A lethal tick-borne encephalitis from an active endemic area in Slovakia

Litvová S.[1,2], Štefkovičová M.[1], Grežďová M.[3], Drľová A.[3], Krištúfková Z.[4], Kopilec Garabášová M.[5]

[1]Faculty of Healthcare, Alexander Dubček University of Trenčín, Trenčín, Slovakia
[2]Regional Public Health Authority, Trenčín, Slovakia
[3]Faculty Hospital, Trenčín, Slovakia
[5]Faculty of Public Health, Slovak Medical University Bratislava, Bratislava, Slovakia
[4]Dolnooravian Hospital of Dr. L. N. Jégé, Dolný Kubín, Slovakia

ABSTRACT
Tick-borne encephalitis (TBE) is a neglected zoonotic neuroinvasive disease. Most cases of TBE have a mild course, but some patients with encephalitis develop long-term neurological or neuropsychic sequelae. We report a fatal case of TBE in a patient living in an endemic area. The case occurred in a middle-aged man with no epidemiological evidence of tick bites, no consumption of raw dairy products, and who was not vaccinated against TBE. The aim of this paper is to draw attention to the need for better information of the risk factors associated with TBE with the long-term sequelae, to improve case management and to stimulate the development of new vaccination strategies. To our knowledge, this is the first reported case of rare fatal TBE in a middle-aged man with no severe comorbidities in Slovakia.

KEY WORDS
endemicity – tick-borne encephalitis – long-term sequelae – fatal outcome

SÚHRN
Litvová S., Štefkovičová M., Grežďová M., Drľová A., Krištúfková Z., Kopilec Garabášová M.: Smrteľná kliešťová encefalitída z aktívnej endemickej oblasti Slovenska

Kliešťová encefalitída (KE) je opomínaná neuroinvazívna antropozoonóza. Väčšina prípadov KE má mierny priebeh, ale u niektorých pacientov s encefalitídou sa vyvinú dlhodobé neurologické alebo neuropsychické následky. Uvádzame fatálny prípad KE z endemickej oblasti. Prípad sa vyskytol u muža v strednom veku bez epidemiologických dôkazov o uhryznutí kliešťom alebo konzumácii surových mliečnych výrobkov a ktorý nebol očkovaný proti KE. Cieľom tohto príspevku je upozorniť na potrebu lepšej znalosti rizikových faktorov spojených s kliešťovou encefalitídou s dlhodobými následkami, zlepšiť manažment prípadov a podnietiť vývoj nových vakcinačných stratégií. Podľa našich vedomostí ide o prvý hlásený prípad zriedkavej fatálnej KE u muža stredného veku bez závažných komorbidít na Slovensku.

KĽÚČOVÉ SLOVÁ
endemicita – kliešťová encefalitída – dlhodobé následky – fatálny dopad

Epidemiol Mikrobiol Imunol, 2025; 74(2): 126–130
https://doi.org/10.61568/emi/11-6492/20250428/140418

INTRODUCTION

In Slovakia, tick-borne encephalitis (TBE) is endemic disease. Around 35% of Slovakia's population lives in areas with high TBE endemicity (> 5 cases/100,000 inhabitants). In 2022, Slovakia reported 215 cases TBE (3.4 cases per 100 000). Most of the cases were autochthonous (N = 211. 98.1%), only 4 cases (1.8%) were travel associated (Austria, Czechia, Germany). Tick bite was reported as the most frequently probable mode of transmission (64.7% cases, N = 139 cases). Consumption of infected milk and dairy products was reported in 10.7% (N = 23) cases, and for 24.6% (N = 53) cases the mode of transmission was not known. A total of 3 cases (1.4%) occurred in vaccinated persons and 1 death was recorded (0.47%). Cases were recorded in every age group except group of 0 years and 1–4 years, with the highest age-specific incidence in the 45–54 years (5.52/100,000) and 15–19 years (4.99/100,000) age groups. The incidence of disease was higher in males (5.00/100 000) compared to females (2.6/100 000). A 74.9% (N = 161) of them were recorded in endemic areas with an incidence rate > 5/100,000. The regions demonstrating the highest levels of endemicity include Region of Trenčín

