## **CASE REPORT**

## Endophthalmitis Caused by *Listeria monocytogenes*

CARMEN BETRIU,<sup>1\*</sup> SANTOS FUENTEMILLA,<sup>2</sup> ROSALÍA MÉNDEZ,<sup>2</sup> JUAN J. PICAZO,<sup>1</sup> AND JULIÁN GARCÍA-SÁNCHEZ<sup>2</sup>

Department of Clinical Microbiology<sup>1</sup> and Department of Ophthalmology,<sup>2</sup> Hospital Clínico San Carlos, 28040 Madrid, Spain

Received 20 December 2000/Returned for modification 14 March 2001/Accepted 23 April 2001

*Listeria monocytogenes* was isolated from the aqueous chamber of an immunodepressed patient with acute hypertensive uveitis, who developed a dark hypopyon and pigment dispersion. No extraocular septic focus was found. Treatment was successful with intravitreal vancomycin, anterior chamber irrigation with vancomycin, orally administered ciprofloxacin, and topical fortified vancomycin.

## CASE REPORT

A 62-year-old man presented to the emergency department with pain, redness, and decreased vision in the left eve. The patient had a history of larvngeal carcinoma, for which he had undergone laryngectomy and had been treated with radiation therapy and steroids. Examination of the eye on admission revealed acute hypertensive uveitis, and treatment with corticosteroids was begun but did not provide significant improvement. The patient developed a dark hypopyon with pigment dispersion and uveal ectropion. A differential diagnosis was made between endogenous endophthalmitis and a neoplastic process of the ciliary body (either primary ciliary body melanoma or metastatic melanoma from larynx carcinoma). Results from laboratory studies were unremarkable, except for the leukocyte count (14,030/mm<sup>3</sup> with 77% polymorphonuclear neutrophils). The chest X ray was normal. Blood cultures were negative. An ultrasound scan of the eye showed dispersion of echoes, and no evidence of retinal detachment was noted. B-scan ultrasonography revealed inflammatory deposition and pigmentary epithelium detachment. No proliferation was detected in the stromal iris.

Anterior chamber paracentesis was performed and submitted for culture and histopathology. Cytological examination showed polymorphonuclear leukocytes and no evidence of neoplastic cells. Because the patient reported a history of penicillin allergy, combined treatment with oral administration of ciprofloxacin (750 mg twice a day), anterior chamber irrigation with vancomycin, and intravitreal vancomycin (1 mg) was started. Topical fortified vancomycin (1 g) and corticotherapy were also applied. The patient's condition improved with treatment. Within 7 days, the hypopyon disappeared and the intraocular pressure decreased. However, visual acuity was limited to appreciation of hand motion, because of a severe corneal edema and a cataract which developed in the patient's left eye.

A small amount of fluid obtained by aspiration from the anterior chamber was directly plated onto blood agar and chocolate agar and distributed into aerobic and anaerobic blood culture bottles processed by the BACTEC 9050 system (Becton Dickinson Microbiology Systems, Cockeysville, Md.). Gram staining was performed and no organisms were observed. After a 24-h incubation of plates at 35°C in a 5% CO<sub>2</sub>-enriched atmosphere, catalase-positive, gram-positive coccobacilli grew, producing beta-hemolysis on blood agar. The isolate was identified as Listeria monocytogenes by both the Wider system (Francisco Soria Melguizo, S.A., Madrid, Spain) and the API Listeria system (bioMérieux, Marcy l'Etoile, France). Pure culture of L. monocytogenes was also isolated from both aerobic and anaerobic bottles that were positive after 24 h of incubation. Antibiotic susceptibility was determined in accordance with the recommendations of the National Committee for Clinical Laboratory Standards (23) using a broth microdilution procedure (Sensititre; Radiometer, Copenhagen, Denmark) with cation-adjusted Mueller-Hinton broth with 5% lysed horse blood. The MICs were as follows: penicillin, 0.12  $\mu$ g/ml; ampicillin,  $\leq 0.5 \mu$ g/ml; chloramphenicol, 4 µg/ml; vancomycin, 1 µg/ml; ciprofloxacin, 1 µg/ml; rifampin,  $\leq 1 \ \mu g/ml$ ; trimethoprim-sulfamethoxazole,  $\leq 0.5 \ \mu g/ml$ ml; tetracycline,  $\leq 2 \mu g/ml$ ; gentamicin,  $\leq 4 \mu g/ml$ ; and cefotaxime,  $\geq 8 \ \mu g/ml$ .

