PERITONEAL MACROPHAGES TRANSFUSION IN THE TREATMENT OF CHRONIC POSTOPERATIVE WOUND INFECTIONS

Pages with reference to book, From 310 To 312

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Abstract

Four patients with chronic post-operative wound infections and wound gapping that failed to respond to antibiotics were treated by allogeneic macrophage transfusions. No harmful effects were observed following macrophage transfusion and the chronic infections were eradicated in the treated patients with complete healing of wounds. Haemoglobin and white cell count were increased after cell transfusion. It could be concluded that allogeneic macrophage transfusion can combat chronic resistant infections and stimulate both wound healing and haemopoiesis (JPMA 39: 310, 1989).

INTRODUCTION

Chronic infections might be the result of failure of antibiotics to eradicate microorganisms. This is partly, due to both the inability of antibiotics to reach effective levels at the site of infections and increasing resistance of bacteria to antibiotic therapy. However, failure of antibiotics may reflect depressed immune functions in the patients. On the other hand, macrophages play a major role in the defence against a variety of infectious agents. Recently, we have found that human peritoneal macrophages, obtained from unrelated donors under-going peritoneal dialysis for recently developed renal failure, could eradicate acute urinary infections which were resistant to antibiotic therapy[1]. Furthermore, it has been found that xenogeneic macrophage transfusions, from human to rabbit[2] and from human to guinea pigs (Al-Waili, unpublished observation) could eradicate severe or otherwise fatal septicaemia due to infection with E. Colt This new approach for treatment of acute resistant infections by macrophage transfusion encouraged us to investigate it in the treatment of four patients with chronic resistant infections.

PATIENTS AND METHODS

Collection of Macrophages:

Human peritoneal macrophages were collected from adult patients undergoing peritoneal dialysis as part of their management of renal failure[1-3]. Therapeutic high concentration of cells (2-5x 10^7 cell/ml) were obtained from 5/25 patients undergoing peritoneal dialysis for recently developed renal failure[1]. The penitoneal washout were centrifuged thrice and washed with normal saline. Differential counts of the cells showed 80-90% macrophages, and the remainder was a collection of lymphocytes and granulocytes.

Patients:

Four patients with chronic post-operative wound infections and gapping were included in the study (Table 1).

TABLE 1. Pre-therapy informations on four patients.

Patients Number	Sex	Age	Type of operation	Bacterial wounds infections	Antibiotics used	Period of treatment
1	Male	30	Appendicectomy	E. coli and Proteus spp.	Gentamycin Cephalexin	7 months
2	Female	25	Caesarean section	E. coli and Staphylococcus aureus	Rifampicin Cephalexin	4 months
3	Male	18	Appendicectomy	E. coli	Gentamycin Co-trimexazole	3 months
4	Female	38	Cholycestectomy	E. coli and Staphylococcus aureus	Gentamycin Cloxacillin	7months

The patients had developed wound infections and then gapping during early post-operative periods. Treatment with daily dressing and local and systemic antibiotics were continued for a period of 4-7 months post-operatively without healing. At the time of presentation the surgical wounds were found open with pus and yellowish discharges. Wound swabs were collected for culture and sensitivity. Laboratory investigations including WBC, RBC, ESR, Haemoglobin, Blood urea, Blood sugar, Serum creatinine, and liver function tests were performed. The study was fully explained to the patients and informed consents were obtained.

Infusion of Macrophages:

Patients were asked to stop taking antibiotics for a period of a week prior to infusion. After this washout period, each patient received a total of 200-250ml of macrophages suspension (1-3 x 10^7 cells/ml) intravenously (30 drops/minute); and after ten minutes evaluations of temperature, blood pressure and pulse rate were recorded. The patients were discharged 6-10 hours late, and instructed to attend the clinic daily for follow-up (dressing and side effects). Wound swabs were done every day after cell transfusion. Laboratory investigations were repeated weekly.

