Possible role of low dose dexamethasone administration in listeria monocytogenes meningoencephalitis: A case series

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Abstract. *Listeria (L.) monocytogenes* is a gram-positive, non-sporulating, facultatively anaerobic bacillus transmitted to humans through ingestion of contaminated foods. Listeriosis represents the third most common cause of death from food-borne illness, with a mortality rate of 20-30%, especially for patients affected by an invasive disease, which typically affects immunocompromised patients, pregnant women, the elderly, and neonates. It causes several clinical syndromes, of which meningitis, meningoencephalitis, and sepsis are the most challenging to deal with. Here, five cases of *L. monocytogenes* meningitis/meningoencephalitis affecting two previously healthy immunocompetent and three immunocompromised adult patients treated with ampicillin plus gentamicin are reported. In addition, all the patients described in this report received a low dose of intravenous dexamethasone; four of them made a full recovery. Additionally, a literature search was performed to better explain the appropriate clinical and therapeutic management approaches for these patients, highlighting the value of dexamethasone administration as part of the therapy.

Introduction

Listeria (L.) monocytogenes is a gram-positive, non-sporulating, facultatively anaerobic bacillus that is transmitted to humans through ingestion of foods contaminated with high-bacterial concentrations (1-3).

Listeriosis is a relatively rare disease (0.1 to 10 cases per 1 million individuals per year according to WHO) with a mortality rate of 20-30%, especially for those who developed an invasive disease (4).

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Invasive Listeriosis typically affects immunocompromised patients, pregnant women, the elderly, and neonates (5). It causes several clinical syndromes, of which meningitis, meningoencephalitis, and sepsis are the most challenging to deal with (6,7). Listeria meningitis should be suspected in children <3 years of age and adults >50 years of age who show meningeal symptoms without clear etiology (8).

Ampicillin plays a key role in Listeria treatment, and it is often combined with gentamicin which may be a suitable adjuvant due to its favorable pharmacodynamic synergistic action with penicillin (9). Optimal treatment durations have not been assessed; however, ampicillin should be administered for at least 21 days and gentamicin can be discontinued after 1 week of treatment, taking into consideration the patients' clinical conditions (9). Conversely, gentamicin administration may be prolonged for up to 3 weeks, although the renal function and plasma concentrations of gentamicin should be monitored in such a case (9,10).

Although there are limited data and inconclusive evidence, adjunctive dexamethasone administration is discouraged, as it has been associated with unfavorable outcomes or no beneficial effects; however, other studies tend to reconsider dexamethasone therapy due to its effects on inflammation and edema (11).

The present report describes five cases of *L. monocytogenes* meningitis affecting two previously healthy immunocompetent and three immunocompromised adult patients treated according to the international guidelines. All the patients described received a low dose of dexamethasone.

To discuss the appropriate clinical and therapeutic management of these patients and to argue the possible role of dexamethasone administration in Listeria meningitis, a brief literature review including only documented adult cases (≥18 years old) treated with an antibiotic and dexamethasone combination was also performed.

Case reports

Consent. The patients signed written informed consent forms. Within the consent form, it was specified that data collected during the diagnostic and therapeutic process can be anonymously used for scientific purposes.

Patient 1. This patient was a 69-year-old healthy Italian man with 5 days of fever, nausea, and loss of appetite, followed by a progressive headache and impaired mental status. His past medical history was unremarkable; he did not take any medications.

On admission, the patient was febrile (39˚C), poorly responsive to vocal and painful stimuli, and was in a state of stupor [Glasgow Coma Scale (GCS)] (8). Clinical examination showed neck stiffness along with positive Kernig's sign. Babinski's sign was negative.

Blood tests revealed an elevated white blood cell (WBC) count (18,800/mm^3, 89.8% neutrophils), mild anemia (Hb 11.8 g/dl), normal platelet count (160,000/mm^3), as well as elevated C-reactive-protein (CRP) levels (35.7 mg/dl) and procalcitonin (PCT) levels (3 ng/dl). Renal and liver function were normal. The HIV test was negative.

