MANAGEMENT OF FLAVOBACTERIUM MENINGITIS IN THE NEONATES: EXPERIENCE WITH 18 CONSECUTIVE CASES

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ABSTRACT

18 neonates with bacteriologically confirmed Flavobacterium meningitis and ventriculitis were treated with various antibiotic regimens, including the use of intraventricular antibiotics. During the course of treatment, four patients died. 8/14 patients developed progressive hydrocephalus which required insertion of ventriculo-peritoneal shunts. The remainder 6/14 patients had normal ventricles or only mild ventriculomegaly. 5/8 patients with progressive hydrocephalus and 5/6 patients with normal or mildly dilated ventricles were followed up for at least 24 months. 4/5 of the patients with progressive hydrocephalus had severe bilateral hearing loss and delayed milestones. All the 5 patients with normal or mildly dilated ventricles had normal hearing although 2 of them had gross motor delay due to spastic paraplegia.

Patients with progressive hydrocephalus received effective antibiotic treatment more than 8 days after the onset of infection while those with normal or mildly dilated ventricles within 8 days of infection. Onset of ventricular dilatation was associated with ventriculitis. Daily ultrasound scanning of the ventricles in the early stage helped to determine the need for early instillation of intraventricular antibiotics. Combined use of intravenous rifampicin, moxalactam and piperacillin showed promise as an effective antibiotic regimen in treating patients with normal or mildly dilated ventricles. Once significant ventriculomegaly has occurred, concomitant intravenous and intraventricular administration of antibiotics, to which the organisms were sensitive, was necessary to eradicate the infection.

Keywords: Flavobacterium meningitis, neonates, management.

SING MED J. 1989; No 30: 177 — 183

INTRODUCTION

Flavobacterium meningosepticum is a gram negative rod which produces a yellow-green pigment from which the name Flavobacterium is derived (1). It is a common organism in soil and water.

Although it is usually an innocuous organism, it can cause meningitis and ventriculitis in the neonates (1, 2, 3, 4, 5, 6, 7, 8, 9). Outbreaks of neonatal meningitis due to this organism were reported as early as 1958 by Brody et al (10). 6 serological types of Flavobacterium meningosepticum, types A to F, have been identified. Type C is the most common organism which causes neonatal meningitis (1, 9, 11).

Three unique characteristics of this organism are: i) its multiresistence to antibiotics, ii) its unusual antibiotic sensitivity (4, 5, 6, 8, 9, 11, 12, 13) and iii) its tendency to cause ventriculitis (6). More than 50 percent of the reported cases died (9). In those who survived, hydrocephalus was a common sequela (9).

Various antibiotics had been used singly or in combination by various authors in the last 25 years to treat Flavobacterium meningitis. These antibiotics include: penicillin, ampicillin, sulfonamide, cotrimoxazole, sulfadiazin, chloramphenicol, neomycin, kanamycin, gentamicin, amikicin, vancomycin, carbenicillin, polymycin B, erythromycin, azlocillin and rifamycin (3, 4, 6, 7, 8, 9, 11, 13, 14, 15, 16). The only antibiotic regimen which produced a favourable response repeatedly when given to different patients was that reported by Lee et al (4). In his regimen rifampicin was given both intravenously and intraventricularly simultaneously to patients. All of Lee's patients had hydrocephalus and required shunts.

Over a period of 21 months, between June 1983 and February 1985, 18 cases of Flavobacterium meningitis were admitted to the University Unit in the Kuala Lumpur General Hospital.

The following is a report of our experience in the management of these cases.

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METHODOLOGY

Baseline investigations

Before specific antibiotics against Flavobacterium infection were commenced, all the patients were subjected to the following investigations: full blood picture, blood culture, urine culture, throat swab culture, chest X ray and cerebral spinal fluid for cytological examination, biochemical analysis and culture. Specimens of blood were also taken for assessment of liver function, renal profile and prothrombin time. Cerebral spinal fluid (CSF) were obtained by ventricular tap from patients with enlarged head due to ventriculomegaly.

Ultrasound Examination

All scans were done through the anterior fontanelle with the use of a Phillips SDR 1500 sector scanner via a 3 MHz scan head. All the patients were scanned as soon as possible after admission, preferably within 48 hours after admission. Due to logistic reasons, however, some of our patients were scanned later than planned. Subsequently weekly scans were performed whenever it was possible until discharge.

