



CASE REPORT

Toscana Virus (TOSV) Meningitis in Two Travelers in Southeastern Spain

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Abstract

Two Irish tourists, a 72-year-old male and his 60-year-old wife, developed symptoms of meningoencephalitis after traveling to Spain. Both complained of a holocranial headache, vomiting, and fevers. Toscana virus (TOSV) infection was diagnosed based on serology. Cultures and PCR were negative for other pathogens. Both blood (serum) and cerebrospinal fluid (CSF) samples were tested to diagnose TOSV infection. Specifically, CSF and serum samples were processed using real-time RT-PCR and ELISA serologic assays. Symptomatic treatment led to quick recovery and both patients were discharged from the hospital within 1 week. These cases highlight the importance of considering TOSV in the differential diagnosis of acute meningitis, especially in travelers to endemic regions. The lack of awareness among clinicians and specific screening recommendations may lead to underestimation of the TOSV incidence.

Keywords: Toscana virus, Viral Meningitis, Travel-related Illness, Arboviruses, Meningoencephalitis

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INTRODUCTION

Toscana virus (TOSV) is an arbovirus transmitted by *Phlebotomus* sandflies that causes central nervous system infections, like meningitis, in Mediterranean countries, including Spain. TOSV was first isolated in Spain in 1988 [1]. Sporadic cases of meningeal symptoms and encephalitis have been reported although most TOSV infections are asymptomatic. TOSV circulates in southern Spain where clinical cases have been documented [2]. Herein, we present two patients evaluated and treated in the Infectious Diseases Unit of San Juan University Clinical Hospital (Alicante, Spain).

Case 1: 72-year-old male

A 72-year-old male presented to our hospital complaining of a holocranial headache, vomiting, and fevers that evolved over 3 days. The medical history included paroxysmal atrial fibrillation and adenocarcinoma of the prostate that was treated with radiotherapy in 2024. He was taking the anticoagulant, apixaban. The physical examination was significant for the following: blood pressure, 106/66 mmHg; heart rate, 66 bpm; oxygen saturation, 94%; and temperature, 37.2°C. He was conscious but exhibited meningeal signs. Laboratory testing revealed an elevated leukocyte count ($12.1 \times 10^9/L$) and pleocytosis ($184/mm^3$). The cultures

and PCR were negative but he was initially given symptomatic treatment with paracetamol for suspected meningitis. Both CSF and blood (serum) samples were analyzed for PCR and serology to confirm infection.

A CSF analysis performed on 7 October 2024 revealed glucose and protein concentrations of 54 mg/dL and 128.2 mg/dL, respectively. The leukocyte count was elevated at 184 cells/mm³ (38.1% polymorphonuclear and 61.9% mononuclear cells). The CSF sample had no red blood cells. These findings are consistent with lymphocytic pleocytosis and elevated protein, supporting the diagnosis of viral meningitis. CSF and serum samples were processed at the National Microbiology Centre (Majadahonda, Spain) using real-time RT-PCR (L segment primers) and EUROIMMUN ELISA kits (Lübeck, Germany). The TOSV serologic findings were as follows: TOSV IgM (enzyme-linked immunosorbent assay), 11.2 (positive); and IgG, 5.04 with reference to acute-phase serum. The high IgM titers confirmed an acute-phase infection. The diagnosis was confirmed to be an acute infection based on a positive CSF PCR and IgM seroconversion. No cross-reactivity was detected with other phleboviruses in neutralization assays. Symptomatic treatment led to quick recovery and he was discharged from the hospital within 1 week.

Case 2: 60-year-old female

A 60-year-old woman, the spouse of Case 1, presented on 8 October 2024, with a 2-day history of holocranial headache, photophobia, and fevers (38.5°C). Her medical history included hypertension, dyslipidaemia, and chronic ischemic heart disease that were managed with aspirin, atorvastatin, and bisoprolol.

A CSF analysis performed on 11 October 2024 showed glucose and protein concentrations of 50 mg/dL and 115.5 mg/dL, respectively. The leukocyte count was elevated at 285 cells/mm³ with a predominance of mononuclear cells (97.6%) and a small proportion of polymorphonuclear cells (2.4%). The CSF sample had no red blood cells. These findings were consistent with a marked lymphocytic pleocytosis and elevated protein, supporting the diagnosis of viral meningitis. CSF and serum samples were collected within 24–48 h of symptom onset and stored at –80°C for PCR and ELISA testing. The CSF and serum samples were transported and processed at the National Microbiology Centre (Majadahonda, Spain) using real-time RT-PCR (L segment primers) and EUROIMMUN ELISA kits. The TOSV serologic findings were as follows: TOSV IgM (enzyme-linked immunosorbent assay), 3.83 (positive); and IgG 4.69 (positive) with reference to acute-phase serum. The case was confirmed to be an acute infection based on a positive CSF PCR and IgM seroconversion. No cross-reactivity was detected with other phleboviruses in neutralization assays. The patient improved with symptomatic treatment and was discharged. Recent travel prompted testing for vector-borne diseases.

