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The journal will publish original full-length articles of high scientific standard, with appropriate trial design and analysis, in fundamental surgical science. Retrospective reviews and short reports of negative results will also be accepted and, occasionally, didactic case reports.

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SCHEDULED PERITONEAL LAVAGE IN PERITONITIS – ITS IMPLICATIONS ON HUMORAL AND CELLULAR DEFENSE MECHANISMS

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(Accepted for publication 21 August 1988)

Peritonitis exudates from the initial operation and exudates from programmed reoperations were analysed for their ability to promote particle opsonisation and for phagocyte activity. The results indicate that even long courses of lavage treatment do not essentially alter the opsonic deficit and the enhanced phagocyte activation status found in original exudates as long as the source of peritonitis cannot be cured surgically. The clinical improvement resulting in clear exudates is connected with a pronounced recovery of opsonisation and decrease of exudate elastase levels.

KEY WORDS: Peritonitis, peritoneal lavage, opsonic capacity (OC), opsonin level (OL), phagocytosis.

INTRODUCTION

In the management of severe peritonitis open treatment with scheduled reoperations and lavage procedures has been established during the last decade. Several different techniques have been promoted. Due to the heterogeneity of the patient groups, evaluation of these therapeutic approaches is difficult and comparison on base of survival rates can be misleading. The effect of repeated lavage procedures on the intraabdominal environment and local defense mechanisms has been little investigated.

In our clinic we employ a concept of scheduled reoperations with lavage of the abdominal cavity and a preliminary closure of the abdominal wall without drainages in between.¹

In previous studies we could demonstrate a strong impairment of particle opsonisation in peritonitis exudate with pronounced degradation of the main opsonins C3 and IgG.² The chemiluminescence response of phagocytes as an indication of cell activation in such exudates was intact.

We have now investigated the influence of the lavage therapy on the local humoral and cellular resistance.

MATERIALS AND METHODS

During initial operations for diffuse purulent peritonitis and lavage-reoperations, exudate and blood samples were drawn simultaneously to measure the phagocytosis

activity of the local and circulating leukocytes. For evaluation of the samples' opsonic capacity exudates were centrifuged, while blood was processed to serum or EDTA-plasma.

Chemiluminescence (CL) Assay

Cell-free samples capacity for opsonisation (OC) of zymosan was determined with a Luminol enhanced chemiluminescence assay as described previously.² For the evaluation of the release of oxygen derived free radicals from local or circulation leukocytes a similar assay was applied: In an exudate dilution of 1:300 spontaneous CL of the cells was measured without zymosan stimulation and CL response was also quantified after stimulation of the phagocytes with 1 mg of normal serum-preopsonized zymosan.

Other Assays

Immunological C3 and IgG opsonin levels (OL) were measured with a standard radial immunodiffusion assay (Behringwerke, Marburg, FRG; normal values = 100%: C3 82 mg/dl and IgG 1250 mg/dl). C3a was determined by radioimmunosassay available from Upjohn.³ Elastase in complex with α_1 -proteinase inhibitor (α_1 PI) was measured by ELISA (test kits from E. Merck, Darmstadt, FRG)⁴ with a reference range for complexed plasma elastase from 50–181 μ g/l.

Protein content was determined by the Biuret method. Serum and exudate protein electrophoresis was performed according to Grabner *et al.*⁵ WBC was carried out in a Neubauer chamber after staining with Türk's solution (from E. Merck, Darmstadt, FRG).

Aerobic and anaerobic bacterial cultures were prepared from all exudates immediately after sampling.

RESULTS

For analysis samples were classified in exudates from the initial operation, purulent exudates from reoperation (> 2000 leukocytes/ μ l) and clear exudates (generally from the last reoperation, ≤ 2000 leukocytes/ μ l).

HUMORAL FACTORS

Exudates from the *initial peritonitis* were characterized by a protein content of 65% of patients' serum concentration. Mean opsonin (C3 and IgG) concentration was 280 mg/l and 4.7 g/l respectively (Table I). The mean level of anaphylatoxin C3a in these exudates exceeded 58 times the normal plasma value. Exudate elastase concentrations were more than 800 fold the normal plasma level.

Purulent lavage exudates showed no significant difference of total protein content but a shift towards higher IgG and decreased C3 levels compared to primary exudates was observed. The concentration of complexed elastase was even elevated. The amount of C3a was significantly reduced (Table I).