Ventricular dilatation was diagnosed if the distance from the roof to the floor of the lateral ventricle exceeded 6 mm (17). Hydrocephalus was considered present when ventricular dilatation was associated with tense and/or bulging anterior fontanelle with or without clinically big head in the early stages of obstruction.

Computer axial tomography of the brain (C.A.T. Scan) was arranged whenever ultrasound scanning suggested loculation of fluid or abscess in the brain or ventricles.

CSF reservoir

When ventriculitis was diagnosed, patients were referred to the neurosurgeon for insertion of a Standard Ommaya CSF reservoir (Heyer Schutz, USA) to facilitate ventricular taps. However, owing to shortage of reservoirs, this was carried out in only 3 of the patients.

Choice of Antibiotics

Only parenteral antibiotics were used when the ventricular system was not dilated. Usually two to three antibiotics were used in combination via the intravenous route. The choice of antibiotics was influenced not only by the sensitivity and MIC results, but also, to a large extent, by the availability of the antibiotics in the hospital at the time of treatment. Thus, although Rifampicin was one of the drugs of choice, it was not used in all the patients because at times the supply was interrupted.

When parenteral antibiotics failed to sterilise the CSF after 72 hours of treatment, and the ventricular system was not dilated, other antibiotics to which the organism was sensitive were used instead. However, if the organism was only sensitive to Rifampicin and Erythromycin, then intrathecal injection of Rifampicin was administered in addition to parenteral antibiotics.

Intraventricular antibiotics were used concomitantly with parenteral antibiotics when the ventricles were dilated.

The dosages of the various antibiotics used intravenously are as follows: Rifampicin 30 mg/kg/day in two divided doses, Erythromycin lactobionate 100 mg/kg/day in three divided doses, piperacillin sodium 600mg/kg/day in six divided doses, moxalactam disodium 150mg/kg/day in three divided doses, vancomycin 50mg/kg/day in three divided doses, chloramphenicol 50mg/kg/day in four divided doses and cefotaxime 200mg/kg/day in four divided doses.

The dosage of intrathecal or intraventricular antibiotics was one-tenth of the parenteral antibiotic dose.

The duration of parenteral antibiotics given was between four and six weeks. Treatment was considered adequate when all the following criteria were met : a) at least three consecutive weeks of sterile CSF culture, b) absence of fever, c) tolerance of oral feed in the absence of raised intracranial pressure, d) progressive weight gain, e) general well-being of the child, f) serial improvement of CSF cytology with white cell count below 10/ml (in the absence of traumatic tap) at the end of the period of treatment and a concomitant rise in CSF sugar.

The duration of daily intraventricular injection of antibiotics was at least 10 days. The criteria to stop intraventricular injection were: a) persistently sterile CSF culture for at least ten consecutive days, b) CSF cell count less then 10/ml with a majority of lymphocytes, c) serial increase in CSF sugar, and d) general well-being of patient with absence of fever.

Bacteriology

Flavobacterium meningosepticum was identified on the following basis. It was a Gram negative short, plump rod which was non-motile, oxidase positive and catalase positive. There was either poor or no growth on MacConkey agar. On nutrient agar at room temperature after 48-72 hours, it formed bright yellow pigmented colonies. Biochemically, it was indole-positive after 48 hours incubation and gelatin positive. The O/F (glucose) test was oxidative. The Voges-Prausker reaction, methyl red test and citrate utilisation tests were all negative. The urease was negative. The triple sugar iron reaction showed an alkaline butt and slant with no gas or hydrogen sulphide formation. Identification was often aided by its characteristic antibiotics susceptibility pattern — it being sensitive to rifampicin, erythromycin, and vancomycin and resistant to almost all aminoglycosides and beta-lactam antibiotics. In addition, Flavobacterium menigosepticum type C was identified using an agglutination test with specific antiserum.

Disc diffusion tests and minimal inhibition concentration (MIC) were both used in determining the bacteria sensitivity in our patients.

Monitoring

Blood cultures were repeated every 48 to 72 hrs until negative. Whenever fever or other symptoms suggestive of infection recurred, blood cultures were repeated.

