

# Likely False-Positive Pneumococcal Antigen Test BinaxNOW Due to *Parvimonas micra*

## A Four-Case Series



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We retrospectively report four cases from two hospitals of nonpneumococcal pleural empyema with a likely false-positive result on the pneumococcal antigen test BinaxNOW (PATB) (Alere) performed in pleural fluid samples in patients with aspiration pneumonia risk factors. To determine whether the positive reaction was due to cross-reactivity, we separately tested the isolates from the pleural fluid samples, along with collection and reference strains. All patients had polymicrobial aerobic and anaerobic positive cultures, including *Parvimonas micra* in every case. In all cases, 16S rDNA polymerase chain reaction sequencing yielded *Fusobacterium nucleatum*. Samples for culture and specific polymerase chain reaction were negative for *Streptococcus pneumoniae*. We found that the false-positive PATB finding was likely due to *P micra*, a previously unknown cross-reactivity. In case of aspiration pneumonia risk factors, a positive PATB result must be interpreted with caution because there can be a false positivity due to anaerobic infection or co-infection.

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**KEY WORDS:** cross-reaction; pleural empyema; pneumococcal antigenic test

### Introduction

Empyema is a serious complication of pneumonia involving significant morbidity. It has an increasing incidence in the United States and Europe despite the introduction of the pneumococcal conjugate vaccine in the 2000s.<sup>1</sup> Rapid diagnosis of the causative agent is required for effective antibiotic treatment and good outcome.<sup>2</sup> However, in > 60% of cases, pleural fluid specimens fail to yield a pathogen on standard laboratory cultures,<sup>3,4</sup> hence the benefit of using the pneumococcal antigenic test BinaxNOW

(PATB) (Alere), which reportedly has good performance in pleural fluid analysis.<sup>5</sup>

We report here four cases of false-positive PATB (Alere) findings in the pleural fluid of patients with nonpneumococcal pleural empyema.

### Case Reports

#### Patients

We retrospectively report four cases from two hospitals. Patient 1 was an 8-year-old girl with a history of epileptic

**ABBREVIATION:** PATB = pneumococcal antigen test BinaxNOW

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encephalopathy with long-term tracheostomy ventilation. Patient 2 was a 34-year-old man with congenital mental impairment and neuroleptic treatment. Patient 3 was a 22-month-old girl with no medical history. Patient 4 was a 16-year-old boy who had a neurodevelopmental disorder caused by a mutation in the ADNP (activity dependent neuroprotective protein) gene and notably causing merycism. All patients presented with febrile respiratory distress, and imaging yielded pleural effusion (right-sided except for patient 4). All underwent thoracentesis for fluid analysis, and fluid drainage was performed in patients 1 through 3. All the patients made a full recovery under appropriate antibiotic therapy.

Pleural fluid analysis yielded inflammatory cytology (WBC count  $> 5,000/\text{mm}^3$  and neutrophil count  $> 70\%$ ) except for patient 4 (cytology results were not available). All had a positive result on PATB. The 48-h bacteriologic culture yielded the following: patient 1, *Eikenella corrodens* and *Parvimonas micra*; patient 2, *P micra* and *Streptococcus intermedius*; patient 3, *S intermedius*, *P micra*, *Prevotella intermedia*, and *Prevotella loescheii*; and patient 4, *P micra*, *Streptococcus anginosus*, *Streptococcus salivarius*, *Staphylococcus aureus*, and *Aggregatibacter aphrophilus*.

The 16S ribosomal DNA polymerase chain reaction sequencing also found *Fusobacterium nucleatum* in all patients and *Prevotella oris* in patient 4. The pneumococcal antigenic test result was negative in the urine when it was performed (patients 1 and 3). Blood culture results remained sterile.

### Microbiologic Analysis

To determine whether the positive reaction of PATB was due to cross-reactivity, we separately tested the isolates of *P micra*, *E corrodens*, and *S intermedius* from the pleural fluid samples with the PATB (according to the manufacturer, the other isolated species are known not to present any cross-reactivity with the PATB). Because we did not isolate any *F nucleatum*, we challenged another strain of *F nucleatum* from our collection. A false-positive test result was recorded for *P micra* and a negative test result for all other species.

To corroborate the results, we acquired the *Parvimonas* strain AIP 2013/00661 from the National Reference Laboratory for Anaerobes at Pasteur Institute and challenged it with the same test. Once again, we found a false-positive test. Finally, we performed specific pneumococcal polymerase chain reaction<sup>6</sup> directly on

the four pleural fluid samples, which proved negative. Consequently, the false-positive result for all patients was due to the presence of *P micra* in the pleural fluid specimens.

### Discussion

*Streptococcus pneumoniae* is the leading cause of pleural empyema. When not properly diagnosed and treated, these infections can be life-threatening. The PATB is an in vitro rapid and simple immunochromatographic membrane assay for the detection of *S pneumoniae* soluble antigen (polysaccharide C) in the urine of patients with pneumonia and in the cerebral spinal fluid of patients with meningitis.<sup>7</sup> Although the manufacturer does not specify that the test can be used in pleural fluid specimens, several studies have proved it useful in the microbiologic diagnosis of pleural empyema.<sup>5</sup>

According to the manufacturer's advertisement, the PATB has been tested for cross-reactivity against most common bacterial agents of meningitis, pneumonia, urinary tract infection, and those found in the urogenital tract normal flora. *P micra*, *Fusobacterium*, *S intermedius*, and the *Eikenella* strains were not among the potential cross-reactants tested.

Although false-positive PATB findings have been reported,<sup>8</sup> no false-positive PATB reactivity due to *Parvimonas* has been described in the literature. *P micra*, formerly known as *Peptostreptococcus micros*, is a anaerobic gram-positive bacterium of the oral microflora<sup>9,10</sup> and an opportunistic pathogenic. This microorganism is mostly responsible for oral infections but can also cause pleural empyema, bone and joint infection, meningitis, and abscesses. *P micra* is known to be susceptible to penicillin, amoxicillin/clavulanic acid, carbapenems, levofloxacin, clindamycin, doxycycline, vancomycin, and metronidazole.<sup>11</sup> However, three strains were described as highly resistant to metronidazole.<sup>11,12</sup>

All serotypes of *S pneumoniae* strains carry a common C-polysaccharide found in the cell wall and, detected by PATB, our results indicate that *P micra* probably harbors a similar polysaccharide. This polysaccharide does not seem to be shared with different species of *Peptostreptococcus* because no cross-reactivity has been observed by the manufacturer with the *Peptostreptococcus anaerobius* reference strain.

All of the study patients but one had risk factors for aspiration pneumonia. In such a context, the use of

PATB and its interpretation must be very cautious because false-positive findings can occur due to the presence of anaerobic bacteria. Indeed, even if *P micra* is fully susceptible to amoxicillin, anaerobic infections are frequently polymicrobial and require antibiotic treatment with  $\beta$ -lactamase inhibitors or metronidazole.

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