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Monocyte phagocytosis in non-small cell lung cancer patients

Fagocytoza monocytów u pacjentów z niedrobnokomórkowym rakiem płuca

INTRODUCTION

Infections more often occur in cancer patients than in patients with benign tumours [1]. This statement is also true in lung cancer. About 25% of neoplastic patients suffer from pneumonias [2]. Additionally, the main pulmonary tissue resection complication is chronic pleural empyema, which occurs in 2–16% cases [3]. Moreover, the major reason of lung cancer mortality (20–40% of patients) are secondary infections of the lung [1]. The reasons of such frequent infections in lung cancer are still unknown. The malnutrition of these patients, which disturb the immunological system functions, cannot be suitable explanation of this phenomenon [8]. Bronchial obstructions in cancer patients cannot explain it clearly, too. A lot of papers clearly showing immunological disturbances in neoplastic patients strongly suggest that impaired immunity must play a key role in this process [4, 5, 6, 7].

One of the very important host defence against infections is innate, non-specific defence. Phagocytosis is one of the key components of it. In the present study we decided to evaluate peripheral blood monocyte phagocytosis in Non-Small Cell Lung Cancer (NSCLC) patients in comparison with volunteer healthy blood donors.

MATERIAL AND METHODS

Phagocytosis was measured in 26 NSCLC patients (pre-operation and 7 days after operation) and 15 healthy individuals. Three women and 23 men were included in the study group. The mean age of NSCLC patients was 59.4 years. The number of patients in clinical stage was as follows: I — 2 pts, II — 9 pts, III — 12 pts, and IV — 3 pts, respectively.

Phagocytosis was measured using Phagotest (ORPEGEN Pharma) as described in protocol. Briefly, 100 μl of whole heparinized peripheral blood were incubated with 20 μl suspension of FITC-labelled *E. coli* for 10 min. (control sample in ice-bath, test sample in 37°C). Just after stopping the phagocytosis by adding cold Quenching Solution the cells were washed twice. Then erythrocytes were lysed for 20 min. in room temperature. After washing the remaining cells were stained with DNA Staining Solution. Just after staining cells were analysed by flow cytometry (CytoronAbsolute, Ortho). Mann–Whitney and Wilcoxon tests, as well as Statistica 5.0 software were applied for statistical analysis.

RESULTS

The results were shown in Table I. A percentage of monocytes, which phagocyted *E. coli* (FITC positive) and as green mean fluorescent intensity (MFI), which reflects the number of phagocyted *E. coli* by a single monocyte were presented there. Percentages of monocytes which phagocyted *E. coli* were significantly decreased in NSCLC patients prior to operation ($p<0.05$) compared with healthy blood donors (Fig. 1). No significant differences were found between MFIs of NSCLC monocytes (Fig. 2), as well as between percentages of FITC positive monocytes in patients before and after operation (Fig. 1). Fig. 3 shows a typical histogram of monocyte phagocytosis.

Table I. Phagocytosis of peripheral blood granulocytes. The results are shown as mean ± SD (median). Significant differences are marked as ♦ ($p<0.05$).

	%	MFI
Healthy control	48.5±12.6♦ (50.6)	142.7±28.8 (130.6)
Patients pre-operation	36.4±13.8♦ (34)	128±12.1 (127.7)
Patients 7 days post-operation	43.7±13.2 (45)	132.9±9.5 (132.2)

DISCUSSION

Significantly decreased lung cancer monocyte phagocytosis found in our study could explain more frequent appearance of inflammatory complications in lung cancer patients. In the paper of Shirai et al. was shown otherwise. Significant increase of monocyte phagocytosis with no significant changes of neutrophil phagocytosis were presented there. No MFI analysis was performed in this study. Moreover, they used *Staphylococcus aureus* conjugated with fluorescein to measure phagocytosis [8] instead of *E. coli* used in our study. In other paper was shown that blood phagocytes have

