Successful Treatment of Listerial Brain Abscess: A Case Report and Literature Review

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Abstract

Listerial brain abscess is extremely rare; only two cases have been reported in Japan. We encountered a female patient with immunoblastic lymphadenopathy, who developed listerial brain abscess after 8 years of treatment with anti-neoplastic agents and corticosteroids. Brain MRI revealed multiple space occupying lesions, suggesting abscesses which were possibly caused by hematogenous spread of the bacteria. Immediate blood culture enabled early diagnosis, and she entered into complete remission with high-dose ampicillin. Blood culture and brain imaging seem to play a crucial role in making an early diagnosis, and the administration of high dose of antibiotics is recommended for improvement of this disease.

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Key words: *Listeria monocytogenes*, opportunistic infection, blood culture

Introduction

Listerial brain abscess is an opportunistic infection, often associated with underlying disorders such as malignancy, organ transplantation, or the use of immunosuppressive agents (1). *Listeria monocytogenes* is also one of the most common causes for meningitis (2, 3), but brain abscess is very rare, and only two cases have been reported in Japan (4, 5). Furthermore, there have been no reviews on listerial brain abscess except for the report by Dee and Lorber in 1986 (1). We report here a unique and rare case of brain abscess due to *Listeria monocytogenes*, and discuss it by reviewing the literature pertaining to this entity.

Case Report

A 58-year-old woman was admitted to Yokohama Rosai Hospital in July 2000, five days after the onset of left occipital headache, fever, and anorexia. She had a 7-year history of immunoblastic lymphadenopathy and had been treated with 10 mg to 30 mg of daily prednisolone. She had also suffered from recurrent interstitial pneumonitis with severe eosinophilia since 1995, for which she had received methylprednisolone pulse therapy 8 times. We had tried immunosuppressive agents and COP (cyclophosphamide, vincristine, and prednisolone) therapy in order to reduce the dosage of daily prednisolone, but they were not effective at all. She finally developed steroid-induced diabetes mellitus in 1997.

On admission, she was drowsy with high fever of around 38°C, while her blood pressure was normal (114/80 mmHg). Physical examination revealed dysarthria, dysdiadochokinesis, neck stiffness, and right-sided hemiparesis. The remainder of the examinations did not show any abnormalities.

The blood cell count showed 10,500 leukocytes per mm³ with 92% neutrophils, associated with highly positive levels of C-reactive protein (7.21 mg/dl), and high plasma glucose level (244 mg/dl). Cerebrospinal fluid (CSF) showed 141 leucocytes per mm³, with 64% mononuclear and 36% polymorphonuclear cells. The protein level of CSF was 668.8 mg/dl and the glucose level was 90 mg/dl. The culture of CSF was negative. Computed tomography (CT) of brain showed a low density lesion in the superior left pons which was suggestive of a brain abscess.

Then, antibiotic therapy with piperacillin sodium (2 g/day) was started. An afebrile state was obtained within a few days, and CRP decreased to 0.6 mg/dl, while neurologic signs such as those described above did not disappear immediately. Brain magnetic resonance imaging (MRI) with gadolinium enhancement revealed multiple rim enhancing lesions in the left pons, left middle cerebellar peduncle, and left cerebellum (Fig. 1). On the seventh day after admission, *Listeria monocytogenes* was cultured from her blood, which was sampled before using

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Figure 1. Brain MRI at onset revealing multiple space occupying lesions (T1 low, T2 high) with ringed enhancement in pons, cerebellum, and middle cerebellar peduncles.

the antibiotic agent.

The sensitivity test of the blood culture showed effectiveness of penicillin and resistance against cephalosporin. The antibiotic treatment was changed to ampicillin (12 g/day) according to the standard therapy of listerial brain abscess. The neurological signs and symptoms including lethargy, dysarthria, and right-sided hemiparesis gradually began to improve. It took almost 2 weeks until all the neurological signs had disappeared. Brain MRI, which was examined 6 weeks after changing the antibiotics, showed only a small residual lesion with no ringed enhancement in the left pons (Fig. 2). Abnormal shadows in the left middle cerebellar peduncle and left cerebellum had completely disappeared. The ampicillin therapy was discontinued at 8 weeks after admission. She was discharged in September without any sequels. Follow-up studies by MRI taken in September and December 2000 did not show any rim-en-

hancing lesion, suggesting no recurrence of the brain abscess.

Discussion

We encountered a unique case of brain abscess infected by *Listeria monocytogenes*, after long-term treatment with immunosuppressants such as prednisolone.

Although *Listeria monocytogenes*, a gram-positive nonencapsulated bacillus, is one of the most common causes for bacterial meningitis and meningoencephalitis (2, 3), listerial brain abscess is extremely rare. To our knowledge, only 31 cases with macroscopic brain abscess due to *Listeria monocytogenes* were reported from 1968 to 2001 (Table 1). This bacteria is believed to generally reach the central nervous system by hematogenous spread from the gastrointestinal tract to form meningitis or brain abscess (7, 29). The clinical manifestation of

Figure 2. Sequential MRI studies showing the reduction of abscess size, and the disappearance of ringed enhancement on day 45 from admission.

listerial brain abscess is similar to that of brain abscesses due to other causes, most patients show fever, elevated leukocyte counts, headache, focal signs and various other neurological findings (Table 2).