*L. monocytogenes* is a ubiquitous gram-positive bacillus. Its sources include sewage, silage, soil, and animals (28). It causes several illnesses in humans, such as meningitis or septicemia. Other reported forms of disease include endocarditis, abortion, wound infection, pneumonia, encephalitis, and ocular infections (24). Most *L. monocytogenes* infections are sporadic, although during the last few decades several outbreaks have been described (3, 9, 10, 18, 21). Food-borne transmission has been demonstrated both in epidemic and sporadic human listeriosis. A variety of foodstuffs have been associated with listeriosis, including soft cheeses, raw vegetables, fish, meat, and

<sup>\*</sup> Corresponding author. Mailing address: Department of Clinical Microbiology, Hospital Clínico San Carlos, Plaza Cristo Rey s/n, 28040 Madrid, Spain. Phone: 34 913303486. Fax: 34 913303478. E-mail: cbetriu@efd.net.

milk. It is now established that listeriosis can present as a gastrointestinal disease with fever (3). Although *L. monocytogenes* infections most frequently affect neonates, pregnant women, immunosuppressed patients, those receiving corticosteroids, and elderly patients, infection can also occur in previously healthy persons.

Ocular listeriosis is rare, with conjunctivitis being the most frequent manifestation. Keratitis, endophthalmitis, and acute chorioretinitis have also been reported. Infective endophthalmitis is a potentially devastating disease that may lead to loss of vision. Exogenous endophthalmitis occurs after ocular surgery or penetrating ocular trauma. Endogenous endophthalmitis results from the hematogenous spread of bacterial infection to the eye. It is a rare entity that accounts for 2 to 8% of all cases of endophthalmitis. Immunocompromised states, chronic diseases such as diabetes mellitus or renal insufficiency, malignancies, and intravenous drug use have been reported in association with this disease (16, 26). Greenwald et al. (16) reviewed 72 cases of metastatic endophthalmitis published from 1976 to 1985, and found Bacillus cereus as the most frequently reported species (15.3%), followed by Neisseria meningitidis (11.1%) and Staphylococcus aureus and Haemophilus influenzae (each, 9.7%). Gram-negative microorganisms, including Pseudomonas aeruginosa and Enterobacteriaceae, accounted for 25% of isolates. Three cases (4.2%) of endogenous endophthalmitis by L. monocytogenes were included in the study. Later, in 1994, Okada et al. (26) reported, from a series of 28 patients with endogenous endophthalmitis, 71% of cases due to gram-positive organisms with streptococci and S. aureus accounting for 32 and 25% of all isolates, respectively. They found the endocardium to be the most frequent source of infection, followed by the gastrointestinal tract and the genitourinary tract. As endophthalmitis is a severe, vision-threatening infection, early diagnosis and prompt initiation of antibiotic therapy are essential. Therefore, the condition warrants puncture of the anterior chamber or vitreous tap to investigate the etiologic agent and a simultaneous intravitreous antibiotic injection, as well as an intensive intravenous antibiotic administration.

L. monocytogenes is a rare cause of endophthalmitis. Since the first case of endophthalmitis due to L. monocytogenes reported by Goodner and Okumoto (15) in 1967, to our knowledge, only 16 other cases have been published in the literature (1, 2, 4-8, 12-14, 17, 19, 20, 22, 25, 29). Almost all cases showed similar clinical features including decreased vision, elevated intraocular pressure, and fibrinous anterior chamber reaction. Several patients developed a dark hypopyon. In all cases the cause of bacterial endophthalmitis was determined by recovering the organism from cultures of intraocular fluids. Six of the 17 published cases of L. monocytogenes endophthalmitis occurred in immunocompromised patients (2, 5, 7, 20, 22, 25), 6 occurred in elderly patients with good physical health (1, 4, 14, 15, 17, 19), and the remaining 5 cases affected young healthy individuals (6, 8, 12, 13, 29). Our patient had several potentially predisposing factors, including laryngeal carcinoma and immunosuppressive therapy. An exogenous source of infection was not identified in any of the reported cases. The present case was not related to surgical procedures or to local trauma, and there was no evidence of a distant focus of infection from which hematogenous spread occurred. Considering

that the digestive tract is a likely route of entry of *L. monocy-togenes*, we suggest that the organism might have entered the body orally, disrupted the mucosal barriers, and invaded the eye via the bloodstream.

