Anti-CNS Antibodies in Childhood Neurologic Diseases

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Abstract

To study the incidence of circulating anti-CNS antibodies in childhood neurologic diseases, a population study was undertaken. Serum samples were obtained from a total of 348 children and stored at – 80 °C until being studied. The samples were collected when routine blood tests were being performed. In all cases informed consent was obtained. This study was approved by hospital ethics review committees.

One hundred and ninety-nine of the samples were from children with no known neurologic illnesses and served as the control group. One hundred and twenty-one of the samples were from children with epilepsy and the remaining 28 from a number of different neurologic conditions. The serum samples were screened against normal, adult, autopsy-derived cerebellar and frontal cortex tissue sections and Western blots. Serum immunoreactivity was revealed using HRP-conjugated anti-human IgG.

Significant findings included: (1) patients with epilepsy had an increased incidence of anti-CNS reactivity as revealed on frontal cortex immunoblots ($p < 0.05$) but not on cerebellar immunoblots; (2) there was an increase in the incidence of immunoblot reactivity with age in the controls and the neurology cases; (3) there was an increased incidence of immunoblot reactivity in those cases with a presumed inflammatory central or peripheral neurologic disease; (4) in six additional cases with opsoclonus-myoclonus there was cerebellar-specific immunoreactivity with identified antigenic molecular weights of 27 and 35, and 62 kDaltons; (5) in 31 additional cases of systemic lupus erythematosus there was significant immunoblot reactivity ($p < 0.001$) when compared to a subset of age-matched controls.

There was no difference in immunoreactivity between males and females. There was no significant increase in immunoreactivity in those children with cognitive disturbances including developmental delay and mental retardation.

Key words

Autoimmunity – Child neurology – Epilepsy – Immunohistochemistry – Neuroimmunology

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Introduction

Immune-mediated processes have been demonstrated in neurologic illnesses such as myasthenia gravis (1, 44, 59), Guillain-Barre syndrome (43, 50, 60) and multiple sclerosis (4, 61). In adult neurologic disorders, circulating antibody-mediated processes have been implicated in a number of other conditions including paraneoplastic cerebellar degenerations (19, 27, 57), familial spinocerebellar degenerations (34), paraneoplastic sensory neuronopathy (18), Sydenham's chorea (23, 24), Parkinson's disease (15, 25, 48), schizophrenia (7, 30) Creutzfeldt-Jakob disease and Kuru (2, 52).

The presence of anti-CNS antibody activity in childhood neurologic diseases has not been thoroughly studied. Children do suffer from systemic autoimmune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis and are also subject to well documented autoimmune neurologic diseases more commonly seen in adults such as myasthenia gravis, multiple sclerosis and the Guillain-Barre syndrome.

The published literature suggests the possibility of autoimmune processes in several childhood neurologic diseases. In infantile spasms (63) precipitating antibodies to brain extracts have been described (39, 49). Furthermore, infantile spasms frequently respond to immune-modifying medications such as steroids and ACTH (33). A cell-mediated immune response to brain tissue has been described in autism (62) as well as specific defects in cell mediated immunity (17). Antineuronal antibodies have been found in children with neurologic complications from SLE (21, 26, 64). A more thoroughly studied childhood neurologic disease which may have an underlying autoimmune etiology is the opsoclonus-myoclonus syndrome (O-M) (29). This condition responds to immune-modifying medications such as steroids and ACTH (32, 45). There have been reports of increased cerebrospinal fluid immunoglobulin levels (11) and macrophage inhibition by neuroblastoma antigens (55) in this syndrome. Also, anti-neurofilament antibodies have been observed in O-M (5, 41).

To investigate whether circulating anti-central nervous system (CNS) antibodies may play a wider pathogenic role in childhood neurologic diseases, this population study was undertaken.

Serum samples were collected and screened against Western blots and sections of human CNS tissue. Immunoblots have an advantage over tissue sections in that immunoreactivity can be resolved to a finite number of bands whose molecular weights can be determined. Our results are presented in tabular form so that comparisons with other studies will be possible.

As a positive control, serum samples from patients with SLE were included since anti-CNS activity in SLE has been previously documented (8, 21, 22, 26, 64). For com-