Cellular Hypersensitivity to Nervous Antigens in Guillain-Barré Syndrome

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ABSTRACT

Cell-mediated immune responses to various nervous antigens were examined in 12 cases of Guillain-Barré syndrome (GBS), 24 cases of noninflammatory peripheral neuropathy (NIPN), and 18 cases of degenerative disorders of central nervous system (CNSDD), using the lymphocyte-transformation technique. Cellular hypersensitivity to bovine P2 protein (P2) and a synthetic peptide, SP66-78, corresponding to the residues 66-78 of P2, was detected in about two-thirds of GBS cases, especially in the active or improving stages, but not in NIPN and CNSDD. The lymphocytes sensitized to these nervous antigens might play an important role in the pathogenesis of GBS.

Index Entries: Guillain-Barré syndrome; cell-mediated immunity; P2 protein; synthetic peptide.

INTRODUCTION

An autoimmune response to certain components of peripheral nerve myelin has been postulated to be a possible pathogenic factor in Guillain-Barré syndrome (GBS). On the basis of studies on experimental allergic neuritis (EAN), an excellent animal model of GBS, it is now generally accepted that P2 protein (P2), a major basic protein of peripheral nerve my-
elin, can induce EAN in Lewis rats (Kadlubowski and Hughes, 1979; Suzuki et al., 1980; Weise et al., 1980) and that P2 is the antigen most responsible for the induction of EAN. Furthermore, a recent study has revealed that a certain synthetic peptide, corresponding to partial sequences of bovine P2, shows consistent neuritogenic activity in Lewis rats (Uyemura et al., 1982).

In an attempt to clarify the antigen responsible for the pathogenesis of GBS, there have been some reports on the cellular reactivity to P2, but these results are still controversial (Sheremata et al., 1975; Abramsky et al., 1975, 1980; Iqbal et al., 1981; Zweiman et al., 1983; Hughes et al., 1984), and no report has appeared concerning cellular reactivity to the synthetic peptide.

In the present study, we examined the cell-mediated immune response to various nervous antigens in GBS in comparison with those in other neurological disorders of either the peripheral or central nervous system. The relationship between cellular responsiveness and the clinical stages of GBS was also investigated.

**MATERIALS AND METHODS**

Twelve cases of GBS were serially examined during the course of the disease, according to clinical stage. The clinical stage was divided into the following three categories; the active, improving, and stable stages. The active stage represented the period from the onset of neurological signs and symptoms to the peak of them, including the plateau phase; the improving stage, the period from the beginning of improvement to the time when no more improvement was obtained; and the stable stage, the period after the improving stage. Corticosteroids were not used except in one case. The control patients involved 24 with noninflammatory peripheral neuropathy (NIPN): six with Charcot-Marie-Tooth disease, one with Dejerine-Sottas disease, nine with diabetic polyneuropathy, five with polyneuropathy of unknown etiology, and three with compression neuropathy; and 18 with degenerative disorders of the central nervous system (CNSDD): six with amyotrophic lateral sclerosis; six with spinocerebellar degeneration; and six with Parkinson’s disease. Fifty healthy controls were also examined (Table 1).

Cell-mediated immune response to the nervous antigens was evaluated using the lymphocyte-transformation technique. The lymphocytes were obtained from 3 mL of blood by Hypaque-Ficoll density gradient centrifugation. Aliquots of $1 \times 10^6$ lymphocytes were cultured in RPMI 1640 medium containing 1.5% fetal bovine serum and antibiotics. After incubation at 37°C in 5% CO₂ air for 5 d with 10 µg of each of the antigens, the cultures were incubated for 24 h with 1 µCi of [³H]thymidine and harvested by a multiple automated harvester. The assay was performed in quadruplicate, in both antigen-stimulated and -unstimulated cultures, and stimulation index was calculated as the ratio of the mean