MENINGITIS DUE TO *LISTERIA MONOCYTOGENES*

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SUMMARY

To our knowledge, meningitis due to ***Listeria monocytogenes*** *has not previously been reported in Malaysia. We describe here two infants with meningitis due to* ***Listeria monocytogenes*** *occurring within a month of each other in the Universiti Kebangsaan Malaysia Paediatric Unit. The incidence of listeriosis in Malaysia is unknown and it is possible that this infection may have been missed in the past.*

INTRODUCTION

Listeria monocytogenes is a Gram-positive rod-shaped bacterium which is found in a variety of habitats. It has been isolated from humans and animals as well as from environmental sources like sewage and soil. Seeliger and Welshimer [1] reported that *Listeria monocytogenes* has been isolated from no fewer than 50 species of warm and cold blooded animals including rabbits, gerbils, ferrets and chinchillas. Despite its ubiquitous existence human listeriosis is an uncommonly reported infection. Less than 200 cases of human listeriosis are reported in the United States each year. [2] It is likely that many cases either go unrecognised or unreported. Human listeriosis usually occurs sporadically and may present in a variety of clinical forms. Meningo-encephalitis, genital infection and septicaemia are the most common presentations. Conjunctivitis (oculoglandular form), pharyngitis (pharyngoglandular), pneumonia, a typhoid-like syndrome and a cutaneous form also occur. Transplacental transmission gives rise to a particularly severe form of disseminated listeriosis in neonates which is called granulomatis infant septica. Listeriosis occurs predominantly in three groups of patients : (a) neonates who present usually with meningitis and septicaemia (b) pregnant women who experience a non-specific pyrexial 'flu-like' illness usually in the third trimester and (c) the immuno-compromised who present usually with meningitis and septicaemia. We wish to report here two cases of *Listeria monocytogenes* meningitis which occurred recently in the Universiti Kebangsaan Malaysia Paediatric Unit.

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CASE REPORTS

Case 1

A 10 day old Indian baby girl was admitted to the General Hospital Kuala Lumpur on the 13.12.1981 with a history of high fever for the past 24 hours. She was otherwise said to be active and was feeding well on Dumex baby formula. She was delivered in the Maternity Hospital, Kuala Lumpur by Caesarian section because of postmaturity and failed induction. There was no maternal pyrexia during labour. The baby weighed 4 lb and its condition at birth was satisfactory.

Examination on admission revealed an active, dysmature looking baby with a tinge of jaundice. Vital signs were: heart rate-148/min, respiratory rate-44/min, temperature-101°F. She was not unduly irritable. The rest of the examination findings were remarkable.

Investigations revealed: Hb-17.3 gm%, TWBC-11, 400/mm^3 (polys 62%, lymphs 38%), platelets-195,000/mm^3. A lumbar puncture was performed. The CSF was not purulent. CSF biochemistry revealed : glucose-0.4 mmol/L (plasma glucose-3.9 mmol/L), protein-1.6 gm/L, globulin positive, chloride-109 mmol/L. There was 224 white

cells/mm^3 (polys 70%, lymphs 30%). No organisms were seen on the Gram-stained direct smear.

The baby was initially started on benzyl penicillin 200,000 units 12 hourly i/v and gentamicin 8 mg 12 hourly i/m. Following the biochemistry of the CSF, chloramphenicol 22 mg 6 hourly i/v was added to the regime. On the following day scanty growth of *Listeria monocytogenes* from the CSF culture was reported which was sensitive to both penicillin and ampicillin. Ampicillin 200 mg 6 hourly i/v was started and all other antibiotics discontinued. The fever subsided on the third day of admission. Cultures of blood, throat, urine, umbilicus and rectum were negative. Repeat lumbar puncture was performed on 16.12.1981. The CSF had a white cell count of 20 cells (lymphs 100%) and the culture was negative. The baby remained well and afebrile. Ampicillin was discontinued after 2 weeks and the baby discharged.

Case 2

A 1½ month old Chinese baby girl was admitted to the General Hospital Kuala Lumpur on 3.1.1982 with a history of low grade fever for 1 day. She was also vomiting all her feeds. She was given some Chinese traditional medication but continued to be unwell and two hours prior to admission started to have several episodes of generalised convulsions each lasting for about 5 minutes. These attacks were associated with frothing and uprolling of the eyeballs.

Physical examination on admission revealed a fairly active baby. The vital signs were : temperature-37°C, heart rate-160/min, respiratory rate-40/min. The rest of the examination did not reveal anything remarkable.

