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**Cancer Cells in the Circulating Blood of Patients with Larynx Cancer.
Part II. Results — Clinical Groups B and C**

Krążące komórki nowotworowe we krwi żylniej chorych z rakiem krtani. Cz. II.
Wyniki — grupy kliniczne B i C

Свободно циркулирующие клетки злокачественной опухоли в венозной крови больных
раком гортани. Ч. II. Результаты — клинические группы B и B

In this group consisting of 45 patients with laryngeal cancer, f.t.c. were searched for in peripheral venous blood before and after (5—7 days) radical surgery — total laryngectomy, mostly with a dissection of the system of cervical and lymphatic vessels by using the method of Jawdyński-Crile, and in the blood draining from the tumour during operation. To give a clearer comparison of the results of the studies on f.t.c. carried out in successive investigation periods in connection with the clinical data of the subgroups observed, the patients of this group (B) were divided into two subgroups (B₁, B₂).

Subgroup B₁ — 28 persons in which free cancer cells were found in the peripheral venous blood on primary examination before surgical treatment. The clinical condition of the patients of this group and the results of the studies on the presence of f.t.c. in the blood carried out in the successive periods are presented in Table 1.

Subgroup B₂ — 17 persons in whom f.t.c. were not found in the peripheral venous blood on primary examination preceding surgical treatment. The patients clinical condition of this group and the results of the tests for f.t.c. in the successive periods are shown in Table 2. The results of the studies on the occurrence of f.t.c. in the blood of the group of patients treated surgically (jointly for both groups), and the dynamics of changes of the investigation results (in percents) in the successive periods are graphically presented in Fig. 1. The percentage of positive results of the tests for f.t.c. in the blood of the patients examined "++" (numerous cancer cells in the sample from 5 to 10 rarely more) found before the operation was 22%, and it increased to 67% during the operation, and decreased to 4% after surgical treatment. The analogically summarized percentage of positive results of the tests for f.t.c. denoted by "+" (few cancer cells in the sample from 1—5) was 40% before the operation; it decreased to 26% during the operation, and decreased to 18% after surgical treatment. The percentage of negative results (lack of f.t.c. or typical cells) decreased from 38% before the operation to 7% during the operation and it increased considerably to 78% in 5—7 days after the operation.

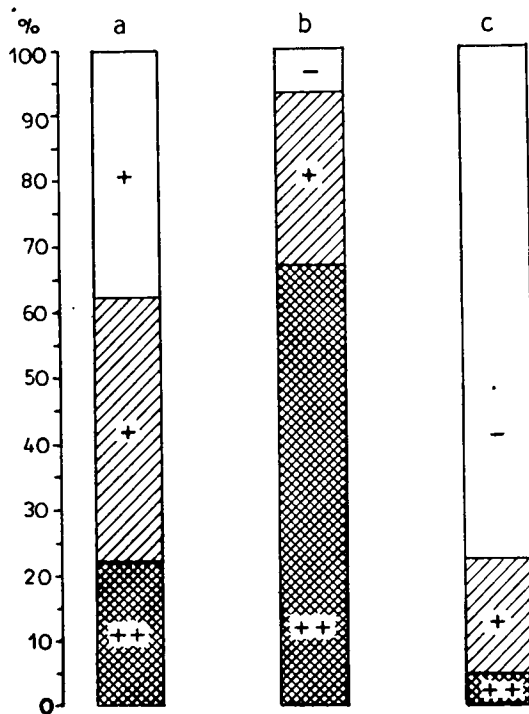


Fig. 1. Distribution of f.t.c. in the blood examined: a — before the operation, b — during the operation, c — 5—7 days after the operation. Results: —: lack of cancer cells, atypical or doubtful cells with regard to malignancy; +: malignant cancer cells, a few — up to 5 in a sample; ++: malignant cancer cells, 5—10 or more in a sample

The influence of the postoperative trauma on the dissemination of f.t.c. into the draining blood was also studied. Among 28 operated patients (Table 1) with f.t.c. present in the blood before the operation, no decrease in the percentage of positive results was observed during the operation. In 16 patients operated the number and level of positive results did not change, whereas in 29 operated persons (83%) of 35 patients in whom no f.t.c. or only a few of them were found in the blood before the operation — an increase in the percentage of positive results and their level ("++" → "++") was observed. This increase was statistically highly significant ($\chi^2=15,11$; $P<0,001$) and it showed a variable dependence of the influence of postoperative trauma on increased dissemination of f.t.c. into the blood draining from the tumour during the operation (Klonowski, 1972).

