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THE HIGH MORBIDITY OF FUNGAL PERITONITIS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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Summary

Eight episodes of fungal peritonitis occurred in seven patients. All had multiple previous bacterial peritonitis episodes and six had antibiotics prior to the onset of the fungal infection. Candida species accounted for most episodes. Treatment consisted of several strategies of catheter removal and antifungal therapy. All were equally unsuccessful. All patients were transferred to haemodialysis and in six of the seven patients extensive intra-abdominal adhesions occurred. This late complication caused loss of peritoneal space and small bowel obstruction. Sclerosing peritonitis was also observed in two patients.

Introduction

Patients on continuous ambulatory peritoneal dialysis are immunocompromised and have an indwelling catheter, making them more susceptible to opportunistic infections. Peritonitis due to bacteria is the commonest complication of continous ambulatory peritoneal dialysis, but fungal peritonitis although uncommon is important in view of its poor response to treatment and subsequent morbidity. We report our experience.

Patients and methods

Between 1980 and 1983, eight episodes of fungal peritonitis occurred in seven patients (6 female, 1 male). Mean age was 37 years (range 25–58) and mean duration of continuous ambulatory peritoneal dialysis was 17 months (range 7–25). Mycological methods consisted of direct microscopy and culture of the dialysate on glucose (4%) – peptone (1%) or malt (4%) agar plates and incubation at 28°, 37° and 45°C. Repeated positive cultures confirmed the diagnosis. Fungi were also isolated from the catheter tip. All isolates were tested for sensitivity to amphotericin, Flucytosine, miconazole and ketoconazole.

TABLE I. Fungal peritonitis

Patient	Fungal peritonitis episode	No. of previous bacterial peritonitis episodes	Fungi	No. of positive fungal cultures	Treatment strategy	Antifungal drugs	Intra-abdominal complications	Outcome
1	1	2	Candida glabrata	4	B	Flucytosine (O)	Multiple adhesions	HD → CAPD → TX
2	2	3	Verticillium sp	6	A	Nil	Multiple adhesions	HD
3	3	4	Candida parapsilosis	5	C	Amphotericin (IP) Flucytosine (IP) Miconazole (O) Ketoconazole (O)	Nil	HD → TX
4	4	6	Candida glabrata	3	B	Amphotericin (IV) Ketoconazole (O)	Multiple adhesions Sclerosing peritonitis	HD → TX
5	5	2	Candida albicans	5	A	Nil	Adhesions Small bowel obstruction Chronic peritonitis	HD → Died
6	6	4	Candida albicans	3	A	Nil	Adhesions	HD → CAPD
	7		Aspergillus fumigatus	2	B	Flucytosine (IV) Miconazole (O) Amphotericin (IV)	Small bowel obstruction Sclerosing peritonitis	HD → Died
7	8	3	Rhodotorula sp	5	C	Amphotericin (IV) Ketoconazole (O) Flucytosine (IP)	Multiple adhesions	HD → TX

HD = Haemodialysis. TX = Transplantation

Treatment regimens consisted of:

A) catheter removal alone (3 cases):

B) catheter removal followed by antifungal drugs (3 cases), and

C) antifungals with the catheter left in situ (2 cases). Combinations of antifungal drugs according to sensitivities were given by various routes (oral), intraperitoneal and intravenous) and for variable duration from three days to two months.

Results

Fungi accounted for five per cent of our total number of peritonitis episodes. All seven patients had multiple previous episodes of bacterial peritonitis, which usually responded to antibiotics, but occasionally required catheter removal. Antibiotic therapy (flucloxacillin, cefuroxime, gentamicin) was given to six of the seven patients within one month prior to the onset of fungal peritonitis for skin exit site infections, bacterial or culture negative peritonitis.

In all episodes typical features of cloudy dialysate (WCC>100μL^{-1}), abdominal pain and rebound tenderness were present and persistent fever (7 out of 8) and peripheral blood leucocytosis (4 out of 8) were noted. The fungi isolated were mainly of the candida species (Table I). Catheter removal resulted in resolution of symptoms and the addition of antifungal drugs did not accelerate recovery. Antifungal agents alone did not relieve symptoms and catheter removal was necessary.

Following fungal peritonitis, six of the seven patients developed troublesome intra-abdominal adhesions, confirmed by laparotomy, which varied in severity from extensive adhesions preventing catheter replacment to small bowel obstruction. Two patients later developed sclerosing peritonitis. The outcome was that all patients discontinued continuous ambulatory peritoneal dialysis and were transferred to haemodialysis. Two patients returned to continuous ambulatory peritoneal dialysis but one had a further episode of fungal peritonitis. Two patients died, one after five months from chronic peritonitis and small bowel obstruction and the other two years later after recurrent small bowel obstruction and sclerosing peritonitis.

Discussion

Fungi are an uncommon but important cause of peritonitis because of the poor response to treatment and the subsequent high morbidity. In our series like others [1], multiple bacterial and culture negative peritonitis occurred prior to the fungal infection. The prolonged and frequent use of antibiotics can alter the commensal flora and is a predisposing factor [2]. Initially it is difficult to clinically distinguish between bacterial and fungal peritonitis but from our data, persistent fever and a blood leucocytosis were commoner in fungal than bacterial infection. Delay in diagnosis is inevitable, but if bacterial cultures are negative and symptoms persist for more than four days despite antibiotic therapy, fungal infection should be suspected. Multiple positive fungal cultures distinguish

contamination from infection. The source of infection can be endogenous or exogenous. All but one patient in our series were female and vaginal candidiasis may have been the route of infection in two of our episodes. In the Rhodotorula infection the organism was cultured initially from a unidirectional microbial in-line filter several days before it was isolated from the dialysate suggesting transluminal catheter spread.

Fungal infections are generally difficult to control, partly due to the delay in diagnosis but also because an effective non-toxic antifungal agent has yet to be established [3]. Response to treatment has been inconsistent, generally disappointing and the best strategy still remains unclear. Some propose peritoneal lavage with antimycotics [4], while others suggest early catheter removal, with or without antifungal agents [5,6]. Early catheter removal has the advantage of removing the foreign body which may be colonized by fungi and resolution of symptoms, but it can result in peritoneal adhesions and transfer to haemodialysis. The other approach is to leave the catheter in situ and use if for peritoneal lavage, intraperitoneal antifungal administration and to continue peritoneal dialysis. This may reduce adhesions but continuous lavage removes phagocytic cells and may impair defence mechanisms [7]. A further alternative combines the above strategies. Keogh [8], has suggested early removal of the colonized catheter, insertion of a temporary catheter for short periods of lavage to continue peritoneal dialysis and administer intraperitoneal antifungal drugs. A new permanent catheter is inserted after resolution of the infection.

Peritonitis can result in adhesion formation, sclerosing and thickening of the peritoneum [9] and our study shows a very high incidence of symptomatic adhesions following fungal peritonitis with consequent small bowel obstruction. Sclerosing peritonitis was also observed later in two patients.

Our results of treatment were unsuccessful whether the catheter was removed early or late and the addition of antifungal drugs did not prevent cessation of continuous ambulatory peritoneal dialysis. Subsequent peritoneal adhesions makes Keogh's approach worthy of consideration. However, more effective antifungal therapy is needed but again there is no agreement to the optimal antimycotic dose, route or duration of treatment. The ideal treatment should not only eradicate the peritoneal infection without disruption of peritoneal dialysis but should prevent intra-abdominal adhesion formation.

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