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Pseudo-outbreak of varicella-zoster virus associated with bronchoscopy in an intensive care unit

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To the Editor—Flexible bronchoscopy is a procedure commonly performed in intensive care units (ICUs). Pathogens can be transmitted via flexible bronchoscopes, most commonly bacteria,[1] but viral transmission is also possible.[2] Varicella-zoster virus (VZV) usually causes self-limited disease in childhood and remains latent. In adulthood, primary infection or reactivation can be severe and disseminated in immunocompromised and critically ill individuals.[3,4]

In December 2021, a 33-year-old man with Crohn's disease treated with adalimumab and methylprednisolone was admitted to the intensive care unit (ICU) due to disseminated VZV infection. Flexible bronchoscopy and bronchoalveolar lavage (BAL) were performed on hospital day 1 and were repeated on hospital days 9, 12, and 23. VZV DNA was detected by polymerase chain reaction (PCR) in the BAL, plasma, and skin vesicles. During the same
3-week period, BAL samples from 4 patients with coronavirus disease 2019 (COVID-19) were positive for VZV. These patients were located in single rooms in a different ICU located on another floor of the hospital. An investigation for a suspected outbreak was launched as soon as the BAL sample from the third COVID-19 patient was positive for VZV.

Methods

Medical records of all patients with VZV-positive BAL specimens between January 19, 2021, and October, 19, 2022, were reviewed, bronchoscope cleaning protocols were assessed, and samples were taken from the bronchoscope (lavage and brush samples) and automated endoscope reprocessor (AER; a 100-mL sample of the final rinse water) for VZV DNA testing. The implicated bronchoscope was returned to the manufacturer for inspection. A written consent for publishing a case report was obtained from the index patient.

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We took 200-µL samples from the BAL samples, the bronchoscope lavage samples and from the sample of the AER final rinse water, after which automatic nucleic acid extraction was performed with the 100-µl elution volume on the MagNA Pure Compact Instrument (Roche Diagnostics, Mannheim, Germany). Herpesvirus diagnostics were performed using GeneProof (BRNO, Czech Republic). The following targets were included in the PCR assay: herpes simplex virus (HSV), VZV, cytomegalovirus (CMV), and Epstein-Barr virus (EBV). The assay was performed according to the manufacturer's instructions.

Results

The index patient's first sample that was positive for VZV was obtained on hospital day 1. Between then and hospital day 23, VZV DNA was detected in BAL samples from 4 additional patients, with PCR cycle thresholds ranging from 33.32 to 37.3. All samples had been obtained with the same FB. Bronchoscopy had been performed for these 4 patients due to respiratory deterioration and progression of lung infiltrates in the setting of COVID-19 infection. Detailed clinical and microbiological characteristics of the 5 patients are presented in Table 1. No other BAL samples were positive for VZV among the 214 reviewed BAL samples in the 11 months before and 9 months after the 8 positive samples described above.

According to the hospital protocol, bronchoscopes are cleaned by trained ICU nurses according to manufacturer's instructions (Olympus, Center Valley, PA) and FDA recommendations. Flexible bronchoscopes are brushed manually for 5 minutes with Enzymex diluted to 0.5 % (5 mL/L) solution and placed in the Olympus automated endoscope reprocessor (type miniETD2) for 40 minutes, where a leak test, rinsing, and disinfection are automatically performed. Bronchoscopes are stored in a drying cabinet (Olympus EDC plus).[5] The AER and the drying cabinet are located in a separate room within our ICU and are handled by trained ICU nurses. The protocol was consistent with the manufacturer's instructions. Direct observation of bronchoscope reprocessing

Table 1. Patient Demographic, Clinical and Microbiologic Characteristics

Patient	Presenting Illness	Chronic Disease	Timing of Bronchoscopy After Admission of the Index Patient[a]	Glucocorticoid Therapy	Viral DNA Detected in BAL Fluid	PCR Cycle Threshold	VZV IgG Serology
Index patient	Disseminated varicella	Crohn's disease	Day 1, Day 9 Day 12 Day 23	Yes	VZV	19.68	NA
Patient 1	COVID-19 pneumonia	Ischemic heart disease MDS	Day 6	Yes	HSV-1 VZV EBV	24.2 33.32 34.23	Positive
Patient 2	COVID-19 pneumonia	Arterial hypertension, GERD	Day 6	Yes	HSV-1 VZV	22.28 34.17	Positive
Patient 3	COVID-19 pneumonia	Ulcerative colitis, Chronic pancreatitis Osteoporosis Anemia	Day 14	Yes	CMV EBV VZV	3210 IU/mL (BAL) <35 IU/mL (blood) 35.33 35.9	Positive
Patient 4	COVID-19 pneumonia	Cryptogenic liver cirrhosis (Child B), Esophageal varices Chronic pleural effusion Sarcopenia Osteopenia Sarcoidosis	Day 22	Yes	VZV EBV	37.30 28.1	Positive

Note. BAL, bronchoalveolar lavage; CMV, cytomegalovirus; EBV, Epstein-Barr virus; F, female; GERD, gastroesophageal reflux disease; HSV-1, herpes simplex virus type 1; ICU, intensive care unit; MDS, myelodysplastic syndrome; PCR, polymerase chain reaction; VZV, varicella-zoster virus; BAL, bronchoalveolar lavage; NA, not applicable.
[a]Day 1, first bronchoscopy on index patient.

was performed as part of the investigation. The bronchoscope reprocessing was performed by different nurses at different times; however, all of them were specifically trained to perform the reprocessing. Samples taken from the working channel of the implicated FB and the automated endoscope reprocessor on hospital days 15–16 were negative for VZV DNA by PCR-based testing. The manufacturer's inspection of the bronchoscope, which included a visual inspection, functional inspection, processor checks and inspection of the channel system with a borescope, revealed no defects.

Discussion

The finding of VZV-positive samples in 4 patients with COVID-19 occurred in the setting of acute respiratory deterioration. An initial consideration was reactivation of latent VZV infection, as the patients had well known risk factors,[3,4,6] but high VZV Ct values (meaning low VZV DNA load) and VZV IgG spoke against either acute infection or reactivation. The samples of 2 patients were positive for HSV-1 with low Ct values, which makes HSV-1 reactivation a more likely etiology of respiratory deterioration.[8] The role of the detected CMV and EBV in the patients' illness is less clear as both might reactivate in the critically ill.[9]

The association of all 5 cases with a single flexible bronchoscopy and the high VZV cycle threshold values in the subsequent patients' BAL samples and their VZV IgG positivity suggest a pseudo-outbreak due to VZV virus or VZV DNA contamination of the FB. An alternative explanation could be asymptomatic VZV shedding in these 4 patients, which has been described in healthy individuals, astronauts, and immunocompromised individuals.[7] But before and after the described cluster, 214 BAL samples were VZV negative. This finding refutes this possibility. Contamination of flexible bronchoscopes with an inactive virus has previously been described for HIV.[2] Although not directly observed, we suspect that failures in flexible bronchoscope reprocessing resulted in residual VZV virus or viral DNA in the flexible bronchoscope lumen, which contaminated the lavage fluid used in the other patients. The samples taken from the flexible bronchoscopes were negative for VZV DNA, probably because it had been reprocessed several times before testing was performed. This case highlights the importance of proper flexible bronchoscope reprocessing. Although there appears not to have been disease transmission in this case, insufficient cleaning and/or disinfection of flexible bronchoscopes can result in patient-to-patient transmission of infection.

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