CSF analysis was done every 24 to 48 hours. When intrathecal or intraventricular antibiotics were given, CSF was collected daily. After completion of treatment, CSF analysis was repeated biweekly for another week. In patients who had raised intracranial pressure and awaited shunting of the ventricles, daily tap to release pressure and CSF analysis was done.

At weekly interval, specimens of blood were collected for full blood picture, liver function test, renal profile and prothrombin time.

Insertion of ventriculo-peritoneal shunt

Patients with progressive hydrocephalus were referred to the neurosurgeon for insertion of ventriculo-peritoneal shunt when antibiotics treatment was completed.

Long term follow-up

Patients were followed-up at three monthly interval. During each visit, the following areas were evaluated: 1) weight gain, 2) head growth, 3) developmental milestone by using the DENVER developmental screening test (18), 4) general well-being, 5) presence of squint.

Hearing ability was assessed initially by behavior response to whispered words and soft rattle at ear level at the age of seven months. Whenever deafness was suspected, patients were referred to the otolaryngologists for testing of brainstem auditory evoked potential under sedation.

RESULTS

7/18 of the patients were born in Kuala Lumpur while 11/18 were from four other states in Malaysia. All the patients were delivered in hospitals except one who was born at home.

10/18 patients were referred with the diagnosis of Flavobacterium meningitis, having had the organisms isolated in the referring hospitals. The rest of the 8/18 patients were referred for the following reasons: two for pseudomonas meningitis, one for queried septicemia, one for recurrent cynotic spells, one for sacrocoxygeal teratoma associated with fever, one for failure to thrive and two for insertion of ventriculo-peritoneal shunts because of gross hydrocephalus. All of them had the organism isolated from the CSF after admission.

Tables 1 and 2 show the basic data and clinical features of the patients, respectively. None of the patients had history of maternal pyrexia during pregnancy or labour. Only 3/18 of the patients had history of prolonged rupture of membranes.

Various antibiotics were given to the patients in the referring hospitals (Table 3). Case 4, who had the organism isolated from her CSF in the referring hospital, was the only case given Rifampicin intraventricularly for four days before her transfer to our hospital. All the patients, except case No. 4, continued to have positive CSF culture and 10/18 of them had positive blood culture after their arrival in our hospital (Table 3). No organisms were isolated from the CSF and blood of case 4 while she was alive in our hospital. She was treated with a course of intraventricular and intravenous Cefotaxime and Erythromycin in our hospital. She had insertion of ventriculoperitoneal shunt which was infected two weeks after operation. She died and her ventricular CSF grew Staphylococcus aureas but her intracardiac blood grew Flavobacterium meningosepticum Type C.

16/18 of the patients had Type C Flavobacterium meningosepticum isolated from them (Table 3). None of the patients had the organisms cultured from their throat swabs.

Low CSF sugar, high protein, positive globulin and high white count with predominence of polymorphs were present in the CSF of all the patients at the time of infection.

The organisms were resistant to most antibiotics including aminoglycosides, cephalosporins and penicillins (Tables 4 & 5). There was discrepancies between disc sensitivity results and MIC values of both Moxalactam and Piperacillin sodium. The MICs were high even though the disc tests indicated bacterial inhibition.

Based on the MIC and disc results, Rifampicin was the antibiotic to which the organisms were most sensitive, followed by Erythromycin, Vancomycin and Novobiocin.

Table 6 shows the response of patients to the different antibiotic regimens used. 13/18 of the patients were admitted with normal or mildly dilated ventricles. Among these thirteen patients, 3 died (2 from the infection and one from sacrococcygeal tumour) and 10 survived. 6 of

Table 1.
PATIENT CHARACTERISTICS

Sex: (no.)	
male	10
female	8
Race: (no.)	
Chinese	9
Malay	4
Indian	5
Modes of Delivery: (no.)	
Spontaneous vaginal delivery	11
Low forceps delivery	3
Vacuum extraction	1
LSCS	3
Gestational Age (weeks):	
mean	38.1
standard deviation	3.6
range	28-43
Birth Weight (grams):	
mean	2517
standard deviation	603
Age of onset of Symptoms (days):	
mean	5.4
standard deviation	3.1
range	1-11

