

UPON THE FORMATION OF VIRUS NEUTRALIZING ANTIBODIES AGAINST POLIOVIRUSES TYPE 3 IN CENTRAL AND PERIPHERIC NERVOUS SYSTEM AFFECTIONS

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The process of specific immunity formation with enteroviral infections is complex and insufficiently clarified. It is supposed that the course of the latter is determined to a great extent by the immune status of the organism. According to some authors (1, 2) secretory antibodies play an important but transitory role in the defence of the organism against polioviral infection of the digestive tract. Serum virus-neutralizing antibodies are the basis of a reliable and long enough defence against paralytic forms, indeed.

The purpose of the present study was to determine the level of virus-neutralizing antibodies (VNA) against poliovirus type 3 with different genetic characteristics which circulated recently more frequently among the inhabitants of Varna city and caused diseases with paralytic manifestations in spite of systemically performed prophylaxis by using vaccine against poliomyelitis.

Material and methods

During the period from 1977 till 1982 a total of 180 cases with suggested enteroviral infection were studied. In the present paper only 8 of them were discussed including mainly children up to 8 years old with central and peripheric nervous system affections. Various cell cultures were used to isolate and typify the viruses. The genetic characteristics of polioviruses was established by means of antigen, temperature and plaque markers (1—3). Serum VNA level was determined on the same cultures by testing the Ist and IInd serum samples.

Results and discussion

It can be seen on table 1 that polioviruses type 3 with pertaining to virulent, intermediary and vaccinal variations according to genetic markers were isolated from various materials mainly from cerebrospinal fluid. The case No 8/81 was a six-months old suckling without immunization with live poliovaccine (LPV) presented with the picture of paralytical poliomyelitis. We isolated a virulent poliovirus type 3 from the liquor and LPV titre increased more than fourfold in the second serum sample (Ist 1:32, IInd above 1:128). According to M. K. Voroshilova (1) LPV titre increase could not be considered absolutely determining the etiological role of polioviral agent because sometimes these titres were not higher than that against the other poliovirus types acquired by means of immunization or latent infection. In our case VNA level against poliovirus type 1 and type 2 was

Table 1

Virological and serological studies of patients with affections of the central nervous system and paralytic manifestations in whom polioviruses type 3 are isolated

Patient's code	Age	Clinical diagnosis	Poliovirus type 3 isolated from	Genetic characteristics of the strain	VNA level in		Etiological role of poliovirus type 3
					Serum 1 st	Serum 2 nd	
8/81	6 months	paralytical poliomyelitis	CSF	virulent	1:32	over 1:128	yes
43/80	2 months	polioliike disease	CSF	vaccinal	under 1:8	1:16	yes
1/79	1 years 3 months	serous meningitis	CSF	virulent	1:8	1:8	yes
18/80	1 year 2 months	polioliike disease	CSF	virulent	1:8	1:8	yes
11/81	17 years	meningoencephalitis	CSF	virulent	under 1:8	1:16	yes
16/81	14 years	encephalitis	CSF	intermed.	under 1:8	1:8	probable
21/80	8 years	ser. mening.	foecal	vaccinal	under 1:8	1:16	no
10/81	4 years	encephalitis	nasal smear	vaccinal	under 1:8	under 1:8	no

between 1:8 and 1:16 while no VNA against enterovirus 71 could be established. It was known that blockade of virus transmission to the central nervous system did not require demonstratively high VNA titres and that only blood traces of them could prevent viremia (1, 6, 10). In our cases in spite of VNA presence a polioinfection developed which was most probably determined by the particular virulence of the viral strain.