proLékaře.cz | 13.2.2026

(5.2 cases per 100,000), Region of Žilina (9.4 cases per 100,000) and Region of Banská Bystrica (10.6 cases per 100,000) [1]. The data on the number of cases are considered to be relatively accurate given the forty-years tradition of mandatory reporting of TBE laboratory results supplemented by active epidemiological investigation of cases in infectious disease wards. In contrast, much less is known about number of cases that contract long-term or permanent sequelae including a fatal outcome. The development of a severe course may not always be recorded in the surveillance system due to the time latency from the onset of the disease [2, 3]. More follow-up is necessary to update the data on serious TBE cases, including fatal outcomes.

The potentially severe course of infection and the risk of permanent neurological sequelae make TBE an important health problem in many European countries. Many aspects of this infection are still not fully understood.

Notwithstanding the clinical severity of the disease and the relatively large number of persons at risk of exposure to the causative agent in view of the large endemic areas in our country, the most effective form of prevention by vaccination is used relatively little in Slovakia.

THE COURSE OF THE DISEASE

In June 2021 a 45-year-old male was admitted to the hospital due to a two-day fever, weakness, loss of appetite, and dyskinesia of the limbs. His condition progressed with clinical presentation of consciousness disorders including snoring and occasional agitation. Symptoms such as dysphagia and loss of palatal reflexes, breathing alternating with irregular periods of apnea, severe left-sided hemiparesis, dysarthria and other symptoms characteristic of bulbar palsy with persistent meningeal irritation were observed. During hospitalization, he was intensively treated, rehabilitated, and admitted to the intensive care unit. After the 12-week hospitalisation, he was discharged to a long-term care facility due to his inability to perform self-care activities. The findings were classified as a severe tick-borne meningoencephalitis, initially with a qualitative-quantitative disorder of consciousness and bulbar symptomatology, left-sided hemiparesis accentuated in the left upper limb, an organic psychosyndrome in the foreground with a decrease in memory-cognitive functions with intermittent psychomotor restlessness, hypobulimia, severe depressive syndrome and motoric instability with falls during his hospital stay; the CT brain scan showed no signs of trauma. A tonic-clonic seizure was recorded at the 32nd week after the onset of disease. The seizure was secondary to the resolution of TBE, possibly complicating pharmacotherapy with Elontril. A focal orofacial epiparoxysm was recorded 4 weeks later. The EEG showed no specific epileptiform abnormalities. Laboratory analysis showed only a slight increase in inflammatory parameters, and the brain CT scan was without abnormalities. Three lumbar punctures were performed (weeks 1, 2 and 34 after the onset of symptoms). The cerebrospinal fluid (CSF) showed a slightly elevated cell count, proteins, and lactate with normal glucose levels. The results of serological and RT-PCR tests were negative both in blood and CSF (dif. dg. other viral and bacterial pathogens). The CFS cultures were negative. TBEV RNA detection by RT-PCR was not performed. Serum and CSF were analysed for the presence of specific TBEV antibodies by enzyme-linked immunosorbent assay (EUROIMMUN DYNEX ELISA). TBEV IgG and IgM antibodies were positive in serum, with IgM also in CSF. The TBEV IgM antibody index was 2.93 in the second CSF sample. The albumin quotient was positive in the first and second samples and negative in the third sample. Intrathecal production of IgM antibodies was present in the second and third samples, and intrathecal production of IgG antibodies was present only in the third sample of CSF (Table 1).