Table 2.
CLINICAL FEATURES OF PATIENTS AT ONSET OF FLAVOBACTERIUM MENINGITIS

Clinical features	Number of patients
Fever	18
Absent or Incomplete Moro Reflex	18
Bulging anterior fontanelle	12
Irritability on handling	11
Convulsion	11
Jaundice	10
Hypertonia	9
Poor sucking reflex	9
Lethargy	7
Big Head	5
Recurrent apnea	3

Table 3.
RELATIONSHIP BETWEEN PATIENTS' PREVIOUS ANTIBIOTIC TREATMENT AND THE RESULTS OF THEIR CSF AND BLOOD CULTURES ON ADMISSION TO THE GENERAL HOSPITAL, KUALA LUMPUR.

	Antibiotics Given In Referring Hospital									Cultures of	
Case no.	Pen.	Amp.	Chlo.	Gent.	Ami.	Cef.	Cla.	Ery.	Rif.	CSF	Blood
1.	–	–	–	–	–	–	–	–	–	+ve	+ve
2.	–	–	–	–	–	–	–	–	–	+ve	+ve
3.	Y	Y	Y	–	–	–	–	Y	Y	+ve	–ve
4.	–	Y	–	Y	–	Y	–	Y	Y	–ve	–ve
5.	–	–	Y	–	–	Y	–	–	–	+ve	+ve
6.	Y	Y	Y	Y	–	–	Y	–	–	+ve	–ve
7.	Y	–	Y	–	–	Y	–	–	–	+ve	+ve
8.	Y	–	–	Y	–	–	–	–	–	+ve	–ve
9.	–	Y	–	Y	–	–	–	–	–	+ve	+ve
10.	Y	–	Y	–	–	–	Y	–	–	+ve	+ve
11.	–	–	–	–	–	–	–	–	–	+ve	+ve
12.	–	–	–	–	–	–	–	–	–	+ve	–ve
13.	–	–	Y	–	–	Y	–	–	–	+ve	–ve*
14.	Y	Y	Y	Y	–	–	Y	–	–	+ve	–ve*
15.	–	–	–	–	Y	Y	–	–	–	+ve	–ve
16.	Y	–	Y	Y	–	–	–	–	–	+ve	+ve
17.	Y	–	–	Y	–	–	–	–	–	+ve	+ve
18.	Y	–	Y	Y	–	–	Y	Y	–	+ve	+ve

Pen. = Penicillin, Amp. = Ampicillin, Chlo. = Chloramphenicol, Gent. = Gentamicin, Amik = Amikacin, Cef. = Cefuroxime, Cla = Cefotaxime, Ery. = Erythromycin, Rif. = Rifampicin. Y denates antibiotic given, – denotes antibiotic not given, +ve means positive culture of Flavobacterium Meningosepticum was isolated, –ve denotes culture was negative.
*: cases of non-Type C Flavobacterium Meningosepticum.

these 10 patients recovered with normal ventricles while the other 4 developed progressive hydrocephalus.

In patients who were admitted with moderate or gross hydrocephalus, concomitant intravenous and intraventricular administration of antibiotics to which the organism was sensitive was effective in eradicating the organism. In fact when intraventricular antibiotic was given early, as in case number 3, it prevented the development of progressive hydrocephalus.

In patients presented with normal or mildly dilated ventricles, the only effective parenteral antibiotic regimen was that consisting of Rifampicin, Moxalactam and Piperacillin.

All, except one, septicemic patients had their blood sterilised rapidly with all the antibiotic regimens.

Four patients, who developed ventricular dilatation associated with fever while being treated, had sterile CSF obtained from lumbar punctures when Flavobacterium was still cultured from their ventricular CSF.

All the patients, who were treated with Moxalactam for more than one week, developed prolonged prothrombin time from the second week of treatment. This was corrected with vitamin K injection and prevented from recurring with weekly vitamin K without requiring to withdraw the antibiotic.

Massive bleeding was observed in one patient with hydrocephalus during ventricular tap and required blood transfusion. Macroscopically blood stained CSF was observed in two other patients on two separate occasions though they remained well with normal ventricles. All three patients were on Moxalactam when this occurred.

