Adult listeriosis—a review of 18 cases

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Summary

Eighteen cases of adult listeriosis (nine with meningitis, one brain abscess and eight bacteraemia) were diagnosed in the Chaim Sheba Medical Center in the years 1964-1982. The infection seemed to be opportunistic in all. Eleven patients had malignant disease, two had cirrhosis of the liver, one had ulcerative colitis, one had bronchial asthma with chronic obstructive pulmonary disease, one had pemphigus, one had diabetes mellitus and one had a renal transplantation. Twelve patients (66%) received radiation therapy and/or cytotoxic and steroid medication.

Diabetes mellitus as an additional underlying disease was strikingly frequent and was found in eight out of 18 patients (44%), in one as the only underlying disease.

In the meningitis group cerebrospinal fluid (CSF) cultures were positive in five patients, and negative in four who had, however, positive blood cultures. The cells in the CSF were predominantly lymphocytes in five and polymorphs in four.

It may be concluded that diabetes mellitus is an important underlying disease in listeriosis. The results also reinforce the fact that lymphocytosis in the CSF does not exclude bacterial meningitis.

KEY WORDS: diabetes mellitus, meningitis, septicaemia.

Introduction

Adult listeriosis though considered a rare infection, has apparently increased in incidence in the last decade. This is probably due to greater awareness of the characteristics of the micro-organism by bacteriologists, and to increased risk of opportunistic infection due to improved therapy, resulting in prolonged survival of patients with special types of

malignancy, and to a greater number of renal transplant patients with their attendant immune suppression.

The purpose of this paper is to review the incidence and clinical spectrum of listeriosis in the Chaim Sheba Medical Center, and to compare them with previous publications (Nieman and Lorber, 1980).

Material and methods

Study material was obtained from the records of the Department of Microbiology 1964-1982. The clinical charts of all patients whose blood and/or cerebrospinal fluid (CSF) culture grew *Listeria monocytogenes* including post-mortem examinations were reviewed.

Listeriosis was classified in three groups: (1) meningitis, if *Listeria monocytogenes* was isolated from the cerebrospinal fluid (CSF), or if the organism was isolated from blood, and the CSF showed pleocytosis and biochemical changes; (2) brain abscess—the micro-organism was isolated from the abscess contents; (3) primary listeria bacteraemia when the blood culture was positive in the absence of listeria infection elsewhere.

Results

There were 18 cases of *Listeria monocytogenes* infection—nine with meningitis, one with brain abscess and eight with bacteraemia. The age, sex, underlying condition and its treatment, and outcome of the disease are shown in Table 1. Diabetes mellitus was present in six of the nine patients with meningitis and two of the eight bacteraemia patients. In one patient, diabetes mellitus was the only underlying condition.

In the meningeal cases, the clinical picture was of sudden onset in eight cases, and relatively gradual in the ninth. All were febrile but typical meningeal signs with neck rigidity were present in only three patients.

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TABLE 1. Eighteen patients with listeriosis—clinical picture and underlying diseases

Case number	Age	Sex	Underlying disease	Previous treatment			Diabetes	Meningeal signs	Outcome
				X-ray	Cytotoxic	Steroid			
			Meningitis (n = 9)						
1	64	F	Multiple myeloma	+	—	—	—	+	Died
2	76	M	Hodgkin's disease	+	—	+	—	—	"
3	54	F	Leukaemia	—	+	+	+	—	Recovered
4	60	F	Pemphigus	—	+	+	+	+	Died
5	70	M	Waldenstrom's macroglobulinaemia	—	+	+	+	—	"
6	83	F	Arteriosclerosis + diabetes	—	—	+	—	—	"
7	78	M	Chronic lymphatic leukaemia	—	+	+	—	—	"
8	76	F	Chronic obstructive pulmonary disease and bronchial asthma	—	—	+	+	—	"
9	38	M	Renal transplant	—	+	+	+	+	Recovered
			Brain abscess (n = 1)						
10	53	M	Cirrhosis of liver	—	—	—	—	—	Recovered
			Bacteraemia (n = 8)						
11	76	F	Carcinoma of gallbladder	—	—	—	—	—	Died
12	70	F	Carcinoma of caecum	—	—	—	+	—	"
13	70	M	Lymphosarcoma	+	+	+	—	—	Recovered
14	65	M	Lymphoblastic leukaemia	—	+	+	—	—	Died
15	56	F	Carcinoma of colon	—	—	—	—	—	"
16	45	F	Ulcerative colitis	—	+	+	—	—	"
17	70	F	Cirrhosis of liver	—	—	—	+	—	"
18	78	M	Chronic lymphatic leukaemia, asthma	—	+	+	—	—	"

The six others had disturbances in consciousness ranging from drowsiness to confusion and coma. None of them had seizures. In two patients, hemiparesis was found without signs of brain abscess.

Seven of the nine patients had positive blood culture. CSF culture was positive in five out of nine cases. In the other four, it was negative but there was a large number of cells and an elevated protein level in addition to positive blood cultures. The cell count ranged from 125–510/mm³. In only four patients were the cells predominantly polymorphs, the other five had a lymphocytosis. The protein level ranged from 0.55–4.00 g/l, the sugar was reduced but was not always compared with blood sugar value. Various antibiotics were given—chloramphenicol, ampicillin, penicillin and aminoglycosides. Only two of the nine patients recovered, one was treated with ampicillin and chloramphenicol and the other with ampicillin only.