A head CT scan (SOMATOM® Definition Flash scanner, Siemens AG) showed no abnormalities (Fig. 1A). Cerebrospinal fluid (CSF) examination revealed high protein levels (4,175 mg/l; normal range 150-450 mg/l), high lactate dehydrogenase levels (193 IU/l), reduced glucose levels (18 mg/dl), and hypercellularity (152 cells/mcl mostly lymphocytes; normal range <5 cells/mcl). Empirical treatment with ceftriaxone 2 g twice daily, acyclovir 10 mg/kg three times daily, and corticosteroids (dexamethasone 4 mg three times daily) was initiated. Molecular biology [reverse transcription (RT)-PCR] for Listeria detection was performed using a FilmArray Meningitis/Encephalitis Panel (ME) CE-IVD according to the manufacturer's protocol (cat. no. RFIT-PRT-0005, BioFire Diagnostics, LLC) on the CSF, and the results were positive for *L. monocytogenes*, which was confirmed by CSF culture [performed in 5% blood agar with Brain Heart Infusion (BHI) to enhance recovery of Listeria isolates with incubation in aerobic conditions at 37˚C for 24 to 48 h]. Targeted therapy was established with intravenous (i.v.) ampicillin 3 g every 6 h, and gentamicin 400 mg i.v. Dexamethasone 4 mg three times a day was also maintained.

The patient's clinical conditions rapidly improved with notable amelioration 72 h after targeted therapy initiation. Overall, the patient was treated for 21 days with antibiotics and dexamethasone, and the latter was gradually reduced before discontinuation. After 1 month of hospitalization, the patient was discharged with no evidence of neurological deficits.

Patient 2. A previously healthy, 39-year-old man was hospitalized for speech problems and intense dizziness. He reported a 4-day history of fever, headache, and vomiting, which were treated with antiemetics and paracetamol.

On admission, the patient was febrile (39.6˚C), with a normal mental status and with neck stiffness. Other signs of meningeal irritation were absent. Clinical examination showed no abnormalities.

Laboratory tests revealed elevated WBC counts (13,300/mm^3, 73.3% neutrophils), high CRP levels (28.91 mg/dl), and elevated transaminase levels [aspartate transferase (AST) 314 IU/l; alanine transferase (ALT) 116 IU/l]. A head CT scan was normal (Fig. 1B).

CSF analysis showed high protein levels (675 mg/l), low glucose levels (29 mg/dl; serum glucose 109 mg/dl), with 502 cells/mcl (mostly lymphocytes). Empiric treatment was established with ceftriaxone 2 g twice daily, ampicillin 3 g four times daily, acyclovir 10 mg/kg three times daily, and dexamethasone 4 mg three times daily. RT-PCR on CSF was positive for *L. monocytogenes* and this result was then confirmed by CSF culture.

Ampicillin 12 g daily i.v., and gentamicin 4 mg/kg/day i.v. for 21 days were administered along with dexamethasone at the same dosage which was gradually tapered. The patient's clinical conditions improved rapidly, and the fever disappeared after 48 h of antibiotic treatment. In 34 days, he was discharged without complications.

Patient 3. A 49-year-old Italian man with a history of ulcerative colitis presented to the emergency department with abdominal pain, nausea, an intense headache, and a fever ~40˚C. He did not have other comorbidities. He took mesalamine and corticosteroids.

On admission, the patient had intense photophobia, and neck stiffness along with positive signs of meningeal irritation (Brudzinski, Kernig). In addition, he was febrile (39.5°C).

Blood tests revealed an elevated WBC count (11,000/mmc^3, 70% neutrophils), CRP levels (44.2 mg/dl) and PCT levels (25.32 ng/ml).

Head CT scan was negative (Fig. 1C). CSF analysis showed 1,364 leukocytes/μl with a preponderance of lymphocytes. CSF protein levels were 420 mg/l, and the glucose level was 32 mg/dl (blood glucose, 98 mg/dl).

The patient was treated empirically with ceftriaxone 2 g twice daily, acyclovir 10 mg/kg three times daily, vancomycin 15 mg/kg, and dexamethasone 4 mg three times daily.

Gram stains of the CSF showed the presence of Gram-positive rods. RT-PCR showed the presence of *Listeria monocytogenes*, later confirmed by culture.