Among the 18 patients, 14 completed the antibiotic treatment and 4 died during treatment. Of the 14 survivals, 6 recovered with normal ventricles while 8 had gross hydrocephalus. Seven of the hydrocephalic patients had ventriculo-peritoneal shunts inserted because of progressive hydrocephalus. The eighth patient did not have clinical evidence of increasing intracranial pressure and was not shunted. He was grossly delayed in milestones and lost to follow-up subsequently after 5 months of age.

Three of the seven patients who had ventriculo-peritoneal shunts inserted developed infected shunt within the first week post-operation. Two of them died, the organisms isolated were Staphylococcus epidermitis and Staphylococcus aureus respectively. The third patient had Klebsiella species isolated from the shunt and the lateral ventricles. He was treated, and had a second shunt inserted. His milestones were grossly delayed with bilateral hearing loss and visual impairment.

The remainder 4/7 patient had no complications during the immediate post-operative period. One of them, however, developed blocked shunt at the age of eight months and dislogement of the distal end of the shunt at one year of age, thus necessitating two revisions of shunt. A second patient needed one revision of blocked shunt at nine months of age.

On comparing the group of 6 patients with normal or mildly dilated ventricles with the group of 8 patients with progressive hydrocephalus, the following differences were found: i) the interval between onset of first symptoms and commencement of sensitive antibiotics was 8 days or less for the first group (range 3-8 days), and more than 8 days for the second group (range 9-53 days); ii) the interval between the onset of the first symptoms and the sterilisation of CSF was 16 days or less for the first group (range 8-16 days) and 17 days or more for the second group (range 17-65 days); and iii) during treatment, only 2/6 of the patients in first group needed intraventricular antibiotics while all the patients in the second group required this route of treatment.

At the time of writing this report, all the 10 patients on follow-up were 24 months or more. One patient did not have brainstem auditory evoked response potential tested since clinically she was found to hear very well and developed languages appropriate for her age at 2 years. Of the nine patients who were tested, four had normal hearing while four had bilateral hearing loss with no response to stimulation up to 105 db. The ninth patient had moderate hearing loss in the left ear, showing response to stimulation only at 70db and above. All those who had hearing problems were hydrocephalic patients who were shunted.

Serial Denver development screening tests showed that 4/5 of the patients with ventriculo-peritoneal shunts inserted for progressive hydrocephalus had abnormal results while the fifth patient had normal results. As for the five patients with normal or mildly dilated ventricles, three had normal milestones while two had abnormal results due to delay in gross motor skill secondary to spastic paraplegia.

Table 4.
ANTIBIOTIC SENSITIVITIES OF FLAVOBACTERIUM MENINGOSEPTICUM ISOLATED IN OUR HOSPITAL FROM THE PATIENTS

	Case No.																	
Antibiotics	**1.**	**2.**	**3.**	**4.**	**5.**	**6.**	**7.**	**8.**	**9.**	**10.**	**11.**	**12.**	**13.**	**14.**	**15.**	**16.**	**17.**	**18.**
Penicillin	–	–	R	–	R	–	R	–	–	–	–	–	–	–	–	–	–	–
Ampicillin	R	R	R	–	R	–	–	–	–	–	R	R	–	–	–	–	–	–
Piperacillin	–	–	R	–	S	–	S	S	S	S	S	–	R	–	–	R	S	R
Carbenicillin	–	R	R	–	R	–	R	–	–	R	R	–	–	–	–	–	–	–
Tetracyclin	–	–	–	–	R	–	R	–	–	R	R	–	–	–	–	–	–	–
Erythromycin	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
Chloramphenicol	S	R	S	–	S	R	R	R	R	R	R	–	–	–	–	–	–	R
Cotrimoxazole	R	S	S	–	R	–	R	–	–	S	R	–	–	–	–	–	–	–
Streptomycin	–	–	–	–	–	–	R	–	–	R	R	–	–	–	–	–	–	–
Nefticillin	–	–	–	–	S	–	–	–	–	R	–	–	–	–	–	–	–	–
Gentamicin	R	R	R	–	R	R	R	–	–	R	R	–	–	–	–	R	–	–
Kanamycin	R	R	R	–	R	R	R	–	–	R	R	–	–	–	–	–	–	–
Amikacin	–	R	S	–	S	R	S	–	–	R	R	–	–	S	S	R	–	–
Cepholorithin	–	R	R	–	R	R	R	–	–	R	–	–	–	–	–	–	–	R
Cefuroxime	–	–	–	–	R	–	R	–	–	–	R	–	–	–	–	–	–	–
Cefotaxime	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	R	R	R
Moxalactam	–	–	S	–	S	–	S	S	S	–	S	–	R	–	–	R	S	R
Novobiocin	–	–	S	–	S	–	S	–	S	S	S	–	–	–	–	–	–	–
Vancomycin	–	S	S	–	S	S	S	S	–	S	S	S	S	S	S	R	S	S
Rifampicin	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S

