picion of a nosocomial infection among patients with IE and recent hospitalization could justify the empirical use of vancomycin as part of the initial empirical antimicrobial regimen. However, the authors do not provide data to support this conclusion. We believe that more sound evidence is needed before a broader definition of nosocomial IE should be accepted and IE management modified accordingly.

Acknowledgments

Performed within Ricerca Corrente Istituti di Ricovero e Cura a Carattere Scientifico.

Conflict of interest. All authors: No conflict.

Stefania Cicalini,1 Vincenzo Puro,2 Claudio Angeletti,2 Maria Federica Proietti,1 and Nicola Petrosillo1

12nd Infectious Diseases Unit and 2Department of Epidemiology, National Institute for Infectious Diseases Lazzaro Spallanzani, IRCCS, Rome, Italy

References


Reply to Cicalini et al.

Sir—We welcome the effort made by Cicalini et al. [1] to validate our observations [2] in a different population. However, before one concludes that their results contradict our own, several points should be considered. Cicalini et al. [1] state that 4 of the patients with cases included in the broadened definition of hospital-acquired infective endocarditis (IE) had been discharged from the hospital within the previous 6 months. However, it is unclear whether the other 5 patients—whose cases were included because the patients had undergone invasive procedures (i.e., surgery, dental work, endoscopy, and dialysis)—underwent these procedures during hospitalization or as outpatients. In our study, patients who underwent invasive procedures as outpatients were assigned to the true community-acquired IE group: 10 (20%) of 49 episodes of true community-acquired IE were associated with such procedures [2]. Therefore, it is possible that only 4 of the patients described by Cicalini and colleagues had cases that fit our broadened definition of hospital-acquired IE. Because the individual associations of bacterial isolates with specific patients are not provided, the distribution of bacterial species among these 4 patients is unknown. However, the small number of recently hospitalized patients, as well as the high proportion of culture-negative IE episodes (3 of 9 episodes), preclude a meaningful assessment of the bacteriological and clinical characteristics of this group. Finally, we hypothesized that IE in recently hospitalized patients reflects the prevalence of bacterial isolates in the discharging medical institution. Therefore, the characteristics of hospital-acquired IE (as traditionally defined) in the relevant medical institution should also be considered when assessing the significance of recent hospitalization. These data are not reported by Cicalini et al. [1].

Currently, there is no well-established definition of hospital-acquired IE. On the basis of our observations, we proposed that patients who had been discharged from the hospital ≤6 months before the onset of their symptoms should be considered to have hospital-acquired infections. However, we agree with Cicalini et al. [1] that a widely applicable definition should be based on data from diverse epidemiological settings. We hope that our observations will encourage other researchers to examine local data, so that this emerging medical problem can be better addressed.

Acknowledgment

Conflict of interest. All authors: No conflict.

Ronen Ben-Ami,1 Michael Giladi,1 Yehuda Carmeli,2 Ruth Orni-Wasserlauf,1 and Yardena Siegman-Igra1

1Infectious Diseases Unit and 2Department of Epidemiology, Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Israel

References


Reprints or correspondence: Dr. R. Ben-Ami, Infectious Diseases Unit, Sourasky Medical Center, Tel Aviv, Israel 64239

Clinical Infectious Diseases 2004; 39:1085 © 2004 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2004/3907-0035$15.00

Antemortem Diagnosis of Human Rabies

Sir—We previously reported the use of nucleic acid sequence-based amplification (NASBA) for the detection of rabies virus RNA in samples of saliva, CSF, and/or urine obtained during life from 8 patients infected with rabies [1, 2]. Here, we summarize the results of NASBA in correlation with the clinical onset of symptoms of the disease.

