Listeria septicemia accompanied by central nervous system involvement in a patient with multiple myeloma and secondary diabetes

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Patient: Female, 58
Final Diagnosis: Listeria septicemia
Symptoms: Nausea • vomiting • high fever • apathetic intelligence • repeated convulsion
Medication: Levoﬂoxacin
Clinical Procedure: —
Specialty: Hematology

Objective: Rare disease
Background: Multiple myeloma is a hematological malignancy that frequently causes secondary diabetes due to chemotherapy using hormones and infection due to immunosuppression.

Case Reports: The patient was a 58-year-old woman with multiple myeloma and secondary diabetes complicated by listeria septicemia accompanied by central nervous system involvement. She initially received moxa lactam and etimacin sulfate, but blood cultures detected Listeria monocytogenes. Levoﬂoxacin was administered, but the symptoms did not improve. The patient ultimately died.

Conclusions: Listeria septicemia accompanied by central nervous system involvement in a patient with multiple myeloma and secondary diabetes is a relatively rare disease. Prevention, timely diagnosis, and treatment are the key steps for improvement. Blood glucose level control is another important factor that should be considered in the prevention and treatment for Listeria monocytogenes infection.

Key words: Listeria monocytogenes • multiple myeloma • secondary diabetes • immunosuppression • central nervous system involvement

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Background

Multiple myeloma is a hematologic malignancy characterized by a proliferation of plasma cells in bone marrow (antibody-forming cells) and consequently an excess of monoclonal paraprotein [1]. In multiple myeloma patients, secondary diabetes is usually caused by hormone-containing chemotherapy and infection frequently occurs due to immunosuppression. Here, we present a patient with multiple myeloma and secondary diabetes complicated by septicemia and central nervous system involvement caused by Listeria monocytogenes. There are few reports on multiple myeloma patients infected with Listeria monocytogenes [2,3]. The course is described in this article.

Case Report

A 58-year-old Chinese woman was diagnosed as having multiple myeloma in May 2010. She had received regular chemotherapy with M2(remestine, cyclophosphamide, chlorambucil, and prednisone) regimen once, followed by VAD (vincristine, Adriamycin, dexamethasone) regimen 6 times. She had complete remission after the third chemotherapy. However, she had secondary diabetes since the first chemotherapy and the blood glucose control was not good. In March 2011, the patient was admitted for accelerated bone pain. The bone marrow showed 6% myeloma cells. The results of hematological examinations were as follows: white blood cell (WBC) count, 7.7×10^9/L; red blood cell count, 121×10^12/L; hemoglobin, 21 g/L; platelet count, 383×10^9/L; albumin, 29.8 g/L; glutamic-pyruvic transaminase, 41 U/L; aspartate amino-transferase, 25 U/L; creatinine, 48 umol/L; urea nitrogen, 5.74 mmol/L; fasting blood-glucose, 7.48 mmol/L; Ca^2+, 2.03 mmol/L; immunoglobulin G, 15.7 g/L; immunoglobulin A, 3.2 g/L; immunoglobulin M, 0.4 g/L; serum β2 microglobulin, 2.8 mg/L; urine β2 microglobulin, 0.7 mg/L; serum xlight chain, 2.0 g/L; serum λ light chain, 2.0 g/L; urine xlight chain, 102 mg/L; and urine λ light chain, 15.4 mg/L. The patient received CT (cyclophosphamide, dexamethasone, and thalidomide) regimen. On the first day after chemotherapy, she had nausea and vomiting without diarrhea, abdominal pain, and fever. The regular therapy to control vomiting was not effective. On the second day after chemotherapy, she had high fever (39.2°C) and severe vomiting. The results of hematological examinations were as follows: WBC count, 4.4×10^9/L; hemoglobin, 128 g/L; platelet count, 230×10^9/L; and random blood glucose, 21 mmol/L. On physical examination, lungs, heart, and abdomen were normal. Neurological examination disclosed no evidence. She received moxalactam and etimicin sulfate. On the third day after chemotherapy, she showed apathetic intelligence and had repeated convulsions. Neurological examination disclosed nuchal stiffness. The blood cultures showed Listeria monocytogenes and the drug sensitivity results are shown in Table 1. She was diagnosed as having Listeria septicemia and suspicious central nervous system involvement. Her family members refused further examination, including brain CT and cerebral spinal fluid examination. She received levofloxacin at a dose of 0.4 g every 12 h and gammaglobulin at a dose of 5 g every day. However, she rapidly developed to coma and died 2 days later.

