

# VENTRICULAR CSF IMMUNOGLOBULINS IN BRAIN TUMOURS

Pages with reference to book, From 88 To 89

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## ABSTRACT

Ventricular CSF glucose, total protein, protein electrophoresis, IgG, IgA, IgM and CSF cytology were determined in thirty seven patients with brain tumours. CSF glucose was unchanged and total protein was significantly high. Protein electrophoresis showed higher albumin and gamma globulin fractions. Mean IgG and IgA were significantly higher (Pc 0.001) in malignant tumours than in benign ones. IgM was detectable in 7 of 37 cases. The higher concentration of total protein, albumin and gamma globulin shows some degree of impairment of blood brain barrier. Increased concentration of IgG, IgA and IgM indicates humoral immune response of the brain against the tumours (JPMA42: 88, 1992).

## INTRODUCTION

The brain has long been regarded as an immunologically privileged site and this essentially is due to the blood brain barrier and absence of lymphatic channels<sup>1</sup>. Later experimental and human studies on gliomas showed some immunologic response and the term suggested was changed to "brain is a partially privileged site"<sup>2,3</sup>. This study was carried out to see the humoral immune response of the brain against tumours by CSF electrophoresis and immunochemical analysis.

## PATIENTS AND METHODS

Thirty seven patients with brain tumours were selected from the department of neurosurgery, Lahore General Hospital, Lahore. There were 26 males and 11 females with ages ranging between 34 - 60 years. Selection was based on initial signs and symptoms of space occupying lesion in the brain and histological diagnosis after craniotomy. Cerebrospinal fluid was collected from patients in the operation theatre by inserting a brain cannula in the ventricles. CSF was kept in 2 aliquots and a smear was prepared for microscopic examination of malignant cells. From one aliquot glucose and total protein were measured on the same day while the other was frozen at -40°C.

Cerebrospinal fluid was concentrated for electrophoresis and immunoglobulin assay. As immunoglobulins were not detectable even in low level kits of RID supplied by Kallisted Laboratories USA. Concentration was done by freeze drying method in Consol 12, Vitris USA. Electrophoresis was done on cellulose acetate membrane in Elvi 70 tank and different protein fractions measured quantitatively by feeding level of total, protein in un concentrated sample on Elvi 165 densitometer. Student 't' test was used for comparison.

## RESULTS

The mean ventricular CSF glucose was  $77.85 \pm 2.71$  pg/dl and it ranged from 45.40 to 110 mg/dl. The total CSF proteins with the electrophoresis pattern and immunoglobulin assay are shown in Table I.

**TABLE I. Total ventricular CSF proteins, electrophoretic protein fractions, IgG, IgA and IgM in brain tumour patients.**

Protein	Mean	±SD	SEM	Range
T. Protein (mg/dl)	23.09	6.90	1.14	15.5-50
Pre-albumin (%)	2.76	1.11	0.18	1.6-6.1
Albumin (%)	59.11	6.11	1.00	49-72.1
Alpha-1 (%)	2.66	0.88	0.14	1.1-5.0
Alpha-2 (%)	3.15	0.86	0.14	1.9-6.1
Beta (%)	12.28	3.72	0.61	7-20.1
Gamma (%)	16.67	3.77	0.62	9.6-24.2
IgG (mg/dl)	784.51	306.38	50.36	242-1165
IgA (mg/dl)	223.03	239.73	41.11	15.15-1195
IgM (mg/dl)	171.78	39.13	14.79	112.5-210

Immunoglobulin G (mean ± SEM was 784.5 ± 50.36 ug/dl. No significant difference was noted in the IgG levels of children and adults, males and females and among the different age groups. However, level of IgG in malignant tumours was significantly higher (Pc 0.00 1) than in benign tumours (Table II). IgA was detectable in 34 cases, the level ranged between 26 and 520 ug/dl. There was again no difference between the various groups. But it was significantly higher (Pc 0.05) in malignant tumours (Table II).

**TABLE II. CSF immunoglobulins in benign and malignant brain tumours. The results are expressed as mean SEM. The number of observations and range values are given in parenthesis.**

Group	IgG (µg/dl)	IgA (µg/dl)	IgM (µg/dl)
Benign (30)	741.30 ± 59.20 (318-1109)	173.15 ± 34.98 (15-552)	155.87 ± 22.31 (112.5-210)
Malignant (7)	969.14 ± 54.91 (666-1082)	415.42 ± 135.30 (171-1195)	193 ± 11.93 (171-212)
P value			
Benign vs malignant	< 0.001	< 0.05	Non-significant

IgM was detectable in only 7 patients and values ranged between 171 and 212ug/dl (Table II). In all 37 patients with benign and malignant tumours CSF cytology showed no malignant cells.

