Case Report

Orthotopic Liver Transplantation: Is There a Risk for Listeria monocytogenes Infection?

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Immunosuppression of any kind is a known risk factor for infection with Listeria monocytogenes (L. monocytogenes). Particularly, patients with impaired liver function are at increased risk of developing an aggravated course of infection with this bacterial pathogen (see Nolla-Salas et al.; 2002 and Cabellos et al.; 2008). It is a well-known pathogen in immunocompromised patients, but has only seldom been reported following orthotopic liver transplantation. Invasion of the central nervous system presenting as meningitis or meningoencephalitis and bacteremia are the principal clinical manifestations of listerial infections (see Brouwer et al.; 2006). We present an account of a case of a patient who developed L. monocytogenes meningitis during the early period after liver transplantation.

1. Case Report

We report the case of a 57-year old man diagnosed with liver cirrhosis Child-Turcotte-Pugh C resulting from chronic hepatitis C. He underwent liver transplantation in June 2007, at a transplantation center in Germany. The operation itself was uneventful and no complications were reported after surgery. Furthermore the preexistent hepato-renal syndrome resolved after transplantation. His immunosuppressive medication included tacrolimus (2 × 4 mg), mycophenolate-mofetil (2 × 1 g) and prednisolone (10 mg).

In August 2007 the patient was admitted to our hospital because of impaired consciousness since the previous day. In our emergency ward elevated body temperature was noticed and shortly after admittance the patient suffered a focal epileptic seizure accompanied by worsening of the mental status and the respiratory situation. He became unconscious and had to be transferred to our intensive care unit. For further evaluation a lumbar puncture was performed. The laboratory-chemical analysis indicated bacterial meningitis (see Table 1). In the microscopical analysis gram-positive rods were observed. A parenteral antibiotic therapy with ampicillin (4 g three times daily) and gentamicin (5 mg/kg) was initiated. In the following days, L. monocytogenes grew in culture of cerebrospinal fluid (CSF). The patient responded well to the above-mentioned therapy. The elevated laboratory parameters of inflammation (CRP on admission: 234 mg/l, CRP hospital day 6: 44 mg/l) normalized and the clinical status improved. In a followup lumbar puncture on day 6 of the clinical illness the cell count was normalizing. The patient was transferred to the normal ward after his clinical situation improved. He was discharged on the 25th day following admittance. Before the infection occurred there was no exposure to potentially contaminated food known.

2. Discussion

Listeria monocytogenes is a ubiquitous pathogen in the environment, capable of causing human and animal infection. Although uncommon in humans, it causes illness in sporadic and epidemic forms throughout the world. The pathogen is a facultative intracellular, aerobic, facultatively anaerobic gram-positive rod [1]. The organism is normally found in soil and decaying vegetable material. Listeria is exceptionally resistant to environmental conditions and able to grow in temperatures ranging from 4°C to 37°C. It is most often
transmitted to humans via contaminated foods like milk, cheese, undercooked meat, or uncooked vegetables. The pathogen has also been isolated from asymptomatic humans. About one to five percent of healthy individuals are fecal excretors of Listeria species [2]. The Center of Disease Control and Prevention (CDC) declares that in the United States an estimated 2,500 persons become seriously ill with listeriosis each year; of these 500 die.

After the introduction of the Haemophilus influenzae type b conjugate vaccine in the USA, meningitis caused by L. monocytogenes became the fourth most common cause of bacterial meningitis, following Streptococcus pneumoniae, Neisseria meningitides and group B streptococcus [3].

Most of the systemic invasive infections with Listeria are in individuals with one or more predisposing conditions. The risk factors are mainly pregnancy, corticosteroid therapy, other immunosuppressive therapy, and age. In a study from Finland seventy four cases of systemic listeriosis were analysed. Of these patients, 66% had an underlying disease, most commonly malignancy, diabetes mellitus, or renal transplantation, and 43% had received immunosuppressive therapy within one week before onset of listeriosis. Bacteremia and central nervous system infections were the most common clinical entities; both accounted for 43% of cases [4]. In a review analysing Listeria-meningitis-meningoencephalitis outside of pregnancy, hematologic malignancy and kidney transplantation were the leading predisposing factors. But in 36% of patients no underlying diseases were detectable. Listeriosis occurred throughout life, with a higher incidence before the age of 3 and after the age of 45–50 years [5]. Thirteen cases of spontaneous bacterial peritonitis due to L. monocytogenes in individuals with cirrhosis suggest that liver cirrhosis is also a significant risk factor for listeriosis [6].