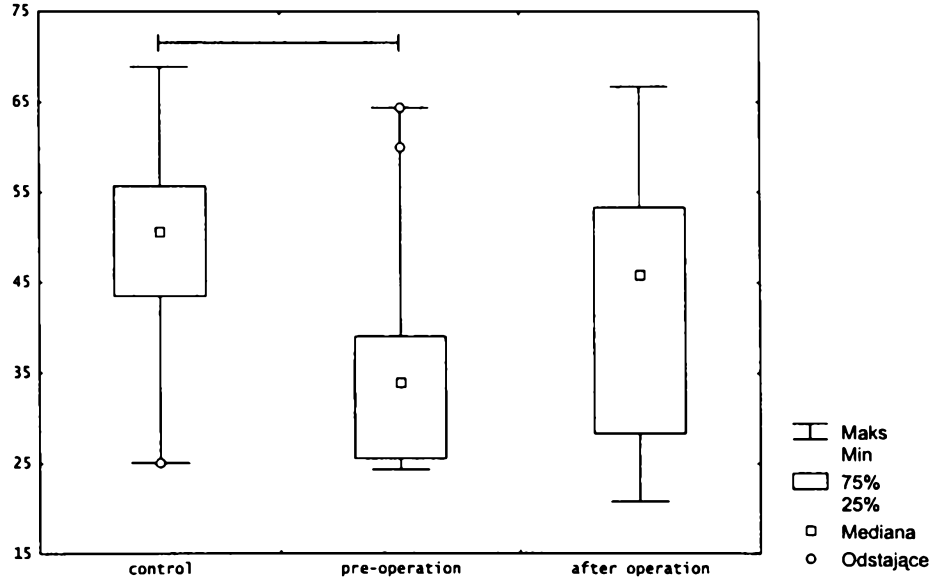

Fig.1. Percentage of peripheral blood monocyte phagocytosis in NSCLC patients (pre- and post-operation) and in healthy blood donors. Significant differences are marked

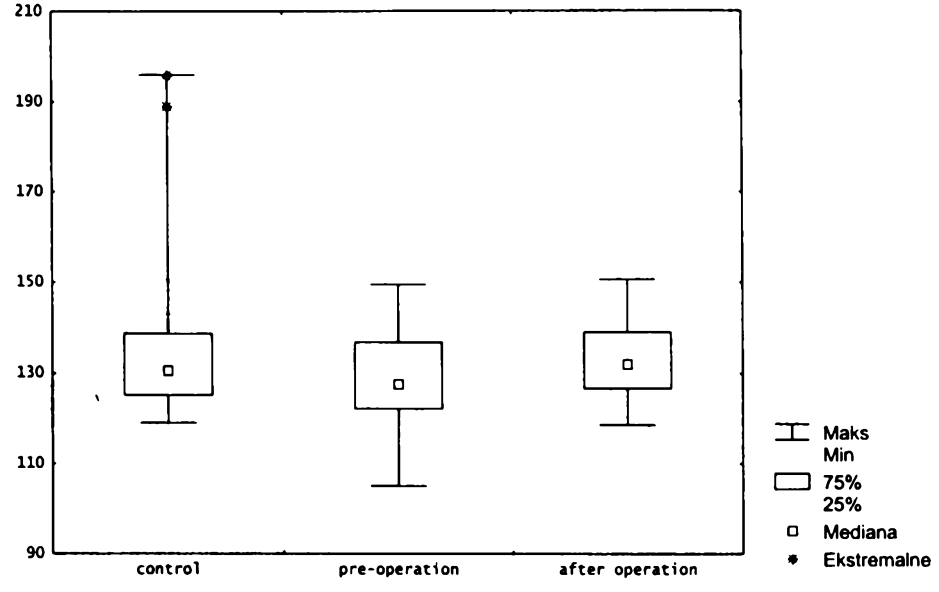

Fig. 2. Green mean fluorescence intensity of peripheral blood monocyte phagocytosis in NSCLC patients (pre- and post-operation) and in healthy blood donors

