 (99.8% of cases) could be classified into one of three clinical syndromes [Table 2]. Three patients died, giving a four year case fatality rate of 0.5%.

Table 2

Number of tickborne encephalitis cases by clinical syndrome, Poland, 1999-2002

Clinical syndrome	1999	2000	2001	2002	Total
Aseptic meningitis	71 (70.3%)	130 (75.1%)	155 (75.2%)	97 (77.0%)	453 (74.7%)
Meningo-encephalitis	24 (23.8%)	29 (16.8%)	34 (16.5%)	22 (17.5%)	109 (18.0%)
Meningo-encephalo-myelitis	6 (6.0%)	14 (8.1%)	17 (8.2%)	7 (5.6%)	44 (7.3%)
Total	101 (100%)	173 (100%)	206 (100%)	126 (100%)	606 (100%)

Of the 607 cases reported, 602 (99.2%) could be classified as a possible, probable, or confirmed case [Table 3]. Four cases could not be classified because their symptoms started after the tick activity season. One person didn't meet the clinical compatibility requirement and had been diagnosed exclusively on serologic results. 153 patients (25.4%) were confirmed TBE cases, 343 (57.0%) were probable cases and 106 (17.6%) were possible cases.

Table 3

Number of tickborne encephalitis cases by case classification, Poland, 1999-2002

Possible cases	**106**	**17.6%**
a. Clinically compatible	106	100%
b. Onset during tick activity season	106	100%
Probable cases	**343**	**57.0%**
a. Visit to endemic area	NA*	-
b. Specific IgM in serum	343	100%
Confirmed cases	**153**	**25.4%**
a. Specific IgM or IgG in CSF	142	92.8%
b. 4-fold rise in antibody Ig titre	17	11.1%
c. viral isolation from tissue	NA**	-

* NA = not available, data not reported in the forms.
** NA = not available, test not performed in 1999-2002.

There was a significant difference in case classification by gender with 28.6% of male cases classified as confirmed, compared with 19.7% of female cases (2=10.48, p=0.0053) [Figure 2]. There was a significant difference in case classification by clinical diagnosis: 32.4% of cases with meningoencephalitis were classified as confirmed cases, compared with 24.7% of cases with aseptic meningitis (X2=11.79, p=0.019) [Figure 3]. The comparison of case classification by province showed highly significant differences by region (X2=94.36, p<0.0001) [Figure 4]. The comparison of case classification for other demographic factors, such as year of onset, season of onset, age, occupation, type of residence (urban/rural), revealed no significant differences.