According to a Spanish study bacterial meningitis in cirrhotic patients was associated with a high mortality and a large number of complications; a case fatality rate of 53.1% was observed. Of the classic pathogens, L. monocytogenes was more prevalent than in other immunocompromised patients. The authors suggest that this could be the result of the easy translocation of the organism into the bloodstream from the gastrointestinal tract [7]. According to a review of the literature, it seems that liver disease is not the only predisposing factor of infection with Listeria: liver transplantation; L. monocytogenes was grown in culture from the CSF and blood [8]. In another case report a 29-year old man diagnosed with autoimmune hepatitis suffered bacteremia and peritonitis in the early postoperative period after cadaveric liver transplantation [22]. Data from the literature show that listeriosis can present within days to years after transplantation [9, 10]. Nosocomial acquisition in the present case is unlikely because there were no further cases of listeriosis in our hospital at the same time. There was also no evidence that the transmission was caused by the donor. We speculate that the source of infection is through the intestinal tract following previous enteric colonization probably after ingestion of contaminated food products.

Even though there are still no satisfactory data regarding the incidence of Listeria infection following liver transplantation it seems that patients after transplantation suffer a greater risk to develop an aggravated course of infection with this pathogen. Including this case there are 16 reported cases of listeriosis after liver transplantation (see Table 2).

The clinical signs of meningitis caused by Listeria include fever, headache and altered mental status and the signs of Listeria meningitis do not for the most part differ from those found in patients with community-acquired non-listerial bacterial meningitis [23]. All of the typical symptoms were present in 43% of the patients. Almost all patients presented with at least two of the four classical symptoms, headache, fever, neck stiffness, and altered mental status. The above-mentioned symptoms of bacterial meningitis were reported equally in meningitis patients due to other causes [24]. On the contrary in some previous reports an atypical course of meningitis was reported. In a study by Mylonakis et al., patients with Listeria infection had a significantly lower incidence of meningeal signs compared with patients with acute meningitis due to other bacterial pathogens. The CSF profile was significantly less likely to have a high cell count or a high protein concentration [5]. The course of meningitis ranges from mild illness with fever and changes of mental status to a fulminant course with coma. A subacute presentation with cranial nerve palsies, lymphocytic pleocytosis, elevated CSF protein and low glucose may mimic tuberculous or fungal meningitis. Additionally focal signs can be present. Beside cranial nerve abnormalities, there may be ataxia, tremors, hemiplegia and deafness. In the later course seizures may occur [5]. In a large proportion of patients, symptoms may be present for more than 4 days. In the literature, meningitis caused by Listeria is characterized by high case-fatality rates (24%–62%) due to the occurrence in the elderly and the immunocompromised [25]. A recent prospective study demonstrates a mortality rate of 17% [23].

We present a case of Listeria meningitis shortly after orthotopic liver transplantation. Because of the low incidence and the high mortality rate of Listeria infection, physicians must be aware of this pathogen most notably in immunocompromised patients, particularly because the therapy of Listeria meningitis diverges from the “normal” regime used for other bacterial pathogens causing meningitis. Third-generation cephalosporins are the beta-lactams

### Table 1: Cerebrospinal fluid analysis.

|                    | Reference range, adults | On admission | Hospital day 6 |
|--------------------|-------------------------|--------------|----------------|
| Total cell count (per mm³) | 0–5                    | 1220         | 724            |
| Proteine (mg/dl)    | 5–55                    | 519          | 311            |
| Glucose (mg/dl)     | 50–57                   | 36           | 101            |
| Lactate (mmol/l)    | 16.6                    | 4.7          |                |

Reference range, adults: Glucose (mg/dl) 50–57, Proteine (mg/dl) 5–55, Glucose (mg/dl) 50–57, Lactate (mmol/l) 16.6.
of choice in the empiric treatment of meningitis. These drugs have potent activity against all the major pathogens of bacterial meningitis with the notable exception of L. monocytogenes since Listeria has an innate resistance to cephalosporin antibiotics. The treatment of choice against Listeria has traditionally been ampicillin (2 g every 4 hours) since resistance to this drug is rare [26]. Some authors recommend the addition of gentamicin to ampicillin treatment on the basis of the synergistic effect observed in vitro in animal models, but gentamicin is poor in penetrating the intracellular compartment and the CSF and is a well-recognized nephrotoxic agent. Ampicillin is given for two to four weeks in immunocompetent patients and for four to eight weeks in immunocompromised patients. Gentamicin is given for 10 to 14 days until the patient improves; in poor responders, it can be given for up to three weeks.