Brain MRI at that time showed a non-specific hyperintense white matter lesion on axial FLAIR image in the left cella media without hemosiderin deposition, without acute ischaemic and haemorrhagic changes, and without evidence of focal meningeal thickening in both the native and the post-contrast. This MRI finding persisted on repeat MRI (week 47 after the disease onset). In addition, hyperintense signal changes in the basal ganglia were described bilaterally, which were also vaguely visible on the initial MRI. Empirical antimicrobial therapy with ceftriaxone and acyclovir and symptomatic treatment were initiated. Due to the atient's deteriorated condition, corticosteriods were added. Epidemiological investigation revealed that the patient had lived for a long time in the Western Carpathian Mountains in the Váh River basin (Trenčín Region), which is one of the most active TBE endemic areas in Slovakia.

The man reported no recent tick bites, no consumption of raw milk products, and no professional exposure. He only mentioned frequent walks with his dog. In the 47th week after the onset of the disease, during a hospital readmission due to choreatic dyskinesia, cardiopulmonary insufficiency occurred, leading to the patient's death. He had not been vaccinated against TBE. In 2009–2023, 1992 TBE cases were reported in Slovakia; 99,4% (1793/1803) of TBE cases with known vaccination history were unvaccinated. Current legislation regulates TBE vaccination as the recommended vaccination for persons who are occupationally exposed to an increased risk of TBE (primarily occupations in agriculture, forestry, tourism and recreation sectors). Based on an assessment of occupational exposure, the vaccine is reimbursed by the employer. Other citizens may be vaccinated at their own request through self-payment of the vaccine or through health insurance benefits.

proLékaře.cz | 13.2.2026

Table 1. Main laboratory findings

Laboratory data					
	Sample collection (in the week following the onset of symptoms)				
Charakteristic	1.	2.	33.	44.	cut-off
Blood					
Albumin (g/l)	42.09	37.95	44.46		35.0–52.0
Imunoglobulín M (g/l)	1	1.2	0.67		0.4–2.3
Imunoglobulín G (g/l)	12.09	10.93	9.89		7.0–16.0
anti TBEV IgM (U/l)	3.38	4.02	0.44	0.23	≥1.1
anti TBEV IgG (U/l)	1.27	2.91	1.06	2.5	≥1.1
CSF					
Albumin (mg/l)	427	317	173		120– 300
Imunoglobulín M (mg/l)	2.69	7.72	3.33		0.20– 1.20
Imunoglobulín G (mg/l)	50.2	51.3	48.4		12.0–40.0
anti TBEV IgM	negat	pozit	negat		
anti TBEV IgG	negat	negat	negat		
specific TBEV IgM antibody index		2,96			> 1.5
Element	625/3	35/3	17//3		0.00–10.0
Erytrocyte	832/3	3.3	1.0/3		
Glucose (mmol/l)	3.19	3.38	3.57		2.25–4.50
Protein (g/l)	0.54	0.49	0.28		0.00–0.50
Chlorid (mmol/l)	121.2	116.1	119.1		115–135
Lactate	3.11	2.73	–		1.2–2.10
Cytology	pleocytosis*	pleocytosis**			
*polynuclear and monocytic, erythrophages, **monocytic, lymphocytic					
Blood-CSF barrier					
Q Alb= Alb(CSF)/AlB(S)	10.14	8.35	3.88		< 7.4
barrier function	impairment	impairment	non-impairment		
Intrathecal IgM antibody syntesis by using Reiber's graph					
intrathecal syntesis	not present (0%)	present (67%)	present (86%)		
Index IgM	0.27	0.77	1.28		< 0.75
Intrathecal IgG antibody syntesis by using Reiber's graph					
intrathecal syntesis	not present (0%)	not present (0%)	present (47%)		
Index IgG	0.41	0.56	1.21		< 0.75