Figure 2

TBE case classification by gender, Poland, 1999-2002

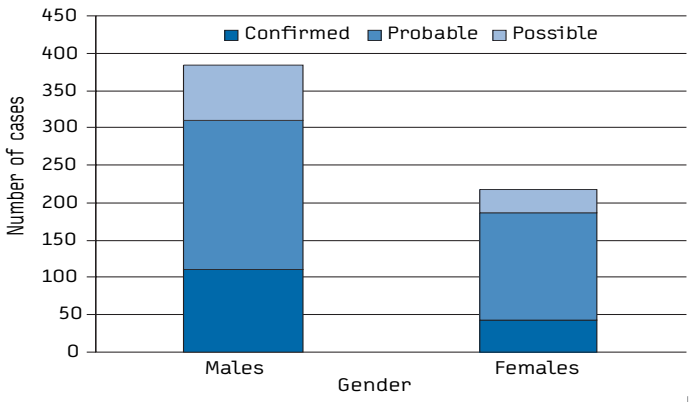


FIGURE 3

TBE case classification by clinical diagnosis, Poland, 1999-2002

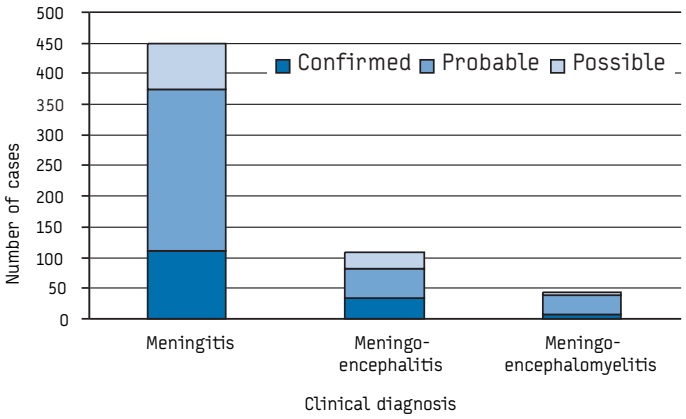
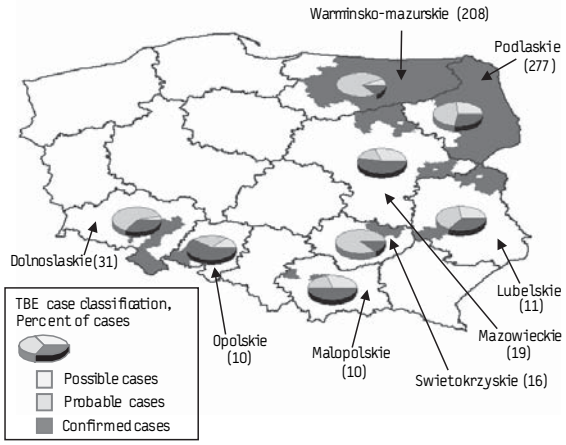


FIGURE 4

Geographic distribution of TBE classification, Poland, 1999-2002



Notes

The names of provinces are accompanied by number of cases reported from 1999 through 2002

Districts with at least one case reported during > 1 year

The probability of being classified as a confirmed case was modelled. Controlling for geographic location, males were more likely to be classified as confirmed cases, compared to females (OR=1.92, 95% CI: 1.21–3.11). Compared with other provinces, patients living in Warminsko-mazurskie (OR=3.99, 95% CI: 1.65–10.76) and Podlaskie province (OR=1.68, 95% CI: 1.04–2.69) were more likely to be classified as a probable or possible case. Geographical differences in case classification were directly linked to important differences in diagnostic tests used to confirm TBE. The serum IgM test was used extensively in Warminsko-mazurskie (81.3% of cases were classified as probable) and in Podlaskie (45.1% of cases were classified as probable). IgM and IgG tests of cerebrospinal fluid were used to confirm a higher proportion of cases in Opolskie (58.8%), Mazowieckie (52.6%), and Malopolskie (50.0%) provinces.

Discussion

TBE is an emerging disease spreading from central Europe to western and northern Europe, possibly because of climate change. The disease is endemic in the northeast of Poland with approximately 200 cases a year reported countrywide. For appropriate monitoring of TBE trends, a uniform and valid case definition should be used in European countries. This need is illustrated by the observation that only 25% of cases reported in Poland in 1999-2002 had sufficient diagnostic tests to meet the criteria of a confirmed TBE case. The fact that male TBE cases were more likely to receive a confirmatory diagnosis, needs to be further investigated. The higher incidence of TBE among males may reflect more rigorous investigation. Interview, follow-up and diagnostic procedures were not uniform across various regions of Poland.

Local health departments used different surveillance forms and hospital laboratories used different ELISA tests, resulting in reporting differences. Some endemic northeastern regions of Poland, particularly Warminsko-mazurskie province, were less likely to perform confirmatory diagnostic testing of the cerebrospinal fluid and were more likely to rely on serologic results. The introduction of a new case definition will help to standardise procedures and encourage proper diagnostic methods. Finally, a more accurate surveillance system is crucial to better focus preventive campaigns including immunisation.

The case report form needs to be modified to collect missing information (e.g. residing or visiting an endemic area). Forms of infection that are not symptomatic and which are typically not hospitalised should be included as probable illnesses, based on epidemiological or serological evidence. Also, the case report should include the presence of tick bite and risk factors related to exposure (i.e. forest activities). The present criteria for suspect cases are insufficient to differentiate TBE from other illnesses involving meningitis. Additionally, since a viral isolation test was never used to confirm TBE over a 4 year period, the usefulness of this diagnostic test should be reviewed. The implementation of the new case definition needs to be linked to better education about the appropriate diagnosis of the disease and the need for standard, uniform diagnostic protocols. There is a need to modify diagnostic procedures in clinical settings. Carrying out lumbar puncture should be more systematic for diagnosis confirmation and for the elimination of potential differential diagnosis (herpetic meningoencephalitis, neuroborreliosis, etc.). Moreover, an effort to carry out a second serologic examination seems necessary, especially in cases with no neurological symptoms that are not hospitalised.

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