**Massilia timonae** Infection Presenting as Generalized Lymphadenopathy in a Man Returning to Belgium from Nigeria

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We report a case of apparent malaria infection presented with a syndrome of painless, generalized lymphadenopathy without granulomas shortly after exposure to fresh water in rural West Africa. Residual infection with *Massilia timonae* was diagnosed and successfully treated with co-trimoxazole.

**CASE REPORT**

A 52-year-old man, born in Nigeria and living in Belgium since 1996, was admitted to our hospital with a 7-day history of fever, myalgia, and lymphadenitis. The fever was intermittent, with spikes of fever following chills on alternating days. Two weeks earlier, he had returned from a 2-month visit to his family in Nigeria. He did not take any malaria prophylaxis and reported swimming in a lake outside Lagos. Once returned in Belgium, he continued his usual life as an unemployed person, spending most of his time indoors. His medical history revealed diabetes mellitus and previous malaria.

At the time of admission, the patient was conscious and alert; he had a temperature of 38.5°C, a pulse rate of 120 beats/min, and blood pressure of 120/80 mm Hg. Physical examination revealed multiple firm and nontender cervical, axillary, and inguinal lymphadenopathies, with a size up to 2 cm. Abdominal examination showed tenderness in the right upper quadrant. The rest of the physical examination was unremarkable.

Hematological investigations showed a hemoglobin level of 11.5 g/dl (reference values, 12.9 to 16.4 g/dl), a platelet count of 11.5 g/dl (reference values, 12.9 to 16.4 g/dl), a platelet count of 13.1 × 10^9/liter (reference values, 142 to 9.76 × 10^9/liter), and a total leukocyte count of 13.1 × 10^9/liter (reference values, 3.45 × 10^9 to 9.76 × 10^9/liter) with a normal differentiation. Biochemical investigations were normal, except for mildly elevated lactic dehydrogenase (LDH) (790 U/liter [reference values, 313 to 618 U/liter]) and elevated C-reactive protein (CRP) (30 mg/dl [reference value, <0.5 mg/dl]).

A rapid diagnostic test (RDT) for malaria (BinaxNOW malaria test; Inverness Medical Binax, Inc., Scarborough, ME) was positive for *Plasmodium falciparum* malaria. The BinaxNOW malaria test in an endemic population is 95.3% sensitive (95% confidence interval [CI], 93 to 97%) and the overall specificity for the same antigen is 99.8% (95% CI, 99 to 100%). Similar performance characteristics of the test were found in rounds 1 and 2 of the WHO RDT testing scheme (sensitivity, 100% in high-parasite density samples; specificity, 95%). Blood and urine cultures were sterile. Computed tomography scans were performed and showed diffuse lymphadenopathies with a diameter of 2 to 3 cm in the cervical, mediastinal, axillary, and pelvic regions. The liver and spleen were normal in size.

The patient was treated for malaria with oral quinine (1,500 mg daily) and doxycycline (100 mg twice daily) for 7 days. The clinical state of the patient improved, and he became afebrile within 3 days.

The enlargement of the lymph nodes persisted, and therefore a biopsy of a cervical lymph node was performed 2 weeks later. Histocytological analysis of the biopsy specimen revealed a diffuse nonspecific inflammation with infiltration by small and large lymphocytes. Immunohistochemical staining for the B-cell marker CD20 showed a preserved architectural structure of the lymph node with no arguments for B-cell lymphoma. There was some positivity for CD30, but the absence of cells with typical Reed-Sternberg morphology and negative staining for CD15 of these CD30-positive cells made a diagnosis of Hodgkin lymphoma very unlikely. In conclusion, no arguments for hematologic disease could be found.

Direct examination of the lymph node by Gram staining and Ziehl-Neelsen staining was negative. Lymph node culture on blood agar at 37°C showed growth of nonfermentative Gram-negative bacilli after 2 days. Tests for oxidase and catalase were positive.

Using a standardized disk diffusion technique with Neo-Sensitabs (Rosco Diagnostica A/S, Taastrup, Denmark) for *Pseudomonas aeruginosa*, the Gram-negative bacilli appeared to be susceptible to meropenem, piperacillin-tazobactam, cefazidime, amikacin, ciprofloxacin, and co-trimoxazole and resistant to ampicillin, amoxicillin-clavulanate, and cefuroxime. The patient was treated with co-trimoxazole, and the lymphadenopathy resolved within 3 weeks.