DISCUSSION

The diagnosis of TBE is based on the detection of specific IgM antibodies in the cerebrospinal fluid. These antibodies develop with a slight delay and may not be detectable at the onset of the disease. This may cause underreporting of TBE compared to the real number of cases. The reasons for the underreporting of TBE in Europe are multifactorial; only 8% of European countries use the current ECDC diagnostic criteria. Other reasons include specific symptoms in paediatric patients, access to diagnostic tests, and suboptimal surveillance systems or passive surveillance [2]. Through active-passive surveillance with the integration of microbiological and epidemiological information systems, we strive to improve the quality of data on acute cases of TBE.

proLékaře.cz | 13.2.2026

Tick bites go unnoticed in about one third of patients, and initial symptoms are not specific, making diagnosis of TBE in its early stages difficult [4]. The mode of TBE transmission is unknown in 26.3% of cases in Slovakia) [3]. In the case we reported, it was not possible to determine the mechanism of transmission. It may be related to nymph bites, when the bite is easily overlooked, or the small nymphs are unknowingly removed when undressing or scratching the skin. Living in an endemic area is, therefore, the only information that focuses attention on the possible route of transmission of TBEV. In our case, this route of transmission is supported by two facts: the patient lived in an area with high endemicity, and he liked to take his dog for long walks.

TBE is a disease that may present as meningitis, meningoencephalitis, or meningoencephalomyelitis. The case-fatality of TBE in EU/EEA countries is less than 2%, generally reported to be around 0.5% [5]. Long-term sequelae have been reported in 10–40% of patients with neurological symptoms, but different study designs and definitions make it difficult to compare [6, 7, 8]. Information on the monophasic course is limited. Several clinical studies proved that the monophasic form of neuroinfection is associated with a more severe outcome [7, 9]. In a comparative study of a group of patients with a monophasic and a biphasic course, the age of the patients, presence of underlying disease, previous vaccination against TBE, and the duration of neurological involvement before CSF examination remained statistically significantly associated, even on multivariate testing, suggesting that these factors were independently associated with a monophasic course of illness [10]. After acute TBE, a minority of patients experience long-term neurological deficits [6]. Some papers demonstrated that patients with sequelae after TBE had significantly more neuropsychic symptoms than patients who completely recovered and more than the subjects in control group [7, 8].

Most of the symptoms reported in the literature were present in our patient. At the onset of the disease, respiratory disorders and bulbar syndrome required admission to the intensive care unit. During hospitalisation, left-sided hemiparesis, organic psychosyndrome with significant impairment of memory-cognitive functions and depressive syndrome were diagnosed. Subsequently, epiparoxysms appeared. In the 47th week after the onset of the disease, the patient was rehospitalized because of choreatiform dyskinesia. The mentioned sequelae of the TBE disease caused a significant deterioration in the quality of life, including the loss of performing self-care. Intensive psychiatric, psychotherapeutic, neurological treatment, including oxygen therapy in a hyperbaric chamber, did not eliminate the sequelae of the disease in our patient to enable him to perform self-care activities. The long-term sequelae resulted in disability, a fundamental change in the way of life, and led to his premature death. Studies on the long-term sequelae of TBE in Slovakia, like those in Central and Eastern Europe, are not frequent. In our report, we present the course of TBE with serious sequelae and a fatal outcome. We want to raise the awareness that the course of TBE is often unpredictable. Further research is necessary to develop effective managment for the neurological complications of TBE. TBE vaccination is highly effective in prevention of this disease. Despite the availability of highly effective vaccines in the Czech Republic, 3648 cases of TBE were recorded between 2018–2022 (7.0/100,000 inhabitants). 98.1% (3105/3166) of TBE cases with known vaccination history were unvaccinated. It is estimated that during the monitoring period, vaccination against TBE prevented 1020 TBE cases, including 964 hospitalizations, in a population of 10.4 million people [11]. The situation in vaccination in Slovakia is like the Czech Republic, with 99.4% of diseases occurring in unvaccinated individuals in our country. To increase the protection of the population through vaccination, it is necessary to achieve at least partial coverage of the vaccine costs by health insurance companies preferable in regions with the highest endemicity and also to increase public awareness of the potential risks of the disease and the benefits of vaccination.

