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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 • vomitting • 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 moxalactam and etimicin 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(carmustine, 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, 121×10^9/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;crea,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 microglobin, 2.8 mg/L; urine β2 microglobin, 0.7 mg/L; serum κlight chain, 2.0 g/L; serum λlight chain, 2.0 g/L; urine κlight chain,102 mg/L; and urine λlight chain, 15.4 mg/L. The patient received CTD (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 severer 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, 21mmol/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 hemotherapy, 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].

Listeria monocytogenes promotes its internalization into host epithelial cells. Adhesion to host cells and invasion of the intracellular space are critical steps in the traversal of host barriers, leading to organ infection and bacterial spread in the body [9]. The ability of *Listeria monocytogenes* to colonize and affect the central nervous system can be explained by direct invasion of endothelial cells, invasion via infected phagocytes, and entrance into a neural pathway [10].

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 merely bacteriostatic concentrations *in vivo* and is not effective intracellularly [12].

Determination of the MIC *in vitro* is often used as the basis for predicting the clinical efficacy of antibiotics [13]. Immunity treatment also plays an important role. Infection with *Listeria monocytogenes* evokes a complex immune response

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

characterized by the influx of neutrophils and a predominantly proinflammatory cytokine response [14]. The importance of myeloid cells in defense against *Listeria monocytogenes* infection was first demonstrated by Rosen et al. The administration 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 glucocorticoid. 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 examination, 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 nervous system involvement in a patient with multiple myeloma and secondary diabetes is relatively rare. Prevention and timely diagnosis and treatment are the key steps for improvement. However, patients with multiple myeloma must receive hormone-containing chemotherapy and prevention is the most important step. Blood glucose level control is another important 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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