



## Case report

## Detection of *Fusobacterium nucleatum* in culture-negative brain abscess by broad-spectrum bacterial 16S rRNA Gene PCR



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## ABSTRACT

**Background:** *Fusobacterium nucleatum* is a strict anaerobic microorganism commensal to the human oropharynx and gastrointestinal tract, which causes a wide spectrum of human diseases and it is an important pathogen in abscesses.

**Case presentation:** We report the case of a previously healthy 64-year-old woman with multiple abscesses due to *Fusobacterium nucleatum*, involving liver, pleura and brain. *Fusobacterium* was not recovered from blood cultures nor from culture of hepatic, pleural and brain drain fluid. The diagnosis was obtained by polymerase chain reaction amplification of bacterial deoxyribonucleic acid in brain abscess drain.

**Conclusions:** *Fusobacterium* spp., should be considered in patients with any organ abscess, especially in case of invasive disease with multiple secondary site involving brain.

**Molecular:** techniques might be of special usefulness in cases that remain negative in culture to obtain the diagnosis and perform adequate treatment.

## Background

*Fusobacterium nucleatum*, is a Gram-negative anaerobic microorganism that is indigenous to the human oral cavity. It can also be found in the gastrointestinal, urogenital and upper respiratory tract and can induce a wide spectrum of human diseases, such as adverse pregnancy outcome, pulmonary and intraabdominal infections, and it is an important pathogen in abscesses, especially in patients with comorbidities such as cancer [1].

We describe a case of woman with multiple abscesses due to *Fusobacterium nucleatum*.

## Case presentation

A 64-year-old woman, with no significant past medical history, was admitted to intensive care unit with confusion and fever.

On clinical examination, temperature was of 38.8 °C, blood pressure at 105/73 mmHg, heart rate at 129 bpm. She presented significant agitated behavior and abdominal sensitivity.

Blood tests showed a white blood cells (WBC) at 14.000/mm<sup>3</sup>

(normal 4.000–10.000 mm<sup>3</sup>), an elevated C-reactive protein (CRP) at 160.6 mg/l (normal < 3.0 mg/l), and creatinine at 126 μmol/l (normal 49–90 μmol/L). All blood cultures were negative. Screening for HIV, HCV and HBV as well as for syphilis was negative.

A magnetic resonance imaging (MRI) of the head, performed on admission showed 4 ring enhancing lesions with a surrounding edema consistent with cerebral abscesses: a 28 mm cerebellar lesion, a 15 mm frontal right image, a 17 mm parietal and a 15 mm occipital lesion. A lumbar puncture found 275/mm<sup>3</sup> WBC, 4% PNN and 89% lymphocytes. No germ was retrieved.

A total body scan imaging revealed an 11 cm liver abscess and a right-sided pleural effusion with negative microbiological cultures from thoracentesis and liver drains which recovered a brown purulent liquid.

An intravenous Ceftriaxone and oral Metronidazole was started on day of admission and led to clinical and biological improvement. Patient became afebrile five days after the beginning of antibiotic treatment and neurological symptoms have resolved. She was transferred in infectious diseases unit. A cerebral MRI performed at 3 weeks of treatment found no major difference in the size of the brain abscesses. An ultrasound showed stagnation in the size of the liver

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abscess. Neurosurgeons recommended craniotomy with drainage of brain abscesses. A brain biopsy found a mixed inflammatory reaction with an important macrophagic infiltrate and granulomas, without any evident pathogenic microorganism. Aerobic and anaerobic cultures were performed but remained negative. Polymerase chain reaction (PCR) product was detected with 16S ribosomal deoxyribonucleic acid (RNA) from *Fusobacterium nucleatum*.

Ceftriaxone was changed by Clindamycine and Metronidazole was continued.

An 18F-fludeoxyglucose positron emission tomography (FDG-PET) didn't show any other infection site besides the liver, pleura and the brain.

An MRI of brain performed 12 weeks after the beginning of treatment showed brain abscesses decrease in size: a 28 mm cerebellar lesion decrease to 8 mm, a 15 mm frontal right image to 6.5 mm, a 17 mm parietal and a 15 mm occipital to 6.5 mm for the both. Decrease of ring enhancing intensity and surrounding edema. The treatment with only oral metronidazole was continued for total duration of 20 weeks.

Brain, hepatic and pulmonary images performed 6 months after the initial presentation showed a stability of brain images and complete recovery of hepatic abscesses and pleural effusion.

The patient shows a good clinical recovery, especially in neuro cognitive function as well as a good biological evolution with CRP at 3.7 mg/l and no fever.

## Discussion and conclusion

*Fusobacterium*, especially *Fusobacterium Nucleatum* and *Fusobacterium Necrophorum*, is a major cause of the well-known Lemierre's Syndrome, described for the first time in 1936: a septic thrombophlebitis of the internal jugular vein that typically begins with an oropharyngeal infection but it is also one of the main protagonists of abscesses in many organs [1–3].

In the study reporting clinical and biological features of 78 cases of *Fusobacterium nucleatum* infections, abscess was the most common type of infection, 43 patients (55%), involving many organs but principally skin, pleura and liver [1].

The available bacteriological data is, however, variable on the role of *Fusobacterium* spp. in brain abscesses. Even if anaerobes are major aetiological agents of intracranial abscess (nearly 60%), the prevalence of *Fusobacterium* spp varies from 5% to 33% according to several studies on the microbiological spectrum of brain abscesses [4–7].

We present the case of woman with multiple abscesses due to *Fusobacterium nucleatum*, which was not recovered from blood cultures nor from culture of the patient's hepatic, brain and pleural drain fluid.

The microbiological diagnosis was performed by nucleic acid amplification technique on brain abscess.

In the past the importance of anaerobic organisms in abscesses was

underestimated probably because of lack of use the appropriate collection methods of anaerobic cultures and rapid transportation to the laboratory which lead to the failure to identify the bacteria. Recent studies showed an important increase in the detection of anaerobic pathogens causing abscess [5,7].

Furthermore, a review of the literature showed that diagnosis of *Fusobacterium nucleatum* infection in most cases is based on culture (81.25%) and only few cases on nucleic acid amplification technique [8]. The sensitivity of blood cultures is however poor, especially in association with abscesses [1].

In our patient, pre-culture antibiotic therapy may contribute to the negativity of culture, but the severity of initial presentation didn't permit the delay of antibiotic treatment.

The exact origin of infection was difficult to determine in our patient. The imaging exams revealed the presence of intra-uterine device which was removed but the culture of device remained negative.

Concerning the underlying comorbidities, the FDG-PET didn't revealed malignancies.

To conclude, *Fusobacterium* spp, should be considered in patients with any organ abscess, especially with peritonsillar, oropharyngeal, lung and liver abscess, but also in case of invasive disease with multiple secondary site involving brain.

Indeed, PCR is not to perform routinely but PCR-mediated amplification and sequencing of 16S ribosomal RNA might be of special usefulness in cases that remain negative in culture, possibly due to prior antibiotic treatment, to obtain the diagnosis and perform adequate treatment.

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