Antibiotic therapy was switched to ampicillin 12 g daily i.v. plus gentamicin 4 mg/kg/day i.v. Dexamethasone was maintained at the same dosage, and was gradually decreased. He was treated for 4 weeks, with complete recovery of symptoms. After 1 month, the patient was discharged without neurological sequelae.

Patient 4. A 67-year-old man presented to the emergency department with a worsening frontal headache associated with a high fever (up to 40˚C), and impaired consciousness (GCS 12). His medical history included a B-cell lymphoma, treated with rituximab, and secondary hypoglobulinemia.

On admission, he had marked neck stiffness; Kernig's and Lasegue's signs were positive. He was febrile (38.4˚C) and confused.

Blood tests revealed elevated CRP levels (18 mg/dl), reduced WBC counts (3,500/mm^3) with normal formula, mild anemia (11.3 g/dl), and normal PCT levels. A head CT scan showed no abnormalities (Fig. 1D).

CSF examination revealed a glucose level of 0.24 mg/dl, a protein level of 1,400 mg/l, and a cell count of 425/mcl (with a predominance of mononuclear cells). Empirical therapy was started with vancomycin 15 mg/kg daily plus dexamethasone 4 mg three times daily.

CSF was positive for *L. monocytogenes* and antibiotic therapy was administered with ampicillin 12 g daily i.v. and gentamicin 4 mg/kg/day i.v. for 21 days. Dexamethasone 4 mg three times daily i.v. was also prolonged for 21 days and was

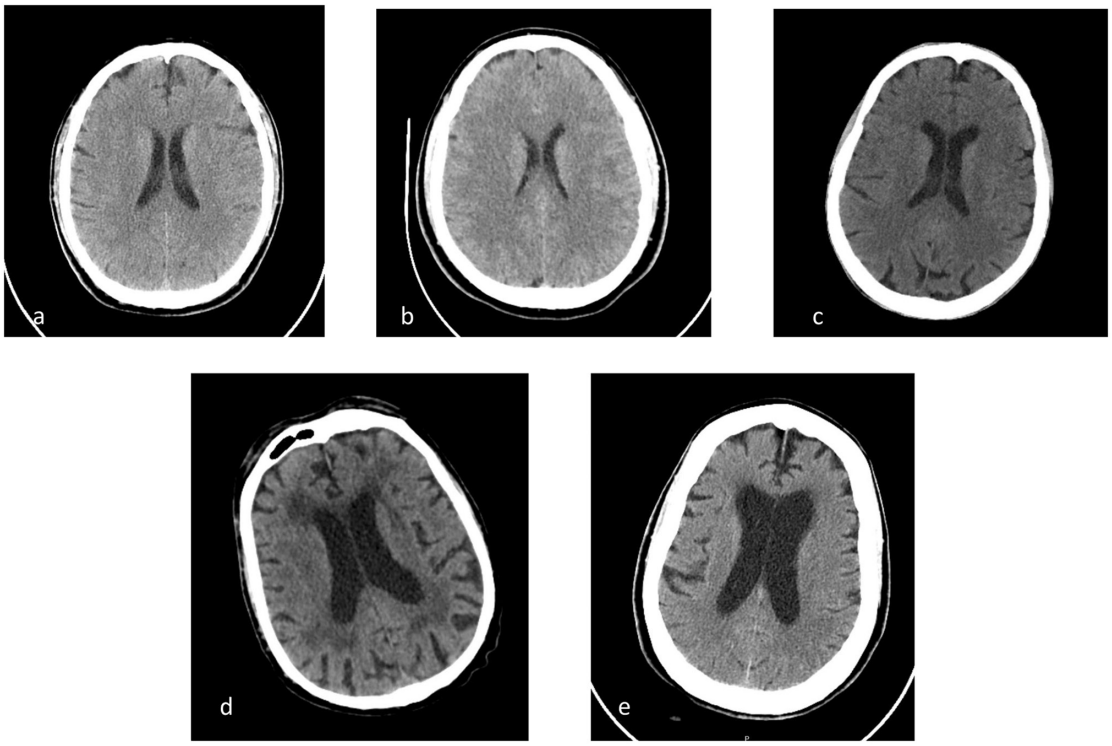

Figure 1. Patients' head CT scan. CT scans of the (a) first, (b) second, (c) third, (d) fourth, and (e) fifth patients' head.

gradually reduced. He was discharged 35 days after hospitalization without complications.