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### References

[1] B. Swaminathan, J. Roccourt, and J. Bille, “Listeria,” in Manual of Clinical Microbiology, p. 341, ASM Press, Washington, DC, USA, 6th edition, 1995.

[2] A. Schuchat, B. Swaminathan, and C. V. Broome, “Epidemiology of human listeriosis,” Clinical Microbiology Reviews, vol. 4, no. 2, pp. 169–183, 1991.

[3] A. Schuchat, K. Robinson, J. D. Wenger, et al., “Bacterial meningitis in the United States in 1995,” The New England Journal of Medicine, vol. 337, no. 14, pp. 970–976, 1997.

[4] K. Skogberg, J. Siryjanen, M. Jähkola, et al., “Clinical presentation and outcome of listeriosis in patients with and without immunosuppressive therapy,” Clinical Infectious Diseases, vol. 14, no. 4, pp. 815–821, 1992.

[5] E. Mylonakis, E. L. Hohmann, and S. B. Calderwood, “Central nervous system infection with Listeria monocytogenes: 33 years’ experience at a general hospital and review of 776 episodes from the literature,” Medicine, vol. 77, no. 5, pp. 313–336, 1998.

[6] J. Nolla-Salas, M. Almela, I. Gasser, et al., “Spontaneous bacteremia with Listeria monocytogenes peritonitis: a population-based study of 13 cases collected in Spain,” American Journal of Gastroenterology, vol. 97, no. 6, pp. 1507–1511, 2002.

[7] C. Cabellos, P. F. Viladrich, J. Ariza, et al., “Community-acquired bacterial meningitis in cirrhotic patients,” Clinical Microbiology and Infection, vol. 14, no. 1, pp. 35–40, 2008.

[8] S. Mizuno, “Listeria monocytogenes following orthotopic liver transplantation: central nervous system involvement and review of the literature,” World Journal of Gastroenterology, vol. 13, no. 32, pp. 4391–4393, 2007.

[9] C. A. Retally and K. V. Speeg, “Infection with Listeria monocytogenes following orthotopic liver transplantation: case report and review of the literature,” Transplantation Proceedings, vol. 35, no. 4, pp. 1485–1487, 2003.

[10] A. P. Limaye, J. D. Perkins, and K. V. Kowdley, “Listeria infection after liver transplantation: report of a case and review of the literature,” American Journal of Gastroenterology, vol. 93, no. 10, pp. 1942–1944, 1998.

[11] H. A. Elsner, W. Tenschert, L. Fischer, et al., “Nosocomial infections by Listeria monocytogenes: analysis of a cluster of septicemias in immunocompromised patients,” Infection, vol. 25, no. 3, pp. 135–139, 1997.

[12] W. E. Peertmans, H. P. Endtz, A. R. Janssen, et al., “Recurrent Listeria monocytogenes bacteraemia in a liver transplant patient,” Infection, vol. 18, no. 2, pp. 107–108, 1990.

[13] P. G. Spitzer, S. M. Hammer, and A. W. Karchmer, “Treatment of Listeria monocytogenes infection with trimethoprim-sulfamethoxazole: case report and review of the literature,” Reviews of Infectious Diseases, vol. 8, p. 427, 1986.

[14] V. Vargas, C. Aleman, I. de Torres, et al., “Listeria monocytogenes associated acute hepatitis in a liver transplant recipient,” Liver, vol. 18, no. 3, pp. 213–215, 1998.

[15] N. Bourgeois, F. Jacobs, M. L. Tavares, et al., “Listeria monocytogenes hepatitis in a liver transplant recipient: a case report

