J Infect Chemother (2013) 19:517–523
DOI 10.1007/s10156-012-0475-7

CASE REPORT

Usefulness of gram-stained sputum obtained just after administration of antimicrobial agents as the earliest therapeutic indicator for evaluating the effectiveness of empiric therapy in community-acquired pneumonia caused by pneumococcus or *Moraxella catarrhalis*

Ryuichi Fujisaki · Toshimori Yamaoka · Michiko Yamamura · Sayoko Kawakami · Yasuo Ono · Yukihisa Miyazawa · Tamio Teramoto · Hajime Nishiya

Received: 28 June 2012 / Accepted: 4 September 2012 / Published online: 17 October 2012

Abstract We present here three cases in which morphological changes and/or a decreased number of *Streptococcus pneumoniae* or *Moraxella catarrhalis* could be observed in gram-stained sputum obtained just after the first administration of an antimicrobial agent. Case 1 was a 53-year-old man with pneumonia caused by gram-positive diplococcus, identified as *S. pneumoniae*, who was administered 2 g of ampicillin over a period of 1 h. Gram-stained sputum showed smaller or gram-negative pneumococci at the completion of administration of the agent, a decreased number of cocci at 1 h after administration, and almost no cocci at 12 h after the completion of administration. Case 2 was a 72-year-old woman with pneumonia caused by diplococcus, identified as *S. pneumoniae*, who was administered 2 g of ampicillin over a period of 1 h. Gram-stained sputum showed weakly stained, small cocci at the completion of administration of the agent and few cocci at 1 h after the completion of administration. Case 3 was a 58-year-old woman with pneumonia caused by a gram-negative diplococcus, identified as *Moraxella catarrhalis*, who was administered 1 g of cefotaxime over a period of 30 min. Gram-stained sputum showed few extracellular cocci and some intracellular cocci inside neutrophils 1 h after administration and no cocci 2 h after the completion of administration. These three cases showed that gram-stained sputum obtained just after and/or 1 h after administration of the first antimicrobial agent were suitable as the quickest therapeutic indicator of the effectiveness of empiric therapy, with the effectiveness of the agent being shown much earlier than with markers such as the white blood cell count and C-reactive protein level.

Keywords *Streptococcus pneumoniae* · *Moraxella catarrhalis* · Gram staining · Therapeutic indicator · Community-acquired pneumonia

R. Fujisaki · T. Yamaoka · M. Yamamura · T. Teramoto · H. Nishiya (✉)
Department of Internal Medicine, Teikyo University School of Medicine, Kaga 2-11-1, Itabashi-ku, Tokyo 173-8605, Japan
e-mail: hnishiya@med.teikyo-u.ac.jp

S. Kawakami · Y. Miyazawa
Department of Central Clinical Laboratory, Teikyo University Hospital, Tokyo, Japan

Y. Ono
Department of Microbiology, Teikyo University Hospital, Tokyo, Japan

Introduction

Community-acquired pneumonia (CAP) is an important infectious disease causing hospitalization and death [1], particularly in elderly patients and patients who are susceptible to resistant pathogens [2, 3]. *Streptococcus pneumoniae* is the most common pathogen implicated in CAP, and in hospitalized patients it accounts for two-thirds of the mortality associated with CAP [4]. In CAP, it is said that gram staining of sputum is useful in only a small percentage of patients as a tool for the diagnosis of bacterial pneumonia and that the role of sputum examination in the management of patients with CAP is limited [5, 6]. However, the usefulness of the gram stain in the management of CAP is controversial [7, 8]. Most clinicians prescribe empiric antimicrobial agents in accordance with guidelines. To evaluate the effectiveness of the antimicrobial

agents, some markers including the white blood cell count (WBC), serum C-reactive protein (CRP) level, body temperature, and the extent of consolidation shadows on an X-ray film of the chest are useful and are frequently checked. With these methods, the effectiveness of the antimicrobial agents can be evaluated 2 or 3 days after starting the therapy [9]. Most patients with CAP will have an adequate clinical response within 3 days, and the initial antibiotic therapy should not be changed in the first 72 h in most patients, unless there is marked clinical deterioration [8]. However, we suggest that a more rapidly changing therapeutic marker with more certainty is needed in dealing with CAP. We present here three cases in which morphological changes and/or a decreased number of *Streptococcus pneumoniae* or *Moraxella catarrhalis* could be observed in gram-stained sputum obtained just after the first administration of antimicrobial agents.

