

EFFECTS OF RADIATION THERAPY ON BLOOD-BORNE LEUCOCYTES IN PATIENTS WITH MAMMARY CARCINOMA

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Ionizing radiation is well known to cause changes in the bone marrow and peripheral blood, among other things in leucopenia (LAWRENCE et coll. 1948, JACOBSON et coll. 1949, BOND et coll. 1965, LEHAR et coll. 1966). The leucopenia is mainly attributed to a reduction in blood-borne lymphocytes and segmented neutrophils. ELVES (1970) has shown that antecedents to macrophages in the blood are highly resistant to irradiation in the rat, and it has earlier been revealed (REBUCK et coll. 1961, VOLKMAN & GOWANS 1965, VOLKMAN 1966) that the blood-borne precursor to the macrophages probably takes the form of a small mononuclear cell or monocyte. LEHAR et coll. presented the results of focal human bone marrow irradiation in nine patients; the number of blood-borne monocytes remained virtually unchanged during the irradiation. The same findings were reported by RENNER & HASSENSTEIN (1972).

The present report describes the changes in the amount of blood-borne leucocytes in patients with mammary carcinoma after external radiation therapy.

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Table 1*Leucocyte changes after operation in 12 patients. Differences not significant*

Cell type	No. of cases			Mean of individual leucocyte differences	
	Increase	Decrease	Unchanged	Mean, per cent	SE
Juvenile neutrophils	4	7	1	-0.6	0.6
Segmented neutrophils	5	6	1	-1.6	1.9
Eosinophils	7	5	0	+0.7	0.5
Basophils	4	4	4	0	0.2
Lymphocytes	6	6	0	+0.9	1.8
Monocytes	7	5	0	+0.6	1.0
Total, absolute values	8	4	0	+180	510

Material and Methods

The material consisted of 48 female patients from Radiumhemmet's series of mammary carcinoma, randomly selected so that 33 received preoperative (group A) and 15 postoperative irradiation (group B).

White blood cells were counted under standardized conditions 0 to 21 days (mean 14.8) before and 10 to 21 days (mean 14.0) after end of treatment. For group A, the postirradiation values were obtained before any surgical intervention had been undertaken, and for group B the time interval between the operation and the preirradiation leucocyte counts was at least three weeks. In 12 of the 15 patients in group B, the leucocytes were also determined immediately before and 21 to 49 days (mean 26.0) after the operation, but before radiation therapy.

The leucocytes were stained with May-Grünwald-Giemsa and the total number of leucocytes and their percentage differential were determined. For practical reasons, there was no possibility to have all the tests counted in the morning with the patients fasting. In a single case, the blood tests before and after the radiation therapy were performed at the same time of the day in order to minimize the changes in the leucocyte count during the day. The patients had a mean age of 55 years, the youngest being 36 and the oldest 70 years of age; 25 had a left-sided and 23 a right-sided carcinoma.

The dose given was 4 500 rad to the mammary, axillary and supraclavicular regions with a tumour dose of 175 rad at each irradiation. For the preoperative group, ^{60}Co was used throughout and the mammary gland was irradiated using two opposed wedge-fields; for the postoperative group the axillary and supra-

Table 2*Number of leucocytes before radiation therapy in 48 patients*

Cell type	Absolute number		Relative number	
	Mean value	SE	Mean, per cent	SE
Juvenile neutrophils	240	27	3.9	0.4
Segmented neutrophils	3160	177	51.2	1.4
Eosinophils	190	19	3.3	0.3
Basophils	50	5	0.8	0.1
Lymphocytes	2000	502	34.1	1.4
Monocytes	390	36	6.7	0.5
Total	6030	229	100.0	

clavicular regions were irradiated with ^{60}Co and the thoracic region with electrons having a mean energy of 12.5 MeV (10—15 MeV). The mammary regions received the prescribed dose in 5 weeks and the total irradiation time for both groups was 48 days (37—52). There was no significant difference as regards irradiation time between groups A and B. Using the data presented by MECHANIK (1926) it was estimated that approximately 10 per cent of the bone marrow was included in the treatment area. Thus, the major part of the radiation dose is given to the blood-borne leucocytes.

The statistical calculations were performed using the Student's t-test.

Results

No significant change in the number and relative differential of the leucocytes was observed in group B postoperatively as compared with preoperative values (Table 1). The results of tests before irradiation are given in Table 2. No significant differences were observed between the pre- and postoperative groups of patients regarding the number of leucocytes and their percentage differential before radiation therapy.

As expected, a significant reduction ($p < 0.001$) in the total number of blood-borne leucocytes was observed after irradiation. This was due to the reduction in lymphocytes ($p < 0.001$) and segmented neutrophils ($p < 0.001$, Table 3). The number of juvenile neutrophils, eosinophils, basophils and monocytes for the combined group of patients remained virtually constant after radiation therapy. No significant difference between patients with right- and left-sided carcinomas, respectively, is evident in Tables 1, 2 and 3.

