Chlamydia trachomatis and Parainfluenza 2 Virus: a Shared Antigenic Determinant?

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A tracheal aspirate from which parainfluenza 2 (PI-2) virus but not chlamydiae was isolated demonstrated positive immunofluorescence of elementary body- and reticulate body-like particles on direct examination with anti-chlamydia monoclonal antibodies (Syva Co.). In subsequent studies, we found this reagent to show specific staining of this strain of PI-2 as well as of 3 of 18 additional PI-2 strains that were evaluated.

A tracheal aspirate specimen was simultaneously evaluated by both viral and chlamydial culture techniques and led us to examine the possibility that Chlamydia trachomatis and parainfluenza virus 2 (PI-2) might share a common antigenic determinant. McCoy cell cultures of the specimen, as well as smears of the original specimen, demonstrated fluorescence staining that resembled scattered but abundant chlamydial elementary and reticulate bodies when reacted with fluorescein-conjugated anti-chlamydia monoclonal antibodies (Syva Co.) directed to the major outer membrane (OMP) protein (OMP reagent) (2). However, no inclusions were seen, and the staining material diminished and was ultimately lost on successive passages. The Rhesus monkey kidney (RMK) cell cultures inoculated with the tracheal aspirate developed cytopathic changes and hemadsorption and showed cytoplasmic fluorescence in a pattern typical for parainfluenza viruses when reacted with polyclonal antiserum raised to the Greer strain (National Institute of Allergy and Infectious Diseases, Bethesda, Md.) of PI-2 and a fluoresceinated secondary antibody (5, 8). Furthermore, the OMP reagent stained these RMK cells in a like manner. When infected RMK cells were simultaneously stained with PI-2 antiserum by using a rhodamine-conjugated secondary antibody and the OMP reagent, photographs demonstrated identical distributions and patterns of staining within cells.

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To learn more about the nature and extent of this cross-reactivity, we obtained 18 additional PI-2 isolates: 3 from Boston (Kenneth McIntosh), 12 from Houston (Paul Glezen), and 3 from our own laboratory. No clinical data were available regarding the patients from whom these isolates were obtained. These isolates were inoculated into RMK cell (University of Chicago) culture tubes, and the cells were harvested when they were strongly hemadsorption positive. Suspensions of infected cells were spotted onto 12-well (4-mm-diameter) slides, air dried, fixed in cold acetone for 10 min, and stored at -90°C before they were stained.

We then determined the reaction of each strain with the following: PI-2 polyclonal antiserum (National Institute of Allergy and Infectious Diseases) raised to the Greer strain of PI-2 by using a biotin-avidin rhodamine system, the OMP reagent, and the fluoresceinated monoclonal antibodies (Bar-tels Immunodiagnostics) directed to the chlamydial lipopolysaccharide reagent. Cells of strains that exhibited staining with the chlamydia monoclonal antibodies were stained simultaneously with the PI-2 antiserum by using a biotin-avidin system of rhodamine as the chromagen and the fluoresceinated chlamydia monoclonal antibody to examine for concordance of the staining pattern. They were then examined by fluorescence microscopy, and suitable fields were successively photographed under illumination appropriate for fluorescein and rhodamine, thereby enabling each staining pattern to be examined independently.

All viral strains reacted with the PI-2 viral antiserum. In addition to the strain from our patient, 3 strains (1 from Boston and 2 from Houston) of the 18 additional viral isolates also stained with the OMP reagent. None of the 19 isolates demonstrated positive staining with the lipopolysaccharide reagent. In the double labeling experiment, the pattern of staining of the cells with the PI-2 antiserum and the OMP reagent was identical (Fig. 1).

Antigenic cross-reactivity could be caused by a shared antigenic determinant or by a close resemblance between antigenic determinants. Many examples of antigenic mimicry exist. There are reports of chlamydial antigenic components cross-reacting with other species, i.e., Acinetobacter anitratus and Coxiella burnetii (1, 4, 10). However, a cross-reaction between chlamydiae and a viral antigen has not been described previously.

PI-2, one of four serotypes of parainfluenza virus, is a common cause of respiratory infection in children. It is believed to have at least seven viral polypeptides, including the fusion (F) and hemagglutinin and neuraminidase (HN) glycoproteins (9). These glycoproteins are common to all the parainfluenza viruses and correspond to the glycoproteins of the simian virus SV-5. Antigenic variation is frequent among human PI-3 viruses and has also been described among clinical strains of mumps virus, another member of the paramyxovirus group (7). Van Wyke Coelingh and colleagues (12), using monoclonal antibodies to the HN protein, demonstrated that this antigenic diversity represents genetic heterogeneity since some 1983 isolates appeared to be identical to the 1957 prototype and other 1983 isolates did not. PI-2 has been less well studied. However, in two isolates variable gel electrophoresis migration patterns of the nucleoprotein and the HN and F glycoproteins have been dem-

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onstrated (3). Furthermore, the cleavage products of the F protein may vary from strain to strain (6, 11). This variability might account for the fact that positive immunofluorescence with the C. trachomatis monoclonal antibodies was observed in only 3 of 18 additional PI-2 isolates, suggesting that one of these proteins is involved in this cross-reaction. It is unclear which of the proteins of these isolates shares a common antigenic determinant with the chlamydial OMP. Nonetheless, a shared antigenic determinant may lead to an error in clinical diagnoses.

Direct staining of respiratory tract secretions with the OMP reagent may show positive fluorescence when the patient does not have chlamydial pneumonia, but rather PI-2 infection. This misdiagnosis may cause the initiation of unnecessary antimicrobial therapy; therefore, the OMP reagent should not be used for direct staining of respiratory specimens without the benefit of culture confirmation. In addition, one should be cautious to interpret all positive laboratory findings within the clinical context of the patient. However, in the appropriate clinical setting, rapid viral diagnosis with monoclonal antibodies can be a highly useful tool.

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FIG. 1. (A) PI-2 isolate stained with PI-2 antiserum raised against the Greer strain by a biotin-avidin rhodamine system. (B) PI-2 isolate stained with the fluoresceinated chlamydial OMP reagent (Syva Co.). Magnifications, ×400.