To identify the bacterial isolate, a 16S rRNA sequence analysis was performed on the culture originating from the lymph node. Following DNA extraction, PCR amplification was executed using the MicroSeq 500 16S rDNA PCR kit (Applied Biosystems). After purification of the PCR product, analysis was performed with the ABI PRISM 310 genetic analyzer. The obtained sequences of the strain were aligned with the EMBL
Nucleotide Sequence Database (accession number U54470) and displayed 99.7% homology for Massilia timonae. Based on the morphological characteristics, conventional biochemical tests results, and 16S RNA sequence analysis, the diagnosis of Massilia timonae lymphadenitis was made.

The genus Massilia belongs to the family Oxalobacteraceae (Betaproteobacteria) and, up to now, comprises five species: M. timonae, M. dura, M. albidaflava, M. plicata, and M. lutea (17). M. timonae was first described by La Scola et al. in 1998 based on a single isolate from the blood of an immunocompromised patient with meningoencephalitis (8). It was classified as a novel bacterium based on its unique phenotypic and genotypic characteristics. The use of 16S rRNA sequence analysis has led to the identification of five additional cases of Massilia timonae infection in humans (Table 1) and resulted in an emended species. Recently, other species of the genus Massilia isolated from different soil samples from southeast China (17, 18), confirms the environmental nature of the species. Recently, other Massilia strains have been isolated from air (11–13) and drinking water (6).

Malaria is widespread in tropical and subtropical regions, including parts of Africa, Asia, and Latin America. It is a mosquito-borne infectious disease caused by a microorganism of the genus Plasmodium. For travelers to areas in which the disease is endemic, malaria is a serious health hazard, and the disease is often diagnosed on return to the country of residence. Coinfection with malaria and a second pathogen is rarely reported in travelers. This could be explained by the fact that infection with a species of Plasmodium is responsible for most of the fevers in travelers to countries in which the infection is endemic. According to surveillance data from GeoSentinel, the global surveillance network of the International Society of Travel Medicine, and the Centers for Disease Control and Prevention, malaria is responsible for 62% of systemic febrile illness in travelers returning from sub-Saharan Africa (15). Additionally, malaria is easier to diagnose than many other infectious diseases, and consequently, other infections are not suspected unless patients remain symptomatic after treatment for malaria. Simultaneous infection and malaria have been reported with dengue (1), leptospirosis (16), brucellosis (2), nontyphoidal Salmonella (7), and Q fever (4). To our knowledge, this is the first report of M. timonae and malaria coinfection in the literature. Because the association of two diseases may result in an atypical clinical presentation, it is not easy to diagnose a coinfection based only upon clinical and epidemiologic characteristics. Therefore, extensive biological testing is crucial to establish the presence of coinfections when other signs and symptoms of residual disease persist after malaria treatment.

We thank Anne Willems (LM-UGent) for the sequence alignment with the EMBL Nucleotide Sequence Database.

### Table 1. Summary of six reported cases in literature of M. timonae infection

<table>
<thead>
<tr>
<th>Patient age (yr), sex</th>
<th>Underlying medical condition</th>
<th>Diagnosis</th>
<th>Type of isolate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>25, male</td>
<td>Common variable immunodeficiency</td>
<td>Meningoencephalitis</td>
<td>Blood</td>
<td>La Scola et al. (8)</td>
</tr>
<tr>
<td>36, male</td>
<td>None</td>
<td>Wound infection following elective orthopedic surgery</td>
<td>Pus collected intraoperatively</td>
<td>Sintchenko et al. (10)</td>
</tr>
<tr>
<td>29, male</td>
<td>None</td>
<td>Osteomyelitis</td>
<td>Femur</td>
<td>Lindquist et al. (9)</td>
</tr>
<tr>
<td>49, female</td>
<td>None</td>
<td>Cerebral pseudotumor</td>
<td>Cerebrospinal fluid fluid</td>
<td>Lindquist et al. (9)</td>
</tr>
<tr>
<td>41, male</td>
<td>End-stage renal disease secondary to diabetic nephropathy and hypertension, hemodialysis</td>
<td>Sepsis</td>
<td>Blood</td>
<td>Lindquist et al. (9)</td>
</tr>
<tr>
<td>39, female</td>
<td>None</td>
<td>Sepsis</td>
<td>Blood</td>
<td>Lindquist et al. (9)</td>
</tr>
</tbody>
</table>
REFERENCES