INTERLEUKIN-2 AND TUMOUR NECROSIS FACTOR VALUES IN INTRACRANIAL TUMOURS

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SUMMARY

Tumour Necrosis Factor (TNF) and Interleukin-2 (IL-2) values were determined in 44 intracranial tumour patients pre-and postoperatively and compared with the values in 20 healthy persons and 14 with Behçet's disease, who were usde as the control group.

There was no significant difference in IL-2 values of the control group and preoperative values of the tumour group except for meningioma and acustic neurinoma. We think that macrophages and glycoaminogaycans which encapsulate the tumour prevent stimulation of T helpers by the tumour antigens, so IL-2 is not secreted from the T helpers.

Probably for the same reason we could not find significant TNF values between the control group and the preoperative tumour group. Postoperative decrease in IL-2 is considered to be the result of corticosteroids used for 7 days. Increased TNF values in the postoperative tumour group can be due to the breakdown of the glycoaminoglycan barrier and stimulation of macrophages by the tumour antigens.

KEY WORDS:

Intracranial tumour, tumour necrosis factor, interleukin-2.

INTRODUCTION

Immunohistological studies have demonstrated that central nervous system CNS tumours are infiltrated with mononuclear cells (TIL), most of which are T lymphocytes or macrophages (6,9,15).

Central nervous tissue has special histochemical and histological characteristics which differ from other tissues. There some defects in the afferent and efferent pathways of immunological reaction. This property of the system causes a unique immunological reaction (1,7,11,13,20).

Microglias are a special form of reticuloendothelial cells and an analogue of macrophages (6,9).

Extra cranial tumors show 15 % brain metastase whereas extracranial metastase of intracranial tumours are very rare (8,9).

In this study we investigated the tumour necrosis factor (TNF) and interleukin-2 (IL-2) levels in blood samples both pre-and postoperatively in 44 cases with different intracranial tumours.

Our results are compared and discussed in the light of current literature concerning tumour immunology.

MATERIALS AND METHODS

Venous blood samples from 44 intracranial tumour cases were taken one day prior to and

7 days following the operation. Supernatants were separated immediately and stored at 20°C. IL-2 values were determined using a radioimmunossay kit (IL-2, RIA, ILE, Medgenix, Flercus, Belgium) and expressed as U/ml.

TNF values were determined by using a TNF-alfa, IRMA, Medgenix Brussels-Belgium kit and expressed as pg/ml.

Each patient received 16 mg/day dexamethasone for 7 days, beginning 2 days before the operation. TNF and IL-2 values of 20 healthy persons and 14 with Behçet's disease were used as the control group. Statistical analyses were obtained with the aid of an IBM 4361-3 system s2-x 2.1 pocket programme.

RESULTS

We investigated 44 intracranial tumour patients (13 women and 31 men) with a mean age 44.7 years.

Twenty healthy persons (11 women, 9 men) with a mean age of 33.3 and 14 Behçet's disease patients (11 men, 3 women) with a mean age of 36 were used as the control group.

Histological distribution of the tumours was as follows: glioblastoma multiforme 10, oligodendroglioma 5, pituitary adenoma 5, medulloblastoma 3, pinealoma 2 craniopharyngioma 3, astrocytoma grades I, II: 4, meningioma 5, acustic neurinoma 3, metastase (adenocarcinoma) 3.

IL-2 and TNF levels of the control and tumour groups both pre and postoperatively are shown in Table 1.

Table 1 :

Group	Number of cases	Mean age	Mean Values Of TNF Preop	Postop
Normal	20	33,3	14.546 ± 0.282	
Behçet's disease	14	37,6	116.485 ± 131.798	
Glioblastoma	10	53,0	14.48±0.721	14.842±1.26
Oligodendroglioma.	5	48,0	15.094±2.31	18.430±9.23
Pituitar adenoma	5	44,2	14.241±0.275	14.667±0.324
Medulloblastoma	3	11,3	14.258±0.631	14.680±0.54
Mature teratoma	1	18,0	14.206	14.625
Pinealoma	2	16,5	14.201±0.26	14.59±0.527
Astrocytoma I-II	4	27,5	15.26±2.05	21.945±14.82
Craniopharyngioma	3	22,0	14.432±0.288	14.804±0.187
Meningioma	5	38,1	14.219±0.123	17.021±1.24
Neurinoma	3	29,3	117.68±176.87	22.876±15.21
Metastatic adeno ca	3	65,6	31.73±20.17	15.25±0.235
			Mean values of IL - 2	
Normal	20	33,3	0.642 ± 0.262	
Behçet's disease	14	37,6	0.334 ± 0.167	
Glioblastoma	53,0	1.473±1.33	0.666±0.233	
Oligodendroglioma	5	48,0	0.926±0.267	0.99±0.425
Pituitary adenoma	5	44,2	0.298±0.15	0.393±0.15
Medulloblastoma	3	11,3	1.091±0.332	0.544±0.165
Mature teratoma	1	18,0	0.410	0.343
Pinealoma	2	16,5	0.947±0.042	0.56±0.184
Astrocytoma	4	27,5	0.933±0.533	0.925±0.236
Craniopharyngioma	3	22,0	0.625±0.153	0.615±0.178
Meningioma	5	38,1	1.054±0.099	0.745±0.190
Neurinoma	3	29,3	1.340±0.629	0.481±0.235
Metastatik	3	65,6	0.436±0.287	0.331±0.133