A comparison was also made of the difference in the relative differential of

Table 3*Leucocyte changes after radiation therapy in 48 patients. Absolute numbers*

Cell type	No. of cases			Mean of individual leucocyte differences		Significance of the difference, p
	Increase	Decrease	Un-changed	Mean	SE	
Juvenile neutrophils	27	21	0	+19	33	—
Segmented neutrophils	12	36	0	—733	175	< 0.001
Eosinophils	22	25	1	+1	25	—
Basophils	23	24	1	+7	10	—
Lymphocytes	1	47	0	—1127	87	< 0.001
Monocytes	26	22	0	+21	36	—
Total	4	44	0	—1812	266	< 0.001

the leucocyte values before and after irradiation. For the lymphocytes, a highly significant reduction was observed ($p < 0.001$). A highly significant increase ($p < 0.001$) of the juvenile and segmented neutrophil and monocyte cells occurred. Eosinophil and basophil values were significantly increased ($p < 0.01$ and $p < 0.05$, respectively, Table 4).

Discussion

In the peripheral blood monocytes are considered to be the most difficult cells to differentiate from other leucocytes and especially from neutrophils and me-

Table 4*Leucocyte changes in per cent after radiation therapy in 48 patients*

Cell type	No. of cases			Mean of individual leucocyte differences		Significance of the difference, p
	Increase	Decrease	Un-changed	Mean	SE	
Juvenile neutrophils	32	10	6	+2.3	0.5	< 0.001
Segmented neutrophils	35	13	0	+5.5	1.4	< 0.001
Eosinophils	28	12	8	+1.5	0.5	< 0.01
Basophils	25	13	10	+0.4	0.2	< 0.05
Lymphocytes	4	44	0	—13.0	1.4	< 0.001
Monocytes	37	10	1	+3.3	0.6	< 0.001

dium-sized or large lymphocytes (DIGGS et coll. 1954, COPENHAVER & JOHNSON 1958). A percentage increase in juvenile and segmented neutrophils and monocytes might then be of importance in immunologic investigations as the results are often given as stimulation values for a certain number of lymphocytes. Thus, a false value might be obtained if the lymphocytes are not properly isolated from the monocytes, as may occur for instance when lymphocyte stimulation values before and after radiation therapy are compared.

Several authors have reported an increase in the number of peripheral eosinophils after irradiation, especially when treating the abdominal region (MORCZEK & CHRISTOPH 1958, CHONÉ & FUCHS 1969). On the other hand, unchanged or decreased eosinophil counts have also been reported (SPIETHOFF 1930, PARLAVECCHIO 1940, RENNER & HASSENSTEIN). In the present material no significant differences were observed after irradiation in the number of eosinophils, basophils and monocytes, nor any significant change in the number and relative distribution of the leucocytes in group B postoperatively as compared with the preoperative values after irradiation. As no difference was found between right- and left-sided carcinomas, it is hardly conceivable that the position of the thoracic duct would influence the results obtained.

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SUMMARY

The results of absolute and relative leucocyte counts in 48 pre- or postoperatively irradiated patients with mammary carcinoma have been evaluated. A reduction in the number of lymphocytes and segmented neutrophils occurred whereas the juvenile neutrophils, eosinophils, basophils and monocytes remained unchanged. In the differential leucocyte counts, a significant increase of juvenile and segmented neutrophils, monocytes, eosinophils and basophils was encountered, however. These results may be of importance in immunologic investigations when lymphocyte stimulation values before and after irradiation are evaluated.

ZUSAMMENFASSUNG

Die Ergebnisse der absoluten und relativen Leukozytenwerte bei 48 prä- oder postoperativ bestrahlten Patienten mit einem Brustkarzinom sind zusammengestellt worden. Es trat eine Verringerung der Zahl der Lymphozyten und segmentförmigen Neutrophilen auf, während die jungen Neutrophilen, Eosinophilen, Basophilen und Monozyten unverändert blieben. Bei den Differential-Leukozytenwerten stiegen die jungen und segmentförmigen Neutrophilen, Monozyten, Eosinophilen und Basophilen jedoch. Diese Ergebnisse mögen von Bedeutung in immunologischen Untersuchungen sein, wenn Lymphozyten-Stimulierungswerte vor und nach Bestrahlung festgestellt werden.

RÉSUMÉ

L'auteur examine les résultats de numérations leucocytaires absolue et relative chez 48 malades atteintes de cancer du sein et irradiées avant ou après l'opération. Il a constaté une réduction du nombre des lymphocytes et des neutrophiles segmentés alors que les neutrophiles jeunes, les éosinophiles, les basophiles et monocytes restent sans changement. Il a constaté cependant dans la numération leucocytaire différentielle une augmentation significative des neutrophiles jeunes et segmentés, des monocytes, des éosinophiles et des basophiles. Ces résultats peuvent être d'importance dans des études immunologiques pour évaluer les valeurs de stimulation lymphocytaire avant et après irradiation.

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