

# Necrotizing pneumonia caused by *Streptococcus pneumoniae* serotype 3 despite PCV13

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## ABSTRACT

*Streptococcus pneumoniae* is the most common cause of complicated pneumonia. Pneumococcal necrotizing pneumonia (PNP) is a rare and serotype related complication. Serotypes 1, 3, 14, 15, 19A and 33 were the most reported serotypes in children with PNP before immunization. Despite widespread vaccination, *S. pneumoniae* is still cause of invasive diseases. We reported a child, fully immunized with 13-valent conjugated pneumococcal vaccine (PCV13) who was diagnosed PNP due to serotype 3. Breakthrough invasive infection caused by *S. pneumoniae* must be considered in mind despite fully vaccination.

**Key words:** *Streptococcus pneumoniae*, necrotizing pneumonia, immunization, child.

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## INTRODUCTION

*S. pneumoniae* is the most common cause of invasive diseases, such as pneumonia, meningitis, bacteremia and sepsis in children. To date 91 different capsular types have been identified on basis of capsular polysaccharide. Different serotypes exhibit differences in clinical expression of the disease. About 13 serotypes are responsible for > 75 % of invasive pneumococcal diseases (IPD) in children.<sup>1</sup> Conjugated pneumococcal

vaccine 7 (PCV7) which include 4, 6B, 9V, 14, 18C, 19F, 23F serotypes, was introduced to Turkish national immunization program in 2009 and then was replaced by PCV13 which includes 1, 3, 5, 6A, 7F and 19A serotypes.<sup>2</sup> In a multicenter study from Turkey, the potential serotype coverages of PCV-7, PCV-10 and, PCV-13 were 16.3 %, 45.4 %, and 60 %, respectively, for pediatric parapneumonic empyema.<sup>3</sup> By the end of 2015, the vaccination rate for PCV13 was reported as 97 % in Turkey. Despite high vaccination rates and strong immunoreaction to conjugate vaccines, life-threatening complications such as pneumococcal necrotizing pneumonia (PNP) or empyema still occur.

## CASE REPORT

A previously healthy 20-month-old boy was admitted to hospital with a 3 days history of cough and fever. His medical and family history was unremarkable. He had been vaccinated with PCV13 at 2, 4, 6 and 12 months of age. On physical examination his body temperature was 39 °C, pulse rate was 160 beats/min and respiratory rate was 56 breaths/min. His weight and height were 13 kg (percentile 75 %) and 90 cm (percentile 90 %), respectively. The physical examination does not show suggestive findings of a determined syndromic picture. Decreased breath sounds were noted over the left lung field. The result of other system examinations was normal.

Laboratory data: white blood cells count  $14,6 \times 10^3 / \text{mm}^3$ , neutrophils 65 %, lymphocytes 10 %, hemoglobin 10 g/dl, platelets  $179000 / \text{mm}^3$ , erythrocyte sedimentation rate 31 mm/hr, C-reactive protein 42 mg/dl, biochemical parameters were normal. Chest X-ray showed total opacity of the left lung. Thorax tomography (CT) showed extensive consolidation with necrotizing pneumonitis in the left lower lobe and moderate left pleural effusion (Figure 1). Thoracic drainage tube was inserted and, about 250 mL purulent fluid drained. Gram positive diplococci were seen on gram stain. Intravenous ampicillin-sulbactam (200 mg/kg/day) and clindamycin (40 mg/

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kg/day) were started. Penicillin-susceptible *S. pneumoniae* grew in empyema culture. Isolate was identified as serotype 3 by the Quellung reaction using serotype-specific antisera (Staten's Serum Institute, Copenhagen, Denmark). Fever was resolved within 2 days, but despite the presence of a drainage tube, respiratory distress and pleural effusion were not resolved and, left lung did not expand on chest x-ray. On the 30th day of treatment, pleural thickening as 4 mm with fully atelectatic left lung and thick pleural effusion were detected by thorax tomography (CT). After left pleural decortication was performed, left lung expanded rapidly (Figure 2). Immunologic screening tests (blood cell counts, peripheral blood lymphocyte subsets, serum total immunoglobulin levels, dihydrorhodamine test, complement system) were all in normal limits, and ELISA for human immunodeficiency virus was negative. Spleen was seen normal by ultrasound, Howell-Jolly bodies was not detected on peripheral smear. The total pneumococcal IgG titer was 2.2 microgr/ml. Antibiotic treatment was completed for 6 week and the patient was discharged. The patient has been followed up for 1 year without sequelae.

