Short Report

Effect of *Candida* infection on outcome in patients with perforation peritonitis

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Peritonitis is caused most commonly by perforation of the hollow viscus and grave consequences of the disease are attributed to the microbial infection of the peritoneal cavity. Factors predicting outcome in cases of perforation peritonitis are well known and have been well documented in the construction of various scoring systems.\(^1,2\) Increasing awareness of worse outcome after fungal co-infection,\(^3,4,5\) and the knowledge that intra-abdominal microbiological findings do not correlate with severity of illness as judged by the scoring systems,\(^6\) prompted us to conduct this study.

**Methods**

Eighty-four consecutive patients of gastrointestinal perforation peritonitis undergoing surgery were prospectively followed between May 2005 and September 2006 at the Department of Surgery, Government NSCB Medical College, Jabalpur. The ethical committee of the institute approved the protocol. Patients who presented with primary peritonitis or peritonitis due to anastomotic leak or trauma were excluded. Based on the site of perforation, patients were categorized as those with peptic, ileal or colonic perforation. Peritoneal fluid samples (2 mL) were collected, intra-operatively, under aseptic precautions, in sterile disposable syringes.

Microbial culture and biochemical tests for bacteria and fungi and their respective antibiotic sensitivities were done at the Regional Medical Research Centre for Tribals (ICMR), Jabalpur. The Jabalpur Prognostic Score was calculated. Forty-two of the 84 patients had positive peritoneal fluid cultures. *Escherichia coli* was the most common bacterium (n=26) and *Candida* (n=13) the most common fungus isolated. Bacterial isolates were largely sensitive to amikacin while all the *Candida* isolates were sensitive to fluconazole. Mortality was significantly higher in patients with positive peritoneal cultures (15/42) compared with those with negative peritoneal cultures (0/42, p<0.001), and in patients with mixed bacterial and fungal-positive cultures (10/13) compared with those with isolated bacterial cultures (5/29, p<0.001). Using the Jabalpur Prognostic Score, positive fungal cultures were found to be associated with a significantly higher than expected mortality. Patients with gastrointestinal perforations and positive peritoneal cultures have a poor prognosis, which is significantly worsened by the association of positive fungal cultures. Early recognition and treatment of fungal infection is advisable.


Peritonitis is treated with surgery and antibiotics. This study was conducted to identify bacterial and fungal microorganisms responsible for peritonitis in patients with hollow viscus perforation and to examine the influence of these microorganisms on the outcome. A prospective study was conducted from May 2005 to September 2006 involving 84 consecutive patients with spontaneous gastrointestinal perforation peritonitis, who were referred for surgery. Peritoneal fluid was analyzed by microbial culture and biochemical tests for bacteria and fungi. The Jabalpur Prognostic Score was calculated. Escharichia coli was the most common bacterium (n=26) and Candida (n=13) the most common fungus isolated. Bacterial isolates were largely sensitive to amikacin while all the Candida isolates were sensitive to fluconazole. Mortality was significantly higher in patients with positive peritoneal cultures (15/42) compared with those with negative peritoneal cultures (0/42, p<0.001), and in patients with mixed bacterial and fungal-positive cultures (10/13) compared with those with isolated bacterial cultures (5/29, p<0.001). Using the Jabalpur Prognostic Score, positive fungal cultures were found to be associated with a significantly higher than expected mortality. Patients with gastrointestinal perforations and positive peritoneal cultures have a poor prognosis, which is significantly worsened by the association of positive fungal cultures. Early recognition and treatment of fungal infection is advisable.
availability.

Categorical variables were analyzed using the Fisher exact test.

**Results**

Eighty-four patients (mean age 37.0 years [range: 11–65 years]; 68 men) were included in the study. Fifty-nine patients (70%) had peptic perforation, and the remaining 25 (30%) had ileal perforation. Samples of 42 patients (50%) turned out to be culture positive while, in the remaining, the cultures were sterile. Bacteria were isolated from all 42 patients with positive culture, while 13 additionally had isolation of fungi from culture. Of the 42 culture-positive samples, 21 (50%) were peptic in origin while the other 21 (50%) were ileal in origin. Of the 29 patients with only bacteria isolated from the peritoneal fluid, 18 (62%) were peptic in origin while 11 (38%) were ileal in origin. Among the 13 cultures that had both bacteria and fungus isolated, 3 (23%) were peptic while 10 (77%) were ileal perforations.

