Imported Chikungunya Infection, Italy

To the Editor: Chikungunya virus (CHIKV) infection is a self-limiting illness characterized by fever, headache, weakness, rash, and arthralgia. Some patients have prolonged weakness or arthralgia lasting several months. In 2006, several Indian Ocean states and India had an outbreak of CHIKV infection (1,2). During the epidemic’s peak, some European and American travelers returning from these areas were infected (3–6).

Because the foci of *Aedes albopictus*, 1 of the 2 main vectors of CHIKV, are now in Italy and many travelers visit CHIKV-epidemic areas, surveillance for imported cases is mandatory in Italy (7). From July to September 2006, a total of 17 confirmed cases of CHIKV infection were observed in travelers at 5 Gruppo di Interesse e Studio delle Patologie di Importazione (GISPI) centers (Italian network of Institutes of Infectious and Tropical Diseases). Serologic diagnosis was performed with a hemagglutination-inhibition test and confirmed by a plaque-reduction neutralization test (8). Demographic and epidemiologic characteristics of these patients are reported in the Table.

Cases were distributed throughout the year with a peak from March to May 2006 (n = 10). Nine patients (53%) were men. Median age was 43 years (range 31–66 years). Several reasons for travel were reported: tourism (64.6%), visits to relatives or friends (11.8%), business (11.8%), and missionary work (5.9%). One patient was a resident in the disease-epidemic area. The median exposure time in the CHIKV-endemic area for the 15 travelers was 15 days (range 9–93 days) (missionary and resident patients were excluded). The median delay before being seen at a clinic after return was 2 days (range 0–73 days). Only 7 patients (41.2%) were hospitalized. The remainder were outpatients.

All patients had fever; arthralgia (88.2%, n = 15), weakness (70.6%, n = 12), headache (11.8%, n = 2), diarrhea (11.8%, n = 2), and gum bleeding and epistaxis (5.9%, n = 1) were other reported symptoms. The median duration of fever was 5 days (range 2–12 days). Only 7 of 16 patients (43.8%) were still febrile when first seen. Physical examination showed diffuse macular erythematous rash in 13 patients (76.5%), a similar rate to that reported among French travelers (4). Hepatomegaly was found in 2 patients (11.8%), splenomegaly in 2 (11.8%), and peripheral lymphadenopathy in 2 (11.8%).

Twelve acute-phase patients were admitted to the hospital for blood testing within 3 days of the initial examination. In contrast with results of other studies, leukopenia and thrombocytopenia were uncommon in our study. Leukopenia (leukocyte count ≤4,000/μL) was present in 4 patients (33.3%) and thrombocytopenia (platelet count ≤150,000/μL) in 1 patient (8.3%). This finding may help distinguish CHIKV infection from dengue fever (4). Anemia (hemoglobin level ≤12 g/dL) was found in only 1 patient (8.3%). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) determination were available for 12 patients. ALT and AST levels were elevated (>40 IU/L) in 5 (41.7%) and 2 (16.7%) patients, respectively. Seven (46.7%) of 15 patients fully recovered within 1 month; 8 patients (53.3%) reported persistent arthralgia.

Because the GISPI network provides regional coverage only, the number of imported CHIKV cases in all of Italy in 2006 was likely higher. Moreover, most patients probably did not seek medical care, and when they did, physicians may have failed to recognize the disease because of lack of familiarity with it or limited diagnostic facilities. Differential diagnosis with other arthropodborne viruses of the *Alphavirus* genus (Ross River, Barmah Forest, o’nyong nyong, Sindbis, and Mayaro viruses) is difficult, but these are comparatively rare. In contrast, dengue and CHIKV epidemics may overlap, and potential patients should be screened for both.

The potential risk for introduction and establishment of CHIKV reservoirs in areas with mosquito vectors was discussed in March 2006 by a multidisciplinary European expert panel (9). In Italy, *A. albopictus* was first recorded in 1990; it has since quickly spread across the country. Scattered foci are now reported in almost all regions, mainly along the coastal plains, from the sea to the inlands, up to an altitude of ≈500–600 m (7).

The ability of *A. albopictus* to colonize new areas and its adaptability to the mild Italian climate allow vector populations to be active throughout the year (10). The patient is thought to be viremic for only 6–7 days (shortly before and during the febrile period) (6). We were unable to directly assess
viremia levels; however, almost half the patients were still febrile on return to Italy, which suggests a potential risk.

Although the same mosquito is a potential vector of dengue, no autochthonous case has been reported as yet, despite annual reports of many imported dengue cases in Italy. On the other hand, the clinical manifestations of both conditions are nonspecific, and a hypothetical autochthonous case would most likely go undiagnosed unless a targeted surveillance system were established. Prompt reporting of imported CHIKV infections is essential for monitoring of potential risk. The possibility of introducing CHIKV into Italy cannot be ruled out on the basis of current evidence.

