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RELATION OF MALIGNANT TUMOR TO PROSTACYCLIN AND THROMBOXANE

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The level of 6-keto-$PGF_{1\alpha}$ and thromboxane B_2 (TXB_2) in plasma was determined with radioimmunoassay in 58 normal subjects and 92 patients with various cancers (including lung, hepatic, gastric, esophageal and pancreatic carcinoma). The results showed that 6-keto-$PGF_{1\alpha}$ in plasma was 10.21±2.75 Pg/ml, and TXB_2 146.03±37.31 Pg/ml in normal individuals, the ratio of 6-keto-$PGF_{1\alpha}$ to TXB_2 was 0.07; while in cancer patients 6-keto-$PGF_{1\alpha}$ was 27.5±16.9 Pg/ml and TXB_2 315.4±173.4 Pg/ml, the ratio of 6-keto-$PGF_{1\alpha}$ to TXB_2 was 0.08. The values of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma of cancer patients were 2.69 folds and 2.16 folds higher than that of the two groups, respectively. The difference between the two groups was statistically significant ($P<0.01$). It indicates that, the synthesis and release of PGI_2 and TXA_2 of cancer tissues increases greatly as compared to the normals.

The study also revealed that the size of tumor, metastasis and histological classification had no obvious relation to PGs.

Key words: Prostaglandin, Prostacyclin, Thromboxane, Arachidonic acid

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Up to now no conclusion can be made about the relationship between malignant tumor and prostaglandin. Since Prostacyclin (PGI_2) and Thromboxane (TXA_2) were discovered as derivatives of arachidonic acid in the mid-term of 1970s, the pathogenesis of some diseases such as coronary atherosclerosis, hypertension, diabetes mellitus and pulmonary hypertension etc. have been gained new recognition. All of the above-mentioned disease have relation to the imbalance of PGI_2 and TXA_2. Little is known about the role of PGI_2 and TXA_2 within human malignant tumors. PGI_2 and TXA_2 are unstable, their half-lifes are 3 minutes and 30 seconds respectively, and rapidly degrade into nearly inactivated 6-keto-$PGF_{1\alpha}$ and TXB_2. In order to analyses the change of PGI_2 and TXA_2 within patients of malignant tumor, the contents of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma were determined by radioimmunoassay in normal subjects as well as in patients with malignant tumors.

MATERIALS AND METHODS

Objects to Be Examined

Normal Individual Group

A total of 58 blood donors as control, 41 members were male and 17 female. Ages ranged from 20 to 53 years and averaged 34.8 years.

Patients with Malignant Tumor Group

Ninety-two patients with various cancer were studied. Among them, 43 are with lung cancer, 29 with hepatic cancer, 11 with gastric cancer, 3 with esophageal cancer, 3 with pancreatic cancer, 1 with ileocecal cancer, 1 with duodenal cancer and 1 with mesenteric liposarcoma.

Methods

Venous blood 3 ml was taken by silicified syringe, and then poured into the silicified glass tube, 2% EDTA (1:9) was added for prevention of coagula-tion and separation of blood plasma. The tube should be kept under -20°C for determination.

The concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma was determined by RIA in order to reflect the levels of PGI_2 and TXA_2.

PGI_2 and TXA_2 kits were supplied by Thrombus RM, Institute of Blood Diseases, Suzhou Medical College. See instruction of the kits for operation.

RESULTS

Determined Results (Table 1)

The results revealed that the contents of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma of cancer patient group were 2.69 folds and 2.16 folds notably higher than those of normal subjects group ($P<0.01$), respectively. The positive rate of 6-keto-$PGF_{1\alpha}$ was 67.6% (exceeding the normal value by $\bar{x}+2s$), 76.9% (exceeding $\bar{x}+1s$), and that of TXB_2 was 60% (exceeding $\bar{x}+2s$), 75.4% (exceeding $\bar{x}+1s$) respectively.

Relation of Cancer Size to PGs (Table 2)

Table 2 showed that the longitudinal meridian of cancer had no relation to the concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2.

Table 1. Concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma in normal subjects and cancer patients

Group	No. of cases	$PGF_{1\alpha}$ TXB_2	6-keto-$PGF_{1\alpha}$ (Pg/ml)			TXB_2 (Pg/ml)		
			$\bar{x}\pm s$	Increasing folds	P value	$\bar{x}\pm s$	Increasing folds	P value
Normal subjects	58	0.07	10.21± 2.75			146.03± 37.31		
Cancer patients	92	0.08	27.5± 16..9	2.69	$P<0.01$	315.4± 173.4	2.16	$P<0.01$
lung cancer	43	0.09	26.1± 18.7	2.56	$P<0.01$	306.6± 178.7	2.10	$P<0.01$
liver cancer	29	0.10	36.9± 19.1	3.61	$P<0.01$	366.5± 175.4	2.51	$P<0.01$
gastric cancer	11	0.06	18.0± 8.9	1.76	$P<0.05$	296.6± 162.5	2.03	$P<0.05$
esophageal cancer	3		18.1± 7.1	1.77		202.7± 43.6	1.39	
pancreatic cancer	3		10.2± 9.9			228.8± 246.7		
ileocecal cancer	1		33.4			250.0		
duodenal cancer	1		11.6			273.8		
mesenteric liposarcoma	1		15.1			126.8		