S denotes sensitive, R indicates resistant, – means test was not performed.

Table 5.
MIC OF ANTIBIOTICS TOWARDS FLAVOBACTERIUM MENINGOSEPTICUM

Case No.	MICs of Antibiotics in mg/L				
	Rifampicin	Erythromycin	Vancomycin	Moxalactam	Piperacillin
1.	0.5	4	–	128	–
2.	–	–	–	–	–
3.	–	–	–	–	–
4.	1.0	16	–	–	–
5.	1.0	8	–	–	–
6.	2.0	16	–	32	>128
7.	1.0	16	–	32	>128
8.	–	–	–	–	–
9.	0.5	64	–	>128	>128
10.	2.0	8	–	32	128
11.	1.0	8	–	128	>128
12.	–	–	–	–	–
13.	1.0	16	–	128	>128
14.	1.0	128	16	–	>128
15.	0.5	2	16	64	128
16.	1.0	8	16	64	128
17.	0.5	16	16	32	64
18.	2.0	8	8	>128	>128

Table 6.
RESPONSE OF PATIENTS TO DIFFERENT ANTIBIOTIC REGIMENS

Case No.	Presence of Ventriculomegaly when admitted	Antibiotic Regimens			Interval between onset of treatment and sterilisation of CSF (days)	Outcome
		Intravenous only	Intravenous and (intrathecal)	Intravenous and (intra-ventricular)		
1.	no	Rif, Ery, Chlo	–	Rif, Ery, (Rif, Ery)	8	alive, hydrocephalic, shunted.
2.	no	Rif, Ery,	Rif, Ery, (Rif)	–	7	alive, normal.
3.	yes	–	–	Rif, Ery,(Rif, Ery)	5	alive, normal
4.	yes	–	–	Rif, Ery, Claf, (Rif) (Ery, Claf)	2	died, hydrocephalic, infected shunt.
5.	no	Ery, Claf, Van	–	–	7	alive, spastic cerebral palsy.
6.	yes	–	–	Rif, Ery (Rif, Ery)	1	died, congestive cardiac failure.
7.	yes	Rif, Mox, Pip,	–	–	7	alive, normal, defaulted
8.	no	Rif, Ery,	Rif, Ery, (Rif)	Rif, Mox, Pip, (Rif, Mox)	8	alive, hydrocephalic, shunted.
9.	no	Rif, Mox, Pip	–	–	3	alive, normal.
10.	yes	Rif, Mox, Pip	–	Rif, Mox, Pip (Mox)	6	died, hydrocephalic, infected shunt.
11.	no	Rif, Mox, Pip	–	–	3	died, sacral coccygeal teratoma.
12.	yes	Rif, Mox, Pip	–	–	3	alive, spastic cerebral palsy.
13.	yes	Rif, Ery, Van	–	Rif, Ery, Van, (Ery)	8	alive, hydrocephalic, shunted.
14.	yes	–	–	Rif, Ery, Van, (Ery)	6	alive, hydrocephalic, infected shunt.
15.	yes	–	–	Rif, Ery, (Ery)	1	alive, hydrocephalic, defaulted,
16.	no	Rif, Ery, Van	Rif, Ery, Van, (Rif)	Rif, Ery, (Rif)	never	died from Flavobacterial ventriculitis.
17.	no	–	Rif, Ery, (Rif)	Rif, Ery, (Rif)	5	died from Flavobacterial septicemia.
18.	no	Rif, Ery, Pip	–	Rif, Ery, (Rif)	9	alive, hydrocephalic, shunted.

