Local T cell subsets in mumps meningitis

H NAGAI, T MORISHIMA, Y MORISHIMA, S ISOMURA, AND S SUZUKI

Department of Pediatrics, and First Department of Internal Medicine, Nagoya University School of Medicine, Japan

SUMMARY In the acute phase of mumps meningitis, more than 85% of the cells in cerebrospinal fluid (CSF) were OKT 3 positive, while 76% of the peripheral mononuclear cells (PMN) were OKT 3 positive. The ratio of OKT 4:8 positive cells in CSF was significantly lower than that in PMN, showing that suppressor/cytotoxic T cells had selectively accumulated in CSF. In addition, 58% of CSF cells were immune associated (Ia) positive, probably activated T cells.

It has recently become clear that cell mediated immunity plays an important role in various viral infections. How the viruses are cleared from the actual infected foci is still, however, uncertain. To find effective treatments in central nervous system (CNS) viral infections, it may be necessary to ascertain what defence mechanism operates at the site of virus invasion and which factor is activated first among the immune systems. We endeavoured to determine the nature of T lymphocytes in cerebrospinal fluid (CSF) and to examine the difference between systemic and local T cell responses in patients with mumps and mumps meningitis.

Patients and methods

Patients. We studied 15 children with mumps meningitis and 12 mumps patients who did not develop meningitis. The children were aged between one and 8 years. The diagnosis of mumps parotitis was based on swelling of the parotid gland and serologic evaluation. The diagnosis of meningitis was confirmed by clinical manifestations and by lymphocytic pleocytosis in the patients' CSF after parotid gland swelling.

Methods. CSF and heparinized blood samples were taken from the patients during the acute phase of their illness. Peripheral mononuclear cells (PMN) were then separated by Ficoll-Paque density gradient centrifugation. As almost all the cells in CSF were mononuclear (>90%), CSF cells were collected directly by low speed centrifugation.

The hybridoma derived monoclonal antibodies

OKT 3, 4, and 8 (Ortho Pharmaceutical Corporation, USA) were used—OKT 3 identifies human peripheral T lymphocytes;¹ OKT 4 recognises an antigen on the surface of the human inducer/helper subclass; and OKT 8 is specific for the suppressor/cytotoxic subclass.¹ Ia like antigens on the cell surface were determined by the monoclonal antibody, Ia-6A1,² and activated T cells by monoclonal antibody 5E9.³ Analysis was performed by indirect immunofluorescence using these monoclonal antibodies.

Results

In mumps meningitis patients, more than 85% of

Fig. 1 Ratios of OKT 4:8 positive cells in peripheral mononuclear cells (PMN) and cerebrospinal fluid (CSF) cells.

The shaded area represents the ratio of mean (SD) OKT 4:8 in age matched controls. Bars indicate mean (SD). The P value was determined by Student's *t* test.

Fig. 2 Percentages of Ia positive cells in peripheral mononuclear cells (PMN) and cerebrospinal fluid (CSF) cells.

Bars indicate mean (SD). The P value was determined by Student's *t* test.

the mononuclear cells in CSF were OKT 3 positive, while 76% in PMN were OKT 3 positive ($P<0.01$). A difference in the percentage of OKT 3 positive PMN in patients with mumps and those with mumps meningitis (66% and 76% respectively, $P<0.02$) was found. The percentage of OKT 4 and OKT 8 positive cells and the ratio of OKT 4:8 positive cells were calculated. As shown in Fig. 1, the OKT 4:8 ratio was, mean (SD) 2.50 (0.45) in healthy controls, but in mumps patients, with and without meningitis, PMN showed a much lower ratio,—mean (SD) (1.20 (0.35) and 1.25 (0.42), respectively. Of particular interest, the OKT 4:8 ratio in CSF T cells was, mean (SD) 0.67 (0.24); significantly lower than that in PMN ($P<0.001$). In further experiments, it became clear that mean (SD) 58% (10%) of CSF cells possessed Ia like antigens (Fig. 2). In contrast, only mean (SD) 26% (7%) of PMN in mumps meningitis were Ia positive. Approximately 30% of CSF cells and less than 10% of PMN were 5E9 positive.

Discussion

We have shown that in mumps meningitis, antibody

and interferon synthesis occurred independently in the CNS.⁴ In the present study, the percentage of OKT 3 positive cells in CSF was significantly higher than in PMN. Moreover, when compared with the systemic reactions (in PMN), CSF T cells comprised more OKT 8 suppressor/cytotoxic T cells. Ia positive cells were also predominant among CSF cells. It was recently reported that, besides B cells and monocytes, activated T cells also possess Ia like antigen on the cell surface.⁵ As the population of B cells, or monocytes, or both was less than 15% among CSF cells, these Ia positive cells seemed to be activated T cells. This result was confirmed by 5E9 monoclonal antibody that reacted only with activated or some malignantly transformed cells.³ Indeed, Kreth *et al.* have reported that virus specific cytotoxic T cells were induced in a patient with mumps meningitis.⁶

These results lead to the conclusion that numerous suppressor/cytotoxic T cells, probably cytotoxic T cells, are selectively accumulated in the CNS and that these cells may perhaps be activated by antigenic stimulation caused by mumps virus.

We thank Dr B F Haynes (Duke University, USA) for supplying 5E9.

References

- 1 Van Wauwe J, Goossens J. Monoclonal anti-human T-lymphocyte antibodies: Enumeration and characterization of T-cell subsets. *Immunology* 1981;**42**:157-64.
- 2 Morishima Y, Kobayashi M, Yang SY, Collins NH, Hoffman MK, Dupont B. Functionally different T lymphocyte subpopulations determined by their sensitivity to complement-dependent cell lysis with the monoclonal antibody 4A. *J Immunol* 1982;**129**:1091-8.
- 3 Haynes BF, Hemler M, Cotner T, *et al.* Characterization of a monoclonal antibody (5E9) that defines a human cell surface antigen of cell activation. *J Immunol* 1981;**127**:347-51.
- 4 Morishima T, Miyazu M, Ozaki T, Isomura S, Suzuki S. Local immunity in mumps meningitis. *Am J Dis Child* 1980;**134**:1060-4.
- 5 Fu SM, Chiorazzi N, Wang CY, *et al.* Ia-bearing T lymphocytes in man. *J Exp Med* 1978;**148**:1423-8.
- 6 Kreth HW, Kress L, Kress HG, Ott HF, Eckert G. Demonstration of primary cytotoxic T cells in venous blood and cerebrospinal fluid of children with mumps meningitis. *J Immunol* 1982;**128**:2411-5.

Correspondence to Dr Hideshi Nagai, Department of Pediatrics, Nagoya University School of Medicine, 65, Tsurumai-cho, Showa-ku, Nagoya, Japan.

Received 19 July 1983.