

## LISTERIOSIS AND AIDS: CASE REPORT AND LITERATURE REVIEW

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### SUMMARY

Listeriosis is a not uncommon infection in humans, usually associated with immunodeficient states and with newborns. However, relatively few cases have been reported in HIV-infected patients. This scarcity of reported cases has aroused interest in the association of listeriosis and AIDS.

In this paper we present a case of meningitis and septicemia caused by *Listeria monocytogenes* in a female patient with AIDS. A review of recent medical literature indicates that association of listeriosis and AIDS may be more common than it seems.

Recent research in host-parasite interaction in listerial infection suggests an important role for tumor necrosis factor (TNF) and for integralin, a bacterial protein, in modulating listerial disease in AIDS patients. Inadequate diagnosis may be in part responsible for the scarcity of reports.

**KEYWORDS:** Listeriosis; AIDS; Meningitis; *Listeria meningitis*; Septicemia

### INTRODUCTION

*Listeria monocytogenes* is a motile gram-positive bacillus that not infrequently causes disease in humans<sup>1, 11</sup>. The majority of cases are during pregnancy and in newborns, as well as in immunosuppressed patients with a variety of underlying diseases of therapies<sup>1</sup>. Assymptomatic infections are common and tend to reflect proximity to animals or animal-derived products. Although considered a zoonosis, there is sufficient evidence to support human to human transmission<sup>1, 11</sup>.

The exact prevalence of the infection is difficult to establish. European data report a prevalence of 2 to 3 cases per million, which is possibly the approximate prevalence in the United States<sup>1, 11</sup>. France reports a prevalence of 11 cases per million, probably due to better reporting<sup>1</sup>. Adequate data from Brazil or other developing countries is lacking, but isolated reports show that the preva-

lence of listeriosis in Brazil and other developing countries does not differ significantly from the industrialized countries<sup>15, 16</sup>.

Notwithstanding its relatively common occurrence, listeriosis has only infrequently<sup>2, 7, 12, 13, 14</sup> been reported as an opportunistic infection in AIDS, contrary to the expected, as listeriosis tends to occur in immunodeficient states. We describe an AIDS patient with *L. monocytogenes* meningitis and septicemia and review the reports of this association.

### CASE REPORT

A 36 years-old female iv drug abuser with a history of sexual promiscuity, was admitted to the hospital with a history of fever for the last 6 months and headache and nausea for the last 15 days. The patient had never received AZT.

Physical examination revealed a conscious,

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well oriented woman with a disseminated erythematous rash, meningeal irritation and hepatosplenomegaly.

Neurological examination disclosed a stiff neck, but no other signs.

Initial laboratory examinations revealed a white blood count (WBC) of  $8.3 \times 10^9/L$  (67% polymorphonuclear leukocytes, 5% band forms, 23% lymphocytes and 2% monocytes), a platelet count of  $111 \times 10^9/L$  and a hemoglobin concentration of 93 g/L. A biochemical profile and urinalysis were essentially normal.

CSF examination yielded 3750 cells/mm<sup>3</sup> (100% PMN cells), 91 mg% protein and 36% glucose. Small, gram-positive thin bacilli were visualized in a gram stain (after centrifugation for 15' at 1,500 rpm). A presumptive diagnosis of listeria meningitis was made, and subsequently confirmed(\*) by growth of *Listeria monocytogenes* in CSF and blood cultures (2 samples). All growths were ampicillin-sensitive.

A tube agglutination test (Behring®) for listeria was positive for serotypes 1 (O=1:320 and H = 1:40) and 4b (O = 1:320 and H = 1:40). A CD4 (T-helper) lymphocyte count was 382/mm<sup>3</sup>, and the CD4/CD8 ratio was 0.36.

An echo cardiogram and an abdominal ultrasound examination were normal.

Treatment with iv ampicillin, 2g q.i.d., was initiated and maintained for 28 days. After 2 days the patient was much better, although she was febrile up to the 20 th day of treatment. A CSF examination was normal on day 28.

She was discharged after a 28-day course of i.v. ampicillin. CSF examination on discharge was normal. The patient died five months later apparently as a consequence of multi focal progressive leukoencephalopathy, without evidence of active *Listeria* infection. Consent for a postmortem was not granted.

