Organisms causing spontaneous bacterial peritonitis in children with liver disease and ascites in Southern Iran

Mahmood Haghighat, Seyed Mohsen Dehghani, Abdolvahab Alborzi, Mohammad Hadi Imanieh, Bahman Pourabbas, Mehdi Kalani

AIM: To determine the causative agents of spontaneous bacterial peritonitis (SBP) in children with liver disease and ascites in our center.

METHODS: During a 2.5 year period, from September 2003 to March 2006, 12 patients with 13 episodes of SBP were studied. In all cases at the time of admission serum albumin and glucose, urinalysis and urine culture was performed. Analysis [white blood cell (WBC) count with differential, albumin, glucose], gram stain, culture by BACTEC method and antibioticogram was done on ascitic fluids. Abdominal paracentesis was repeated after 48 h of antibiotic therapy for bacteriologic assay. The patients were followed for at least three months in a gastroenterology clinic.

RESULTS: There were 7 girls (58%) and 5 boys (42%) with a median age of 5.2 years (range, 6 mo to 16 years). All cases had positive ascitic fluid culture. Gram stain was positive in 5 (38.5%) of them. The isolated organisms were S. pneumoniae in 5 (38.5%), E. coli in 2 (15.3%), S. viridans in 2 (15.3%), and K. pneumoniae, H. influenza, Enterococci, and nontypable Streptococcus each in one (7.7%). All of them except Enterococci were sensitive to ciprofloxacin and ceftriaxone. All ascitic fluid cultures were negative after 48 h of antibiotic therapy.

CONCLUSION: S. pneumoniae is the most common cause of SBP in the pediatric age group and we recommend a third generation cephalosporine (e.g., Ceftriaxone or Cefotaxime) for empirical therapy in children with SBP.

Key words: Spontaneous bacterial peritonitis; Children;

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without a demonstrable intra-abdominal cause[1]. It is a well known complication of cirrhosis in adults, occurring in 8% to 13% of patients[2-5]. The diagnosis is established by a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥ 2.5 × 10³/L). In adults, the organisms of SBP are usually gram-negative bacteria[2-4,6], but they may differ in children[5,7]. The aim of the present study was to determine the causative agents of SBP in children with liver disease and ascites in our center.

MATERIALS AND METHODS

During a period of 2.5 years, from September 2003 to March 2006, 63 children with liver disease and ascites were prospectively studied in the Department of Pediatric Gastroenterology in Nemazee Hospital affiliated with Shiraz University of Medical Sciences, the major referral center in Southern Iran. Written consent was obtained from all patients after informing them about this study which was approved by the Ethics Committee of the University.

Of the children involved in this study 12 had met the criteria for SBP (polymorphonuclear leukocyte count greater than 2.5 × 10³/L and positive ascitic fluid culture). In total 13 episodes of SBP were documented, of which two occurred with one patient, 4 mo apart. The patients and their parents answered a structured questionnaire, which included name, age, sex, clinical history, underlying liver diseases, history of antibiotic and diuretic use, history of previous variceal bleeding and episodes of SBP. All children had undergone a thorough physical examination.

Serum albumin and glucose, urinalysis and urine culture were done in all patients. Paracentesis was performed
on all patients under sterile conditions and analysis of fluid (Albumin, glucose, WBC count and differential) and gram stain was done. Ten milliliters of ascitic fluid was inoculated at the bedside in a blood culture bottle (BACTEC, PEDS PLUS/F medium, Becton, Dickinson Co. USA) using the BACTEC 9240 system (Becton, Dickinson Co. USA). Anti-biogram was performed with the disk diffusion method (Kirby-Bauer method) for ciprofloxacin (5), cefotaxime (30), ceftriaxone (30), gentamicin (10) and ceftriaxone (1.25-23.15) (MAST Co. UK). Intravenous ceftriaxone (100 mg per kilogram body weight) was started empirically for all patients after paracentesis, as recommended in adult series [8]. After 48 h of antibiotic therapy ascites were resolved in 4 patients. We could not obtain ascitic fluid despite sonographic guidance. One patient expired. Abdominal paracentesis was repeated in 8 cases for analysis and culture. The patients were followed for at least three months in our gastroenterology clinic.

RESULTS

Of the patients involved in this study, 27 had normal ascitic fluid analysis and negative cultures. In 22 patients fluid analysis showed greater than $2.5 \times 10^5$ per liter, but fluid cultures were negative. These patients were treated as culture negative neutrocytic ascites and were excluded from this study. Two patients had normal ascitic fluid analysis, but ascitic fluid cultures were positive for staphylococcus coagulase positive and negative, which were considered as non-neutrocytic Bacterascites. These were excluded from this study.

