

Caso  
clinico

Case  
report

# Multiple abscesses of the left brain hemisphere due to *Listeria monocytogenes* in an immunocompromised patient: a case report

**Ascessi multipli dell'emisfero cerebrale sinistro dovuti a *Listeria monocytogenes* in un paziente immunocompromesso: un caso clinico**

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## INTRODUCTION

*Listeria* is a genus of gram-positive, non-encapsulated, motile bacilli. *Listeria monocytogenes* is reported to be an ubiquitous environmental organism, which may live as a commensal of up to 10% of healthy humans [1]. In immunosuppression states and following gastroenterologic disorders, the transition from asymptomatic carrier to infected patient with an invasive illness is often observed [1, 2]. Listeriosis may also clinically present as a flu-like syndrome, as a food-borne infection and more importantly as a sepsis and infection of the central nervous system [2].

In the last two pathologies the mortality rate is high (13-34%); among non-immunosuppressed patients, 80% had a CNS infection, and 52% of immunosuppressed patients had sepsis [2]. We describe a lethal case of single brain hemisphere multiple abscesses caused by *Listeria monocytogenes* in a cirrhotic and diabetic 57-year-old woman.

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## CASE REPORT

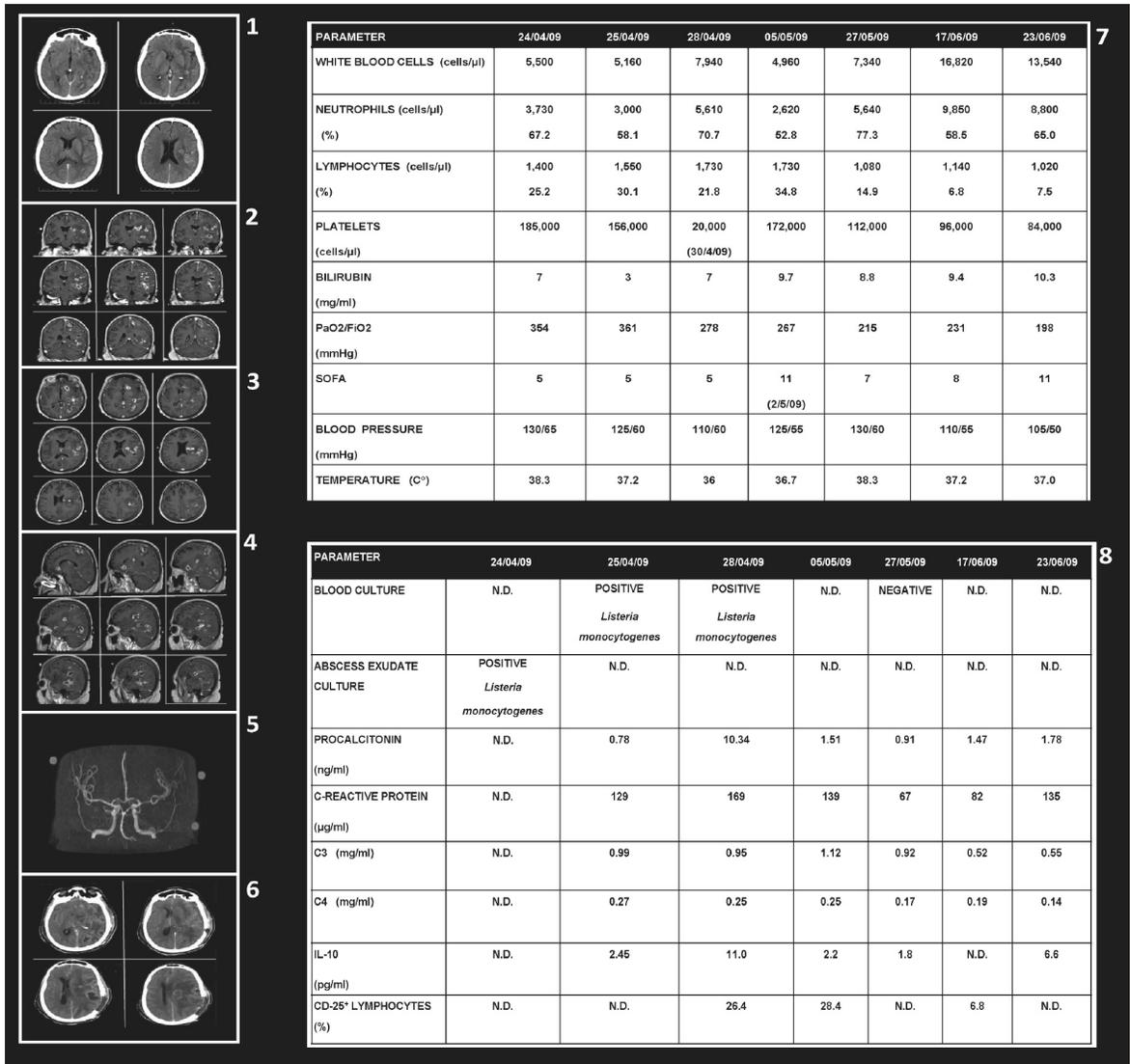
A 57-year-old woman with a history of cirrhosis and diabetes was admitted to the University Hospital of Catanzaro with a clinical picture of high fever, aphasia, right hemiparesis, left facial palsy and seizures that had been seen 3 weeks earlier in another hospital, where an MRI and proton MR spectroscopy suggested an ischemic lesion of the left cerebral hemisphere. Angio-MRI investigation showed a thrombosis of the left middle cerebral artery. She was then transferred to the Neurosurgical Department of the same Hospital due to the worsening of neurological conditions and the appearance of respiratory insufficiency.