RESULTS

After cell transfusions wound swabs from the. four patients yielded no growth at 7-10 days. Pus discharge were reduced gradually and stopped within two weeks. Complete closure of wound gappingwere evidentin 1-2monthspost treatment. Haematological investigations (Table II)

TABLE II. Haematological indices before and after therapy with macrophages transfusions.

Patient Number	Pre-therapy			Post-therapy Week2			Post-therapy Week 4		
	WBC	Hb	ESR	WBC	Hb	ESR	WBC	Hb	ESR
1	8100	12	70	9200	13	35	10100	13.5	10
2	7600	10	76	8700	11	43	10200	12.8	8
3	8000	10.5	66	9150	10.9	54	9320	12.2	12
4	7100	11.2	78	7800	12.7	27	9700	12.9	15

revealed elevation of WBC, Hb and lowering of ESR. No changes in blood urea and other investigations were noted. No side effects were recorded during and after macrophages transfusions, apart from mildheadache, rigors and tachycardia. These were overcome using antipyretics. On the other hand, wound swabs from one patient with cholecystec¬tomy still yielded heavy growth of Staphylococcus aureus with mild pus discharge at 3 weeks post-therapy. This patient received another macro¬phage transfusion in similar dosage. At 7 day, wound swabs yielded no growth and complete

closure of wound was evident in 1 month.

DISCUSSION

The results confirm the observation that allogeneic macrophage transfusion did not elicit graft-host or host-graft reactions[1,4]. In addition, repeated macrophage transfusions, obtained from two unrelated individuals and given to one patient, did not initiate adverse reactions. The transfused cells could combat chronic infection and stimulate wound healing and recipient haemopoiesis. In all patients, microorganisms were sensitive to some antibiotics but failed to respond to treatment, presumably due to chronic illness or/and defective immunocompetence. Surgical trauma and chronic inflammations caused a progressive defect in immunity and secondary anaemia which resulted probably from over production of prostaglandins from inflamed and damaged tissues[5-7].. Moreover, tissue damage and necrosis might hinder antibiotics to reach therapeutic level at the site of infection. The transfused macrophages might enhance immunity of the host against the invading microorganisms since they possess immunostimulatory properties. They might represent the bacteria to be recognisedby host T-cells causing T-cell activation induction of killer T-cells, helper T-cells and elaboration of lymphokines. The activation of recipient helper T-cell might potentiate the differentiation of B-cells into antibody producing plasma cells[8,9]. On the other hand, the transfused cells might be chemotactically attracted to the infected wounds by some substances including bacteria and bacterial products, antibody antigen complexes, complements and lymphokines[9]. Cell wall product, lipopolysaccharides, from gram negative bacteria activate peritonealmacrophages to become non-specifically cytotoxic[10]. Following chemotaxis to the infected wound, the cell might phagocytize the invading bacteria and eliminate infections. However, further studies are needed to substantiate these suggestions. Regarding the effect of macrophages on haemopoietic system, the results show that the recipients, baemoglobin and white blood cells were both increased alter cell transfusions. This means that macrophages might stimulate haemopoiesis. It has been known that macrophages produce a colony stimulating factor which is essential to form colonies of both granulocytes and monocytes[11]. Other reports showed that monocytes and macrophages are the main source of colony stimulating factor in man[12]. In addition, macrophages have been reported to produce erythropotetin, territm, transterrm and they are a source of iron for developing normoblast in the bone marrow[13]. On the other hand, increased haemoglobin after cell transfusion might be, in part due to elimination of infection. Of great concern is the effect of macrophage transfusion on wound repair. The results show that the post-operative wound gapping and discharging sinuses were completely repaired after cell trans-fusion. When macrophages attracted to the site of the infected area they ingested wound material and acted to debride the wound by releasing proteases, like collagenase. This influenced the rate of collagen degradation[14]. Macrophages also participate in the wound healing by releasing substances that induce fibroblast proliferation and neovascularization[14].

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