Of the SBP patients, there were 7 girls (58.3%) and 5 boys (41.6%) with a mean age of 5.2 years (range, 6 mo to 16 years). The most common clinical manifestations were as follows: fever in 12 (92.3%), abdominal pain in 12 (92.3%), abdominal tenderness in 12 (92.3%), change in level of consciousness in 5 (38.5%) and decreased bowel sounds in 3 (23%). Urinalyses were normal and urine cultures were negative in all patients. Serum-ascitic fluid albunin gradient was greater than 11 g/L in all (100%) patients. Total protein concentration of ascitic fluid was less than 10 g/L in 11 (85%) patients. Ascitic fluid glucose was greater than 0.5 g/L in all but one. Gram stains of ascitic fluid were positive in five patients (38.5%), including four gram positive cocci and one gram negative bacilli. Results of BACTEC cultures are shown in Table 1. The most common organism of SBP in this study was Streptococcus pneumoniae (38.5%). All organisms except Enterococci and one case of E. coli were sensitive to cefotaxime, and all of them except Enterococci were sensitive to ceftriaxone and ciprofloxacin. All patients became asymptomatic after 72 h of antibiotic therapy, except one infant with diagnosis of neonatal hepatitis and cirrhosis, who expired after 48 h due to encephalopathy. Abdominal paracentesis repeated in 8 cases after 48 h of antibiotic therapy. The results are shown in Table 2. Total WBC declined to 30% of primary counts, and PMN count halved after 48 h. All ascitic fluid cultures were negative after 48 h of antibiotic therapy.

### Table 1 Results of ascitic fluid cultures in 12 patients with SBP

| Organism           | n  | %   |
|--------------------|----|-----|
| S. pneumoniae      | 5  | 38.5|
| E. coli            | 2  | 15.3|
| S. viridans        | 2  | 15.3|
| K. pneumoniae      | 1  | 7.7 |
| H. influenza       | 1  | 7.7 |
| Enterococci        | 1  | 7.7 |
| Nontypable streptococcus | 1 | 7.7 |

1 White blood cell; 2 Polymorphonuclear leukocyte.

### Table 2 Ascitic fluid analysis on admission and after 48 h of antibiotic therapy in SBP patients

| Patient No. | WBC Count on Admission | WBC Count after 48 h | Rate of WBC Decline (%) | PMN Count on Admission | PMN Count after 48 h | Rate of PMN Decline (%) |
|-------------|------------------------|----------------------|-------------------------|------------------------|----------------------|-------------------------|
| 1           | 6600                   | 3000                 | 0.45                    | 5940                   | 1200                 | 0.44                    |
| 2           | 1400                   | 500                  | 0.36                    | 910                    | 200                  | 0.61                    |
| 3           | 600                    | 550                  | 0.92                    | 480                    | 165                  | 0.37                    |
| 4           | 950                    | 140                  | 0.15                    | 684                    | 56                   | 0.55                    |
| 5           | 4000                   | 3200                 | 0.80                    | 3000                   | 704                  | 0.29                    |
| 6           | 3680                   | 85                   | 0.02                    | 3496                   | 70                   | 0.86                    |
| 7           | 840                    | 100                  | 0.12                    | 689                    | 53                   | 0.65                    |
| 8           | 1000                   | 78                   | 0.08                    | 800                    | 37                   | 0.60                    |

DISCUSSION

Since the first descriptions of SBP by Kerr et al in 1963 and Conn and Fessel in 1964, the clinical presentation, treatment and prognosis of this disease have been well established. However, other aspects are still subject to investigation such as its pathogenesis, diagnosis and prevention.

Although most episodes of SBP occur in patients with advanced cirrhosis with ascites, occasionally it has been observed in non-cirrhotic patients such as fulminant hepatic failure, nephrotic syndrome and congestive heart failure. SBP is a serious infection in patients with ascites, and it is the largest abscess in humans. To date, most studies of SBP have been done in adults with cirrhosis. The lack of reports focusing on pediatric patients is remarkable. The prevalence of SBP in our patients was 20.6%, which is relatively similar to Vieira et al study (19.5%). The mean age of our cases was 5.2 years (6 mo to 16 years), which is relatively similar to the Larcher et al series (5.5 years). Fever and abdominal pain were the most common clinical presentations in our cases, which is also similar to previous reports. In all cases in our study, urinalysis was normal and urine cultures were negative, so we conclude that there is no association between SBP and urinary tract infections. This result differs from the Hoefs et al study which concluded that the urinary tract can be a source of infection in SBP patients. The high incidence of pneumococcal infection (38.5%) in our study, which was lower than that reported by Larcher et al (75%).

www.wignet.com
distinguishes our series from most adult series. In our series there were 9 cases (69%) of gram positive and 4 cases (31%) of gram negative organisms, which is different from the adult series. In this study all organisms except one Enterococci were sensitive to ceftriaxone and ciprofloxacin.

