Disseminated Spiroplasma apis Infection in Patient with Agammaglobulinemia, France
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and serology testing for 12 pathogens. Results from viral cultures on a BAL sample, taken 8 days after hospital admission, showed a cytopathogenic effect on 3 available cell lines (Vero, HEp-2, and MRC5) 7 days after incubation. Results from a PCR, administered in an effort to identify the positive viral culture, for herpes simplex virus and enterovirus were both negative.

Because the general condition of the patient had improved and stabilized, he was weaned from intubation 14 days after admission to the intensive care unit. He was discharged to the geriatric department and slowly recovered consciousness; his neurologic status also normalized. Three months after onset of the infection, the patient described having some memory loss and no memory at all of the days when the infection first started.

Because routine testing did not lead to a diagnosis, a BAL sample and a viral culture were sent to the University Hospital Leuven (Leuven, Belgium). The cell culture was subjected to next-generation sequencing (NGS) with the Novel enrichment technique of VIRomes protocol (5). This protocol includes purification of viral particles, nucleic acid extraction, and random PCR amplification, followed by library preparation and sequencing using NextSeq 500 system NGS technology (Illumina, San Diego, CA, USA) (6). The sequence reads obtained were filtered and trimmed, de novo assembled, and taxonomically classified (7,8). Analysis of the NGS results identified a complete West Nile virus genome (11,060 nt). To confirm this result, a novel RNA extraction and a reverse transcription PCR (QIAGEN, Venlo, the Netherlands) with newly developed primers were performed on the BAL sample and cell culture, followed by Sanger sequencing (9). The sequence obtained from the positive sample was identical to the sequence from the complete genome obtained by NGS.

The WNV lineage 2 strain in this study, WNV-2|Belgium|2017|Antwerp (GenBank accession number: MH021189), is closely related (99.4%–99.6% nucleotide similarity) to a strain from Hungary and other Balkan countries identified between 2010 and 2015 (Figure), reinforcing the conclusion that this WNV infection was acquired in Hungary. This case illustrates that the combined use of cell cultures and NGS can be a powerful tool for identifying unknown pathogens in clinical specimens when results from routine tests are negative and the patient’s condition is undiagnosed.

About the Author
Elke Wollants currently works as laboratory manager in the Clinical Virology Lab at the Rega Institute, KU Leuven. Her research interests are identifying pathogens not detected in routine diagnostic laboratory tests and next-generation sequencing.

References

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Disseminated Spiroplasma apis Infection in Patient with Agammaglobulinemia, France

Nicolas Etienne, Laurent Bret, Cécile Le Brun, Hervé Lecuyer, Josquin Moraly, Fanny Lanternaire, Olivier Hermine, Agnès Ferroni, Marc Lecuit, Sabine Pereyre, Laure Beven, Olivier Lortholary

Author affiliations: Paris Descartes University Hospital, Paris, France (N. Etienne, H. Lecuyer, F. Lanternaire, O. Hermine, A. Ferroni, M. Lecuit, O. Lortholary); Centre Hospitalier Régional,
We report a disseminated infection caused by *Spiroplasma apis*, a honeybee pathogen, in a patient in France who had X-linked agammaglobulinemia. Identification was challenging because initial bacterial cultures and direct examination by Gram staining were negative. Unexplained sepsis in patients with agammaglobulinemia warrants specific investigation to identify fastidious bacteria such as *Spiroplasma* spp.

In February 2017, a 40-year-old man in France who was under immunoglobulin replacement therapy for X-linked agammaglobulinemia experienced a migrating nonitchy papular eruption. Skin biopsy revealed nonspecific lymphocytic dermatitis. One month later, he experienced distal interphalangeal arthritis. Histology of a synovial biopsy sample found a nonspecific lymphocytic infiltrate. Bacterial cultures were negative. In April 2017, febrile arthritis of the left ankle and right knee appeared, along with bilateral wrist and finger tenosynovitis. Culture results of aerobic culture were negative. Unexplained sepsis in patients with agammaglobulinemia warrants specific investigation to identify fastidious bacteria such as *Spiroplasma* spp.

**These authors contributed equally to this article.**
than honeybees. The insect stings in this patient are a likely gateway of the reported infection.

In summary, clinicians and microbiologists should be aware of fastidious organisms in atypical infections in immunocompromised patients. Our findings indicate a need for prolonged culture on specific agar on all joint fluids in patients with agammaglobulinemia and targeted molecular methods to identify *S. apis* organisms.

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**About the Author**

Dr. Etienne is an infectious disease clinician and a clinical immunologist in Necker-Pasteur Center for Infectious Diseases, Paris. His research interest focuses on infections in immunocompromised patients.

**References**


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**Figure.** Direct examination with dark-field microscopy of specimens from a patient with agammaglobulinemia who had *Spiroplasma apis* infection, France. A) Helical and motile bacteria in blood culture. B) Elongated and coccoid bacteria in joint fluid. C) Helical and motile bacteria in culture from joint fluid in modified SP4 broth medium. Scale bar indicates 10 µm.

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**Mycoplasma ovipneumoniae in Wildlife Species beyond Subfamily Caprinae**

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