CONCLUSION

Our short report with a fatal outcome aims to complement the mosaic of serious cases, as well as to draw attention to the need for better information of the risk factors associated with TBE with long-lasting sequelae. The report is also intended to highlight the improvement of case management and to stimulate the creation of new vaccination strategies.

REFERENCES

1. Úrad verejného zdravotníctva SR. Analýza epidemiologickej situácie a činnosti odborov epidemiológie v Slovenskej republike za rok 2022. (Analysis of the epidemiological situation and activities of epidemiology departments in the Slovak Republic for 2022), ÚVZ SR. [cit. 2024-11-20] Available at: https://www.uvzsr.sk/web/uvz/vyrocne-spravy-epidemiologia
2. Kunze M, Banović P, Bogovič P, at al. Recommendations to Improve Tick-Borne Encephalitis Surveillance and Vaccine Uptake in Europe. *Microorganisms,* 2022,10(7):1283–1298. doi: 10.3390/microorganisms10071283.
3. Kerlik J, Avdičová M, Štefkovičová M, at al. Slovakia reports highest occurrence of alimentary tick-borne encephalitis in Europe: Analysis of tick-borne encephalitis outbreaks in Slovakia during 2007– 2016. *Travel Med Infect Dis*., 2018,26(11– 12):37– 42. doi: 10.1016/j.tmaid.2018.07.001.
4. Lindquist L, Vapalahti O. Tick-borne encephalitis. *Lancet,* 2008,371:1861–1871. doi: 10.1016/S0140-6736(08)60800-4.
5. European Centre for Disease Prevention and Control. The risk of tick-borne encephalitis virus transmission via substances of human origin. Stockholm: ECDC; 2024. ISBN 978-92-9498-746-4 doi 10.2900/4129451.

proLékaře.cz | 13.2.2026

6. Kaiser R. Tick-borne encephalitis: Clinical findings and prognosis in adults. *Wien Med Wochenschr*, 2012,162(11– 12):239–243.
7. Haglund M, Günther G. Tick-borne encephalitis--pathogenesis, clinical course and long-term follow-up. *Vaccine*, 2003,1(21) Suppl 1:S11– 18. doi: 10.1016/s0264-410x(02)00811-3.
8. Mickiene A, Laiskonis A, Günther G, at al. Tickborne encephalitis in an area of high endemicity in Lithuania: disease severity and long-term prognosis. *Clin Infect Dis*., 2002,35(6):650– 658. doi: 10.1086/342059.
9. Bogovič P, Stupica D, Rojko T, et al. The long-term outcome of tick-borne encephalitis in Central Europe. *Ticks Tick Borne Dis*., 2018,9(2):369– 378. doi: 10.1016/j.ttbdis.2017.12.001.
10. Bogovič P, Lotrič-Furlan S, Avšič-Županc T, et al. Comparison of Clinical, Laboratory and Immune Characteristics of the Monophasic and Biphasic Course of Tick-Borne Encephalitis. *Microorganisms,* 2021,9(4):796– 808. doi: 10.1007/s10354-012-0105-0.
11. Kyncl J, Angulo FJ, Orlikova H, Zhang P, Vlckova I, Maly M, Krivohlavkova D, Harper LR, Edwards J, Bender C, Pilz A, Erber W, Madhava H, Moïsi JC. Effectiveness of Vaccination Against Tick-Borne Encephalitis in the Czech Republic, 2018– 2022. *Vector Borne Zoonotic Dis*., 2024,24(9):607– 613. doi: 10.1089/vbz.2023.0166.

Do redakce došlo dne 13. 11. 2024.

Adresa pro korespondenci:
prof. MUDr. Mária Štefkovičová, PhD., MPH
Fakulta zdravotníctva
Trenčianská univerzita Alexandra Dubčeka v Trenčíně
Študenská 1
911 01 Trenčín
Slovenská republika
e-mail: stefkovicova@gmail.com