LETTERS

Jean-Marc Collard, Zaneidou Maman, Harouna Yacouba, Saacou Djibo, Pierre Nicolas, Jean-François Jusot, Jocelyne Rocourt, and Rabi Maitournam

Acknowledgments

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References


Address for correspondence: Jean-Marc Collard, Biology Unit, CERMES, 634 blvd de la Nation, YN034 BP 10887, Niamey, Niger; email: jmcollard@cermes.org

Toscana Virus Infection in American Traveler Returning from Sicily, 2009

To the Editor: Since the discovery of Toscana virus (TOSV) in 1971 in Tuscany (1), sandfly-borne TOSV has become recognized as a leading cause of acute meningitis in central Italy during the summer (2). France, Spain, Portugal, Greece, and Cyprus have also reported cases of TOSV infection (2). Although TOSV has been detected in sandflies in Sicily (3), we are not aware of any historically documented human infection with TOSV in this southernmost region of Italy.

We report TOSV infection of an American male physician, 65 years of age, who traveled to Sicily for 3 weeks and returned to the United States in October 2009. Two days after his return, he awoke with a headache, and hours later he noticed difficulty finding words. His headache progressed, and during the next few hours, he experienced severe expressive dysphasia. At admission to the hospital, he denied having fever, nuchal rigidity, photophobia, nausea, vomiting, or diarrhea.

Other than changing planes in Milan, the patient had remained in Sicily during the entire 3 weeks of his visit. He had sustained both mosquito and what he thought were flea bites while in Sicily. He had no known exposure to bats, rabid animals, or ticks.

Computed tomographic scan and magnetic resonance imaging of the brain showed no mass lesions or abnormality of the cerebral vessels. A sample of cerebrospinal fluid (CSF) obtained at admission showed 14 leukocytes/mm³ (reference range 0–5 leukocytes/mm³) with 100% lymphocytes, a protein level of 126 mg/dL (reference range 15–45 mg/dL), and a glucose level of 63 mg/dL (reference range 50–80 mg/dL). A nasopharyn-
geal swab specimen was negative for influenza A and B virus antigens. Other than a decreased thrombocyte count and an elevated serum glucose level, the results of complete blood count, comprehensive chemical panel, and coagulation studies were within normal limits. PCR results for CSF were negative for herpes simplex virus, enterovirus, and parechovirus. Test results for acute-phase and convalescent-phase serum specimens performed at the Washington State Department of Health Laboratory were negative for West Nile virus and St. Louis encephalitis virus immunoglobulin M.

Serum and CSF were sent to the Centers for Disease Control and Prevention in Fort Collins, Colorado. TOSV RNA was detected in a CSF sample collected on day 1 of illness by using reverse transcription–PCR (4). Plaque-reduction neutralization assays demonstrated a >4-fold rise in TOSV neutralizing antibodies between paired serum specimens collected on days 1 (titer <1:10) and 21 (titer 1:320) of illness. No similar rise in neutralizing antibodies to serologically related phleboviruses (e.g., sandfly fever Naples virus and sandfly fever Sicilian virus) was detected. The patient received supportive care only. He had a complete neurologic recovery in 10 days and was able to return to work.

Phylogenetic analyses indicate that 2 geographically distinct genotypes, the Italian and Spanish lineages of TOSV, circulate throughout the Mediterranean region (5). To determine the lineage of the infecting strain, we performed advanced molecular analyses of TOSV RNA isolated from the infected traveler’s CSF. These analyses used published consensus primers that target the small (S) segment (4) as well as primers newly designed to target the medium (M) segment: M 851F, 5′-ACCAAATACACATAGCCCC-3′ (forward) and M 1327c, 5′-ATACAATTCCACAGTCGGTA-3′ (reverse) of the multisegment TOSV genome. Reverse transcription–PCR amplification and nucleotide sequencing generated 2 nt sequences of 332 (S segment) and 424 (M segment) nucleotides in length. Phylogenetic analyses of the newly determined sequences and sequences previously determined for Mediterranean TOSV isolates of diverse origin were carried out by using MEGA version 4 (6). According to phylogenetic inference, the TOSV RNA identified in the returning traveler is of the Italian lineage (Figure). Of interest, the TOSV M segment sequence generated from this patient aggregates with extreme bootstrap support along with that generated previously from a strain of TOSV that was isolated from sand flies in Palermo, Sicily, in 1993 (Figure), indicating that the infecting strain is likely representative of strains that have circulated in Sicily for years.

