JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 1997, p. 334–335 Vol. 35, No. 1
0095-1137/97/$04.00+0

Letters to the Editor

Poliovirus Genomic Sequences in the Central Nervous Systems of Patients with Postpolio Syndrome

In a recent study by Leparc-Goffart et al., poliovirus-specific genomic sequences were detected during the amplification of genomic sequences in the conserved part of the 5′ untranslated region (5′-UTR) as well as the poliovirus-specific VP1 region only in 5 of 10 patients with postpolio syndrome (PPS) and in none of the control patients (5). No information is given about concurrent human immunodeficiency virus (HIV) infection or otherwise among the 10 PPS patients or 23 control patients in Lyon, France. A 26-month-old HIV-infected female in Romania was afflicted with a type 2 poliomyelitis after 4 doses of live poliovirus vaccine (Sabin) (4). An HIV coinfection in PPS patients could selectively enhance the replication of poliovirus genomic sequences and their subsequent detection in cerebrospinal fluid (CSF). The absence of poliovirus sequences in five PPS patients could well be related to HIV infectivity status.

The genomic activity of poliovirus in relation to susceptible neurons in different regions of the brain and spinal cord could also be ascertained through T2-weighted magnetic resonance imaging (MRI) in patients with PPS. By MRI, lesions in the dorsal region of the pons to the upper level of the thoracic cord were evident in a patient with poliomyelitis-like syndrome at Ehime in Japan (6). Furthermore, high-intensity areas were observed in the left anterior horn at cervical levels 4 to 6 in a 7-year-old boy who developed acute flaccid paralysis of the left upper limb 4 days after an asthmatic attack (1).

The role of poliovirus genomic sequences in the pathogenesis of PPS could be established by long-term studies of monkeys inoculated with attenuated poliovirus strains. Monkeys survived the mandatory 21-day observation period following an intraspinal injection with attenuated Sabin poliovirus strains (2). They even showed clinical evidence of paralytic poliomyelitis of their limbs. During histopathological examination of the brain and spinal cord, foci of neuronal damage have been found in the spinal cord and in neurons far away from injection sites (3). It would be feasible to carry out reverse transcription-PCR (5) with CSF, MRI (1, 6), and both brain and spinal cord biopsies during the prolonged survival of such monkeys. An in situ PCR would elucidate the precise sites for localization and multiplication of poliovirus genomic sequences.

REFERENCES

1. **Arita, J., Y. Nakae, H. Matsushima, and K. Maekwa.** 1995. Hopkins syndrome: T2-weighted high intensity of anterior horn on spinal MR imaging. Pediatr. Neurol. **13:**263–265.
2. **Boulger, L. R.** 1973. The neurovirulence test for live poliomyelitis vaccine. J. Biol. Stand. **1:**119–138.
3. **Boulger, L. R., S. C. Arya, P. Ahourai, and S. A. Marsden.** 1978. International comparison of species of monkey used for neurovirulence test for oral poliomyelitis vaccine. J. Biol. Stand. **6:**233–242.
4. **Ion-Nedelcu, N., A. Dobrescue, P. M. Strebel, and R. W. Sutter.** 1994. Vaccine-associated paralytic poliomyelitis and HIV infection. Lancet **343:**51–52.
5. **Leparc-Goffart, I., J. Julien, F. Fuchs, I. Janatova, M. Aymard, and H. Kopecka.** 1996. Evidence of presence of poliovirus genomic sequences in cerebrospinal fluid from patients with postpolio syndrome. J. Clin. Microbiol. **34:**2023–2026.
6. **Wakamoto, H., T. Morimoto, H. Nagao, and H. Matsuda.** 1992. MRI in poliomyelitis-like syndrome. Pediatr. Radiol. **22:**533–534.

Subhash C. Arya
Centre for Logistical Research & Innovation
M-122 (of part 2), Greater Kailash-II
New Delhi 110048, India

Authors' Reply

Our study demonstrated the presence of poliovirus genomic sequences in the central nervous systems of patients with PPS and the absence of such sequences in control patients (4). This result suggests a relationship between the persistence of poliovirus RNA and the PPS. PPS is a slow disease, defined as the development of new muscle weakness and fatigue in skeletal or bulbar muscles, unrelated to any known cause, that begins 25 to 30 years after an acute attack of paralytic poliomyelitis. Some of the questions posed by Dr. Arya concern the acute attack of paralytic poliomyelitis and not PPS.