Patient 5. A 72-year-old man with a history of recurrent pulmonary infections, chronic kidney disease (CKD), and diabetes was admitted to the emergency department with fever (38.6˚C), photophobia, and confusion (GCS 11).

Neurological examination revealed neck stiffness with positive Kernig's and Lasegue's signs. Laboratory data showed high WBC counts (5,600/mm^3, 76% neutrophils), high CRP levels (36 mg/dl), creatinine 2.1 mg/dl (eGFR with CKD-EPI 31 ml/min), AST 56 IU/l, ALT 41 IU/l, and glucose 176 mg/dl. A head CT scan was normal (Fig. 1E).

CSF showed 1,125 mononuclear cells/mm^3, glucose 0.66 mg/dl and protein 2,100 mg/dl. Empiric therapy was started with ceftriaxone, acyclovir, ampicillin, and dexamethasone 4 mg three times daily. The CSF molecular panel was positive for *L. monocytogenes*, which was confirmed on CSF culture.

Antimicrobial therapy with ampicillin 3 g four times daily along with intravenous gentamicin 3 mg/kg/day was initiated. Due to the impaired kidney function, diminished doses of gentamicin were administered for 10 days, strictly monitoring creatinine and eGFR, the levels of which remained constant. Dexamethasone therapy was maintained for 21 days, although gradually reduced.

Unfortunately, despite appropriate therapy, the patient's condition deteriorated rapidly, especially his mental status, and he died on the 11th day after admission.

Discussion

Worldwide, *Listeria monocytogenes* is the third leading cause of community-acquired meningitis, accounting for 5% of all cases (1). Aging, chronic disease, sepsis, and malignancies represent the most important predictors of mortality in patients with Listeria meningitis (12).

Two of the patients reported on in this study were healthy and immunocompetent men who were not involved in farming or animal husbandry. We consider as 'immunosuppressed' every patient with impaired immunity or an impaired immune response due to congenital or acquired disease or those patients who took drugs that can induce an impaired immune status (e.g. chemotherapy, chronic corticosteroid administration). The third patient was immunosuppressed due to chronic corticosteroid treatment but reported no contact with animals or unknown foods prior to infection. The fourth patient had a history of hematologic disease; the fifth patient was affected by CKD due to diabetes, which could be considered an immunosuppressive disease, and reported multiple respiratory infections previously. None of them had a clear exposure to foods classically associated with an increased risk of Listeria infection (1). None of them were HIV positive, as performing an HIV test is strongly suggested in the presence of Listeria meningeal infection (13,14), nor were they HCV or HBV positive (15-17). It is hypothesized that they were asymptomatic intestinal carriers since the incidence of fecal carriers is estimated to be 1-10% of the population (11,18). In addition, head CT scans of all patients described did not reveal signs of rhombencephalitis. Perhaps, MRI would have been a better method to address this issue, but it was not performed due to the patients' serious clinical conditions.

Concerning Listeria meningitis, lumbar puncture is essential for diagnosis since these patients are clinically indistinguishable from those with more common pathogens (9). However, according to various studies, the incidence of

meningeal signs in patients with *L. monocytogenes* is lower than in patients with other bacterial CNS infections (19). Signs and symptoms may include fever, headache, vomiting, diarrhea, and altered mental status, such as those reported in these reports (20). CSF analysis in most cases shows pleocytosis with neutrophilia, reduced glucose concentrations, and increased protein levels (21).

As stated for meningitis caused by other microorganisms, even in neurolisteriosis, an earlier diagnosis correlates with better outcomes and reduced neurological sequelae rates (9).

Typical CSF findings of bacterial meningitis are present in 77% of patients, and Gram staining of the CSF reveals Gram-positive rods in only one-third of cases (21). Therefore, culture or PCR of CSF is required to detect *L. monocytogenes* (sensitivity and specificity of 80%) (9). Multiplex PCR may reduce the appropriate treatment delay, improving results and leading to the initiation of proper antibiotic therapy (22). In our cases, RT-PCR provided a positive result quickly for Listeria and specific treatment was started immediately, whereas microbiological results were confirmed later with positive CSF cultures, as the latter represents the gold standard for assessing bacterial antibiotic susceptibility.