In this group of patients the influence of surgical treatment on the dissemination of f.t.c. into peripheral venous blood was also traced (Klonowski, 1972). Among 45 persons tested for the presence of f.t.c. in venous blood during 5—7 days after the operation, an increase in the percentage of positive results and their levels was only observed in 2 patients in the direct post-operative period. In 22 persons, no changes in the tests for f.t.c. were found, whereas in 21 patients after the operation a decrease in the percentage of positive results and their

Table 1. The distribution of f.t.c. in peripheral blood and in blood draining from tumour before, during and 5-7 days after radical surgery (total laryngectomy) in 28 patients — group B₁ — according to the state of clinical advancement of the disease (TNM), to the site of origin of larynx cancer and the stage of its clinical malignancy

Clinical advancement		Results of searching for f.t.c.	Before operation - in peripheral blood						During operation - in blood draining from tumour						5-7 days after operation - in peripheral blood				
			SITE OF ORIGIN OF LARYNX CANCER												Subgroup A without clinical recurrence		Subgroup B with clinical recurrence		
			Supraglottis			Glottis			Supraglottis			Glottis			Results of searching for f.t.c.		Total		
			Stage of histological malignancy			Total			Stage of histological malignancy			Total			positive	negative			
Stage	TNM	1°	2°	3°	Total	1°	2°	3°	Total	1°	2°	3°	Total	positive	negative	positive	negative		
		++	+	-	++	+	-	++	+	-	++	+	-	++	+	-	++	+	
II°	T ₃ N ₀ M ₀	++																	
		+		1	1														
		-																	
Total				1	1														
III°	T ₃ N ₁ M ₀	++	1	3	4	1	1	5	7	6	13	1	3	4	17		2	2	
		+	1	6	4	11	2	2	4	15	1	1	2	1	1	3	2	2	4
		-															14		14
Total			1	7	7	15	2	3	5	20	1	7	7	15	2	3	5	20	
IV°	T ₄ N ₁ M ₀	++			1	1			1	1	1	2			2				
		+	1													1		1	
		-															1		1
	T ₃ N ₂ M ₀	++	1	1	2			2	1	1	1	3			3				
		+	1															1	1
		-															2		2
T ₄ N ₂ M ₀	++	1					1	1		1				1					
	+																1	1	
	-																		
Total			3	1	2	0			6	3	1	2	0		6		1	4	
Total (I°+II°+III°+IV°)			4	9	9	22	3	3	0	21	4	9	9	22	3	3	0	28	
%			14	32	32	78	11	11	22	100	14	32	32	78	11	11	22	100	

levels ("++" → "+") was found. In the group of 21 patients (75%) of 28 operated persons. Tab. 1), in whom no f.t.c. in the blood ("+" or "++") were found before the operation, a decrease in the percentage of positive results and the level of positive results was observed after the operation; this decrease operation was observed only in 2 operated persons, and lack of changes in before the operation, an increase in the number of f.t.c. in the blood after the was statistically highly significant ($\chi^2=8,33$; $P<0,01$). Among 35 patients in whom no f.t.c. in the blood on only few in the sample ("++"), were found positive results and their level — in 21 persons operated (60%).

In the clinical group A as well as in group B, the presence or lack of f.t.c. in the blood after surgical treatment was not analysed with regard to the criteria concerning the methods and technique of this group of patients (group B), f.t.c. were not usually found in the peripheral blood from the 5th — 7 th

Table 2. The distribution of f.t.c. in peripheral blood and in blood draining from tumour before, during and 5-7 days after radical Surgery (total laryngectomy) in 17 patients — group B₂ — according to the stage of clinical advancement of the disease (TNM), to the site of the origin of larynx cancer and to the stage of its clinical malignancy.