*E. coli* was the most common bacterium isolated, being cultured in 26 cases followed by *Klebsiella* in 11, *Pseudomonas* in 5, and *Salmonella* and *Staphylococcus* in one case each. No attempt was made to speciate the *Candida* isolates. *Candida* infection was never found in isolation. Antibiotic sensitivity of the bacterial isolates revealed that most were sensitive to amikacin (88.1%), followed by cefoparazone + sulbactam (64.2%), ceftriaxone (59.5%), ciprofloxacin (42.4%), and norfloxacin (16.6%). All 13 isolates of *Candida* were sensitive to fluconazole (100%) and 6 (46%) were sensitive to both amphotericin B and fluconazole.

None of the 42 patients with sterile peritoneal fluid died (0%), while among culture-positive patients, 15/42 died (36%, $\chi^2=18.24$; $p<0.001$). Only 5/29 patients having isolated positive bacterial cultures died (17%), whereas 10/13 patients with positive bacterial and fungal culture, died (77%, $\chi^2=13.93$; $p<0.001$). The outcome was significantly worse in fungal culture-positive patients as compared to fungal culture-negative patients (Table). On correlating fungal culture positivity with Jabalpur Prognostic Score, it was found that the observed mortality was similar to predicted mortality for fungal-negative patients, but not for fungal-positive patients, being significantly higher than expected mortality (Figure).

**Discussion**

Enteric Gram-negative organisms and anaerobes are the predominant isolates in patients with perforation peritonitis, with *E. coli* and *Bacteroides fragilis*, respectively, being most frequent.7 Our results were similar, with 50% of patients having a negative culture. This figure should be interpreted with caution since anaerobic culture could not be done.

Although the number of patients in the present study is small, several conclusions could be drawn. Patients with perforation peritonitis whose culture was positive had higher mortality than those having a sterile culture. Mortality was higher in patients who had mixed bacterial- and fungal-positive culture as compared with those who had only bacterial-positive culture. Mortality was higher in patients with fungal-positive culture compared with those with fungal-negative culture. The Jabalpur Prognostic Score was accurate in predicting mortality for patients with fungal-negative cultures, but those with fungal-positive culture exhibited significantly greater than expected mortality.
Candida co-infection in patients with perforation peritonitis appears to be a bad prognostic factor. Most studies have found positive peritoneal fungal culture a significant risk factor for adverse outcome in patients with perforation peritonitis. 3,4,5,8 Candida infection was associated with increased mortality, in addition to the predictive effect of the Jabalpur Predictive Score.

Inadequate antimicrobial treatment is an independent determinant of hospital mortality, especially fungal infections are among the type of infection with the highest rates of inappropriate initial treatment. 9 Routine peritoneal culture tests in perforation peritonitis for bacteria and fungi are easily available, easily done, and take only 48 hours to provide information. It is, therefore, recommended that all patients undergoing laparotomy for perforation peritonitis should undergo peritoneal fluid cultures both for bacteria and fungi and respective antibiotic sensitivities and should be treated accordingly. Early recognition and treatment of fungal co-infection can potentially minimize the high mortality seen in these patients.

References


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News and Notices

The 49th Annual Conference of Indian Society of Gastroenterology and the Asia Pacific Digestive Week 2008 will be held at Ashok Hotel, New Delhi, India from September 12-16, 2008.

For details, contact: Dr. Rakesh Tandon, Chairman, Organizing Committee. Websites: www.apdw2008.net; www.isg.org.in. E-mail: apdw@apdw2008.net.

Medical Education Fellowships-2009: CMCL-FAIMER Regional Institute, Christian Medical College, Ludhiana

The CMCL-FAIMER Regional Institute’s Fellowship is a two-year fellowship program designed for Indian medical school faculties who have the potential to play a key role in improving medical education at their institutes. The program is uniquely designed to teach education methods and leadership skills, as well as to develop strong professional bonds with other medical educators. The fellowship is now running in its fourth year.

Sixteen fellowships are on offer for the year 2009. Requirements for selection are submission of a curriculum innovation project proposal and letter of support from applicant’s institute. Limited funding is available to support fellows’ travel, local expenses and course fee.

Applications open from: July 1 to October 15, 2008

For details, please visit http://cmcl.faimer.googlepages.com/home

A conference on “Inflammatory Bowel Disease: Problem-Oriented Approach” will be held at the P D Hinduja National Hospital, Mumbai 400 016, November 8 and 9, 2008.

A Workshop on Clinical Research Methodology will be held in Lucknow on 10-12 December, 2008, under the aegis of the U.S. National Institutes of Health and the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow.

Applicants should email a short summary of their experience, expertise and current activities in clinical research by October 31, 2008 to Paolo Miotti, U.S. Embassy, New Delhi (pm122m@nh.gov). A selection committee will notify the successful applicants of their acceptance. Participants’ travel and hotel expenses will be covered by the workshop organizers.