## DISCUSSION

Necrotizing pneumonia is characterized by destruction of the lung parenchyma resulting in multiple cavities and is often accompanied with empyema. Generally, PNP is diagnosed by serial radiography and thoracic CT. *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae* are the most common cause of PNP.

Surgical resection is indicated in cases of sepsis, persistent fever, empyema or refractory to antibiotic treatment.<sup>1,4-5</sup>

*S. pneumoniae* serotypes such as 1, 3, 14, 15, 19A and 33 were the most reported serotypes in children with PNP before immunization, especially serotype 3 was more likely to cause it.<sup>6</sup> Although the mechanism of necrosis for serotype 3 is not clear, it has been hypothesized to be related with rapid accumulation of capsular polysaccharides leading to a large antigenic load and possible reduced humoral immune responses.<sup>7</sup>

Despite widespread vaccination, reports of vaccine failure from PCV13 (included serotype 3) have been documented for parapneumonic effusion. Antachopoulos et al. reported the failure of PCV13 serotype 3 vaccine with complicated pneumonia from Greek. They reported 5 children with empyema due to serotype 3, although they were fully immunized with PCV13. Patients were treated with antibiotic, chest tube and fibrinolysis. None of them required surgery. Multivariate vaccines cannot protective at the same level in every serotype. In some studies, pneumococcal polysaccharide IgG responses for serotype 3 before and after toddler dose were lower than other serotypes.<sup>8,9</sup>

The greatest spread of pneumococci to the lungs comes from the oropharynx. Bacteremic pneumonia accounts for about 12–16 % of invasive pneumococcal disease among children 2 years old or younger.<sup>10</sup> PCV is particularly effective in infections with bacteremia. Low protection of vaccine in complicated non-bacteremic

FIGURE 1. Thorax CT: Extensive consolidation with necrotizing pneumonitis and moderate left pleural effusion



FIGURE 2. Chest X-ray: Left lung expanded after decortication



pneumonia can be related with this condition. The patient blood culture was sterile, despite no antibiotic use. On the other hand, pneumococcal antibiotic resistance is a worldwide challenge of disease. Antimicrobial resistance causes different clinical presentation of disease, making it more difficult to diagnose and to treat.<sup>11</sup> However, our patient's culture susceptible to penicillin, the clinical response was inadequate to therapy. Antibiotic resistance, and immunodeficiency should be kept in mind on complicated cases. Primary immunodeficiency known to underlie clinical disease caused by *S. pneumoniae*, include congenital asplenia, complement deficiency, antibody deficiency, mutations of *NEMO*, *IRAK4* or *MYD88* genes. The patient immunologic screening tests was normal. Clinical infectious phenotype of *IRAK-4* and *MyD88* deficiencies are extremely severe. Laboratory (CRP concentration, total leukocyte counts, and neutrophil numbers) and clinical (temperature) signs of inflammation are typically low even in such infections.<sup>12</sup> The patient's clinic and laboratory features were not compatible with *IRAK-4* or *MyD88* deficiencies.

According to our knowledge, a case of PNP in a child fully immunized has not been reported in literature. The patient total pneumococcal Ig G was positive but, unfortunately, we could not measure the serotype-specific antibody levels. We cannot define this case a serotype specific vaccine failure.

PNP has required longer duration of treatment, pleural drainage and surgery. Irrespective of high vaccination rate, pediatricians should be alert to possible complications of IPD. Early definition of *Streptococcus pneumoniae* serotypes can be useful for treatment approach. Continuing active surveillance is important for determination of vaccine failure and design of new vaccines. ■

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