L. monocytogenes is susceptible to a wide range of antibiotics but not to cephalosporins. Nevertheless, since the isolation of the first multiresistant strain of L. monocytogenes in France in 1988 (27), strains resistant to one or several antibiotics, such as trimethoprim, erythromycin, streptomycin, tetracycline, or chloramphenicol, have become more frequent (11). The treatment of choice for systemic L. monocytogenes infection is the administration of ampicillin or penicillin G combined with an aminoglycoside such as gentamicin. Trimethoprim-sulfamethoxazole alone or with rifampin is considered an alternative treatment for patients who are allergic to penicillin. For our isolate, MICs of almost all antibiotics tested, including ciprofloxacin, were low. To our knowledge, this is the first case of L. monocytogenes endophthalmitis which has been treated with oral ciprofloxacin combined with intravitreal and topical vancomvcin.

This paper points out the importance of prompt and accurate identification of the infectious agent by the microbiologist in the management of endophthalmitis. Although endophthalmitis due to *L. monocytogenes* is uncommon, the possible presence of this entity should be kept in mind regardless of the age or immunological status of the patient.

## REFERENCES

- Abbott, R. L., R. K. Forster, and G. Rebell. 1978. Listeria monocytogenes endophthalmitis with a black hypopyon. Am. J. Ophthalmol. 86:715–719.
- Algan, M., B. Jonon, J. L. George, C. Lion, M. Kessler, and J. C. Burdin. 1990. *Listeria monocytogenes* endophthalmitis in a renal-transplant patient receiving ciclosporin. Ophthalmologica 201:23–27.
- Aureli, P., G. C. Fiorucci, D. Caroli, G. Marchiaro, O. Novara, L. Leone, and S. Salmaso. 2000. An outbreak of febrile gastroenteritis associated with corn contaminated by *Listeria monocytogenes*. N. Engl. J. Med. 342:1236–1241.
- Bagnarello, A. G., A. J. Berlin, A. J. Weinstein, M. C. McHenry, and P. S. O'Connor. 1977. *Listeria monocytogenes* endophthalmitis. Arch. Ophthalmol. 95:1004–1005.
- Ballen, P. H., F. R. Loffredo, and B. Painter. 1979. *Listeria* endophthalmitis Arch. Ophthalmol. 97:101–102.
- Beuchaf, L., B. Hirschel, C. Tabatabay, and I. Filthuth. 1985. Intraocular listeriosis. J. Fr. Ophthalmol. 8:797–799.
- Brasseur, G., A. Retout, T. Didier, J. F. Charlin, and J. F. Lemeland. 1989. Listeria endophthalmitis: an uncommon etiology. Bull. Soc. Ophthalmol. Fr. 89:1463–1466.
- Brian, G. R., and M. C. Treplin. 1988. Listeria monocytogenes endophthalmitis: a case report. Aust. N. Z. J. Ophthalmol. 16:329–331.
  Bula, C. J., J. Bille, and M. P. Glauser. 1995. An epidemic of food-borne
- Bula, C. J., J. Bille, and M. P. Glauser. 1995. An epidemic of food-borne listeriosis in western Switzerland: description of 57 cases involving adults. Clin. Infect. Dis. 20:66–72.
- Centers for Disease Control and Prevention. Update: multistate outbreak of listeriosis—United States, 1998–1999. Morb. Mortal. Wkly. Rep. 47:1117– 1118.
- Charpentier, E., G. Gerbaud, C. Jacquet, J. Rocourt, and P. Courvalin. 1995. Incidence of antibiotic resistance in *Listeria* species. J. Infect. Dis. 172:277–281.
- Deramo, V. A., G. K. Shah, M. Garden, and J. I. Maguire. 1999. Good visual outcome after *Listeria monocytogenes* endogenous endophthalmitis. Retina 19:566–568.
- Duch, S. T., M. C. Quintana, and O. G. Pujol. 1991. Listeria monocytogenes endophthalmitis. Acta Ophthalmol. 69:108–110.
- Eliott, D., T. P. O'Brien, W. R. Green, H. D. Jampel, and M. F. Goldberg. 1992. Elevated intraocular pressure, pigment dispersion and dark hypopyon in endogenous endophthalmitis from *Listeria monocytogenes*. Surv. Ophthalmol. 37:117–124.
- Goodner, E. K., and M. Okumoto. 1967. Intraocular listeriosis. Am. J. Ophthalmol. 64:682–686.
- Greenwald, M. J., L. G. Wohl, and C. H. Sell. 1986. Metastatic bacterial endophthalmitis: a contemporary reappraisal. Surv. Ophthalmol. 31:81–101.
- 17. Heidemann, D. G., M. Trese, S. F. Murphy, D. Bradford, M. Lewis, and S. P.