Paired samples could not be obtained from the patients because they returned to their usual place of residence in Ireland.

The patients began their travel on 16 September 2024, departing from Ericeira, Portugal. On 17 September they stayed at a campsite in the northern area of Albufeira, Portugal. On 18 and 19 September they travelled to Spain and spent 2 nights camping in Dos Hermanas, Seville. Their itinerary continued with a stay in La Zubia, Granada from 20–22 September and concluded with arrival in Alicante, Spain on 23 September 2024, where they remained.

Between 1 and 7 October the couple's daughter visited them in Alicante before returning to Ireland; she did not develop any symptoms. The male patient had the onset of meningoencephalitis symptoms on 5 October 2024; his wife became symptomatic on 8 October 2024. The timing of symptom onset in conjunction with the typical incubation period for TOSV (3–7 d), supports the conclusion that the infection was acquired locally in Alicante. This assessment was corroborated by the Valencian Public Health Department, which classified both cases as autochthonous. Both patients were evaluated and treated in the Infectious Diseases Unit of San Juan University Clinical Hospital (Alicante, Spain).

Both cases met the ECDC criteria for confirmed TOSV infection (PCR positivity in CSF or IgM seroconversion with exclusion of cross-reactivity). Both cases highlight the importance of considering TOSV as a cause of acute meningitis, especially in regions where TOSV is prevalent.

DISCUSSION

Spain is the most popular destination for UK and Irish tourists with >20.5 million visits annually. Ireland is the largest source market per capita. In 2024, a total of 21,176,480 tourists coming from British Isles visited Spain, which was a 9.8% increase from 2023 according to the INE Border Movements Survey [3]. British Isles are listed as one of the international markets contributing to tourism in the Valencian Community, a Mediterranean tourist area. The Valencian Community received a total of 11,914,970 tourists from January–September 2024, most of whom came from UK and Ireland [3].

TOSV is the only pathogenic arbovirus for humans detected to date in Spain. TOSV causes aseptic meningitis and is usually benign. The virus is commonly found in the Mediterranean region and has been identified in Spain through research involving travellers from Sweden [4] and Germany [5]. According to some published studies, TOSV has emerged as a major cause of meningitis in the Mediterranean, especially during the summer months when there is increased sandfly activity [6,7].

A study in Granada, Spain reported a 24.9% seroprevalence of TOSV with rates increasing significantly with age. The virus was identified in 3 of 103 groups of

sandflies through viral culture or PCR, suggesting the presence of at least 2 distinct lineages (Italian and Spanish) in the Mediterranean region [8,9].

Climate change and globalization worsen the spread of the virus, emphasizing the need for additional research to tackle this health threat. A review covering the period from 1985–2023 reported a total of 1381 cases from 12 countries with the majority of cases ($n = 1064$ [77%]) occurring in Italy. Spain was the second most frequent source of infections. Ireland was not represented in this TOSV local and imported case distribution [9]. Few cases of symptomatic TOSV infection have been identified in travellers returning to the United Kingdom or Ireland from Italy or Portugal [10–12].

Finally, we note that a lack of awareness among clinicians and the absence of recommendations for screening suspected cases using specific laboratory tests could contribute significantly to the underestimation of TOSV incidence, despite its importance for public health.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this case report are available from the corresponding author upon reasonable request. Due to patient privacy and confidentiality, some data may not be publicly available.

ETHICS STATEMENT

This study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from both patients for publication of these case reports. The Research Ethics Committee of Hospital Universitario San Juan de Alicante approved the study entitled “Toscana Virus (TOSV) Meningitis in Two Travelers in Southeastern Spain” (Code: 25/050), confirming the protocol, investigator capacity, consent procedures, and data protection compliance according to relevant Spanish and European regulations.

AUTHOR CONTRIBUTIONS

Leticia Espinosa-Del Barrio and Elisabet Delgado-Sánchez collected the clinical data and contributed to patient management. Fernando Buñuel performed the microbiological analyses. Francisco Jover-Díaz supervised the study, coordinated the writing of the manuscript, and is the corresponding author. All authors contributed to the manuscript preparation, critically revised the work, and approved the final version.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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