Neuroimaging techniques (both CT and MRI) provided evidence of several small to medium-sized lesions of the left hemisphere, perivascular cuffs along transcerebral medullary vessels. Most of such lesions were surrounded by a hypodense halo and produced a shift of the ventricular complex to the right (Figure 1, panels 1-4). Angio-MR allowed a narrowing of the middle cerebral artery to be detected (Figure 1, panel 5).

Due to the worsening of the neurological condition with appearance of coma and anisocoria an

emergency decompressive craniotomy and drainage of the major abscesses were performed and the patient was transferred to the intensive care unit (ICU).

Examination of the purulent sample obtained after craniotomy demonstrated the presence of gram-positive bacilli, whose typical characteristics were compatible with those of *Listeria spp.*



**Figure 1** - Neuroimaging findings, clinical and hematochemical, microbiological and pathogenetic data of the studied case. **Panel 1:** CT scan with contrast enhancement (April 14, 2009). Diffuse white matter hypodensity of the left hemisphere and multiple mostly subcortical ring-like foci produce mass effect and right side shift of the cerebral ventricles. **Panel 2:** Contrast-enhanced volumetric MRI (April 17, 2009). Coronal T1-weighted images showing enlarged transcerebral medullary vessels with perivascular cuffs as well multiple ring-like iuxtacortical and subcortical focal lesions with a fan-like distribution. **Panel 3:** Contrast-enhanced volumetric MRI (April 17, 2009). Axial T1-weighted images showing the multiple abscesses spanning from the frontal to the occipital lobe only on the left hemisphere. **Panel 4:** Contrast-enhanced volumetric MRI (April 17, 2009). Sagittal T1-weighted images showing the very extensive compromise of the left hemisphere with lesions of various size. **Panel 5:** Angio-MR (April 17, 2009). TOF-3D showing the narrowing of the M1 segment of the left middle cerebral artery. There is also a shift of the anterior cerebral arteries to the right. **Panel 6:** Contrast-enhanced CT (April 11, 2009). Left parietal craniotomy. Marked increase of the size of the abscesses and of the transfalcial brain herniation. **Panel 7:** Kinetic of clinical and haemato-chemical parameters of the studied case. Sampling date is reported as heading of each column, unless otherwise specified. **Panel 8:** Kinetic of the microbiological and pathogenetic variables. N.D.: not done.