Clear exudates from the end of lavage treatment contained still rather high protein

TABLE I

Humoral opsonisation related factors in primary peritonitis exudate and in purulent and clear lavage exudate (OC = opsonic capacity for zymosan), mean \pm standard deviation

	Prim. perit.	Pur. lavage	Clear lavage
Protein content (g/l)	32.5 \pm 11	36 \pm 8	42 \pm 11
IgG (g/l)	4.7 \pm 2.3	6.9 \pm 3	6.3 \pm 2.7
C3 (mg/l)	280 \pm 150	212 \pm 84	400 \pm 170
C3a (mg/l)	7.4 \pm 10.8	4 \pm 3	2 \pm 0.7
OC (% of normal serum)	12.9 \pm 15.1	6 \pm 6.8	53 \pm 19
Elastase α_1 -PI (mg/l)	47 \pm 45	80 \pm 57	3 \pm 3

concentrations with recovered levels of C3. Elastase- α_1 PI-complex and C3a were low in such exudates.

According to the opsonin amount peritonitis exudates should provide sufficient opsonisation. The effective opsonic activity in purulent exudates, however, revealed a pronounced impairment of zymosan opsonisation. Clear exudates in contrast opsonized foreign particles as expected from their opsonin content (Table I).

Case Report

In a 63 years old man, leakage of the anastomosis after partial gastric resection lead to diffuse purulent peritonitis. Due to anatomical reasons the source of peritonitis could not be cured. 10 lavage procedures were performed within 20 days. The patient died eventually because of a septic multiorgan failure. The follow-up of OC and OL

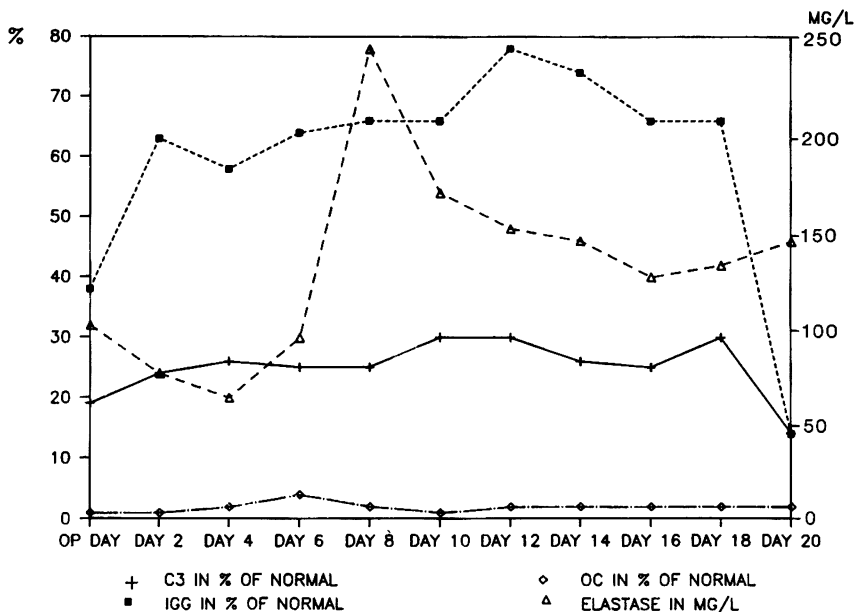


FIGURE 1 Humoral opsonisation related factors in peritonitis exudate in a patient under programmed lavage (OC = opsonic capacity, % of normal serum).