Discussion

Listeria monocytogenes is a small, facultatively anaerobic, gram-positive motile bacillus. Infection is spread through contaminated raw materials, bacterial spread, and ineffective cleaning procedures [4]. Listeria monocytogenes causes life-threatening infections with high mortality, especially in neonates, pregnant women, the elderly, and immunosuppressed patients [5–7]. Meningitis is usually seen in immunosuppressed people [8].

Diabetes is one of predisposing factors of Listeria monocytogenes infection. On the contrary, bacterial meningitis also influences blood glucose levels. The majority of patients with bacterial meningitis have high blood glucose levels on admission. Hyperglycemia can be caused by a physical stress reaction, the central nervous system insult leading to disturbed blood-glucose regulation mechanisms, and susceptibility of people with diabetes to pneumococcal meningitis. The vast majority of these known diabetic patients had meningitis due to infection with Streptococcus pneumoniae (67%) or Listeria monocytogenes (13%) and were at high risk for unfavorable outcome (52%) [11].

Four factors make therapy of listeriosis difficult: (1) The host's susceptibility to infection (compromised host, extreme age groups) is linked with atypical onset of disease; (2) intracellular survival and involvement of granulomatous tissue prevent prompt and successful therapy, even with highly potent antibiotics; (3) diagnosis and treatment are delayed because of the previous 2 factors; and (4) ampicillin often attains mere bactericidal effect for predicting the clinical efficacy of antibiotics [13]. Immunity treatment also plays an important role. Infection with Listeria monocytogenes evokes a complex immune response.
characterized by the influx of neutrophils and a predominant
ly proinflammatory cytokine response [14]. The importance of
myeloid cells in defense against *Listeria monocytogenes*
infection was first demonstrated by Rosen et al. The administra-
tion of 5C6 monoclonal antibody at the initiation of infection
resulted in uncontrolled growth of *Listeria monocytogenes*
in the livers of infected mice [15]. Meeks et al. [16] suggested
IL-23 is required for protection against systemic infection with
*Listeria monocytogenes*.

Our patient had multiple myeloma and secondary diabetes. She
received chemotherapy containing a high dose of glucocorti-
coid. Her positive blood cultures confirmed the diagnosis and
the percentage of positive blood cultures is 59–73% [17,18].
Our patient had obvious symptoms of central nervous system
involvement, but the definite diagnosis of meningitis could not
be ascertained because her relatives refused further examina-
tion, including brain CT and CSF examination. Her WBC was
always in the normal range. She was treated with levofloxacin
and gamma globulin, but she did not recover and soon died.

**Conclusions**

In conclusion, *Listeria septicemia* accompanied by central ner-
vous system involvement in a patient with multiple myeloma
and secondary diabetes is relatively rare. Prevention and time-
ly diagnosis and treatment are the key steps for improvement.
However, patients with multiple myeloma must receive hor-
mone-containing chemotherapy and prevention is the most
important step. Blood glucose level control is another impor-
tant factor that should be considered for the prevention and
treatment of *Listeria monocytogenes* infection.

**Conflict of interest**

The authors declare no conflict of interest.

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**Table 1.** Minimum inhibitory concentrations (MICs) of several antibiotics to *Listeria monocytogenes* isolated from the blood.

| Drug          | MIC (µg/ml) | Normal range (µg/ml) | R/S |
|---------------|-------------|----------------------|-----|
| Oxacillin     | 6           | 11–13                | R   |
| Penicillin    | 26          | 29–29                | R   |
| Teicoplanin   | 20          | 11–14                | S   |
| Vancomycin    | 21          | 15–15                | S   |
| Nitrofurantoin| 24          | 15–17                | S   |
| Cefoxitin     | 10          | 22–22                | R   |
| Gentamicin    | 24          | 13–15                | S   |
| SMZCo         | 33          | 11–16                | S   |
| Tigecycline   | 29          | 0–19                 | S   |
| Rifampicin    | 30          | 17–20                | S   |
| Clindamycin   | 7           | 15–21                | R   |
| Linezolid     | 31          | 21–21                | S   |
| Chloromycetin | 27          | 15–21                | S   |
| Erythromycin  | 26          | 14–23                | S   |
| Ciprofloxacin | 23          | 16–21                | S   |
| Levofloxacin  | 22          | 16–19                | S   |

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