The diagnosis of PPS is a clinical diagnosis that adopts strict criteria of inclusion and exclusion. Among the exclusion criteria, we included any other chronic pathology. None of our PPS patients had another chronic disease associated with PPS, and none were immunodeficient. However, these patients were not specifically tested for HIV infection. We do not believe there is a relationship between the presence of poliovirus genomic sequences in the central nervous systems of PPS patients and the HIV status of these patients. Indeed, our patients had no other chronic diseases and the mean age of PPS patients for whom we found poliovirus RNA in the CSF was 68. There are actually no reports in the literature of a possible association between HIV infection and PPS. Ion-Nedelcu et al. report a case of vaccine-associated paralytic poliomyelitis in a child infected with HIV (2). This case report did not establish a causal relation between HIV infection and vaccine-associated paralytic poliomyelitis.

MRI could detect some inflammatory areas in patients with acute disease, but results will be completely normal for those with chronic disease.

Persistence of poliovirus in the central nervous system could be studied with monkeys as suggested by Dr. Arya. A search for poliovirus genomic sequences in the CSF of monkeys inoculated with wild-type poliovirus over a period of time will help to define the link between the persistence of poliovirus genomic sequences and PPS. Another animal model, transgenic mice with the human poliovirus receptor, or poliovirus-adapted mutant mice, could be considered (1, 5).

By in situ PCR, poliovirus genomic sequences were localized in the central nervous system of a patient with acute paralytic poliomyelitis (3). Poliovirus RNA was found only in neurons in the anterior horn of the human spinal cord. For PPS, it will also be very interesting to localize poliovirus RNA in the central nervous system by in situ PCR.

REFERENCES

1. **Couderc, T., J. Destombes, D. Thiesson, S. Girard, S. G. Wilt, and B. Blondel.** 1996. Persistence of poliovirus in the mouse spinal cord, abstr. F17. *In* Abstracts of the IXth Meeting of the European Study Group on the Molecular Biology of Picornaviruses.
2. **Ion-Nedelcu, N., A. Dobrescu, P. M. Strebel, and R. W. Sutter.** 1994. Vaccine-associated paralytic poliomyelitis and HIV infection. Lancet **343:**51–52.
3. **Isaacson, S. H., K. Sivakumar, D. M. Asher, K. L. Pomeroy, M. Ramos-Alvarez, C. J. Gibbs, Jr., D. C. Gajdusek, and M. C. Dalakas.** 1995. Cellular localization of poliovirus RNA in the spinal cord during acute paralytic poliomyelitis. Ann. N.Y. Acad. Sci. **753:**194–200.
4. **Leparc-Goffart, I., J. Julien, F. Fuchs, I. Janatova, M. Aymard, and H. Kopecka.** 1996. Evidence of presence of poliovirus genomic sequences in cerebrospinal fluid from patients with postpolio syndrome. J. Clin. Microbiol. **34:**2023–2026.
5. **Ren, R., F. C. Costantini, E. J. Gorgacz, J. J. Lee, and V. R. Racaniello.** 1990. Transgenic mice expressing a human poliovirus receptor: a new model for poliomyelitis. Cell **63:**353–362.

Isabelle Leparc-Goffart
Department of Microbiology
University of Pennsylvania
Abramson Center, 8th Floor, 34th & Civic Center Blvd.
Philadelphia, Pennsylvania 19104-4318

Jean Julien
Service de Neurologie Hôpital du Haut-Lévêque, CHU Bordeaux Avenue de Magellan
33604 Pessac, France

Florence Fuchs
Agence du Médicament, Unité de Virologie
321 Avenue de Jean Jaures
69007 Lyon, France

Michele Aymard
Laboratoire de Virologie, Centre National de Référence des Entérovirus
8 Avenue Rockefeller
69373 Lyon Cedex 08, France

Helena Kopecka
Institut Pasteur Paris, Unité de Virologie Moléculaire, URA 1966 CNRS
28 Rue du Docteur Roux
75015 Paris, France