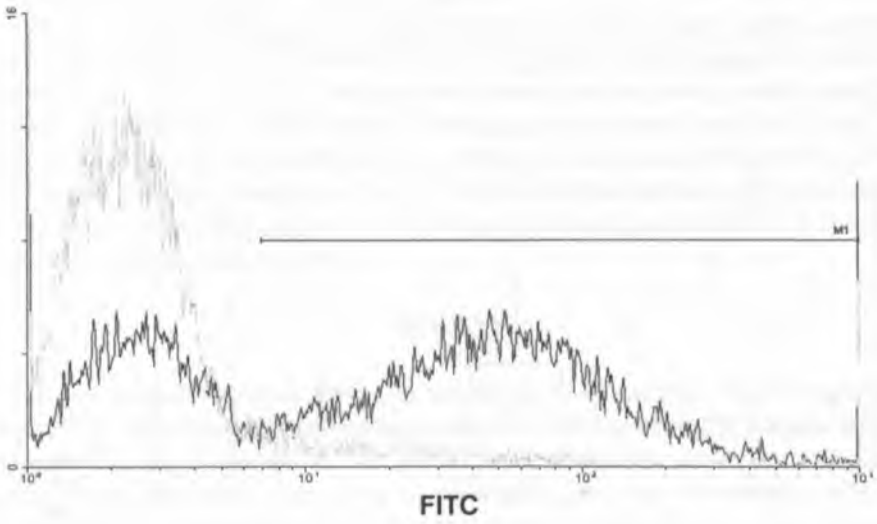

Fig. 3. Histogram of typical monocyte phagocytosis (M1 gate) — 54.2%
(dark line — phagocytosis, grey line — control)

different phagocytic ability against different yeast species [9]. Similar situation could take place in phagocytosis of different bacteria, too. This could be the explanation of conflicting results of their and our studies.

It is very interesting to understand why lung cancer monocytes have aberrant phagocytosis. The most likely explanation of this phenomenon is tumour influence on peripheral blood cells probably via secreted chemo- or cytokines. On the other hand, smoking [10], malnutrition of these patients [8] and hypoxic influence [11] on the immune system could also be a partial explanation of this phenomenon. In our study the monocyte phagocytosis normalise in NSCLC patients 7 days after tumour removal, which could support the first hypothesis. It is worth mention that impaired phagocytosis could influent upon derivation, maturation and antigen presentation of dendritic cells. This must deeply change not only immune response against bacteria or fungi, but against neoplastic cell as well.

CONCLUSION

In conclusion we want to state that phagocytic activities of monocytes of NSCLC are slightly decreased. This can explain partly the inflammatory complication in NSCLC patients.

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STRESZCZENIE

Ostatnie doniesienia w literaturze światowej niedwuznacznie sugerują supresyjny wpływ różnych nowotwór na układ immunologiczny człowieka. W naszych badaniach chcieliśmy ocenić stan obrony niespecyficznej u pacjentów z niedrobnokomórkowym rakiem płuca. W tym celu zmierzyliśmy fagocytozę *E. coli* przez monocyty u 26 pacjentów z niedrobnokomórkowym rakiem płuca (przed i 7 dni po zabiegu operacyjnym) oraz u 15 zdrowych dawców krwi. Stwierdziliśmy, że odsetek monocytów fagocytujących *E. coli* był statystycznie istotnie niższy u pacjentów przed zabiegiem operacyjnym, niż u zdrowych dawców krwi. Co więcej zbliżał on się do wartości prawidłowych już w 7 dni po operacji. Średnia intensywność fluorescencji (odzwierciedlająca średnią ilość *E. coli* zfagocytowanych przez monocyt) nie różniła się statystycznie istotnie pomiędzy badanymi grupami. Podsumowując należy stwierdzić, że fagocytoza monocytów jest zaburzona u pacjentów z niedrobnokomórkowym rakiem płuca.