## DISCUSSION

Studies of general immunocompetence in patients with brain tumours are almost non-existent, presumably due to popular emphasis upon cell mediated mechanism of host response to neoplasia<sup>4</sup>. Mean ventricular CSP glucose is higher than lumbar CSF glucose<sup>5</sup>, and in this study it is not affected

by tumours. Mean total protein was significantly higher than normal values<sup>6</sup>. Whether this increase is transudate of serum or produced intrathecally, needs to be investigated. In this study significant increase of albumin and gammaglobulin fraction than normal levels of other workers<sup>7</sup>, is comparable with the findings of Harter et al<sup>8</sup>, but Tventen<sup>9</sup> described no change in his brain tumour patients. The increase of above fractions suggests impairment of blood brain barrier as also emphasised by other workers<sup>10,12</sup>. Findings of increased IgG and IgA in malignant tumours than in benign tumours is comparable with results of many other workers.<sup>11,12</sup> It is presumed that the elevation of these immunoglobulins is related with humoral immune response of brain against tumours. Sensitivity of method is important as, Nerenberg et al.,<sup>13</sup> using RIA technique detected raised IgM in 19 of 20 cases, while Monari et al.,<sup>14</sup> was unable to detect IgM in any of his cases. It was detected in 7 cases of 37 in this study. Although PID is much less sensitive method for lower levels, finding of IgM suggests some humoral immune response against brain tumours and warrants further investigations in this regard with more sensitive methods.

## REFERENCES

1. Medawar, P.R. Immunity to homologous grafted skin. III. The fate of skin homografts transplanted to the brain, to subcutaneous tissue and to the anterior chamber of the eye. *Br. J. Exp. Pathol.*, 1948; 29:58-69.
2. Coakham, H.B. and Kornblith, P.L. The humoral immune response of patients to their gliomas, *Acta Neurochir. Supp.*, 1979; 28:475-9.
3. Phillips, J.P., Eremin, O. and Anderson, J.R. Lymphoreticular cells in human brain tumours and in normal brain. *Br. J. Cancer*, 1982; 45:61-9.
4. El-Samra, K., Aboul-Enein, I., Kamel, A.M., et al. A clinicopathological and immunological study of primary intracranial neoplasm in children. *Egypt. Natl. Cancer Inst.*, 1986; 2:317-26.
5. Sood, R. *Medical laboratory technology*. New Delhi, Jaypee, 1986, p.190.
6. McMurray, J.R. *Practical clinical biochemistry*. 6th ed. London Heinemann, 1988, p.488.
7. Hill, N.C., Goldstein, N.P., McKenzie, B.P., McGuckin, W.F. and Svien, H. Cerebrospinal fluid-proteins, glycoproteins and lipoproteins, in obstructive lesions of the central nervous system. *Brain*, 1959; 82:581-93.
8. Harter, D.H., Yahr, M.D. and Kabat, E.A. Neurological diseases with elevation of cerebrospinal-fluid gamma globulin; a critical review. *Trans. Am. Neurol. Assoc.*, 1962; 87:210-12.
9. Tventen, L. Cerebrospinal-fluid proteins in obstructive lesions of the central nervous system. *Acta Neurol. Scand.*, 1965; 41:80-91.
10. Osenbruck, M., Rao, M.L. and Quednsu, H.D. Pattern of albumin, immunoglobulins and glucose in cerebrospinal-fluid and serum of patients with disorders of central nervous system. *Eur. Neurol.*, 1985; 24:16-22.
11. Praaad, P. Immunoglobulins in certain CNS disorders; a study of CSF IgG, IgA, IgM, D and E concentrations. *AJCP.*, 1985; 83:190-5.
12. Rao, M.L. and Boker, D.K. Cerebrospinal-fluid and serum levels of albumin, IgG, IgA and IgM in patients with intracranial tumours and lumbar disc herniation. *Euro. Neurol.*, 1987; 26:241-5.
13. Nerenberg, S.T., Prasad, R. and Rothman, M.E. Cerebrospinal-fluid IgG, IgA, IgM, IgD and IgE in CNS disorders. *Neurology*, 1978; 28:988-90.
14. Monari, M., Galvez, S. and Parcas, A. Cerebrospinal-fluid and serum immunoglobulins and C-3 levels in 30 intracranial tumours. *Neurochirurgia*, 1978; 36:75-82.