Note: Rif=Rifampicin, Ery=Erythromycin, Chlo=Chloramphenicol, Claf=Cefotaxime, Van=Vancomycin, Mox=Moxalactam, Pip=Piperacilin.

DISCUSSION

Flavobacterium meningitis in the neonates was a very difficult condition to treat for the following reasons: i) the organism had very unusual antibiotic sensitivities, ii) these antibiotics, viz, rifampicin, erythromycin, vancomycin and nocobiocin, when given parenterally, did not cross the blood brain barrier in high enough levels to kill the organisms in the CSF (13, 19), iii) intrathecal antibiotics were not effective in the majority of the patients in whom this route was used because of the early onset of obstructive hydrocephalus, and iv) ventriculitis was a common complication. In our series, these problems were further compounded by frequent shortage of supply of intravenous rifampicin which was the most effective antibiotic based on in-vitro sensitivity test.

Although our patients showed the same tendency to develop hydrocephalus as those reported in the literature, our series showed that early diagnosis and early commencement of effective antibiotic regimen, viz within 8 days of onset of symptoms, could prevent the development of progressive hydrocephalus.

We have found ultrasound scanning of the ventricles from the early stage of the infection extremely useful. We observed that ventricular dilatation was associated with ventriculitis in the early stages of the infection in our patients. Therefore, daily ultrasound of the ventricles in the early stage will help to decide the timing for early intraventricular instillation of antibiotics. The appearance of ventricular dilatation from normal sized ventricles, together with persistence of fever and irritability, usually indicated that infection was not under control and that ventriculitis was developing in the patient. We suspect that early treatment in two of our patients who had mild and moderate dilatation of the ventricles initially prevented them from developing progressive hydrocephalus subsequently.

Once hydrocephalus was present, the only effective mode of treatment was concomitant intraventricular rifampicin and parenteral rifampicin with one or two other antibiotics to which the organism was sensitive. The main disadvantages of intraventricular injection are: i) trauma to the brain tissue from repeated taps, and ii) intraventricular bleeding. Insertion of an Ommaya reservoir minimised brain tissue damage but there was always the potential danger of colonisation of the reservoir by bacteria and Candida albicans. We also found the reservoir to be costly. Early and late complications following ventriculo-peritoneal shunts, were common in our patients. All these prompted us to search for a parenteral antibiotic regimen which, when given early, would effectively prevent the onset of ventriculitis and subsequent hydrocephalus.

Initially we chose parenteral piperacillin and moxalactam to be used in combination with rifampicin because: i) they were the only 'sensitive' intravenous antibiotics available at that time, ii) they were thought to be sensitive based on the disc sensitivity tests, and iii) both drugs cross the blood brain barrier well. When we found that this regimen of antibiotics worked on the first two patients, we went on to use them on two other patients despite the fact that the serum MIC results were, by then, known. We used very high dosages of both drugs in combination with rifampicin. However, when either piperacillin or moxalactam was used with rifampicin and erythromycin lactobionate, the response was disappointing. One possible explanation was that piperacillin, moxalactam and rifampicin when used in combination, the concentration of the three drugs in the CSF was high enough to kill the organism either by their additive effect or by synergism.

There were worrying features, though, with this regimen. We could not explain the transient mild ventricular dilatation observed in one patient. A second patient had a sudden reappearance of fever associated with a rise in CSF cell count after three weeks of antibiotics although clinically she was gaining weight and neurologically well and the CSF culture was negative. More studies are, therefore, needed regarding the use of this regimen.

In conclusion, neonates with Flavobacterium meningitis, when treated successfully within the first week of illness, generally recover without developing progressive hydrocephalus. Ultrasound scanning of the brain for ventricular dilatations in the early stages of the infection is useful in detecting the onset of ventriculitis, which if treated aggressively with intraventricular instillation of effective antibiotics will prevent the development of progressive hydrocephalus.

The combined use of intravenous piperacillin, moxalactam and rifampicin given early to patients in adequate dosages shows promise against this infection although more studies are required to confirm this. Furthermore, in view of the good response of Flavobacterium ventriculitis to intraventricular rifampicin, should early insertion of reservoir for intraventricular rifampicin be considered in all cases, before the onset of ventriculomegaly? This has to be answered by further study.

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