Table 2. Relation of tumor size to PGs

Diameter of tumor	No. of cases	6-keto-$PGF_{1\alpha}$ (Pg/ml)	TXB_2 (Pg/ml)
<2 cm	6	17.6± 7.5	257.7± 122.0
2 – 5 cm	14	16.8± 7.7	255.2± 124.7
5 – 10 cm	17	21.4± 11.6	251.8± 127.7
>10 cm	7	24.6± 12.8	303.3± 167.8
P value		*P*>0.05	*P*>0.05

Relation of Cancer Metastasis to PGs (Table 3)

Based on the partial cases of lung cancer proved by pathologic diagnosis no affirmative correlation existed between the concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2 to tumor metastasis or absence of metastasis.

Relation of Pathological Type to PGs (Table 4)

In our data, taking the partial patients with lung cancer verified by pathological diagnosis, for example, there was no obvious relation between pathological types and the concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2.

Table 3. Relation of tumor metastasis to PGs

Group	No. of cases	6-keto-$PGF_{1\alpha}$ (Pg/ml)	TXB_2 (Pg/ml)
Metastasis	17	17.1± 8.4	277.2± 144.7
No metastasis	18	18.1± 7.2	200.3± 55.5
P value		*P*>0.05	*P*>0.05

Table 4. Relation of pathologic classification (in partial lung cancer) to PGs

Histological type	No. of cases	6-keto-$PGF_{1\alpha}$ (Pg/ml)	TXB_2 (Pg/ml)
Small cell car.	4	20.2± 7.4	263.3± 92.5
Undifferentiated car.	2	19.8± 5.5	256.6± 49.2
High-differentiated squamous cell car.	5	20.7± 9.1	293..5± 102.6
Low-differentiated squamous cell car.	2	27.0± 8.7	235.7± 26.2
High-differentiated adeno-car.	6	17.7± 10.1	269.0± 93.9
Low-differentiated adeno-car.	3	21.3± 7.8	277.2± 88.7
Adenoid cystic car.	1	18.2	128.0
Unclassified (biopsy)	11	19.6± 11.2	227.0± 102.5
P value		*P*>0.05	*P*>0.05

DISCUSSION

This study showed that the concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma of patients with lung cancers, hepatic cancers and gastric cancers etc. was remarkably higher than that of the normal subjects. This result is in accordance with most authors' study. It is clear that cancer tissue could synthesize and release PGI_2 and TXA_2 in large amounts. Therefore, we consider that determination of the concentration of 6-keto-$PGF_{1\alpha}$ and TXB_2 in plasma in conjunction with clinical and related laboratory data could raise the detactable rate of cancer. It would be beneficial to the diagnosis of malignant tumors.

As for the PGs and malignant tumor correlation, in other words, cancer tissue can produce a large amounts of PGs which acts on the cancer cells as well as the host cells are still not fully understood.[1-3] Some authors maintain that PGs synthesis increase represent a portion of reaction of tumor growth restricted by the internal environment; while other authors claim that the PGs plays an important role in the tumor occurrence and development. Very interestingly, Honn et al. pointed out that the tumor cells could alter the balance between PGI_2 and TXA_2, i.e. the proportional value of PGI_2 to TXA_2 declined, so that it was liable to platelet aggregation. Laekeman[2] observed another result according to his study of 37 patients with breast cancer. He discovered that cancer tissue increases not only synthesized TXA_2, but also synthesized PGI_2, with PGI_2 increasing more than TXA_2. Our results were similar to that of Laekeman's study.

Our study revealed no obvious correlation between PGs and tumor size, metastasis and degree of malignancy, although others have their own opinions.

Bennett's[1] study had pointed out that PGs was released by tumor cells as well as host cells simultaneously, and within the same tumor there might be several sorts of PGs, for instance, human breast cancer can release a considerable amounts of PGs, including arachidonic acid, TXB_2, 6-keto-$PGF_{1\alpha}$, PGD_2, PGE_2 and $PGF_{2\alpha}$ etc. These substances had various functions, some of them may have a contrary action, such as cell hyperplasia, cell differentiation, host defense and tumor cell metastasis and so forth. In addition, some of PGs had relation to inflammation. Inflammation influencing to dissemination of cancer was variable, in mild inflammation there was liable to dissemination of cancer cells, but in severe inflammation could inhibit the cancer cells, therefore the correlation between PGs and tumors were very complex, the mechanism needed to be further studied.

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