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Detection of bacterial pathogens in synovial and pleural fluid with the FilmArray Blood Culture Identification System

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ABSTRACT

We report the use of FilmArray Blood Culture Identification (BCID) multiplex PCR system for pathogen detection from a child with septic arthritis that *Streptococcus pyogenes* was identified directly from synovial fluid and a child with complicated pneumonia with pleural effusion that *Streptococcus pneumoniae* was identified from pleural fluid.

Rapid detection of pathogens in serious infections has been shown to decrease the time to appropriate and optimal antimicrobial therapy, lower mortality, shorten hospital stay, and reduce overall health care costs for these patients [5]. We describe another use of FilmArray Blood Culture Identification (BCID) multiplex PCR system for pathogen detection from pediatric synovial and pleural fluid samples.

Case #1

A 6-year old, previously healthy, fully immunized girl was admitted to the hospital with a 12-h history of sudden onset of fever, rash and a swollen right knee. On physical examination, the patient appeared ill and toxic and had a temperature of 39 °C. She had a pharyngeal inflammation with enanthem without exudation, a scarlatiniform rash all over her trunk, back and extremities. The affected limb was held slightly flexed, externally rotated and abducted to reduce intracapsular pressure. Her right knee was erythematous, warm, swollen and also diffusely painful to palpation. In a few hours since admission to the hospital the inflammation was rapidly spread in the right thigh. The girl was hemodynamically unstable with low blood pressure (75/44 mmHg). The Laboratory studies on admission revealed: Complete Blood Count (CBC): White Blood Cells (WBC): 6390/μl, (Neutrophils (N):78%, Lymphocytes (L): 2%, Monocytes (M): 8%, Bands (B): 12%), C-reactive protein (CRP): 117 mg/lt, Procalcitonin (PCT): 8.06 ng/ml, and Strep-test (Intermedical SRL, Italy) were positive. She was treated with teicoplanin and ceftriaxone for presumed septic arthritis and pyomyositis. The 3rd day of hospitalization, an orthopedic consultation was obtained and the girl underwent a diagnostic synovial knee tap which revealed (from synovial fluid exam): Cells: 60.700/μl (N: 85%), protein: 3890 mg/dl, glucose: 26 mg/dl, Gram stain negative. Next day, patient's condition was deteriorating and new laboratory exams showed CBC: WBC: 11150/μl, (N: 75%, L: 3%, M: 7%, B: 14%), CRP: 411 mg/lt, PCT: 22.4 ng/ml, Prothrombin time (PT): 42 s, Fibrinogen: 451 mg/dl, D-dimers: 4.6 μg/ml. Blood cultures taken on admission as well as synovial fluid cultures remained negative. The MRI of the right thigh and knee showed myositis with an extensive edema and multiple abscesses among muscular groups, the larger with dimensions 12 × 4 × 10 cm and an inflamed fascia. There was also synovitis with pus collection in the right knee without osteomyelitis.

An aliquot of the synovial fluid was tested with the FilmArray Blood Culture Identification System (BioFire Diagnostics, Inc., Salt Lake City, UT). The sample was processed in accordance with the manufacturer's instructions and there was a positive result for *Streptococcus pyogenes*. Teicoplanin and ceftriaxone were discontinued and antimicrobial treatment was modified to penicillin and

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clindamycin. Within three days of treatment, her fever declined and she slowly began to improve. The evolution of the child was favorable as she responded well to the treatment; there was a gradual improvement of the knee mobility and the white blood cells, CRP, and PCT have fallen consistently. The child was discharged after 21 days of treatment and on 1 and 2-month follow-up she is doing very well.

Case #2

A previously healthy 2-year-old male presented with a 4-day history of fever, cough and progressive dyspnea for 2 days. His immunizations were up-to-date and he had received 4 doses of PCV13 at 4, 6, 8 and 12 months of ages. On admission, he had high fever (40 °C) and tachypnea (RR: 40–60/min). Chest examination revealed crackles and a decreased breathing sound over the left lower lung field. Chest radiograph and computed tomography (CT) scan showed consolidation of the left lower lung fields and moderate left pleural fluid accumulation. The rest of the clinical exam was unremarkable. Laboratory values of significance included CBC: WBC: 19,300/μl (N: 80%, L: 15%, M: 4%), Hb: 10.6 g/dl, Ht: 31.6%, PLT: 306,000/μl and CRP: 410 mg/lt.

Following the initial evaluation, empiric intravenous (IV) antibiotics were started with clindamycin and ceftriaxone. Despite therapy, next day the child got worse with persistent fever (up to 39.8 °C), tachycardia (HR: 175) and respiratory distress. A chest ultrasound demonstrated a large left pleural effusion. Debridement of the right pleural space and placement of chest tube (CT) into the posterior left pleural space with video-assisted thoracostomy surgery (VATS) was performed. Gram stain of pleural fluid showed no organisms and blood and pleural fluid cultures were sterile. *Streptococcus* pneumoniae was detected from the pleural effusion by FilmArray BCID, and serotype 3 was identified by polymerase chain reaction.

The antimicrobial therapy was modified to teicoplanin and ceftriaxone and was continued for 14 days. On the 5th hospital day, the child became better, ultrasound of the chest showed only residual fluid and chest tubes were removed. The boy was discharged home after 15 days and he was put on oral amoxicillin/clavulanate one more week.

At 1-month follow-up the child was feeling well, without any respiratory symptoms and chest radiograph revealed only minimal linear opacity in the left lower lobe thought to represent residual scarring.

Rapid molecular tests are changing the landscape of diagnostic microbiology as they provide fast and accurate pathogen identification, that is critical for the optimal management of patients with serious infectious diseases [6].

The FilmArray BCID test is a multiplexed PCR-based diagnostic test approved for use with positive blood culture material that It is designed to identify simultaneously 24 etiologic agents of sepsis (eight Gram-positive, eleven Gram-negative, and five Candida species) as well as three antimicrobial resistance genes (mecA, vanA/B, and bla) in 1 h. This assay has been shown to have good sensitivity and specificity in blood samples from adults and children [7–9].

These cases describe the off-label use of the FilmArray BCID multiplex test to provide diagnostic information for pathogen detection in synovial and pleural fluid. Rapid detection of specific bacterial pathogens allowed children to avoid the unnecessary use of broad spectrum antimicrobials and to limit the cost of treatment. Because in cases of arthritis or pneumonia children have already taken antibiotics most of the times, synovial fluid, blood and pleural cultures are usually negative [3]. In these cases, multiplex PCR systems are bridging some of the gaps that exist in traditional pathogen identification methods providing fast and accurate identification of pathogens [11]. One of the disadvantages of using FilmArray BCID method for testing synovial fluid is that *Kingella kingae*, which is one of the most common bacteria involved, is not included in the pathogens tested [2].

Other studies have used FilmArray BCID test for pathogen detection in other adult clinical specimens like cerebrospinal fluid, joint, pleural and ascitic fluids, bronchoscopy samples or abscesses sonicated fluid from explanted arthroplasties for prosthetic joint infection [1,4,10].

With the presentation of the above cases, we do not encourage the off label use of this test for clinical samples, but we would like emphasize the significance and the impact that such multiplex assays could have in everyday clinical practice, where there is gap in the existence of rapid diagnostic methods.

In conclusion, FilmArray BCID test could support the rapid diagnosis of a variety of infectious pathogens, from direct testing of clinical specimens in pediatric patients, however, that shall be confirmed in larger prospective studies. Rapid identification of bacterial pathogens could benefit patient care, facilitate better use of antibiotics and antimicrobial stewardship when is used timely as part of a routine microbiology service.

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