American Journal of Infectious Diseases and Microbiology, 2021, Vol. 9, No. 1, 1-3
Available online at http://pubs.sciepub.com/ajidm/9/1/1
Published by Science and Education Publishing
DOI:10.12691/ajidm-9-1-1

Tick-borne Encephalitis in a 29-Year-Old Returning Traveller

Abolaji Atomode[1,#,*], Hassan Haruna[1,#], Odega Emmanuel[2,#], Mayode Ajiboye[1], Sarah Mohammed[1], Joseph Ogwuche Onah[3]

[1]Department of Medicine, James Paget University Hospital NHS Foundation Trust, Norfolk, UK
[2]Department of Medicine, Morriston Hospital, Swansea, UK
[3]Department of Medicine, Royal Gwent Hospital, Newport, South Wales, UK
[#]These authors contributed equally to this work.
*Corresponding author: abolajiatomode@gmail.com

Received December 06, 2020; Revised January 09, 2021; Accepted January 18, 2021

Abstract Tick-borne encephalitis (TBE) is a central nervous system (CNS) disease with high morbidity and mortality caused by a *flavivirus* and usually transmitted to humans via the bite of an infected *Ixodes ricinus* tick. It is endemic to central Europe, Germany inclusive. Until 2019, the causative agent, TBE virus, was not considered to occur in the UK. However, with the increase in tourism TBE is becoming a problem also outside endemic regions. It has a varied clinical manifestation ranging from mild symptoms to potentially life-threatening meningoencephalitis or meningoencephalomyelitis. Its diagnosis relies on high index of clinical suspicion and supported by the demonstration of specific IgM- and IgG-serum antibodies by ELISA. Management is largely supportive. We present a unique case of tick-borne encephalitis in a young traveller returning from an endemic region to the UK, managed appropriately with no residual complications.

Keywords: *Tick-borne encephalitis (TBE), Borrelia spp., Ixodes spp, Cerebrospinal fluid (CSF)*

Cite This Article: Abolaji Atomode, Hassan Haruna, Odega Emmanuel, Mayode Ajiboye, Sarah Mohammed, and Joseph Ogwuche Onah, "Tickborne Encephalitis in a 29-Year-Old Returning Traveller." *American Journal of Infectious Diseases and Microbiology*, vol. 9, no. 1 (2021): 1-3. doi: 10.12691/ajidm-9-1-1.

1. Introduction

Tick-borne encephalitis (TBE) is a viral infectious disease that attacks the central nervous system and can result in long-term neurological sequel, and even death. It is the most frequent vector-transmitted infectious disease of the central nervous system (CNS) in Europe and Asia and is considered an emerging disease due to its rising incidence and the spread of endemic areas in recent decades making it a growing public health challenge in Europe and other parts of the world [1,2,3,4].

It is caused by a virus (*Flavivirus* genus, family *Flaviviridae*) which includes five subtypes: European subtype, transmitted by *Ixodes ricinus* ticks, endemic in rural and forested areas of central, eastern and northern Europe; Far eastern subtype, transmitted mainly by *I. persulcatus*, endemic in far-eastern Russia and in forested regions of China and Japan; Siberian subtype, transmitted by *I. persulcatus*, endemic in Urals region, Siberia and far-eastern Russia, and also in some areas in north-eastern Europe; The Baikalian and Himalayan subtype [1]. The clinical picture of TBE has previously been described from different geographic regions in Europe and Asia [5,6]. TBE in Europe is considered to be a milder disease than TBE in the Far East, where even relapsing and chronic courses of infection have been reported [7].

Most cases occur during the highest period of tick activity, in Central Europe mainly from April to November [8,9,10]. TBE caused by European subtype of virus (TBEV) has typically a biphasic clinical course with the second phase presenting as meningitis, meningoencephalitis, or meningoencephalomyelitis in approximately two-thirds of patients and up to 50% of patients have long-term sequelae [4,10]. An occasional clinical manifestation is an abortive form of the disease [11]. Treatment is based on the symptomatic measures. However, TBE can be successfully prevented by safe and highly effective vaccine [10].

2. Case Presentation

Index patient is a 29-years old gentleman with no co-morbidities and not on any regular medications who presented with fever, nausea, generalized body aches, dizziness, clumsiness and felt unsteady on his feet needing support to mobilize of 1-week duration. The symptoms started while he was on holiday in Germany and was bitten by a tick.

Examination showed a young man, who was alert and orientated with evidence of a small healed scar around his right medial popliteal region (site of tick bite), bilateral nystagmus and mild intention tremor. Tone, power and reflexes were normal globally and planters were down going. Gait was however ataxic.

Blood test on admission showed elevated white blood cell count (16.6 x 10^9/L, Neutrophilia 13.3 x 10^9/L), C-Reactive protein of 26mg/L. CSF sampling yielded normal opening pressure, and test for glucose (2.9mmol/L), protein (0.49g/L), viral PCR was negative for HSV 1&2 DNA, VZV DNA, Adenovirus DNA, Enterovirus RNA, Parechovirus RNA. An extended viral panel was carried out which came back *Borrelia* spp. DNA (16S target) and *Borrelia* IgG Immunoblot Negative but TBE virus IgG (1:100) and TBE virus RNA positive. Throat swab was negative for the viruses tested.

