An Italian Study Finding Biochemical Markers of Vaccine Damage

Harris L. Coulter Ph.D.

Comment by Harris L. Coulter: This is, to my knowledge, the first investigation to find biochemical markers of vaccine damage. It has not yet been published but deserves publication. My translation omits the tables and part of the bibliography, but the text is complete. This study should also have an impact on HLA typing, since it shows that vaccinations can have an effect on the individual's HLA type (i.e., that it is not necessarily congenital).

Role of Immunogenetics in the Diagnosis of Postvaccinal CNS Pathology

Massimo Montinari*, Biagio Favoino**, and Angela Roberto***
Dept. Of Pediatric Surgery, University of Bari
**Tissue Typing and Organ Transplantation Service, Bari Hospital and Polyclinic
***Virology Outpatient Clinic. Bari Hospital and Polyclinic

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Resume
This study involves observations of 30 patients with post-vaccinal pathology of the central nervous system and other systems where the first symptoms appeared concomitantly with, or immediately after, administration of a vaccine. All patients were subjected to serologic testing for herpes virus (IgG and IgM) and to HLA (A, B, C) and HLA-DR-DQ tissue typing to see if there was any correlation between the emergence of CNS pathology and these various antigens, thus to show a possible autoimmune-type immunogenetic basis for demyelination processes. Statistical comparison with the Italian population used as controls revealed an increase in the HLA-A3 and HLA-DR7 antigens. The presence of A3 and/or DR-7 was observed in 22/30 (73.3%) of the patients.

Key words
Post-vaccinal pathology; HLA system; autoimmune pathology of the CNS.

Introduction
Post-vaccinal pathology of the central nervous system (CNS) is a topic deserving further investigation. In fact, our own experience with 30 patients of Italian nationality, observed between April, 1994 and October, 1995, shows that clinical

signs of CNS pathology -- associated with dermatitis, food allergies, constipation, and leaking from the anus -- emerged concomitantly or immediately after vaccination with the Salk or Sabin polio vaccine, DT, measles, DPT, anti-tuberculosis, or Hepatitis-B vaccines.

The hypothesis of Herroelen, J. De Keyser, and G. Ebinger on "CNS demyelination after immunization with recombinant hepatitis-B vaccine" (Lancet, 338, November 9, 1991, 1174-1175), as verified by A.P. Brezin, M. Lautier-Frau, M. Hamadani, and O. Rogeaux in their article, "Loss of Vision and Eosinophilia after Recombinant Hepatitis-B Vaccine" (Lancet, Italian Edition, April, 1994), suggests the need for a clinical revaluation and a critical look at all the patients observed up to now in Italian and European clinical centers.

Methods

The patients examined by us came from various regions of Italy, and all presented with a clinical history of convulsions concomitantly with, or immediately after, prophylactic vaccinations. We excluded from the study all patients observed by us whose clinical history was not referable to a vaccination. All the patients were subjected to tissue typing for HLA (A, B, C) and HLA DR-DQ with the aim of defining the relative immunogenetic order. The phenotype was defined by a study of various immune functions: lymphocyte subpopulations, serum immunoglobulin content, sphericity of the antibodies to various viruses (CMV, EBV, HSV-1 and HSV-2, VZV).

This allowed us to relate these data to specific clinical pictures -- patients who had earlier been diagnosed with epilepsy, myoclonic epilepsy, evoving epilepsy, epileptigenic encephalopathy, autism, West Syndrome, and Angelman's Syndrome. All the patients had presented with the first symptoms shortly after receiving the prophylactic vaccination or somewhat later.

The first symptoms were convulsions, very high fever, or diarrhoea immediately following a compulsory vaccination. The parents had told their physicians about this; then, after taking EEGs and visiting neuropsychiatric specialists or pediatricians without getting any satisfaction, the physicians had administered the recall shots of the vaccines leading very shortly to stabilization of the condition with progressive clinical deterioration.