From such purulent matter and from three blood samples obtained following craniotomy, as well as from one blood sample taken before surgery, *Listeria monocytogenes* was cultured. Identification and susceptibility tests were carried out by conventional cultural techniques and allowed immediate administration of aspecific antibiotic therapy: gentamicin (240 mg/d) intravenous (intermittent infusion) and ampicillin/ sulbactam (9 g/d) intravenous (continuous infusion). About two weeks following craniotomy, a CT scan with contrast enhancement indicated a substantial increase in abscesses with profound derangement of the brain anatomical features (Figure 1, panel 6).

Absence of fever and negativity of blood cultures after one week of treatment were observed. Histological evaluation of the sample obtained after surgery showed a pattern of cerebritis with early necrosis of the cerebral parenchyma, oedema and infiltration by lymphocytes, neutrophils and activated microglia. The perivascular spaces in the vicinity were cuffed by lymphocytes and the surrounding nervous tissue was characterized by a mild gliosis. Despite intensive supportive therapy and specific antibiotic administration associated with negative blood cultures, we observed a progressive worsening of the clinical condition finally leading to multiple organ failure (MOF) and death.

Purulent biptic sample following surgery was stained by a standard Gram staining kit, and gram-positive bacilli, morphologically similar to *Listeria spp.*, were microscopically observed. Blood cultures were processed with a BacT/Alert 3D system. In all blood cultures, growth was detected after an incubation of 24 to 36 h. Subcultures on Columbia blood agar yielded circular translucent, and non-haemolytic colonies of homogeneous size after 24 h of incubation. A bacteriological stain of both the direct sampling from the blood culture bottle and also from the subculture disclosed gram-positive bacilli. The purulent sample obtained following surgery grew the same type of colonies. Since all isolates displayed identical biotype and antimicrobial susceptibility, they were considered as a single strain. The microorganism was identified as *Listeria monocytogenes*, based on the typical Gram stain morphology, the reactions obtained by a API *Listeria* biochemical gallery (bioMérieux). We verified identification based on a GP card processed by VITEK 2 instrument (bioMérieux).

In order to follow several inflammatory markers, venous blood samples were obtained at different time points, plasma was separated, aliquoted and immediately frozen (-80 °C) until the time of the assay. Interleukin 10 (IL-10) levels were evaluated by means of sandwich ELISA kits, according to the manufacturer's recommendations (Bender MedSystems, Vienna, Austria).

C-reactive protein, C3 and C4 were measured by a nephelometric method, (Nephelometer BN ProSpec Dade Behring, Marburg, Germany); procalcitonin (PCT) was assayed by ELFA (VIDAS BRAHMS PCT, bioMérieux, France). Blood samples were collected in EDTA Vacutainer tubes (Becton Dickinson) and white cells differential count and platelet count evaluated by automatic Coulter counter MAXM IL; some samples were processed by flow cytometry analysis (FACScan; Beckman Coulter Inc., Fullerton, CA, USA) using fluorescein isothiocyanate (FITC)-labelled anti-CD25+ MAb (Becton Dickinson); data regarding the CD25+ subpopulation were reported as percentages of the CD3+ cells. Bilirubin, haemogas-analysis and SOFA were evaluated by standard methods.

## DISCUSSION

Listeriosis is thought to be a disease of immuno-compromised hosts, and underlying diseases have been described in more than 70% of cases [2, 3].

Although brain abscess has been reported to be caused by different microorganisms including oral saprophytes, it is a very unusual occurrence during listeriosis, sometimes affecting primarily the rhombencephalon [4, 5]. Indeed, only 1% of listeriosis present with a brain abscess. Moreover, only 40 cases have been reported to date and the present study is the fifth describing multiple abscesses (>3) [6]. To our knowledge this is the first report that directly evaluates IL-10 and CD-25+ lymphocytes as an expression of immunoparalysis and as a marker of poor prognosis during a brain abscess due to *L. monocytogenes* in humans.