## DISCUSSION

Our patient did not differ from other patients with AIDS, and apparently her death was unrelated to listeriosis, as she underwent a period of relative well being and there was no evidence of disseminated or localized infection by *L. monocytogenes* during her last hospitalization, despite extensive culturing. Listeriosis is a disease with uncharacteristic manifestations.

Usually non-fatal and without significant sequelae, it is easily mistaken for a number of other diseases<sup>1,11</sup>. Reports of listeriosis in AIDS patients from earlier in the epidemic are scarce but seem to be growing in number. The first case was reported in 1983<sup>17</sup>. Listeriosis is not listed by the Centers for Disease Control as an opportunistic infection in AIDS<sup>4,5,6</sup> and neither was considered as an underlying condition in a review in early 1989<sup>9,11</sup>.

This scarcity drew the attention of JACOBS & MURRAY in 1986<sup>12</sup>. In an editorial in the JAMA, they speculated on the possible reasons, but favored none. Five years later, BERENGUER et al<sup>2</sup> presented a case from Spain and reviewed the literature finding only 20 other cases previously reported. KALES & HOLZMAN<sup>13</sup> reviewed the records of 30 patients with listeriosis treated in Bellevue Hospital in New York City from 1981 to 1988 and found six with AIDS, one with HIV-infection and four others with risk factors HIV infection.

In Brazil, CARVALHO et al<sup>3</sup> presented 11 cases of listeriosis from the Emilio Ribas Hospital, and mentioned AIDS as a underlying disease, but did not specify how many had AIDS. FLEMING<sup>9</sup> in an extensive review of opportunistic infections in AIDS in Africa and other underdeveloped countries makes no mention of listeriosis.

In a recent review, DECKER et al<sup>7</sup> suggest that an elevated tumor necrosis factor (TNF) level, frequently found in AIDS patients, can be protective

(\*) Small, gram-positive, thin, mobile ("umbrella" pattern in blood-agar at room temperature), bacilli that were catalase positive, bile-esculin positive, rhamnose positive, with a positive CAMP-phenomenon and yielding a  $\beta$ -hemolytic halo.

for listeria infection. Activated macrophages, a result of elevated TNF levels, have increased listericidal activity.

*Listeria* invasion of host cells seems to be mediated by a bacterial protein named internalin, different from other known proteins with similar function, such as integrins, found in *Legionella*, *Bordetella pertussis*, *Leishmania* and the tubercle bacillus, and invasin, found in *Yersinia pseudotuberculosis*. Internalin is analogous to the M protein of streptococci, and appears to be largely responsible for the slowly evolving process, characteristic of *Listeria* infection<sup>8,10</sup>.

As the process of host - bacteria interaction in *L. monocytogenes* infection is more adequately understood, an explanation may arise for the apparent paradox of a low incidence of listerial disease in patients with AIDS. To interpret the scarcity of reports simply as a low suspicion and inadequate investigation is naive. However, this may explain the low reporting of *L. monocytogenes* infections associated with AIDS in some regions, possibly in Brazil.

We recommend that listeriosis should be always considered in the differential diagnosis of febrile AIDS patients, particularly those with meningitis, and more attention be given to microbiological processing of specimens, particularly CSF, blood and bone marrow. Although *Listeria* serological tests are very difficult to interpret, their predictive value for active infection in AIDS should be looked upon.

## RESUMO

### Listeriose e AIDS: relato de caso e revisão de literatura

A listeriose é uma infecção não incomum, geralmente associada com recém-nascidos e pacientes imunodeprimidos que tem sido poucas vezes encontrada em pacientes com AIDS. Esta escassez de relatos despertou o interesse de diversos investigadores.

Neste artigo, os autores relatam um caso de septicemia e meningite por *Listeria monocytogenes* em paciente com AIDS e fazem uma revisão da literatura.

Novos conhecimentos sobre a interação agente

- hospedeiro nas infecções por listeria, como o papel do fator de necrose tumoral e da integralina, estão permitindo novas interpretações da aparente escassez de infecções por listeria em pacientes com AIDS.

O número de relatos vem crescendo em período recente, sugerindo que a associação pode ser mais freqüente do que aparenta ser, em parte explicada por inadequação no diagnóstico.

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