Pneumonia Caused by Rhinovirus

Rhinovirus infections, although usually limited to the upper respiratory tract, can extend beyond the oropharynx and may cause complications in the lower respiratory tract, including pneumonia [1–3]. We describe a case of rhinovirus pneumonia in an infant boy in which rhinovirus was recovered from the lung and analysis of hyperimmune serum to the causal rhinovirus revealed localization of rhinovirus antigen in the lung.

At 16 and 22 days of age, an infant boy underwent operations for cardiovascular anomalies, including an interrupted aortic arch and a ventricular septal defect. After the operations, he developed transfusion-associated graft-versus-host disease and died of multiple organ failure at the age of 59 days.

At autopsy, the histopathologic findings for the hematopoietic system and the skin were consistent with transfusion-associated graft-versus-host disease. Examination of the lungs showed mild hyperplasia of the bronchial epithelium with cytological alterations, thickening of the alveolar septum, marked hyperplasia of the alveolar lining cells, and desquamating swollen alveolar epithelial cells and macrophages in the alveoli; however, inflammatory infiltrates were scanty (figure 1).

Two weeks after inoculation of the lung tissue homogenate, human embryonic lung cells had the cytopathic effect typical of enterovirus. The isolated cytopathic agent was resistant to ether and chloroform; its density was 1.3 g/mL, and it was 24 nm in diameter. Its infectivity was sensitive to low pH (pH 3–4), and it was inactivated by heat treatment at 56°C for 30 min. Viral growth at 33°C was prominent compared with that at 37°C. Immunofluorescent antibody testing revealed that antiserum to rhinovirus types 13, 16, and 28 stained the cells infected with the cytopathic agent. The cytopathic agent was not neutralized by antiserum to rhinovirus types 16 and 28 but was neutralized by antiserum to rhinovirus type 13. These findings suggested that the cytopathic agent was rhinovirus type 13.

Hyperimmune serum to the purified virus was obtained 2 weeks after injection of the third booster dose in rabbits and absorption with an uninfected human embryonic lung cell lysate. The specificity of the hyperimmune serum was confirmed by an immunofluorescence study on the human embryonic lung cells that were infected with the isolated agent. Analysis of the hyperimmune serum by means of the modified avidin-biotin peroxidase complex method demonstrated that the rhinovirus antigen was localized in the desquamating swollen alveolar epithelial cells and macrophages in the alveoli and the hyperplastic alveolar lining cells (figure 1B).

Upper respiratory tract infections due to rhinovirus are associated with no histopathologic findings in the nasal epithelium, a brisk leukocyte response, and a paucity of antigen [4]. Only 2 autopsy reports have described the pulmonary pathol-

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Figure 1. Left, Histopathologic analysis of lung tissue from an infant with pneumonia due to rhinovirus shows thickening of the alveolar septum, hyperplasia of the alveolar lining cells, and macrophages in the alveoli (hematoxylin-eosin stain; original magnification, ×350). Right, Analysis of hyperimmune serum (by means of the modified avidin-biotin peroxidase complex method) reveals localization of rhinovirus antigen in the cytoplasms of hyperplastic alveolar lining cells (arrows), desquamating swollen alveolar epithelial cells, and macrophages in the alveoli (original magnification, ×175).
ology of rhinovirus pneumonia in humans with isolation of rhinoviruses from lung tissue [5, 6]. One [5] reports that specific histological changes attributable to the infection were not found in pulmonary tissue, and the other [6] reports that the scattered zones of interstitial pneumonia with hyaline membranes covering some of the affected alveoli were present throughout the lungs.

In our case, examination of the lung showed remarkable histological changes, including hyperplasia and desquamation of the alveolar lining cells, as well as immunohistochemical localization of rhinovirus antigen in the alveolar epithelial cells and macrophages. These findings may suggest that rhinovirus can attack primarily the alveolar lining cells. They are dramatically different from previous descriptions of the pathology associated with rhinovirus infection; however, the nature of our patient’s underlying illness and his multisystem failure may have complicated the lung pathology and made its interpretation difficult.

Coccidioidin Skin Testing in Kern County, California: Decrease in Infection Rate over 58 Years

Skin test surveys in the late 1930s indicated that many people in Kern County, California, had been previously infected by *Coccidioides immitis*. We report the results of serial coccidioidin skin test surveys conducted since 1959 and compare them with the results of the 1937–1945 studies [1–7]. Both sets of surveys were done in the Bakersfield-Delano area, centrally located in California’s southern San Joaquin Valley. We considered a positive test to be 5 mL of induration read at 48 h. Coccidioidin was used until the 1980s (lot 64 from C. E. Smith [Stanford University School of Medicine, Stanford, CA] and, in the first study, some from J. Kessel [University of Southern California School of Medicine, Los Angeles]), when it was replaced by spherulin (ALK Laboratories, Wallingford, CT). For epidemiological purposes, the difference between these 2 reagents is negligible.

Results of the serial coccidioidin skin test surveys (figure 1) are expressed as the infection rate (IR), that is, the number of people infected by *C. immitis* each year. This number is determined from the percentage of positive reactors in subgroups whose members have lived in the study area for different specified periods.

Among students who had lived in the area 10–14 years, the IR was just over 10% in 1937–1939. In 1959, the IR was >4%, and it dropped to ~1% by 1971. It declined further in 1978 and 1984 but returned to the 1971 level in May 1992, early in what proved to be the 1991–1994 epidemic [8]. Among children in kindergarten and first grade who had lived all of their 5–7 years in the area, the IR approached 10% in 1937–1939, then dropped to 2% by 1959 and to ~1% thereafter. Our 6 student surveys from 1959 to 1992 (8491 students were tested) showed an even more dramatic decrease in IR than was seen in the adult studies whose data are presented in figure 1.

Among adults who were 15-year residents, the IR dropped from >10% per year in the late 1930s to ~4% in 1979–1984 and to ~2% in 1995. For 5–9-year residents, the values were >10% in the 1930s, ~5% in 1979–1984, and ~4% in 1995 (with higher levels of exposure during the 1991–1994 epidemic). The IR among adults was greater than that among high school students, which was greater than the IR among children.

Waning of skin test reactivity with time has long been observed, even in areas of endemicity. Maddy et al. [9] found that this waning occurred after 12 years of residence, and Sievers and Fisher [10] used 14 years of exposure for comparative purposes, noting that coccidioidin reactivity decreases in many people after that. Our similar observations suggest that using 15 years of residence as the comparison point may avoid the uncertainties introduced by waning reactivity.

Increasing cultivation, irrigation, and urbanization over the years, all activities expected to decrease the amount of *C. im-