Listerial brain abscess is an opportunistic infection, and most patients (77.4%) have underlying conditions (Table 2), such as a renal transplantation, hematological malignancy, human immunodeficiency virus (HIV) infection, diabetes mellitus, or autoimmune diseases treated with prednisolone (Fig. 3). In our patient, the infection of *Listeria monocytogenes* was also based on such compromising conditions, i.e. she had underlying malignancy, diabetes mellitus, and she was treated with immunosuppressive agents.

Regarding the prognosis, Dee and Lorber reported that 8 among 14 (57.1%) patients with listerial brain abscess died (1), while the prognosis has markedly improved in the past decade as only 2 out of 16 (12.5%) have died of this disease since 1986 (Table 3). Some investigators have reported that the prognosis of brain abscesses due to other causes has also markedly improved in the same period after the introduction of CT (34, 35). This improvement of listerial brain abscess might have been obtainable because of the new diagnostic tests for intracerebral disorders such as CT and MRI. CT or MRI was performed in all cases since 1986 (Table 1), which was helpful to make a diagnosis and follow-up the course of brain abscess. Blood culture was thought to be much more useful than CSF

culture to determine the cause of brain abscess (1, 6), since blood culture was reported to be positive in 77.2% of patients (17/22), while the organism grew in CSF only in 26.1% of the cases (6/23) (Table 2). The timing of blood culture sampling which resulted in positivity was reported in 11 cases; the blood was sampled in most of (8/11) these patients before the use of antibiotics. We could also detect the bacteria by blood culture in the present case, whereas CSF culture did not show any growth of the bacteria. Thus it is suggested that blood culture should be obtained by all means in addition to CSF culture just before starting antibiotics if listerial brain abscess is suspected.

There are two strategies for the treatment of this disease: Surgical treatment and antibiotic therapy. Some reports have described that the remission rate of the disease might be increased by surgical procedure (1, 23). Our review also revealed that surgical procedure might reduce the mortality rate (Table 3), whereas the non-surgical group included some patients who could not undergo a surgical procedure due to their severe condition, which might have made the prognosis of this group poor. Most of the antibiotics except Cephems are reported to be effective against *Listeria monocytogenes*. Among them, chloramphenicol and penicillins can easily infiltrate into the CNS, whereas aminoglycosides do not readily cross the blood brain barrier. There have been no controlled trials to define the best choice of treatment and an adequate duration of therapy for listerial brain abscess, but some investigators recommended