Investigations revealed the following : Hb-9 gm%, TWBC-20, 200/mm^3 (polys 82%, lymphs 18%), platelets-350,000/mm^3, urea-4 mmol/L, sodium-129 mmol/L, potassium-4.3 mmol/L, chloride-94 mmol/L, sugar-6.1 mmol/L (random), calcium-2.14 mmol/L. A lumbar puncture was performed and revealed a non-purulent CSF. The CSF biochemistry was as follows: glucose-1.3 mmol/L, protein-1.7 mmol/L, globulin positive, chloride-107 mmol/L. The CSF contained 228 white cells/mm^3 (polys 13%, lymphs 87%). No organisms were seen on the Gram-stained direct smear.

The baby was started on benzyl penicillin 150,000 units 6 hourly i/v, chloramphenicol 50 mg 6 hourly i/v, gentamicin 12 mg 12 hourly i/m and phenobarbitone 10 mg 12 hourly i/m. On the 6.1.1982 *Listeria monocytogenes* was reported from the CSF culture and was resistant to penicillin and sensitive to ampicillin. Ampicillin 400 mg 6 hourly i/v was started and all other antibiotics discontinued. Blood culture was negative.

The patient stopped having any more convulsions in the ward and the temperature returned to normal by the 11.1.1982. Ampicillin was discontinued on the 15.1.1982 and the patient discharged.

Bacteriology

Listeria monocytogenes was isolated from the CSFs of both patients. *Listeria monocytogenes* was identified on the following criteria : Gram-positive rods which showed the characteristic "tumbling motility" at room temperature. The colonies on blood agar showed beta-haemolysis and on clear agar exhibited a blue-green irridescence when viewed using oblique transmitted light (the Henry effect). Biochemically the bacteria was catalase +, oxidase -, fermentative on O/F test, methyl red +, ferments glucose and trehalose, hydrolyses aesculin and H_2S -. No serotyping was performed on either isolate.

DISCUSSION

Both the patients had evidence of sepsis but no signs that would aid in the recognition of the specific pathogen. Both the CSFs were non-purulent but contained a low glucose, increased protein and increased white cells (both lymphocytes and polymorphs) which is compatible with that of pyogenic meningitis. Gram staining of the CSF deposits did not reveal any organisms and the diagnosis in both cases was established only by culture. Both patients responded satisfactorily to ampicillin. It is possible that meningitis due to *Listeria monocytogenes* may not have been previously recognised in Malaysia.

The largest series of meningitis caused by *Listeria monocytogenes* was documented by Lavetter et al in California. [3] In this review of 25 cases it was noted that signs and symptoms were those that were commonly seen in bacterial central nervous system infections. In up to 70 percent of cases no organisms were seen on the initial CSF deposit. In

the remainder they were reported to have shown a variety of bacterial morphologies including Gram positive cocci and diplococci, Gram positive coccobacilli and Gram positive rods. The mortality rate in this series was as high as 32 percent. All the survivors had no residual deficits at time of discharge except for a three week old infant who had hydrocephalus and a convulsive disorder.

Two distinct clinical syndromes are seen in neonates with listeriosis. [4] They are (a) an early onset, predominantly septicaemic form, characterised by prematurity, a history of obstetrical complications (maternal pyrexia, a 'flu-like' syndrome, pyelitis), a higher frequency of maternal isolates of the causative organism and an increased neonatal mortality rate; (b) a late onset, predominantly meningitic form, characterised by normal birth weight, lower mortality rate and the absence of obstetrical complications. Case 1 would appear to fit into the latter.

The epidemiology remains obscure. Most cases are sporadic although epidemics have been reported. [5] The epidemics are however widespread in animals which may serve as a source of infection in some cases. The late meningitic form may be acquired from congenitally infected babies via their attendants in a newborn nursery. [6]

Listeria monocytogenes tends to be susceptible to a wide range of antibiotics, generally at relatively low concentrations. They include penicillin, ampicillin, gentamicin, kanamycin and chloramphenicol. Penicillin resistant strains are not uncommon (as in Case 2). The treatment of choice however is ampicillin 200 mg/kg/day i/v in 4 divided doses. [3]

Listeria monocytogenes is characteristically a Gram-positive rod. However in clinical specimens it may sometimes appear coccoid and occur in pairs. It may also show variable Gram staining. As a result *Listeria monocytogenes* is easily confused with other pathogens as well as non-pathogens like pneumococci, streptococci, haemophilus and corynebacteria. Moreover primary isolation is often difficult but once isolated it grows quite well on sub-culture. [7] To improve the chances of isolation a "cold enrichment" technique has been recommended. [8] This involves the exposure of the clinical specimen to cold temperature (4°C) for several days to a few weeks, taking cultures at frequent intervals. Because of this difficulty in isolation and mistakes in identification, human listeriosis is often misdiagnosed or unrecognised. It is therefore important that laboratory personnel scrutinise all isolates, especially those designated as "diphtheroids", to ensure that *Listeria monocytogenes* is not missed. This is probably the single most important factor in ensuring the recovery of the bacterium from clinical specimens. [9]

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