The next patient, No 43/80, two-months old suckling, without LPV immunization, had polio-like disease and suspicion on paralytical poliomyelitis. The poliovirus type 3 isolated from the cerebrospinal fluid pertained genetically to the vaccinal variation. Serum VNA against polioviruses type 3 was under 1:8 in 1st and 1:16 in 2nd samples. There were no VNA against polioviruses type 1 and 2 as well as against enterovirus 71. According to other investigators (1, 2, 8) vaccinal poliovirus type 3 possesses weakened immunogenicity and the development of most cases with paralytical manifestations in immunized and contact individuals is probably due to this poliovirus type. Concerning this patient, present serum conversion, poliovirus isolation from the cerebrospinal fluid, the age and the clinical picture allows us to accept the etiological role of the isolated agent in spite of its genetic characteristics. Next two cases, No 1/79 and No 18/80 present infants aged 15 and 14 months, respectively, immunized with LPV and with serous meningitis and polio-like disease, respectively. Polioviruses type 3 virulent according to genetic markers were isolated from their cerebrospinal fluid. VNA level in both serum samples of these patients was 1:8. Most likely, cases with insufficiently intensive humoral immunity against poliovirus type 3 despite specific prophylaxis are considered. The confrontation with a virulent strain caused central nervous system affections and paralytical manifestations. According to A. B. Sabin (9) specific VNA in polioinfection are formed before complete clinical manifestation which makes the lack of seroconversion in some patients possible. This is a probable explanation of the fact that in well outlined

clinical picture (as in the aforementioned cases) there are no changes of VNA level in the course of the infection.

There was a fourfold VNA increase in the IInd sample (Ist under 1:8, IInd 1:16) against virulent poliovirus type 3 isolated from the liquor in patient No 11/81, age 17 years, with meningoencephalitis. The lack of specific VNA in the Ist serum sample gives an evidence that there is no formed immune response before infection to poliovirus type 3 although only as consequence of so-called "home immunization" and of latent infection serum VNA should be already present. In a patient, No 16/81 aged 14 years with encephalitis, poliovirus type 3 was isolated from the liquor and characterized to be an intermediary variation. The serologic examination showed that VNA level was in Ist serum under 1:8 and in the IInd one — 1:8. There was no any active VNA formation as response to antigenic stimulus of poliovirus type 1 and 2, too.

Last two patients as it can be seen on table 1 (No 21/80 and 10/81) had serous meningitis and encephalitis, respectively without evidence of myelopathy. Vaccinal polioviruses type 3 were isolated from faecal samples and nose-throat smears. In the first patient there was a fourfold VNA increase in the IInd serum which was probably due to the regular LPV immunization. In the second patient there were no specific VNA against poliovirus type 3 in both sera tested but the parallelly isolated virus strain Coxackie B1 could be determined as an etiological agent.

We draw the following conclusions:

Despite regularly performed specific prophylaxis there are low VNA titres against poliovirus type 3 in patients with central and peripheric nervous system affections. Our investigations do not confirm the concept of some authors that even VNA traces in the serum only could prevent poliovirus infection by poliovirus type 3 as an etiological agent. The titres of VNA in Ist serum sample (between 1:8 and 1:16) in single patients did not prove to be sufficient barrier for prevention of infection of the nervous system. Independently of their genetic characteristics the polioviruses type 3 isolated by us do not induce in most cases an active VNA formation which results in development of a neuroinfection. The establishing of the etiological role of vaccinal strain poliovirus type 3 in cases of polio-like disease is a serious signal for strengthening the systemic control (virological, immunological and epidemiological) on performed LPV immunization and the quality of vaccine itself.

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**О СОЗДАНИИ ВИРУСНЕЙТРАЛИЗИРУЮЩИХ АНТИТЕЛ ПО ОТНОШЕНИЮ
К ПОЛИОВИРУСАМ III ТИПА ПРИ ЗАТРАГИВАНИИ ЦЕНТРАЛЬНОЙ
И ПЕРИФЕРИЧЕСКОЙ НЕРВНОЙ СИСТЕМЫ**

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Р Е З Ю М Е

Прослеживается образование вируснейтрализирующих антител у больных, преимущественно в возрасте до восьми лет, с затрагиванием центральной и периферической нервной системы. На тканевых культурах, взятых у тех же больных, изолированы из ликвора полиовирусы III типа с различной генетической характеристикой. Установлена этиологическая роль как вирулентных, так и вакцинальных полио III, что является фактом, имеющим особое клиническое и эпидемиологическое значение.

Полученные результаты говорят о необходимости в систематических исследованиях sporadических случаев заболевания с затрагиванием нервной системы.