Clinical advancement	Stage	TNM	Before operation - in peripheral blood						During operation - in blood draining from tumour						5-7 days after operation - in peripheral blood				Total			
			SITE OF ORIGIN OF LARYNX CANCER												Subgroup A without clinical recurrence		Subgroup B with clinical recurrence					
			Supraglottis			Glottis			Supraglottis			Glottis			Positive		Negative					
			Stage of histological malignancy			Total			Stage of histological malignancy			Total			Results of searching for F.t.c.		Total					
1*	2*	3*	Total	1*	2*	3*	Total	1*	2*	3*	Total	1*	2*	3*	Total	Positive	Negative	Positive	Negative			
															++	+	-	++	+	-		
II*	T ₂ N ₀ M ₀	++																				
		+																				
		-	1		1	1	1	2	3	1		1	1	1	2	3			3			3
	T ₃ N ₀ M ₀	++								1		1	2			2						
		+												1		1						
Total		2	1	3	2	1	3	6	2	1	3	2	1	3	6			6			6	
III*	T ₃ N ₁ M ₀	++							1		1				1							
		+							2	3	5	1	1	2	7							
		-	3	3	6	1	1	2	6										6			6
	Total	3	3	6	1	1	2	6	3	3	6	1	1	2	6			6			6	
IV*	T ₄ N ₁ M ₀	++							1		1				1							
		+																		1	1	
		-	1		1			1														
	T ₃ N ₂ M ₀	++							1		1				1							
		+												1		1						
Total		2		2	1		1	3	2		2	1		1	3			2	1		3	
Total (II* III* IV*)		L	7	3	1	11	4	2	6	17	7	3	1	11	4	2	6	17		16	1	17
		%	40	18	6	64	24	12	36	100	40	18	6	64	24	12	36	100		94	6	100

day following the operation; positive results of the determinations after the operation were found only in 10 patients (22%) of this group. Among them were: three persons in whom surgical treatment did not result in cure, they died within a year; five patients who were treated by radiation during one year after the operation because of a clinical recurrence of the disease, and two patients post-operatively treated with X-rays without any success, and over a year's observation f.t.c. were still present in their blood.

Clinical Group C

In this group consisting of 40 persons after the surgical treatment of larynx cancer — total laryngectomy, mostly with a dissection of the cervical lymphatic system, f.t.c. were searched for in the peripheral venous blood in the

Table 3. The stage of clinical advancement of the disease (TNM) in comparison with the site of origin of larynx cancer and its histological malignancy determined before total laryngectomy in 40 patients — group C — examined for f.t.c. in peripheral blood 1–5 years after the surgery

Clinical advancement before treatment		THE SIDE OF ORIGIN OF LARYNX CANCER												
		Supraglottis (AB)			Glottis (C)			Total (ABC)			Total			
		Stage of histological malignancy											Total	
Stage	TNM	1°	2°	3°		1°	2°	3°		1°	2°	3°	L	%
II°	T ₂ N ₀ M ₀		2		2	2	3		5	2	5		7	18
	T ₃ N ₀ M ₀		4		4		2	1	3		6	1	7	18
	Total		6		6	2	5	1	8	2	11	1	14	36
III°	T ₂ N ₁ M ₀	1			1					1			1	2
	T ₃ N ₁ M ₀	5	5	8	18	3	1		4	8	6	8	22	55
	Total	6	5	8	19	3	1		4	9	6	8	23	57
IV°	T ₄ N ₁ M ₀	1			1					1			1	2
	T ₃ N ₂ M ₀	1	1		2					1	1		2	5
	Total	2	1		3					2	1		3	7
Total (II°+III°+IV°)		L	8	12	8	28	5	6	1	12	13	18	9	40
		%	20	30	20	70	13	15	2	30	33	45	22	100