First-line empiric treatment of bacterial meningitis includes third-generation cephalosporins and vancomycin to target the most common pathogens (9). Unfortunately, despite their broad spectrum of action, third-generation cephalosporins generally have no activity against Listeria (23). The most effective treatment for CNS listeriosis has not been determined as there are no randomized controlled trials with an adequate number of patients. Furthermore, an optimal treatment duration has not been determined although a minimum of 21 days of therapy is recommended for Listeria meningitis (9,24). Benzylpenicillin and ampicillin are considered the core of any treatment regimen, either alone or in combination with aminoglycosides (such as gentamicin) due to their synergistic effect on bacterial killing (25).

Although there are no formal recommendations regarding aminoglycoside administration in these patients due to their adverse effects on renal function (9), to enhance ampicillin activity and to improve clinical outcomes, all the subjects we described were treated with gentamicin. The fifth patient received a short-term reduced dose of gentamicin due to his impaired kidney function.

Corticosteroid therapy correlates with decreased CSF inflammation, reversal of brain edema, and improved outcomes (26). Dexamethasone administration could reduce bacterial lysis, which enhances inflammation in the subarachnoid space, resulting in higher morbidity and mortality (26). Considering this, dexamethasone administration is recommended for all meningitis of unknown origin in adults due to its effect on edema, cerebral vasculitis, altered cerebral blood flow, intracranial hypertension, and neuronal damage (25).

Guidelines suggest the cessation of dexamethasone administration if pathogens other than *S. pneumoniae* are present in the culture (26-28) since some cohorts, although small and heterogeneous, showed that standard dexamethasone therapy had no benefits in terms of mortality and morbidity in meningitis caused by other pathogens, such as *Neisseria meningitidis* or *Listeria monocytogenes* (29).

Due to the rarity of L. monocytogenes meningitis, there is a significant lack of clinical trials and studies on dexamethasone administration, and most of the literature consists of case reports or retrospective studies (30). Therefore, it is difficult to make evidence-based recommendations regarding this condition, and the results of clinical studies are varied.

Currently, the prospective Multicentric Observational NAtional Study on LISteriosis and ListeriA (MONALISA) is the largest cohort of patients diagnosed with listeriosis, with 818 cases. However, only 252 cases were neurolisteriosis, and of these, only 32 received dexamethasone. The study showed a significant reduction in the survival of patients treated with dexamethasone within 24 h of admission. However, the treated population was small and this result is not from a clinical trial (31).

An epidemiological study of two Dutch cohorts of patients with neurolisteriosis described no association between dexamethasone administration and poor outcomes. However, the rate of dexamethasone administration was higher in the cohort with a worse outcome (26).

Endorsing the idea of the beneficial effects of corticosteroids, Pelegrín *et al* (32) analyzed 59 patients affected by neurolisteriosis, 29 of those received adjuvant dexamethasone administration. Although no significant differences in mortality or major side effects were recorded and those patients who received dexamethasone were more likely to present with fever at admission than those who had did not, along with a higher number of cells in the CSF, there was a trend toward fewer neurological sequelae in the dexamethasone group. Similarly, Amaya-Villar *et al* (33) described 43 patients with neurolisteriosis, 21 of them received dexamethasone administration; a higher survival rate was observed in patients treated with adjunctive dexamethasone, although it was not statistically significant (Table I).

Overall, Chau *et al* (34), Barocci *et al* (35), and Romero Gutiérrez *et al* (36) reported four cases of Listeria meningitis. Of these, 3 of the 4 patients described were female. The male patient had no risk factors for Listeria infection. In all cases, ampicillin was the antibiotic of choice, with or without other drugs. Out of 4 patients, 3 of them made a complete recovery. One patient died on the 6th day after admission, on the same day the CSF culture came back positive for *Listeria monocytogenes*. In this case, ampicillin was not included in the empiric antibiotic therapy, probably due to the absence of risk factors for neurolisteriosis. Dexamethasone administration was initiated from clinical presentation; however, in 2 cases the dosage is unknown (35,36).