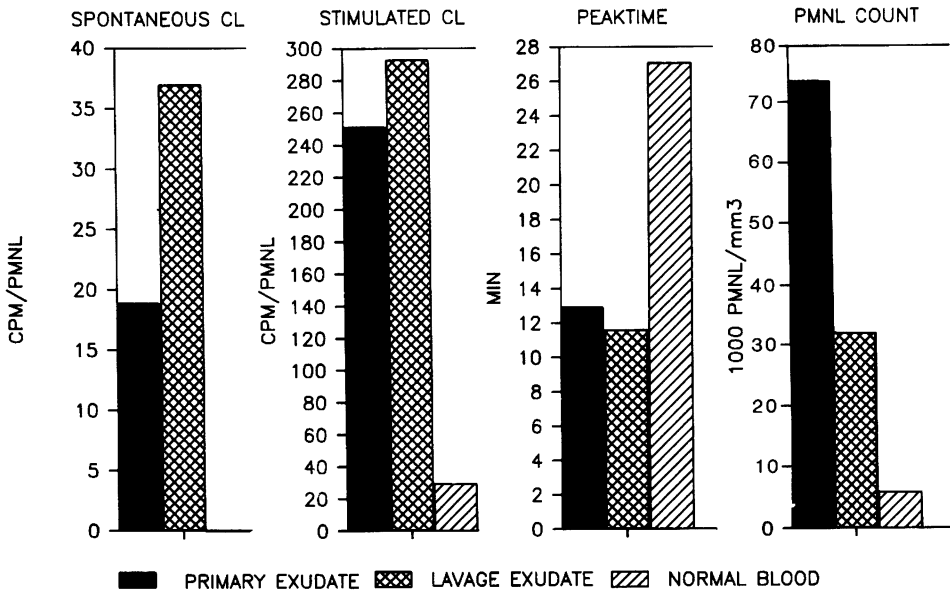


FIGURE 2 Cellular defense in peritonitis exudate: Chemiluminescence (CL) with and without zymosan stimulation, CL-peaktime and white cell count.

reveals low C3 and IgG levels in the beginning with a subsequent increase and prefinal slope. All lavage exudates were purulent as the cause of peritonitis persisted and OC never recovered during the whole treatment (Figure 1).

CELLULAR FACTORS

Exudates from *primary peritonitis* contained excessive leukocyte concentrations with a PMN granulocyte (PMNL) fraction of 98%. In 56% of the exudates we could demonstrate spontaneous CL, that is CL without zymosan stimulation, with a mean activity of 19.2 counts per minute (cpm)/PMNL. Spontaneous CL could never be observed in patients' blood. Zymosan stimulation caused a CL of 252 cpm/PMNL which is 8.5 that of normal blood (Figure 2). CL peak time was critically preponed to 13 minutes compared to 27.1 minutes in normal blood control.

Purulent lavage exudates contained significantly less leukocytes. Spontaneous CL occurred in 63%, stimulated CL was only slightly increased and the peak time shortened. However, compared to the initial exudates these differences were statistically not significant.

Due to the small leukocyte counts CL-experiments could not be performed in *clear exudates*.

MICROBIOLOGICAL FINDINGS

From the primary exudates ($n = 27$) 22% were sterile. *Staphylococcus epidermidis* was never found in these samples, in 40% only one species could be isolated. All

purulent lavage exudates (n = 21) were infected, 34% contained *staphylococcus epidermidis* and 90% revealed multispecies contamination.

DISCUSSION

Opsonisation of foreign particles, the central prerequisite for effective phagocytic response, is mainly mediated by C3 and IgG.⁶

The efficiency of PMNL phagocytosis depends on the quality of opsonisation. Release of oxygen derived free radicals measured as CL serves as a marker for PMNL activity and responsiveness. Shortening of the peak time is a sign of cell preactivation.⁷ The latter can be caused by C3a and several other factors.

In the initial peritonitis exudates we found sufficient levels of immunological detectable opsonins but with an almost complete lack of physiological activity. In previous experiments we could demonstrate a probably proteolytic breakdown of these factors.² The exudates contained plenty of PMNL and extremely high levels of extracellularly released elastase. C3a concentrations were strongly elevated and the CL pattern gave evidence for present production of free radicals which could be further stimulated by exogen zymosan application. Compared to normal blood the exudate PMNL were strongly preactivated.

Little is known about the impact of repeated reoperations and lavage procedures on the local unspecific defense system.⁸ Residual lavage fluid seems to promote abscess formation.⁹ The present results suggest that the peritoneal exudate at the *time of reoperation* is not essentially different from the original exudate when the source of peritonitis has not been cured. We still found a pronounced opsonic deficit despite an increase of IgG levels. Even in the demonstrated long course of lavage therapy levels of OC and OL were rather steady after an initial increase due to acute phase reaction and immune response and with only a prefinal drop. The activation pattern of the PMNL was rather similar to that in primary exudate. Microbiological findings indicated increased contamination and superinfection of the abdominal cavity. These findings match the clinical experience that the prognosis is extremely poor when the source of peritonitis persists.¹⁰ An improvement of the macroscopic aspect of the abdomen with clear exudates corresponded to an almost complete recovery of opsonisation with drastic decrease of PMNL count and extracellularly released lysosomal elastase levels.

For severe cases of purulent peritonitis scheduled reoperations with inspection and lavage of the whole abdomen seems to be superior to relaparotomy only on demand for sepsis.¹¹ Our results indicate, however, that repeated lavage therapy *per se* does not improve the local defense mechanisms. Lavage fluid, however, should be accurately removed in order not to further deteriorate opsonisation.

The benefit of open management of peritonitis is probably due to early recognition of recurrent sepsis and abscess formation.

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