From September 1998 through March 2004, we collected and tested 58 specimens from 23 rabies patients (20 with furious
and 3 with paralytic rabies). Samples collected included: 27 saliva, 14 CSF, 15 urine, and 1 tear specimen; and extracted hairs from 1 patient. All patients had been bitten by stray dogs. Postmortem brain samples from all patients were positive for rabies virus by either fluorescence antibody testing or mouse inoculation; all samples were also positive for rabies virus by either NASBA or RT-PCR. All samples, except the first 4 specimens, which were frozen, stored, and examined retrospectively [1], were kept at 4°C for 24–48 h until examined for the presence of the rabies nucleocapsid gene. In 21 of 23 patients, we identified rabies RNA in specimens obtained on the first day of hospitalization. Specimens collected within 3 days after clinical onset yielded the highest number of positive results with saliva samples having the highest rate of positivity (7 of 8 specimens), followed by CSF (4 of 6) and urine (2 of 5). The sensitivity of all specimens types dropped after 3 days; however, saliva remained the most practical and reliable source for virus detection (11 of 15 specimens positive during days 4–6 after onset and 1 of 2 positive during days 7–9). The test sensitivity for urine (3 of 9 specimens positive for rabies virus RNA) and CSF (2 of 7) was comparable during days 4–6. Test results for 2 saliva specimens, 1 CSF specimen, and 1 urine specimen obtained during days 10–12 were all negative. Of particular interest were the test results for hairs extracted from 1 patient obtained 4 days after onset of symptoms. Fifty hair samples were extracted from this patient instead of excising skin with hair follicles from the nape of the neck [3]. We were able to demonstrate the presence of rabies RNA in the ends of the hair follicles.

Negative results were obtained exclusively from tests performed on samples collected sequentially from 2 patients with paralytic rabies. Samples tested from the first patient included saliva, CSF, and urine collected on day 11 after onset and saliva collected on day 12. Samples tested from the second patient included CSF and urine collected on day 4, saliva and urine collected on days 5 and 6, and tears collected on day 7. For a third patient with paralytic rabies, results from a CSF sample collected on day 3 were positive, but results for saliva samples collected on days 3 and 7 were both negative.

In summary, we conclude that molecular methods, although useful and extremely sensitive, may not always give positive results for patients with rabies. This may be due to the intermittency of virus shedding, the timing of sample collection, and the type of specimens collected. Moreover, the extent the clinical type of rabies (particularly paralytic rabies and cases with atypical features) [4] influences the outcome of laboratory results remains to be determined. We strongly urge that specimens be collected simultaneously from several sources and examined; they should include saliva, urine, and CSF. Sample collection should be repeated until a diagnosis is confirmed [5]. Postmortem examination should also be conducted in all suspected cases of rabies and other encephalitides, regardless of the results of antemortem examination.

Acknowledgments

We are indebted to physicians all over Thailand who participated in rabies surveillance and sent specimens to us. We are grateful to Deborah Briggs for critical review of the manuscript. Financial support. Supported in part by grants from Thai Red Cross Society, Thailand Research Fund, and Japan Health Science Foundation. Conflict of interest. T.H. and S.W.: No conflict.

Thiravat Hemachudha
and Supaporn Wacharapluesadee
Molecular Biology Laboratory for Neurological Diseases, Department of Medicine, Chulalongkorn University Hospital, Bangkok, Thailand

References


Clinical Infectious Diseases 2004; 39:1086–9 © 2004 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2004/3907-0036$15.00

Infection by Drug-Resistant Streptococcus pneumoniae Is Not Linked to Increased Mortality

Sir—We congratulate Dr. Aspa and colleagues and the Pneumococcal Pneumonia in Spain Study Group [1] for their large, labor-intensive study of 638 cases of community-acquired pneumonia due to Streptococcus pneumoniae. We take issue with only one point made in an otherwise excellent study: “The impact of drug-resistant S. pneumoniae on morbidity and mortality is still controversial” [1, p. 795]. The authors underestimate the potency of their own findings when they claim that the issue is controversial. If it is controversial, the authors have provided additional support for the numerous authorities on pneumococcal infection who claim that drug resistance is an artifact of the NCCLS guidelines, with few clinical implications. Their major finding was that in vitro resistance to macrolides and β-lactam agents did not result in increased morbidity or increased mortality—a finding that has been reiterated in >20 peer-reviewed articles, including our own [2]. The authors cited the Centers for Disease Control and Prevention (CDC; Atlanta, GA) study [3] in which mortality was significantly associated with an MIC of penicillin of ≥4 μg/mL, and they suggested that high-level resistance may be associated with an adverse outcome. In fact, the CDC study did not attempt to correlate discordant therapy with out-