Despite current suggestions to stop corticosteroid administration when *Listeria monocytogenes* is detected in CSF (28), dexamethasone is still commonly prescribed for Listeria CNS infections. In our professional experience, as shown in this case series, 4 out of 5 patients treated with a concomitant low dose of dexamethasone made a full recovery without sequelae.

Although the subjects described had no signs of encephalitis nor did they have any systemic complications, and the number of reported cases is too small to make any statistical considerations regarding the effectiveness and safety of dexamethasone in these subjects, it does suggest that patients with neurolisteriosis, in particular those with encephalitis,

Table I. Summary of the clinical characteristic and therapeutic management of patients with neurolisteriosis in the previous literature and present study.

First author, year	Number of patients	Age, years	Sex (n)	Symptoms (n)	Risk factors (n)	Targeted antibiotic therapy (n)	DEX therapy (n)	Outcome (n)	(Refs.)
Chau *et al*, 2010	1	30	M	Fever, headache, emesis, neck stiffness	None	None	Yes	Death	(34)
	1	34	F	Fever, headache, emesis, neck stiffness	Raw milk and soft cheese consumption	AMP 12 gr/die for 11 days	Yes	Complete recovery	(34)
Barocci *et al*, 2015	1	59	F	Fever, headache, altered mental status, altered consciousness, neck stiffness	HT, allo-SCT complicated by cGvHD, soft cheese consumption	AMP 12 g daily and RF 600 mg daily for 14 days, then AMC 1 g every 8 h + RF 600 mg daily for 14 days	Yes	Recovery	(35)
Romero Gutiérrez *et al*, 2012	1	55	F	Fever, headache, sleepiness, reduced mental aptitude, delayed response to stimuli, neck stiffness, left hemiparesis	AA	CTX, AMP, VAN, ACV (for concomitant HSV) encephalitis	Yes	Recovery	(36)
Charlier *et al*, 2017 (MONNALISA cohort)	252	Median age 67	M (152), F (100)	Encephalitis-associated symptoms (218), meningeal involvement without encephalitis (34)	Alcohol abuse (32), cirrhosis (20), DM (55), ESRD (4), SOC (49), HM (34), SOT (5), asplenia (3), neutropenia (8), lympho penia (27), HIV (4), IBD (12), rheumatic disorders (20), other auto-immune diseases (11), age >70 years old (117); corticosteroids (48), anti-TNF biotherapy (6), immunosuppressive therapy (71)	AMX (244), IPM (10), GEN (200), TMP-SMX (42), RF (3), VAN (24), LZD (4), AMX+GEN (192), AMX+TMP-SMX (37), No treatment (1). Mean antibi otic duration 22 days.	Yes (32)	17 of 32 patients receiving dexamethasone survived, 157 of 216 of those who did not receive dexamethasone survived	(31)
Koopmans *et al*, 2013	30	Median age 65	M (15), F (15)	Headache (22), neck stiffness (22), fever (27), altered mental status (21), coma (3), focal neurologic deficits (13), aphasia (7), hemiparesis (2), cranial nerve palsies (2)	Immunocompromised (20)	AMX or penicillin monotherapy (10), third generation cephalosporin monotherapy (5), AMX or penicillin + third-generation cephalosporin (11), other (4)	Yes (5)	Death (5), sequalae (4)	(26)
	62	Median age 69	M (39), F (23)	Headache (44), neck stiffness (39), fever (52), altered mental status (38), coma (8), focal neurologic deficits (21), aphasia (12), hemiparesis (2), cranial nerve palsies (5)	Immunocompromised (42)	AMX or penicillin monotherapy (11), third-generation cephalosporin monotherapy (12), AMX or penicillin + third-generation cephalosporin (36), other (3).	Yes (44)	Death (22), sequelae (12),	(26)

Table I. Continued.