Patient was treated with Doxycycline for a total of 6 weeks after initial Ceftriaxone and he improved remarkably, able to do his usual day to day activities. Patient was followed up as an out-patient in Neurology clinic and discharged from clinic with no neurological complications.

3. Discussion

Most available sequences of the European TBE virus (TBEV) are derived from ticks, because the virus is rarely isolated from patients, and clinical samples generally are PCR negative at onset of neurologic symptoms. This situation hampers TBEV molecular studies [12].

Due to the limitations of laboratory testing for Lyme disease, diagnosis is based primarily on clinical findings [13,14,15,16]. The host antibody response to *B. burgdorferi* infection develops slowly, and only one half of patients with early-stage Lyme disease will have a positive serology. The demonstration of specific IgM- and IgG-serum antibodies by ELISA is the method of choice for the specific diagnosis of TBE. The Immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies appear two to four and four to six weeks, respectively, after the onset of erythema migrans and peak at six to eight weeks. IgM-antibodies may be detectable for several months after infection, whereas IgG-antibodies persist for life and mediate immunity that prevents reinfection [16,17]. A case of TBE is defined by the presence of clinical signs of meningitis, meningoencephalitis or meningoencephalomyelitis with cerebrospinal fluid (CSF) pleocytosis (>5 × 106 cells/l) and the presence of specific TBEV serum immunoglobulin M (IgM) and IgG antibodies, CSF IgM antibodies or TBEV IgG seroconversion [2].

Thus, it is important for clinicians to be aware of this and initiate treatment early if diagnosis is suspected.

This case is unique because treatment for Lymes encephalitis was initiated on based clinical suspicion and continued despite negative test for *Borrelia spp.* Additionally, the decision was justified by the marked improvement experienced after a 6-week course of antibiotics.

Furthermore, a positive TBE virus test, hints at the possibility of a co-infection of with *Borrelia spp.*

TBE is endemic in Germany with the risk areas increased from 129 districts in 2007 to 161 in 2019 [18]. Until 2019, the causative agent, TBE virus, was not considered to occur in the UK when in July, a German infant developed serologically diagnosed TBE following a tick bite in southern England [19,20].

Several classes of antibiotics have been shown to be active against *B burgdorferi* and are used in clinical treatment of Lyme disease [21]. These include penicillins (ampicillin, amoxicillin, penicillin G), some second and third generation cephalosporins (cefuroxime axetil, cefotaxime, ceftriaxone), tetracyclines (tetracycline, doxycycline) and macrolide antibiotics (erythromycin, clarithromycin and azithromycin). The efficacy of penicillin, cephalosporins and tetracyclines has been shown to be equal. Several but not all studies have suggested that macrolides are less efficacious. Of note, first generation cephalosporins are used to treat cellulitis, which is sometimes confused with erythema migrans. These drugs are not effective against *B burgdorferi.* If co-infection with *A phagocytophilum* is possible, doxycycline is typically preferred because of its activity against the organism. Of the oral agents, doxycycline also has among the best bioavailability and central nervous system penetration [22].

This case further stresses the need to continue to view TBE as a travel disease, which make travel history vital in early assessment of these patients.

TBE is partly preventable by wearing trousers, long sleeves and tick-repellents [23]. Early removal of ticks does not prevent disease [8]. The most effective measure is vaccination. The Scientific Working Group of Tick-borne encephalitis stresses the importance of raising awareness in non-endemic regions for travel related TBE and recommends tick-borne encephalitis virus vaccination for Europeans travelling to areas of TBE virus risk if their visits will include extensive outdoor activities, all age groups above 1 year in highly endemic areas, but also for individuals at risk in areas with a lower incidence. Travellers to endemic areas should be vaccinated. [2,18,19,24,25,26].

References

[1] European Centre for Disease Prevention and Control. (2021), Fact-sheet about Tick-borne Encephalitis, Available from: https://www.ecdc.europa.eu/en/tick-borne-encephalitis/facts/factsheet (Accessed 10 January 2021).

[2] Kreusch, T.M., Holding, M., Roger Hewson, R., Harder, T., Medlock, M, J., Hansford, M., K., et'al. (2019), A probable case of tick-borne encephalitis (TBE) acquired in England, July 2019., Euro Surveillance, 24(47): 1900679. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6885749/ /(Accessed 10 January 2021).

[3] World Health Organization (2020), Immunization is the best Protection against Tick-borne Encephalitis, Available from: https://www.who.int/news/item/19-02-2020-immunization-is-the-best-protection-against-tick-borne-encephalitis (Accessed 10 January 2021).

[4] Steffen, R. (2016), Epidemiology of tick-borne encephalitis (TBE) in international travellers to Western/Central Europe and conclusions on vaccination recommendations, *Journal of Travel Medicine*, 23(4), PP. 1-10.