Table 1. Characteristics of 31 Cases of Listerial Brain Abscess

Case	Age/ Sex	Underlying conditions	Immunosuppressive therapy	Head- ache	Fever >38°C	Focal signs	Blood	Culture CSF	Brain	CT/MRI	Surgery	Antibiotics	Outcome
1 (8)	87/M	None	None	NR	Yes	No	+	+	NR	-/-	-	PCG, CP	Died
2 (9)	49/M	Rheumatic fever, alcohol abuse, diabetes	None	NR	Yes	Yes	+	-	NR	-/-	-	PCG	Died
3 (10)	39/M	None	NR	Yes	NR	Yes	NR	-	+	-/-	-	NR	Died
4 (11)	53/M	Seizure, Cirrhosis	NR	No	Yes	Yes	+	-	+	-/-	+	PCG, EM	Survived
5 (12)	49/M	Renal transplant	AZP, PSL	NR	Yes	Yes	+	+	+	-/-	-	CP	Died
6 (13)	68/M	Leukemia	NR	Yes	Yes	Yes	NR	NR	NR	-/-	-	CP	Died
7 (14)	55/M	Renal transplant	AZP, PSL	Yes	Yes	Yes	+	-	+	+/-	+	ABPC	Survived
8 (15)	16/M	Acute lymphocytic leukemia	chemotherapy	Yes	NR	No	+	+	NR	+/-	-	PCG, CP	Survived
9 (16)	54/F	None	None	NR	NR	NR	NR	NR	NR	-/-	-	NR	Died
10 (16)	25/F	Ulcerative colitis	None	NR	NR	NR	NR	NR	NR	-/-	-	NR	Died
11 (17)	45/M	Renal transplant	AZP, PSL	Yes	Yes	Yes	+	-	-	+/-	+	ABPC	Survived
12 (18)	20/M	Acute lymphocytic leukemia	chemotherapy	Yes	Yes	Yes	+	+	NR	+/-	-	ABPC, CP, EM, GM	Survived
13 (19)	NR/M	None	NR	Yes	NR	No	NR	NR	NR	-/-	-	NR	Died
14 (20)	63/F	None	None	Yes	Yes	No	-	-	+	-/-	-	NR	Died
15 (20)	43/F	None	None	Yes	Yes	No	-	-	+	+/-	-	ABPC	Died
16 (1)	58/M	Chronic lymphocytic leukemia	chemotherapy	Yes	No	Yes	ND	ND	+	+/-	+	ABPC, GM	Survived
17 (21)	60/M	HIV infection	None	No	No	Yes	NR	NR	+	+/-	+	PCG, CP	Died
18 (22)	56/M	Acquired immunodeficiency syndrome	None	No	Yes	Yes	+	-	NR	+/-	-	ABPC, GM,	Survived
19 (23)	60/F	Rheumatoid arthritis	PSL	No	No	No	+	-	+	+/-	+	ABPC	Survived
20 (24)	85/M	type 2 Diabetes mellitus, Gout	None	No	No	Yes	+	-	+	+/-	+	ABPC	Died
21 (25)	6/F	Acute lymphocytic leukemia	chemotherapy	No	Yes	No	+	+	NR	+/-	-	ABPC, VCM, netilmicin	Survived
22 (26)	50/M	Sarcoidosis, Aspergilloma	PSL	No	No	Yes	-	-	+	+/-	+	ST	Survived
23 (27)	64/M	type 2 Diabetes mellitus, Aortic valve replacement	None	No	No	Yes	+	-	NR	+/-	-	ABPC, GM	Survived
24 (28)	77/M	Chronic lymphocytic leukemia	chemotherapy	Yes	No	Yes	-	NR	+	+/-	+	CP	NR
25 (29)	61/M	type 2 Diabetes mellitus	None	No	No	Yes	NR	NR	+	+/-	+	ST, CP	Survived
26 (30)	19/M	Juvenile rheumatoid arthritis, Tetralogy of Fallot	PSL	Yes	Yes	No	NR	+	NR	+/-	-	VCM, ABPC	Survived
27 (31)	70/M	None	None	Yes	Yes	No	-	-	+	+/-	+	ABPC	Survived
28 (32)	43/M	Sleep apnea syndrome, alcohol abuse	None	Yes	Yes	No	+	-	-	+/-	+	NR	Survived
29 (4)	58/F	Multiple endocrine neoplasm 2A, Systemic lupus erythematosus	PSL	Yes	Yes	Yes	+	-	NR	-/+	-	PCG, TOB	Survived
30 (33)	0/M	Pronatis	None	No	No	No	+	-	-	+/-	+	ABPC, GM,	Survived
31 (this case)	58/F	Immunoblastic lymphadenopathy	PSL, chemotherapy	Yes	Yes	Yes	+	-	NR	+/-	-	ABPC	Survived

NR: not reported, ND: not done, WBC: white blood cell, AZP: azathioprine, PSL: prednisolone, PCG: Penicillin, CP: Chloramphenicol, EM: Erythromycin, ABPC: Ampicillin, GM: Gentamicin, TOB: Tobramycin, VCM: Vancomycin, ST: sulfamethoxazole-trimethoprim.

Table 2. Characteristics, Laboratory Findings and Therapeutics of Patients with Listerial Brain Abscess

	Underlying conditions	Immunosuppressive therapy	Headache	Fever >38°C	Focal signs	Serum WBC >10,000/ μ l	Culture			Antibiotics		
							Blood	CSF	Brain	PCG	ABPC	ABPC+Aminoglycoside
Number (positive/total)	24/31	13/27	16/26	17/26	18/29	12/20	17/22	6/23	14/17	5/25	9/25	6/25
Ratio of positiveness (%)	77.4	48.1	61.5	65.3	62.0	60.0	77.2	26.1	82.3	20.0	36.0	24.0

penicillins as the first choice because of their effectiveness and permeability into the CNS (1, 6, 7). Our summary obtained from various reports demonstrated that high-dose ampicillin (12–18 g/day) was frequently administered to many cases for 6 to 8 weeks, and that the addition of aminoglycosides to ampicillin might improve the prognosis of this disease (Table 2, 3). [It is suggested that the aminoglycosides can infiltrate into the CNS across the blood brain barrier destroyed by inflammation.] In the present case, we fortunately chose piperacillin in

stead of cephalosporins as an empiric treatment on admission, which might have improved her prognosis. We used high-dose ampicillin according to the recommendation after the diagnosis (6, 7); surgical treatment was not chosen due to the many lesions in the brain stem and cerebellum.

In conclusion, we would like to emphasize that CNS listerial infection should be considered in patients showing abnormal neurological signs associated with multiple brain abscess, in whom there are immunosuppressive conditions such as diabe-

Table 3. Mortality Rate of Patients with Abscess due to *Listeria monocytogenes*

	~1985	1986~	Antibiotics			Surgery		Total
			PCG	ABPC	ABPC+Aminoglycoside	(-)	(+)	
Number of dead patients/Total	8/15	2/16	3/5	2/9	0/6	10/18	2/13	12/30
Mortality rate (%)	53.3	12.5	60.0	22.2	0	55.6	16.7	40.0

Figure 3. Frequency of underlying conditions in CNS listeriosis.

tes mellitus, AIDS, collagen diseases on corticosteroids, and various malignant disorders following chemotherapy. Moreover, it is critical to make a rapid diagnosis of CNS listeriosis by brain imaging studies as well as by several sets of blood culture.

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