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Splenic Rupture and Malignant Mediterranean Spotted Fever

To the Editor: Mediterranean spotted fever (MSF) is a *Rickettsia conorii* infection endemic to the Mediterranean. In this case, a 55-year-old man was referred to the Necker-Enfants Malades Hospital, Paris, France, for fever, myalgia, and hypotensive shock. The patient had been in Southern France (Montpellier) 6 days before symptom onset and had been bitten by a tick on the left hand. Four days later, he reported fatigue, fever (39°C), and myalgia. His medical history showed

polycystic kidney disease, which had necessitated hemodialysis and a kidney transplant. He was receiving ongoing treatment with an immunosuppressive regimen of cyclosporine, prednisolone, and tacrolimus; his baseline hemoglobin level was 15 g/dL, and creatinine level was 230 μmol/L.

At admission, the patient's temperature was 39.5°C, blood pressure 55/40 mm Hg, and heart rate 104 beats/min. Physical examination showed a diffusely tender abdomen with guarding, no hepatosplenomegaly, a nontender renal transplant, and no lymphadenopathy. Results of cardiovascular, respiratory, and neurologic examinations were unremarkable. A diffuse maculopapular cutaneous eruption was noted on the lower limbs; no eschar was detected.

Laboratory analyses showed the following values: hemoglobin 7.9 g/dL, platelet count $115 \times 10^9/L$, leukocyte count $6.7 \times 10^9/L$ (neutrophils $5.2 \times 10^9/L$, lymphocytes $1.4 \times 10^9/L$); serum creatinine 466 μmol/L, and C-reactive protein 156 mg/L. Blood cultures were negative. Serologic study results were negative for HIV, hepatitis viruses, Epstein-Barr virus, cytomegalovirus, *Legionella*, *Mycoplasma*, *Coxiella*, *Bartonella*, *Leishmania*, and *Toxoplasma* spp. Serologic testing obtained at day 1 was negative for spotted fever group (SFG) rickettsiosis.

A computed tomographic scan showed hemoperitoneum secondary to a ruptured subcapsular splenic hematoma (online Appendix Figure, available from www.cdc.gov/EID/content/14/6/995-appG.htm), and an emergency splenectomy was performed. Histopathologic evaluation of the spleen showed white pulp atrophy; the red pulp indicated congestion and ill-defined nodules, varying in size and comprising macrophages, polymorphonuclear neutrophils, and necrotic cells (Figure, panels A, B). Skin biopsy of the macular eruption on day 2 demonstrated a leukocytoclastic vasculitis with nonocclusive luminal

thrombi in the dermal capillaries (Figure, panel C).

Universal 16S rRNA gene PCR amplification on spleen and skin tissue samples and direct sequencing identified an *R. conorii*-specific 16S rRNA sequence match. We confirmed this by using primers for *gltA* and *ompA* specific for *R. conorii*. Immunohistochemical staining demonstrated *Rickettsia* in endothelial cells and macrophages in the spleen and skin (Figure, panels D–F). Blood culture, skin biopsy specimens, and splenic tissue cultures were subsequently *R. conorii* positive. Doxycycline therapy (100 mg intravenously twice a day) was instituted at day 2 because rickettsiosis was suspected. The patient dramatically improved within 72 hours and remained well 36 months after diagnosis.

MSF is a rickettsiosis belonging to the tick-borne SFG caused by *R. conorii*, an obligate intracellular bacteria transmitted by the dog tick *Rhipicephalus sanguineus*. Endemic to Mediterranean countries, MSF generally results in a benign febrile illness accompanied by a maculopapular rash, myalgia, and local black eschar at a tick bite inoculation site. A minority of persons seeking treatment display a malignant form, which results from disseminated vasculitis associated with increased vascular permeability, thrombus-mediated vascular occlusion, and visceral perivascular lymphohistiocytic infiltrates (1). Focal thrombi have been identified in almost all organs of patients with fatal cases. Manifestations of MSF include neurologic involvement, multi-organ failure, gastric hemorrhage, and acute respiratory distress syndrome; the case-fatality rate is 1.4%–5.6%.