This case represents the third report of meningitis or meningoencephalitis caused by TOSV infection in a US traveler to the Mediterranean (all acquired in Italy) (7,8). As is shown by this and other recent reports of TOSV infections in the Mediterranean islands surrounding Italy (9), the geographic range of TOSV human infections is larger than previously known. Reports of TOSV infection among European travelers returning from disease-endemic regions have provided additional evidence of the emergence of TOSV-related illness on a global scale (10).

Although the clinical course varies from asymptomatic infection to severe meningoencephalitis, TOSV should be included in the differential list of viral pathogens among patients who seek treatment with symptoms consistent with meningitis or encephalitis if the patients have recently traveled to Mediterranean areas, including Sicily. Because neither a vaccine nor specific antiviral drug treatment is available to prevent or treat TOSV infection, travelers to TOSV-endemic areas should be advised to take all precautions to prevent insect bites.

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Phylogeny of Toscana viruses (TOSVs) of diverse origin. Partial small (S) and medium (M) segment sequences of interest were aligned by using ClustalW (www.ebi.ac.uk/Tools/clustalw2/index.html), and neighbor-joining and maximum-parsimony trees were generated using 2,000 bootstrap replicates with MEGA version 4 (6). Highly similar topologies and confidence values were derived by all methods, and a neighbor-joining tree generated from a comparison of 424 nt of the M segment polyprotein gene open reading frame is displayed here. GenBank accession numbers appear after the location and source of isolation for each taxon. Scale bar represents the number of nucleotide substitutions per site. Of interest, the 2009 Sicilian TOSV described in this study (Sicily, human, 2009) aggregates with extreme support along with other Italian viruses, including an isolate that was derived from sandflies in Palermo, Sicily, in 1993.
Hospital Discharge Data for Guillain-Barré Syndrome and Influenza A (H1N1) Vaccine Adverse Events

To the Editor: As part of the public health response to the current pandemic (H1N1) 2009, surveillance for adverse events following vaccination for influenza A (H1N1) is a high priority (1). Surveillance for Guillain-Barré syndrome (GBS) has been of particular interest, because the syndrome was associated with the 1976–1977 swine influenza vaccine (2,3). To study this association, reliable ascertainment of recent incident cases of GBS is necessary.

GBS is an acute, immune-mediated paralytic disorder of the peripheral nervous system (3–5) with an estimated annual incidence of 0.8–1.9/100,000 (6). Most cases are associated with an antecedent infection (6). Several surveillance systems are in place to monitor rates of post-vaccination GBS (1–3), most of which include a component of electronic administrative record review for case detection. Analysis of computerized medical databases is a well-established method for monitoring for vaccine adverse events (7). Although the validity of such data varies, depending on the diagnosis and region, few studies have evaluated the use of hospital discharge data for GBS specifically (8,9).

We reviewed the Tennessee Department of Health Uniform Hospital Discharge Dataset for all hospital discharge diagnoses in 4 major metropolitan regions of Tennessee in 2002–2003 with codes from the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), that might indicate acute GBS. Records with ICD-9-CM code 357.0 (acute infective polyneuritis) or other combinations suggestive of GBS within the top 10 diagnoses were requested. These data were compared with information on cases identified by directly requesting lists of patients with discharge diagnoses of GBS from hospital medical record departments. Charts of all reported cases were validated by chart review. Patients were classified as having acute GBS if they met Brighton Criteria Levels 1, 2, or 3 (10).

A total of 344 records of possible cases of acute GBS were identified. Of these cases, 215 (63%) were identified through the state hospital discharge database, 315 (92%) were reported directly by hospitals, and 186 (54%) were identified by both systems. Among all suspected cases identified, only 103 (30%) met criteria for acute GBS, and 14 (4%) were in out-of-state residents, 114 (33%) were nonacute cases that occurred before the study period and patients were readmitted for other reasons, 90 (26%) had no documentation of GBS in the medical record, 17 (5%) were duplicate reports, and 6 (2%) had insufficient information for further investigation. The predictive-value positive of a...