[5] Monath TP, Heinz FX. Fields BN, Knipe DM, Howley PM, et al. *Flaviviruses, Fields' virology*, 1996, vol. Vol. 1 3rd ed. Philadelphia Lippincott-Raven (pg. 961-1034).

[6] Dumpis U, Crook D, Oksi J. *Tick-borne encephalitis*, Clin Infect Dis, 1999, vol. 28 (pg. 882-90).

[7] Vasilenko FI, Grigorjeva IGH. *Early and late recurrences of tick-borne encephalitis [in Russian], 1987, vol. 87 (pg. 178-81). Available from: europepmc.org/article/med/3577500.*

[8] Rendi-Wagner P. *Risk and prevention of tick-borne encephalitis in travellers.* J Travel Med. 2004; 11(5): 307-12.

[9] Kunze U; ISW TBE. Conference report of the 9th meeting of the International Scientific Working Group of TickBorne Encephalitis (ISW TBE). *Tick Borne Encephalitis: from epidemiology to*

current vaccination recommendations. Vaccine. 2007; 25(50): 8350-1

[10] Mansfield KL, Johnson N, Phipps LP, Stephenson JR, Fooks AR, Solomon T. *Tick-borne encephalitis virus-a review of an emerging zoonosis.* J Gen Virol. 2009;90:1781-1794

[11] Kaiser R. *Tick-borne encephalitis.* Infect Dis Clin North Am. 2008; 22: 561-575, x.

[12] Spagnolo, E., V., Mondello, C., Roccuzzo,S., Cardia, L., and Raffino, C. (2018), A lethal Tick-Borne Encephalitis (TBE) due to TBE Virus in Sicily (Italy): a case of IgG+/IgM- response? *La Clinica Terapeutica*, 169(4):e145-e148.

[13] Shapoval AN. *Primary progredient forms of tick-borne encephalitis*, Zh Nevrol Psikhiatr Im S S Korsakova, 1976, vol. 76 (pg. 182-8).

[14] Sigal LH. *Laboratory confirmation of the diagnosis of Lyme disease*. Uptodate. 2002; 11: 1.

[15] Tugwell P, Dennis DT, Weinstein A, Wells G, Shea B, Nichol G, et al. *Laboratory evaluation in the diagnosis of Lyme disease.* Ann Intern Med. 1997; 127: 1109-23.

[16] Bunikis J, Barbour AG. *Laboratory testing for suspected Lyme disease*. Med Clin North Am. 2002; 86: 311-40.

[17] Taba, P., Schmutzhard, E., Forsber,P., Lutsar, I., Ljøstad U., Mygland, A. et'al (2017), EAN consensus review on prevention, diagnosis and management of tick-borne encephalitis, *European Journal of Neurology*, 24(10): 1214-e61.

[18] Human Animal Infections and Risk Surveillance group. HAIRS risk assessment: tick-borne encephalitis. Qualitative assessment of the risk that tick-borne encephalitis presents to the UK population. London: Public Health England; 2019. Available from: https://www.gov.uk/government/publications/hairs-risk-assessment-tick-borne-encephalitis (Accessed 10 January 2021).

[19] Lotric-Furlan S, Avsic-Zupanc T, Strle F. *An abortive form of tick-borne encephalitis (TBE)--a rare clinical manifestation of infection with TBE virus.* Wien Klin Wochenschr. 2002; 114: 627-629.

[20] Hellenbrand W, Kreusch T, Böhmer MM, Wagner-Wiening C, Dobler G, Wichmann O, et al. (2019) Epidemiology of Tick-Borne Encephalitis (TBE) in Germany, 2001-2018, *Pathogen*, 8(2): E42. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6630332/(Accessed 10 January 2021).

[21] Wormser GP, Dattwyler RJ, Shapiro ED , et al. "The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis". Clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2006; 43: 1089-134. [PMID: 17029130]

[22] Linden T. Hu, "Lyme Disease", Annals of Internal Medicine; American College of Physicians, 2016, 10.

[23] Donoso Mantke O, Escadafal C, Niedrig M, Pfeffer M, On Behalf Of The Working Group For Tick-Borne Encephalitis Virus C. *Tick-borne encephalitis in Europe, 2007 to 2009*. Euro Surveill. 2011; 16(39): pii=19976.

[24] Lindquist L, Vapalahti O. *Tick-borne encephalitis*. Lancet. 2008; 371(9627): 1861-71.

[25] Walder G, Falkensammer B, Hein FX, Holzmann H, Dierich MP, Würzner R. *Tick-borne encephalitis in the Tyrol (Austria): changes in incidence and endemicity 2000-2006*. Int J Med Microbiol. 2008; 298 Suppl 1:88-93.

[26] Anna J. Henningsson, A., J., Lindqvist, R., Norberg, P., Lindblom, P., Roth, A., Forsberg, P., et 'al. (2016), Human Tick-Borne Encephalitis and Characterization of Virus from Biting Tick, *Emerging Infecious Disease*, 22(8): 1485-1487.