Splenic rupture has been reported in the course of infection with several microbial agents, including Epstein-Barr virus (2), HIV, rubella virus, *Bartonella* spp. (3), *Salmonella* spp., mycobacteria (4), and *Plasmodium* spp. (5). Splenomegaly as a result of MSF has also been documented previously (6);

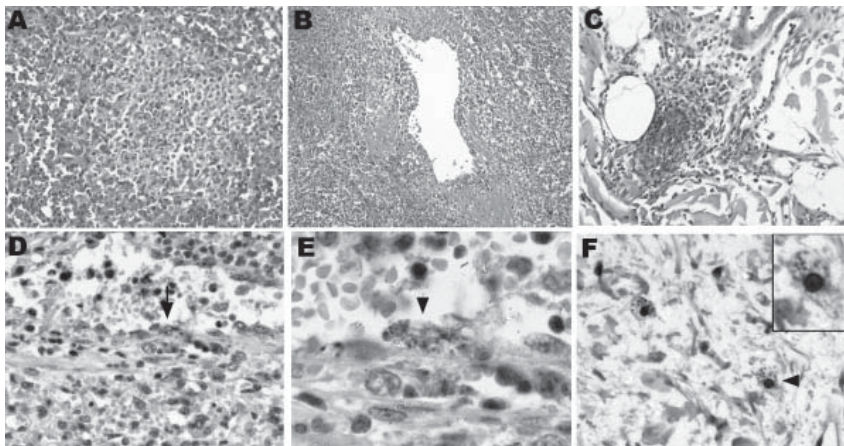


Figure. Histopathologic and immunohistochemical labelings of spleen and skin tissue samples. Tissue samples were fixed in 10% formalin, paraffin-embedded, and examined after hematoxylin-eosin staining, Gimenez staining, or immunostaining with the R47 anti-*Rickettsia conorii* polyclonal rabbit antibody. The spleen red pulp indicated congestion and ill-defined nodules varying in size and comprising macrophages, polymorphonuclear neutrophils, and necrotic cells (A, magnification $\times 100$). A diffuse macrophage infiltration with abundant hemophagocytosis (not shown) and venulitis (B, magnification $\times 50$) was also observed. In the skin, leukocytoclastic vasculitis with focal vascular necrosis and nonocclusive luminal thrombi were noted in dermal capillaries (C, magnification $\times 100$). Intracellular images evocative of rickettsiae were observed in the splenic arteriolar endothelium upon immunohistochemical staining (D, arrow, magnification $\times 200$; magnified view shown in E, arrowhead, magnification $\times 500$). No infected cells were observed in nodular inflammatory splenic lesions. Immunohistochemical staining also disclosed intracellular immunolabeled dots in cells that could correspond to infected dermal macrophages (F, arrowhead, magnification $\times 300$; magnified view shown in inset, magnification $\times 600$), at a distance from the vascular alterations. Endothelial cells of dermal capillaries were also immunolabeled (not shown). A color version of this figure is available online (www.cdc.gov/EID/content/14/6/995-G.htm).

however, splenic rupture in the context of tick-borne illness has only previously been reported for *R. typhi* (7) and *Coxiella burnetii* infections (8).

SFG rickettsioses have rarely been described in transplant recipients. Barrio et al. reported a case of MSF in a liver transplant recipient with clinical resolution of infection (9), and a case of Rocky Mountain spotted fever after heart transplantation has been described (10).

Seroconversion remains the principal diagnostic tool for the rickettsioses, but often no detectable antibody is found in the early phase of the disease. Spleen and skin tissue samples allowed rapid 16S rRNA gene PCR and sequencing before the results of other diagnostic procedures were ob-

tained. Immunostaining allowed detection of *R. conorii* in spleen and skin tissue samples and illustrated the cell tropism of this intracellular bacterium for cells morphologically similar to endothelial cells and possibly macrophages. Although *R. conorii* infection of postmortem human splenic samples from patients with fatal cases has been documented by immunohistochemical testing, *R. conorii* has not been described previously in spleen tissue of those who have survived malignant MSF.

This case expands the spectrum of infectious agents associated with spontaneous splenic rupture and solid organ transplantation. Rickettsioses are a significant risk both for those living in disease-endemic regions and

for international travelers. To facilitate early detection and treatment, physicians must be vigilant for atypical symptoms, especially in immunocompromised persons.