The intracellular location protects the *Listeria* from humoral immune response. In addition, immunocompromised patients are unlikely to produce an adequate supply of specific antibodies. Although *Listeria* was cultured from April 22, 2009, the white blood cell count including neutrophils and lymphocytes percent-

age were among the normal range with the exception of the latest time points (Figure 1, panel 7). Moreover, we observed constantly high values of bilirubin (ranging from 3 µg/ml and 9.7 µg/ml) associated with severe thrombocytopenia and consequently an increasing SOFA score, finally associated with the clinical criteria of MOF. The abscess exudate and blood cultures were both positive for *L. monocytogenes*. Procalcitonin was slightly increased on April 25, 2009, peaked on April 28 2009, showing a mild increase during the whole ICU stay like the C-reactive protein. Regarding complement factors, only C3 showed a substantial decrease from June 17, 2009 until the exitus. Among the indicators of immunoparalysis, IL-10 was constantly elevated (reference value <0.66 pg/ml) during the hospital stay and peaked on April 28, 2009, while CD-25+ lymphocytes were increased on April 28, 2009 and May 5 2009 (Figure 1, panel 8) (7).

At least three different pathways are described in order to explain the ability of *L. monocytogenes* to colonize and affect the central nervous system: direct invasion of endothelial cells, invasion via infected phagocytes, and entrance by a neural pathway [8].

The mechanism of supratentorial listerial brain abscess formation differs from that of listerial meningitis.

The epithelium of the choroid plexus allows *L. monocytogenes* to gain access to CNS and begin a meningitis [9]. On the other hand, *L. monocytogenes* may reach the brain parenchyma via the cerebral capillary endothelium, a single layer of brain microvascular endothelial cells characterized by tight junctions [10].

It has been reported that *L. monocytogenes*-infected macrophages may pass through such endothelial cells via the middle cerebral artery resulting in cerebritis and, subsequently, brain abscess formation [6]. In our case a narrowing of the left middle cerebral artery could be observed by angio-MR and all the lesions were

found downstream this artery and on the same side. Arteritis is a well known pathology due to *L. monocytogenes*; therefore it might be argued that left middle cerebral artery was the starting point of brain-invader bacteria. Multiple abscesses reflect the intensity of the infection associated with immunosuppression.

Diabetes and hepatic disease predispose to brain abscess by *Listeria* as reported by other investigators [1, 11]. Also our data suggest that immunosuppression, indicated by the increase of IL-10 and CD25+, is a marker of a poor prognosis. The absence of abnormal white blood cell count and neutrophil/lymphocyte percentage does not exclude cerebral abscess if a subject exhibits fever and neuroradiology imaging suggestive of this severe pathology [12].

The use of appropriate antibiotic and supportive therapy from the first clinical evidence might avoid a lethal outcome; unfortunately in our patient, microbiological diagnosis with susceptibility test-guided antibiotic therapy was started too late [11]. Therefore blood cultures became negative, but MRI imaging showed larger brain lesions. This apparent contradiction may be accounted for by a systemic and progressive septic condition up to immunoparalysis plus a local cerebral arteritis, in the presence of aggressive and appropriate antibiotic therapy.

In conclusion, we described a poor-outcome case of *L. monocytogenes* with multiple and unilateral brain abscess. Culture of blood and brain samples guided diagnosis and therapeutic approaches. PCT, IL-10, CD25+ lymphocytes and C3 played a significant role as prognostic markers.

**Keywords:** *Listeria monocytogenes*, brain abscess, immunocompromised

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The authors do not have an association that might pose a conflict of interest.

## SUMMARY

We describe a case of brain abscesses in a cirrhotic and diabetic 57-year-old woman showing fever, aphasia, right hemiparesis and seizures. Neuroradiological investigation revealed unilateral cerebritis evolving in multiple abscesses.

From blood and surgical drainage samples *Listeria monocytogenes* grew in pure culture. Despite decompressive craniotomy, the patient died two months after hospital admission.

## RIASSUNTO

Descriviamo un caso clinico di ascessi cerebrali multipli in una paziente di 57 anni cirrotica e diabetica che presentava febbre, afasia, emiparesi destra e convulsioni. Le indagini neuroradiologiche rivelavano cerebrite unilaterale che evolveva in ascessi multipli.

*Listeria monocytogenes* veniva isolata in coltura pura da campioni di sangue e di drenaggio chirurgico. La paziente moriva due mesi dopo il ricovero, nonostante la craniotomia decompressiva.

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