DISCUSSION

Cerebral tumors are infiltrated with lymphocytes which mostly accumulate in the periphery of the maas (3). These cells consist of T cells (70-80 %) and B cells (20-30 %) and B cells (20-30 %) (19). While corticosteroid therapy decreases the number of T helper cells (TH), it increases cytotoxic T cells (Tec) (1,3). We used 16 mg/day dexamethasone in our group of patients beginning 2 days before the operation and continuing for 7 days. We did not find any increase in IL-2 levels released from TH when compared with the control group. In glioblastoma, lymphocytes and macrophages were dominante among the TIL cells (9). The transforming growth factor (TGF) which is cesreted from these cells inhibits IL-2 secretion of TH (1,3,10,14,18). Decreased TH in the circulation causes decreased IL-2 secretion and insufficient function of B cells (1,6).

Most of intracranial tumours and especially glioblastomas secrete TGF, prostaglandin E2 (PGE2), PGF2, PGI2 and proteinkinase all of which suppress immune functions (10,11). We did not find any significant difference between the control group and the other intracranial tumours except meningioma and acoustic neurinoma in comparisons with IL-2 values (Table 1). This result might mean that the tumour antigens could not stimulate TH or the antigens and TH were not countered. If there were/had been any functional deficiency in TH or IL-2 caused by immuno-suppressive substances secreted by the tumour (1,9,14), we should have found compared with decreased preoperative IL-2 levels in comparison with the control group.

High IL-2 levels found in meningioma and acustic neurinoma can be due to the small number of cases, decreased secretion of suppressor factors or extraparenchymal localization of these tumours. Another factor for insufficent reaction of TH againts the tumour antigen can be macrophages which transform from microglia (6,16,19).

Macrophages probably disturb the immunological mechanism by secreting PGE2, PGI2 and leucotriens (1,2,15) and prevent extracranial metastasis by infiltrating the peritumoral and perivascular area (19). Brain tumours have strong angiogenic factors (20). Endothelial cells have the capacity to secrete many factors such as factor VIII angiotensin, convert enzyme, collagen, elastin, glicoaminoglycan and prostoglandins (5,7,12). Some of these factors initiate macrophages to infiltrate this area without the need for antigenic stimulation but only irritiating mitosis (5,15). Stimulation of the immunological mechanism by the endothelial cells is a factor that should be considered. TNF is the most important substance secreted by the macrophage (17).

TNF values can give an idea of the function of macrophages.

We could not find any significant differance between the control group and preoperative TNF values, except in the group with Behçet's disease. This result is considered to be due to the inability of macrophages to counter tumour antigens to be stimulated for TNF secretion. Probably the meeting of macrophages with tumour antigen is prevented by glycoamine which is secreted from the malignant gliomas and is a mucoplysaccaride character (6,14). As a matter of fact TNF values were found to increase after separation though this was not significant. This insignificant increase in TNF values can be due to the berakdown of the glycoaminoglycan barrier between the tumour and macrophages following the operation.

Roszman et al (14) report increased IL-2 values following brain tumour resection and explain it as the result of decreased secretion of immunosuppressive agents. In this study we observed a decrease in IL-2 values in the blood samples taken 6 days following corticosteroid therapy and 7 days after the operation. This observation can be correlated with the inhibition on TH function or lack of immunological stimulation due to the use of steroid (1).

Decreased IL-2 and increased TNF levels after operation can imply independent functions of TH and macrophages in immunological reactions.

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