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Acetobacter indonesiensis Pneumonia after Lung Transplant

To the Editor: Unusual and multiresistant bacterial infections are increasingly reported in cystic fibrosis (CF) patients (1). On January 25, 2007, a 31-year-old man with CF (mutation ΔF 508 and I 507) was admitted to our institution in Marseille, France, for lung transplantation. His immunosuppressive regimen included IV cyclosporin A (for the first 6 days with conversion to oral tacrolimus thereafter), azathioprine, and corticosteroids. Induction therapy that used antithymocyte globulin was administered for the first 3 days (Thymoglobuline, Genzyme Corporation, Naarden, the Netherlands). Since 2003, the patient was chronically colonized by methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* (susceptible only to colistin sulfomethate), and *Candida albicans*. Pre-

agents including colistin sulfomethate, tobramycin sulfate, ceftazidime, and linezolid was administered, starting on posttransplant day 1; prophylactic caspofungin, followed by inhaled amphotericin B, was given for the first month. Six and 9 days, respectively, after surgery, sputa from the patient showed *P. aeruginosa* and MRSA.

On postoperative day 11, the patient's clinical condition worsened. Leukocytes increased to $13.84 \times 10^9/L$. In addition to *P. aeruginosa* (10^4 CFU/mL) and MRSA (10^3 CFU/mL), culture of later sputum samples yielded the growth of 10^4 CFU/mL of gram-negative, catalase-positive, and oxidase-negative bacillus (isolate 7120034) on CEPACIA agar (AES, Combourg, France) after 72 hours of incubation at 30°C. API 20NE, API

20E, and VITEK 2 Auto system (bioMérieux, Marcy l'Etoile, France) did not identify the bacillus. This bacterium was multiresistant to antimicrobial agents, including colistin, and was susceptible only to imipenem, rifampin, and aminoglycosides. The final identification of this isolate as *Acetobacter indonesiensis* was achieved after partial sequencing of 16S rRNA gene, as previously described (2) (GenBank accession no. AJ199841, 99% similarity). The sequence of our isolate has been deposited in GenBank under the accession no. EF681860. The phylogenetic position of isolate 7120034 among other gram-negative bacteria is shown in the Figure.

Tobramycin was stopped at day 11, colistin and ceftazidime were stopped at postoperative day 14, lin-

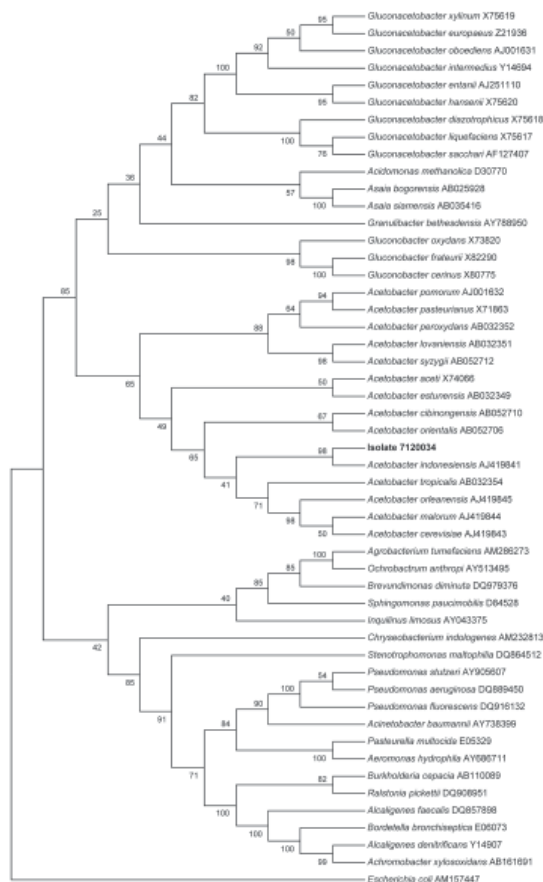


Figure. Phylogenetic tree showing the position of *Acetobacter indonesiensis* (isolate 7120034, GenBank accession no. EF681860), in **boldface**, within acetic acid bacteria and other gram-negative rods. The tree was based on 16S rDNA comparison by the neighbor-joining method. Numbers along the branches indicate bootstrap values.