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**Table 2: Cases of listeria infection following liver transplantation.**

| Age (yr) | Sex | Time post LTX | Clinical presentation | Treatment | Outcome | Ref |
|----------|-----|---------------|-----------------------|-----------|---------|-----|
| 53       | M   | 5 d           | Meningitis with headache, mental decline | Ampicillin | Survived | [8] |
| 66       | F   | 32 mo         | Fever, hypotension, bacteremia | Ampicillin | Survived | [9] |
| 39       | F   | 7 d           | Fever, abdominal pain, bacteremia | Ampicillin | Survived | [10] |
| 66       | F   | 32 mo         | Fever, right flank pain, anorexia, bacteremia | Ampicillin | Survived | [11] |
| 39       | F   | 7 d           | Fever, abdominal pain, bacteremia | Ampicillin | Survived | [12] |
| 55       | F   | 4 mo          | Fever, abdominal pain, bacteremia | TMP-SMX | Survived | [13] |
| 57       | F   | 20 mo         | Bacteremia, hepatitis | Ampicillin | Survived | [14] |
| 56       | F   | 8 mo          | Bacteremia, hepatitis | Ampicillin, Gentamicin | Survived | [15] |
| 41       | F   | 10 mo         | Endocarditis, bacteremia, hepatitis, pulmonary emboli | Ampicillin, Gentamicin | Survived | [16] |
| 47       | F   | NR            | Peritonitis, bacteremia | Ampicillin, Amikacin | Survived | [17] |
| 11 mo    | M   | 7 d           | Meningitis, epididymitis, orchitis | Ampicillin | Survived | [18] |
| NR       | NR  | 14 d          | Meningitis | NR | Survived | [19] |
| 67       | F   | 21 d          | Meningitis | Ampicillin | Died | [20] |
| 13       | F   | 4 mo          | Meningitis | Ampicillin | Died | [21] |
| 29       | M   | 4 d           | Fever, abdominal pain, cholestasis | Ampicillin | Survived | [22] |

Abbreviations: TMP-SMX: trimethoprim-sulfamethoxazole; NR: not reported.
and review of the literature,” *Journal of Hepatology*, vol. 18, no. 3, pp. 284–289, 1993.

[16] R. K. Avery, D. S. Barnes, J. C. Teran, et al., “*Listeria monocytogenes* tricuspid valve endocarditis with septic pulmonary emboli in a liver transplant recipient,” *Transplant Infectious Disease*, vol. 1, no. 4, pp. 284–287, 1999.

[17] C. Chapoutot, P. Perney, G. P. Pageaux, et al., “*Spontaneous Listeria monocytogenes* peritoneal infection complicating hepatic transplantation,” *Gastroenterologie Clinique et Biologique*, vol. 20, no. 8–9, pp. 700–702, 1996.

[18] C. von Schnakenburg, B. Hinrichs, J. Fuchs, et al., “Pretransplant epididymitis and orchitis following *Listeria monocytogenes* septicemia,” *Pediatric Transplantation*, vol. 4, no. 2, pp. 156–158, 2000.

[19] C. V. Paya, P. E. Hermans, J. A. Washington, et al., “Incidence, distribution, and outcome of episodes of infection in 100 orthotopic liver transplantations,” *Mayo Clinic Proceedings*, vol. 64, no. 5, pp. 555–564, 1989.

[20] M. Pouyet, C. Ducerf, P. Gaussorgues, et al., “Fulminant and subfulminant hepatitis treated by orthotopic transplantation of the liver. Apropos of 10 cases,” *Chirurgie*, vol. 115, no. 8, pp. 533–539, 1989.

[21] D. B. Louria, A. Blevins, and D. Armstrong, “*Listeria* infections,” *Annals of the New York Academy of Sciences*, vol. 174, no. 2, pp. 545–551, 1970.

[22] T. Kruszyna, M. Walsh, K. Peltekian, et al., “Early invasive *Listeria monocytogenes* infection after orthotopic liver transplantation: case report and review of the literature,” *Liver Transplantation*, vol. 14, no. 1, pp. 88–91, 2008.

[23] M. C. Brouwer, D. van de Beek, et al., “Community-acquired *Listeria monocytogenes* meningitis in adults,” *Clinical Infectious Diseases*, vol. 43, no. 10, pp. 1233–1238, 2006.

[24] D. van de Beek, J. de Gans, L. Spanjaard, et al., “Clinical features and prognostic factors in adults with bacterial meningitis,” *The New England Journal of Medicine*, vol. 351, no. 18, pp. 1849–1859, 2004.

[25] C. Pigrau, B. Almirante, A. Pahissa, et al., “Clinical presentation and outcome in cases of listeriosis,” *Clinical Infectious Diseases*, vol. 17, no. 1, pp. 143–144, 1993.

[26] E. Charpentier, G. Gerbaud, C. Jacquet, et al., “Incidence of antibiotic resistance in *Listeria* species,” *Journal of Infectious Diseases*, vol. 172, no. 1, pp. 277–281, 1995.