Acknowledgments

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References

2. Mudur G. Failure to control mosquitoes has led to two fever epidemics in India. BMJ. 2006;333:773.

Table. Demographic and epidemiologic data on 17 travelers with chikungunya infection diagnosed in 2006, Italy

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age, y</th>
<th>Reason for travel</th>
<th>Country of origin</th>
<th>Date of return (length of stay, d)</th>
<th>Date of first medical assessment after return (delay, d)</th>
<th>Last date of fever (length of fever, d)</th>
<th>Fever on date of return?</th>
</tr>
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<tr>
<td>1*</td>
<td>M</td>
<td>32</td>
<td>Business</td>
<td>Réunion</td>
<td>Feb 23 (93)</td>
<td>Feb 25 (2)</td>
<td>Feb 26 (4)</td>
<td>Yes</td>
</tr>
<tr>
<td>2†</td>
<td>F</td>
<td>39</td>
<td>Tourism</td>
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<td>Feb 28 (10)</td>
<td>Feb 28 (0)</td>
<td>Feb 28 (4)</td>
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</tr>
<tr>
<td>3†</td>
<td>M</td>
<td>46</td>
<td>Tourism</td>
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<td>Mar 7 (10)</td>
<td>Mar 7 (0)</td>
<td>Mar 6 (5)</td>
<td>No</td>
</tr>
<tr>
<td>4†</td>
<td>M</td>
<td>32</td>
<td>Tourism</td>
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<td>Mar 8 (1)</td>
<td>Mar 4 (4)</td>
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<td>5§</td>
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<td>Mar 15 (7)</td>
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</tr>
<tr>
<td>6‡</td>
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<td>66</td>
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<td>Mar 27 (5)</td>
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<td>8*</td>
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<td>43</td>
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<td>46</td>
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<td>Apr 13 (73)</td>
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<td>–</td>
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<td>10‡</td>
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<td>44</td>
<td>Visit relatives</td>
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</tr>
<tr>
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<td>F</td>
<td>36</td>
<td>Tourism</td>
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<td>May 3 (3)</td>
<td>May 3 (3)</td>
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<td>May 3 (3)</td>
<td>Apr 5 (6)</td>
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<tr>
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<td>38</td>
<td>Tourism</td>
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<td>Jun 12 (2)</td>
<td>May 7 (4)</td>
<td>No</td>
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<tr>
<td>16‡</td>
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<td>Central African Republic</td>
<td>Jun 24 (14 y)</td>
<td>Jul 10 (16)</td>
<td>Apr 26 (12)</td>
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<td>57</td>
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<td>Sep 10 (4)</td>
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</table>

*GISPI (Gruppo di Interesse e Studio delle Patologie di Importazione) centers: Torino.
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‡GISPI center: Negrar. NA, not available.
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BACTEC 9240 system (Becton-Dickinson, Sparks, MD, USA). A catheter-related bacteremia was suspected, and vancomycin (1 g in intravenous drip) was prescribed. Other laboratory findings included a total leucocyte count 14.5 × 10⁹/L (84% neutrophils, 16% lymphocytes), blood urea nitrogen 38 mg/dL, and creatinine 7.9 mg/dL. Urinalysis results were within normal limits. Urine and stool cultures were negative for pathogenic bacteria. The catheter was not removed for culture. On day 4 of incubation, both blood cultures showed growth, which was then placed onto 5% (vol/vol) sheep blood agar for subculture and produced deep yellow colonies. This uniform, gram-negative, oxidase-positive bacterium was not identifiable with manual phenotypic tests and the API 20NE strip (bioMérieux, Durham, NC, USA). It was identified by the Vitek 2 system (bioMérieux) and reported to be Myroides sp. with an excellent confidence level (98.7% probability).

To further confirm the identification, we used 16S rDNA analysis. The primer pair forward 5′-AGAGTTT GATCMTGGCCTCAG-3′ and reverse 5′-ACGGYTACCTTGGTACGAC TT-3′ were used to amplify the 16S rDNA by PCR. DNA extraction and PCR amplification were carried out as described (5). The sequence of 16S rDNA amplicon (1,450 bp) was determined after electrophoresis and performed with the 3100 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) according to the manufacturer’s recommendations. The 16S rDNA sequence of this isolate (strain RB28), deposited in GenBank under accession no. DQ984127, was compared with sequences in GenBank by using the BLAST algorithm (version 2.0; National Center for Biotechnology Information, Bethesda, MD, USA, www.ncbi.nlm.nih.gov/blast). Sequence alignment and distance analysis were performed with Lasergene software (DNASTAR, Inc., Madison, WI, USA). According to the 16S rDNA sequence analysis, our isolate belonged to the family Xanthomonadaeceae of the Gamma Proteobacteria class; the highest sequence similarity (99.2%) was obtained for D. japonica type strain XD53 (6). In contrast, RB28 shared <97% sequence similarity to other species of Dyella and other genera in this family (data not shown). Organisms within the same species should share ≥97% of 16S rDNA sequence similarity (7). Therefore, this isolate was identified as D. japonica.

The biochemical profile of RB28 was also most consistent with D. japonica (Table). MIC values as determined by Etest were amikacin 0.75, cefotaxime 0.064, ceftazidime 0.38, ciprofloxacin <0.002, co-trimoxazole 0.125, gentamicin 1.5, imipenem and meropenem 0.25 mg/L. Because of MIC results, treatment was changed to ceftazidime (1 g intravenously every 8 h). Fever abated within a few days without catheter removal. The patient had a complete recovery with no complications. Follow-up blood cultures 2 and 4 weeks after 14 days of treatment were negative.

The Dyella genus comprises 3 species: D. japonica (6), D. koreensis (8), and D. yeojuensis (9). All are soil isolates and have been neither isolated from clinical samples nor reported to cause human infection. Their pathogenicity in humans is unknown. Because of its rapid onset after hemodialysis, the bacteremia in this patient is thought to have been associated with the dialysis procedures. Contaminated dialyzing fluid may have been a source for the organism, and the permanent catheter was likely to have provided an entry. In addition, blood culture bottles could have been contaminated by environmental samples. However, the diagnosis of catheter-related infection could not be definitive because neither catheter tip nor fluid was available for culture. The severity of D. japonica bacteremia was difficult to determine because the clinical manifestation was