In summary, Gram positive organisms are a more common cause of SBP than gram negative organisms in cirrhotic children in our area and a third generation cephalosporin such as ceftriaxone or cefotaxime can be a suitable antibiotic for empirical therapy of children with SBP. We suggest that pneumococcal vaccination may play a role in the prevention of SBP in children, but its efficacy can only be established by further studies.

REFERENCES

1. Such J, Runyon BA. Spontaneous bacterial peritonitis. Clin Infect Dis 1998; 27: 669-674; quiz 675-676
2. Conn HO, Fessel JM. Spontaneous bacterial peritonitis in cirrhosis: variations on a theme. Medicine (Baltimore) 1971; 50: 161-197
3. Weinstein MP, Iannini PB, Stratton CW, Eickhoff TC. Spontaneous bacterial peritonitis. A review of 28 cases with emphasis on improved survival and factors influencing prognosis. Am J Med 1978; 64: 592-598
4. Bar-Meir S, Lerner E, Conn HO. Analysis of ascitic fluid in cirrhosis. Dig Dis Sci 1979; 24: 136-144
5. Clark JH, Fitzgerald JF, Kleiman MB. Spontaneous bacterial peritonitis. J Pediatr 1984; 104: 495-500
6. Hoefs JC, Canawati HN, Sapico FL, Hopkins RR, Weiner J, Montgomery JZ. Spontaneous bacterial peritonitis. Hepatology 1982; 2: 399-407
7. Larcher VF, Manolaki N, Vegnente A, Vergani D, Mowat AP. Spontaneous bacterial peritonitis in children with chronic liver disease: clinical features and etiologic factors. J Pediatr 1985; 106: 907-912
8. Runyon BA, McHutchison JG, Antillon MR, Akriviadis EA, Montano AA. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis. A randomized controlled study of 100 patients. Gastroenterology 1991; 100: 1737-1742
9. Bhuvu MA, Ganger D, Jensen D. Spontaneous bacterial peritonitis: an update on evaluation, management, and prevention. Am J Med 1994; 97: 169-175
10. KERR DN, PEARSON DT, READ AE. INFECTION OF ASCITIC FLUID IN PATIENTS WITH HEPATIC CIRRHOSIS. Gut 1965; 4: 394-398
11. CONN HO. SPONTANEOUS PERITONITIS AND BACTEREMIA IN LAENNEC’S CIRRHOSIS CAUSED BY ENTERIC ORGANISMS. A RELATIVELY COMMON BUT RARELY RECOGNIZED SYNDROME. Ann Intern Med 1964; 60: 568-580
12. Chiwa M, Guanier C, Poralta C, Llovet T, Gómez G, Soriano G, Balanzó J. Intestinal mucosal oxidative damage and bacterial translocation in cirrhotic rats. Eur J Gastroenterol Hepatol 2003; 15: 145-150
13. Castellote J, López C, Gornalis J, Tremosa G, Farina ER, Baillass C, Domingo A, Xiol X. Rapid diagnosis of spontaneous bacterial peritonitis by use of reagent strips. Hepatology 2003; 37: 893-896
14. Bauer TM, Follo A, Navasa M, Vila J, Planas R, Clemente G, Vargas V, Bory F, Vaquer P, Rodés J. Daily norfloxacin is more effective than weekly rufloxacin in prevention of spontaneous bacterial peritonitis recurrence. Dig Dis Sci 2002; 47: 1356-1361
15. Dhiman RK, Makharia GK, Jain S, Chawla Y. Ascites and spontaneous bacterial peritonitis in fulminant hepatic failure. Am J Gastroenterol 2000; 95: 233-238
16. Hingorani SR, Weiss NS, Watkins SL. Predictors of peritonitis in children with nephrotic syndrome. Pediatr Nephrol 2002; 17: 678-682
17. Shaked Y, Samra Y. Primary pneumococcal peritonitis in patients with cardiac ascites: report of 2 cases. Cardiology 1988; 75: 372-374
18. Puri AS, Puri J, Ghoshal UC, Sharma BC, Saraswat VA, Ayyagari A, Naik SR. Frequency, microbial spectrum and outcome of spontaneous bacterial peritonitis in north India. Indian J Gastroenterol 1996; 15: 86-89
19. Vieira SM, Matte U, Kieling CO, Barth AL, Ferreira CT, Souza AF, Taniguchi A, da Silveira TR. Infected and noninfected ascites in pediatric patients. J Pediatr Gastroenterol Nutr 2005; 40: 289-294
20. Hoefs JC, Runyon BA. Spontaneous bacterial peritonitis. Dis Mon 1985; 31: 1-48
21. Pinzello G, Simonetti RG, Craxi A, Di Piazza S, Spanò C, Pagliaro L. Spontaneous bacterial peritonitis: a prospective investigation in predominantly nonalcoholic cirrhotic patients. Hepatology 1983; 3: 545-549

S-Editor Wang GP  I-Editor Rippe RA  E-Editor Ma WH