Eight patients with bacteraemia had no local documented listerial infection. Non-specific symptoms, such as fatigue, malaise, abdominal pain, nausea and sometimes diarrhoea, were present in almost all. Some of these symptoms were probably due to the underlying disease. Seven of the eight patients (88%) died although they were under what seemed to be appropriate antibiotic therapy. The patient who recovered had lymphosarcoma as underlying disease and was treated with ampicillin.

Discussion

Listeria monocytogenes was first implicated as a cause of human disease by Nyfeldt in 1929. Clinically,

the disease was described as an infectious mononucleosis-like syndrome, hence the name '*Listeria monocytogenes*'. Since then the demographic characteristics of the disease and even its clinical features have changed (Armstrong, 1979). Adult listeriosis has become mainly an opportunistic infection affecting people suffering from malignancy, those receiving immunosuppressive drugs, and renal transplant recipients. We think that diabetes mellitus should be added to this list.

Nieman and Lorber (1980) reviewed 186 published cases of adult listeriosis (including eight of their own) and emphasized the changing pattern in the clinical manifestations of the disease, an infectious mononucleosis-like syndrome now being rarely, if ever, seen. They found that meningitis was the most common manifestation (55% of cases). The special predilection of this opportunistic pathogen for the central nervous system has been noted since the earliest reports (Burn, 1935). Almost 75% of all cases of listeriosis reported to the Center for Disease Control in Atlanta, Georgia, in 1971 were cases of meningitis (Moon and Zehmer, 1973). In our series, meningitis was present in 50% of the cases.

An underlying condition was present in all our cases. The association of listeria meningitis and malignancy was first emphasized by Louria *et al.* (1967). In a review of meningitis in cancer patients (Chernik, Armstrong and Posner, 1973), listeria was the most common cause of bacterial meningitis, accounting for 22%. In Nieman and Lorber's (1980) review of 102 cases of listeria meningitis, 25 patients

had malignancy (19 non-solid tumours). Five out of our nine cases had non-solid malignancies. Pemphigus, not mentioned in the review, was the underlying disease in one of our patients. Diabetes mellitus was found in six (66%) out of nine patients with meningitis, in one as the only underlying disease, while it was found in only three of 102 cases in Nieman and Lorber's review, in two of them as the only associated disease.

The clinical manifestations of listeria meningitis in the cases reported here are similar to those mentioned elsewhere (Nieman and Lorber, 1980). Six patients had no clinical signs of meningitis, but had disturbances in consciousness, ranging from fluctuating mental state to coma as the main feature in addition to fever.

The CSF findings in listeria meningitis are reported as variable, a preponderance of polymorphonuclear leucocytes in the CSF being found in almost three-quarters of the cases, the protein level usually being moderately elevated and sugar reduced. We found lymphocytosis in the CSF in five out of our nine cases. This is a very important point as it indicates that in more than half of the cases with listeria meningitis, the cellular finding in the fluid simulated viral meningitis. We want to emphasize that lymphocytic polycytosis in the CSF in malignant or immunosuppressed patients does not exclude bacterial meningitis, and antibiotic therapy should be given in these cases until the results of CSF and blood cultures are available. The CSF sugar level in our patients was usually reduced but not contributory as it was not always correlated with blood sugar.

Unilateral neurological signs were found in three of 10 cases with central nervous system (CNS) involvement. In one patient only, a cerebral abscess was found, proved by angiography and treated successfully with surgery and antibiotics (Halkin, Shacked and Altmann, 1971). In the other two there were no signs of abscess and diffuse cerebritis or cerebral angiitis may have been present.

Listeria bacteraemia in the absence of documented listerial infection at any other site occurred in one-quarter of patients in Nieman and Lorber's review (1980). In this series it was present in eight out of 18 patients (44%). Six of the eight patients had underlying malignancy (three solid and three non-solid tumours) while in Nieman and Lorber's review 15 out of 46 patients had malignant disease (14 of them with non-solid tumours). Of the remaining two patients, one had cirrhosis of the liver and one ulcerative colitis. In Nieman and Lorber's review, three out of 46 had cirrhosis and none had ulcerative colitis. Diabetes mellitus was again relatively frequent and found in two out of eight cases, while none of the 46 cases in Nieman and Lorber's review had diabetes.

Another interesting point is that in five out of the eight bacteraemic patients, the underlying condition was a gastrointestinal disease (three solid tumours, one ulcerative colitis and one cirrhosis). The source and route of listeriosis are not well known. Healthy faecal excretors of *Listeria monocytogenes* have been investigated in various populations and were found to range from a minimum of 1–62% of office workers and 77% of a group of laboratory workers (Kampelmacher and Jansen, 1980). The high incidence of underlying intestinal disease in our series may suggest that the portal of entry of the organism is the diseased gastrointestinal tract.

The clinical picture of the bacteraemia patients was similar to those reported elsewhere (Nieman and Lorber, 1980), except that four out of eight patients developed septic shock simulating 'gram-negative sepsis', leading to death within 24–48 hr. Of the eight patients, only one, in whom lymphosarcoma was the underlying disease, recovered.

Prognosis of adult listeriosis in general is poor. Only three of 18 patients (17%) recovered. Prognosis apparently depends not only on listeriosis itself but on the type and stage of the underlying disease. The efficacy of the various antimicrobial regimens used could not be well evaluated. The three patients who recovered were treated, one with ampicillin and chloramphenicol and the two others with ampicillin only.

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