**Dunn.** 1990. Endogenous *Listeria monocytogenes* endophthalmitis presenting as keratouveitis. Cornea **9:**179–180.

- Linnan, M. J., L. Mascola, X. D. Lou, V. Goulet, S. May, C. Salminen, D. W. Hird, M. L. Yonekura, P. Hayes, R. Weaver, A. Audurier, B. D. Plikaytis, S. L. Fannin, A. Kleks, and C. V. Broome. 1988. Epidemic listeriosis associated with Mexican-style cheese. N. Engl. J. Med. 319:823–828.
- Lohmann, C. P., V. P. Gabel, M. Heep, H. J. Linde, and U. Reischl. 1999. Listeria monocytogenes-induced endogenous endophthalmitis in an otherwise healthy individual: rapid PCR-diagnosis as the basis for effective treatment. Eur. J. Ophthalmol. 9:53–57.
- Maloney, J. M., F. S. Nolte, and T. A. Meredith. 1990. Listeria monocytogenes endophthalmitis, treatment with vitrectomy and trimethoprim/sulfamethoxazole. Emory J. Med. 4:201–204.
- McLauchlin, J., S. M. Hall, S. K. Velani, and R. J. Gilbert. 1991. Human listeriosis and pate: a possible association. BMJ 303:773–775.
- Melamed, J., S. Kwittko, S. Barcaro, J. M. Verri, and V. F. Petrillo. 1994. Endogenous endophthalmitis due to *Listeria monocytogenes*. Ocul. Immunol. Inflamm. 2:45–48.
- 23. National Committee for Clinical Laboratory Standards. 2000. Methods for

dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 5th ed. Approved standard M7–A5. National Committee for Clinical Laboratory Standards, Wayne, Pa.

- Nieman, R. E., and B. Lorber. 1980. Listeriosis in adults: a changing pattern. Report of eight cases and review of the literature, 1968–1978. Rev. Infect. Dis. 2:207–227.
- Nigrin, J., D. L. Tyrrell, F. L. Jackson, S. R. Ombres, and R. A. Morgan. 1977. *Listeria monocytogenes* endophthalmitis in an immune-suppressed host. Can. Med. Assoc. J. 116:1378–1382.
- Okada, A. A., R. P. Johnson, W. C. Liles, D. J. D'Amico, and A. S. Baker. 1994. Endogenous bacterial endophthalmitis. Report of a ten-year retrospective study. Ophthalmology 101:832–838.
- Poyart-Salmeron, C., C. Carlier, P. Trieu-Cuot, A. L. Courtieu, and P. Courvalin. 1990. Transferable plasmid-mediated antibiotic resistance in *Listeria monocytogenes*. Lancet 335:1422–1426.
- Schuchat, A., B. Swaminathan, and C. V. Broome. 1991. Epidemiology of human listeriosis. Clin. Microbiol. Rev. 4:169–183.
- Snead, J. W., W. H. Stern, J. P. Whitcher, and M. Okumoto. 1977. Listeria monocytogenes endophthalmitis. Am. J. Ophthalmol. 84:337–340.