First author, year	Number of patients	Age, years	Sex (n)	Symptoms (n)	Risk factors (n)	Targeted antibiotic therapy (n)	DEX therapy (n)	Outcome (n)	(Refs.)
Pelegrìn *et al*, 2014	59	Median age 64	M (41), F (18)	Fever (54), meningeal signs (46), altered mental status (44), headache (42), hemiparesis (5), cranial nerve palsy (12), focal signs (15), seizures (7)	DM (14), Chronic corticosteroid therapy (14), cirrhosis (6), SOC (4), HM (3), Immunosuppression (5)	AMP (15), AMP + Aminoglycosides (39). Median duration of therapy 21 days.	Yes (30)	Death (14), sequelae (8)	(32)
Amaya-Villar *et al*, 2010	43	Median age 69	M (24), F (19)	Fever (39), headache (29), vomiting (20), neck stiffness (30), seizures (4), focal neurological deficit (14), cerebellum dysfunction (5)	Immunocompromised (29)	AMP + GEN (18)	Yes (21)	Death (12), sequelae (5)	(33)
Present study	5	69	M	Cough, fever, nausea, headache, decreased consciousness	None	AMP 3 gr x 4 i.v. and GEN 400 mg i.v. for 21 days	Yes	Complete recovery	
		39	M	Fever, headache, emesis, speech problems, dizziness, neck stiffness	None	AMP 3 gr x 4 i.v., GEN 4 mg/kg/day i.v. for 21 days	Yes	Complete recovery	
		49	M	Abdominal pain, nausea, fever, photophobia, neck stiffness	UC	AMP 3 gr x 4 i.v. and GEN 4 mg/kg/day i.v. for 21 days	Yes	Complete recovery	
		67	M	Headache, fever, disorientation, neck stiffness	B-cell lymphoma, hypoglobu linemia	AMP 3 gr x 4 i.v. and GEN 4 mg/kg/day i.v. for 21 days	Yes	Complete recovery	
		72	M	Fever, photophobia, confusion, neck stiffness	CKD, DM	AMP 3 gr x 4 i.v. and GEN 4 mg/kg/day i.v.	Yes	Death	

M, male; F, female; HT, hypertension; allo-SCT, allogenic stem cell transplant; cGvHD, chronic graft-versus-host disease; AA, aplastic anemia; CRD, chronic respiratory disease; CLD, chronic liver disease; DM, diabetes mellitus; ESRD, end stage renal disease; IBD, inflammatory bowel diseases; TMP-SMX, trimethoprim-Sulfamethoxazole; UC, Ulcerative colitis; DEX, dexamethasone; SOC, solid organ cancer; HM, hematologic malignancy; CKD, chronic kidney disease; WBC, white blood cell; NE, neutrophils; CRP, C-reactive protein; PCT, procalcitonin; CSF, cerebrospinal fluid; RBC, red blood cell; HSV-1, human herpes virus 1; AMP, ampicillin; RF, rifampicin; AMC, amoxicillin/clavulanate; CTX, ceftriaxone; VAN, vancomycin; ACV, Acyclovir; AMX, amoxicillin; IPM, imipenem; LZD, linezolid; GEN, gentamicin; i.v., intravenous.

may benefit from a low dose dexamethasone administration, especially considering the effects on inflammations and edema. Presumably, the successful outcomes described here are associated not only with corticosteroid administration but also with the patients' mild disease and the suitable antibiotic treatment.

In conclusion, despite the development of antimicrobial therapy, the mortality and mobility rates of neurolisteriosis remain high. Further studies on antibiotic treatment as well as adjunctive therapies are needed to improve a patient's morbidity and mortality. Dexamethasone has a central role as both an adjunctive empiric therapy for patients affected by meningitis of unknown origin and as a specific therapy for those with pneumococcal meningitis. Concerning listeria meningitis, dexamethasone administration should be carefully evaluated in larger cohort studies and randomized clinical trials to better assess its possible effectiveness and safety in these patients.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

VM, AM, MC, FC, AZ, BMC, GN, and BC contributed to the conception and design of the study. VM wrote the manuscript. AM, MC, and FC searched the literature. AZ and BMC provided clinical assistance to the patients and were responsible for the pharmacological treatments. GN and BC revised the manuscript. GN and BC confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The patients signed written informed consent. Within the consent, it was specified that data collected during the diagnostic and therapeutic process can be anonymously used for scientific purposes.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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