period from 1 to 5 years after the treatment. The clinical condition of this group before the surgical treatment of the laryngeal cancer is presented in Table 3. The results of the tests for the presence of f.t.c. in the peripheral blood of these patients compared with the stage of clinical advancement of cancer before the surgical treatment and the actual clinical condition in the control period are shown in Table 4. In this group the occurrence of f.t.c. in the peripheral venous blood and symptoms of clinical recurrence were traced. In the subgroup with clinical symptoms of recurrence (Table 4) in all patients examined (5 persons), f.t.c. were found in peripheral blood, whereas only in one patient (2,5%) out of 35 observed f.t.c. were found in the blood without symptoms of clinical recurrence. This difference is statistically highly significant ($\chi^2=32,38$; $r=0,90$; $P<0,001$) — (Klonowski, 1971). Among 5 patients with clinical symptoms of tumour recurrence after surgical treatment, in whom f.t.c. were found in the blood, 2 of them died in 2 years and 3 of them in a year.

In one person of this group (Table 4) f.t.c. were found in peripheral blood in the fourth year of observation after surgical treatment of larynx cancer and without clinical recurrence of the tumour; they occurred in three successive determinations, but the patient vanished from observation after the third test.

Table 4. The distribution of f.t.c. in peripheral blood of 40 laryngectomized patients — group C — examined 1—5 years after total laryngectomy according to its actual clinical condition and to the stage of clinical advancement of the disease (TNM) determined before treatment

Clinical advancement before treatment		SUBGROUP A without clinical recurrence				SUBGROUP B with clinical recurrence				total		
		Results of searching for f. t. c. in peripheral blood										
		positive			negative	total	positive				negative	total
Stage	T N M	+	+	+	-		+	+	+	-		
II*	T ₂ N ₀ M ₀				6	6						14
	T ₃ N ₀ M ₀				8	8						
	total				14	14						
III*	T ₂ N ₁ M ₀				1	1						23
	T ₃ N ₁ M ₀			1	17	18	4				4	
	total			1	18	19	4				4	
IV*	T ₄ N ₁ M ₀								1		1	3
	T ₃ N ₂ M ₀				2	2						
	total				2	2			1		1	
Total (II*+III*+IV*)		L		1	34	35	4	1			5	40
		%		2,5	85	87,5	10	2,5			12,5	100,0

It was a remarkable thing, that in this group of 40 persons tested for f.t.c. in the peripheral blood in the period of three years (1969—1972) and remaining under observation from 1 to 5 years after surgical treatment of larynx cancer, recurrences of the disease were observed only in 5 controlled persons — of whom two died, two lived with symptoms of clinical recurrence and the fate of one person was unknown. It should be stressed however, that these observations are not conclusive for the evaluation of the results of treatment, because they concern a selected group. However, the comparison of the clinical conditions of the patients of this group (C) after operation with their positive results of tests for f.t.c. in peripheral blood is very interesting and statistically significant. This, however, concerned the phenomenon of f.t.c. occurrence in the blood of the group of patients being after primary radical surgical treatment which consisted in total laryngectomy with dissection of the cervical lymphatic system according to the methods used in radical treatment of larynx cancer.

REFERENCES

1. Klonowski St.: Badania nad występowaniem i znaczeniem wolnych komórek nowotworowych w krwi chorych na raka krtani. Druk. UMCS, Lublin 1972.

STRESZCZENIE

Przedstawiono wyniki badań na obecność w.k.n. w krwi 45 chorych na raka krtani — grupa B, leczonych operacyjnie. Podano również wyniki badań na obecność w.k.n. w krwi 40 osób kontrolowanych w okresie od 1 roku do 5 lat po radykalnym operacyjnym leczeniu raka krtani.

РЕЗЮМЕ

Представлено результаты исследований на наличие с.к.о. в крови 45 больных раком гортани — группа Б, подвергшихся хирургическому лечению, а также результаты исследований на наличие с.к.о. в крови 40 лиц контролируемых по истечении 1 до 5 лет после радикального хирургического лечения рака гортани.