These children were mostly from 3 to 9 months old. All patients were studied for the presence of metabolic diseases with negative results; then chromosomal mapping was done, also with negative results; encephalic TAC and RMN were performed at first appearance of the symptomatology, also with negative results.

The EEG performed at first appearance of the symptomatology gave a negative result in 92% of the patients. Serologic investigations for herpetic virus (IgG and IgM) were positive in all for IgG and negative for all for IgM, leading us to estimate seropositivity (IgG) for Epstein-Barr virus of 73.8%, for cytomegalovirus of 71.4%, for Herpes Simplex virus of 47.6%, and for Varicella-Zoster Virus of 21.4%. In all the patients we observed diminished sideremia and a deficit of IgA and IgG with a slight increase of GOT and GPT. None of the patients had maternally transmitted viral encephalopathy, and in all the patients the vegetative and relational life was quite normal prior to administration of the first dose of vaccine.

The patients were subjected to HLA tissue typing (A, B, and C), and serologic HLA DR-DQ, with the aim of checking a possible correlation with the emergence of CNS pathology, and these antigens indicate a possible autoimmune immunogenetic basis for the demyelination process. (See A. Svejgard, P. Platz, and L. P. Ryder in Immunology Rev. 70, 1983, 193). The chi-square statistical analysis, with the Italian population as a control (see 11th International Histocompatibility Workship and Conference, 1992) demonstrated an increase in the HLA-A3 antigen (43.3% vs. 25%, $P = 0.04$, after statistical correction) and the HLA-DR7 antigen (48.3% vs. 24.14% $P = 0.007$ after statistical correction). The presence of A3 and/or DR7 was observed in 22/30 (73.3%) of the patients.

Additional cases are under study to better define the possible association of HLA A3 and/or HLA DR7 with appearance of this pathology in the CNS following vaccination. HLA system alleles have an elevated genetic polymorphism and are inherited as autosomal dominant characteristics. The combination of the alleles of various loci in the same chromosomes has been defined as the haplotype or complex gene, and the complexity of the HLA region demonstrates, besides the thousand different possible haplotypes, also the problems: of molecular resemblance (see G. Laurentaci and B. Favoino, "Immunogenetica e malattie HLA Associate," Dedalo Litostampo, Bari, 1991), of discriminating between self- and non-self-antigens, and of determining the function of the Class 2a CMI molecules; any interference with the process of presentation of the antigen can predispose to an autoimmune disease. Alterations which do not occur can be due to the action of viral agents which compromise the specific immune response because of their resemblance to the "self" tissue antigens. The consequence is persistence of the infective agents and a tendency to provoke, through a marked reaction, induction of an autoimmune disease. This can present in conditions of marked reactivity to some viruses and to myelin antigens.

A study of the disease associated with genes of the HLA system has shown that this genetic complex can be responsible for a particular genetic susceptibility, predisposing to various diseases characterized predominantly by immune-system pathogenesis. The observation that many vaccines use Thimerosal as a preservative,

for which we do not have clear dose-response relationships and whose toxic effects take the form essentially of neurologic symptoms, not the least of which are symptoms of the purine pathway of the innervation of the digestive tube, leads us to consider that in 66% of cases there was obstinate constipation and in 31% there was proctic symptomatology with emission of mucus and blood.

Conclusion

All the patients observed presented various physical problems. The various types of CNS pathology could be due to a delatentization of preexisting autoimme damage by viral DNA. It has been observed that the “cleaner" the species, from the virologic or microbiologic point of view, the more likely it is to present autoimmune conditions of the CNS and other apparatuses. The results indicate that autoimmune pathology is more frequent in countries where vaccination is more widespread, i.e., in countries defined as "clean." With this study, and with the individualization of alleles such as A3 and DR7, in the presence of viral DNA, it would be possible to define the subjects at risk of an autoimmune pathology from vaccination. The action of thimerosal used as an excipient in vaccines, and whose toxicity is independent of thedose administered, could demonstrate the possibility of changes in the aminoacids of the molecules which preserve the antigen.

This type of study could even be utilized to individualize the etiopathogenesis of other types of autoimmune pathology.

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