Case reports

Case 1

A 53-year-old man was admitted to our hospital because of fever. He had been well until 1 week previously, when he was travelling in China, and he developed a fever of around 38 °C. The fever decreased to around 37 °C on the next day. He returned to Japan 4 days before admission to our hospital. Three days before admission, he had a fever again, and his body temperature reached around 39 °C on the day of admission.

On admission, his consciousness was clear. His body temperature was 38.6 °C and his pulse was 107 beats/min. His blood pressure was 158/88 mmHg. Oxygen saturation with pulse oximetry showed 98.4 % in room air. Blood gas analysis showed PaO_2, 65.7 torr; $PaCO_2$, 27.5 torr; pH, 7.544; HCO_3^-, 24.0 mEq/l. On physical examination, a fine crackle was heard at the base of the right lung. No murmur was heard. His abdomen sounds were normal and no lymphadenopathy was found. He had no history of contact with birds or of staying at hot springs. Neurologic evaluation was negative. An electrocardiogram showed sinus tachycardia. Urinalysis results were normal. Laboratory tests were performed. The WBC was elevated, at 18400/mm^3 with an increased percentage of neutrophils. The CRP level was elevated, at 12.46 mg/dl. Results of tests for renal and liver function were normal. An X-ray film of the chest showed a consolidation shadow in the S5 segment of the right lung.

Gram staining of the sputum obtained on admission showed a large number of neutrophils and gram-positive diplococci, suggesting *S. pneumoniae* (Fig. 1a). Two grams of ampicillin (ABPC) was intravenously administered over a period of 1 h. At the completion of administration of ABPC, the pneumococci had become smaller in size compared with those seen before the therapy, and some had lost their gram-positive staining and were detected as gram-negative cocci (Fig. 1b). The changes had progressed 1 h after the completion of ABPC administration and the number of cocci had decreased further (Fig. 1c). Twelve hours after the first dose of ABPC, when the second dose was started, gram staining of the sputum showed almost no cocci (Fig. 1d). These changes on gram staining clearly showed the effectiveness of ABPC, which was then repeatedly administered twice a day. The WBC and CRP levels were 16000/mm^3 and 16.93 mg/dl, respectively, 1 day after completion of administration of the first dose of ABPC; these findings did not show the effectiveness of ABPC, and the levels were 9400/mm^3 and 3.08 mg/dl, respectively, 4 days after completion of administration of the first dose of ABPC. Two days after completion of administration of the first dose of ABPC, susceptibility tests of the bacteria showed that the minimum inhibitory concentration (MIC) of benzylpenicillin G (PCG) was 2 μg/ml. ABPC was administered twice a day for 8 days according to the results of gram stains, and the pneumonia was cured.

Case 2

A 72-year-old woman with hypertension and dyslipidemia was transferred to our hospital to receive additional therapy. She had been well until 1 week previously, when she developed a sore throat and rhinorrhea. She visited a clinic and was diagnosed as having a common cold. Six days before admission, she had a fever. Three days before admission, she visited another clinic because of the persistence of fever and was prescribed azithromycin for 3 days. On the day before admission, she had iron-colored sputum. On the next day, she visited the clinic again. Her WBC and CRP levels 3 days before admission were elevated, at 33290/mm^3 and 32.8 mg/dl, respectively. She was admitted to our hospital because of fever and headache. On admission, her body temperature was 39.0 °C. Her pulse was 110 beats/min, and oxygen saturation by pulse oximetry in room air showed 96 %. Her blood pressure was 146/94 mmHg. On physical examination, the patient was alert. No jaundice was noted. A coarse crackle was heard at the base of her right lung. The heart and abdomen were normal. Neurologic evaluation was negative. No neck stiffness and no lymphadenopathy were found. An electrocardiogram showed sinus tachycardia. Laboratory tests were performed. Proteinuria (1+) without pyuria was noted. Slight liver dysfunction was also noted. The WBC was elevated, with an increased percentage of neutrophils (WBC, 18900/mm^3; neutrophils 87 %). The CRP level was elevated, at 16.54 mg/dl. An X-ray film of the chest