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COMMENTARY

Invasive pneumococcal infection due to serotype 15A after the pneumococcal conjugate vaccine implementation in Turkey

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ABSTRACT

Invasive pneumococcal infections among children are a serious public health problem in many countries, including Turkey. Pneumococcal conjugate vaccine has been included in Turkey's National Immunization Programme since 2009. We report the first two pediatric cases of invasive pneumococcal infection due to non-vaccine serotype 15A after pneumococcal conjugate vaccine implementation in Turkey. It is essential to monitor the countries' own local seroepidemiologic data for detecting selective pressure of non-vaccine serotypes of *S. pneumonia*.

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Introduction

Streptococcus pneumoniae is a common pathogen of invasive infections such as bacterial pneumonia, meningitis, and sepsis in children with high morbidity and mortality worldwide. *S. pneumoniae* is responsible for 1.6 million deaths annually especially in young chidren and the elderly, in view of a report of World Health Organization (WHO).[1] In Turkey, PCV7 was implemented into the Turkish National Immunization Program (NIP) in 2009 to be given at 2, 4, 6, and 12 months of age. Furthermore it was switched to PCV13 in November 2011 based on the surveillance data of invasive pneumococcal diseases (IPD) in Turkey.[1] IPD in children has been significantly decreased by widespread implementation of the pneumococcal conjugate vaccines (PCVs) in the world.[2] However IPD continues to occur with the serotype replacement due to circulation of new pneumococcal serotypes not included in the PCV-vaccines in recent years.[3]

With this report we attemped to share the first two pediatric cases of IPD due to non-vaccine serotype 15A in Turkey.

CASE 1: A 13-year-old previously healthy boy was referred to the Hacettepe University Children Hospital Emergency Department with fever, headache, neck pain and vomiting. It was noticed that he had a nasofrontoethmoidal fracture 25 days ago related with a car accident and he was hospitalized for repairing basiler scull fracture, intracranial bleeding and frontal lobe contusions. He was vaccinated with PCV13 at the third post operative day as he didn't have any pneumococcal conjugate vaccines before and for his basiler scull fracture. Administration of pneumococcal polysaccharide vaccine (PPSV23) was planned for 2 months later. He was discharged 10 days ago and received ampicilin-sulbactam (100 mg/kg/d) for 10 days for prophylaxis after hospital stay.

The physical examination revealed that he was febrile (tympanic temperature was 39.7°C) with lethargy, neck stiffness, rhinorrhea and raccoon eye in the emergency department. Other system examination was normal. The laboratory investigations revealed a hemoglobin of 12,5 g/dL, platelet count of 314.000/μL and a white blood cell count of 19.000/μL (neutrophils 86%, lymphocytes 6%, monocytes 8%), with normal liver enzymes and kidney function tests. His eritrocyte sedimentation rate was 54 mm/h and C-reactive protein was 14.7 mg/dL (normal: 0–0.8 mg/dL). The lumbar puncture showed 66 cells/mm^3 leucocytes, 41.25 mg/dL of protein, 64 mg/dL of glucose and 108 mg/dL of concurrent serum glucose was detected concentrations. Gram positive diplococcus was detected in the gram strain of cerebrospinal fluid. The patient hospitalized in the pediatric infection department due to menengitis. Vancomycin (60 mg/kg/day) and cefotaxime (200 mg/kg/day) were started. *S. pneumonia* (penicilline resistant) was isolated from blood culture anf CSF culture (penicillin resistant). Serotype 15A was detected. Magnetic resonance imaging revealed multiple fractures of frontal sinus wall and anterior cranial fossa base. The encephalocele was noted to herniate into the nasofrontoethmoidal region with cerebrospinal fluid leakage with cranial MRG imagination and cisternography. The lomber drainage was performed for 8 days for the patient with cerebrospinal fluid leakage. The patient received vancomycin for 23 d and cefotaxime for 18 days for *S. pneumonia*. The antibiotics could not stop on the 14th day due to intermittent fever. Coronavirüs OC43\HKU1 was detected from nasopharyngeal aspirate by PCR. 4th, 8th, 11th, 17th day of

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blood cultures and 20th day of CSF culture were sterile. The patient discharged after cerebrospinal fluid leakage improvement with any complications at the 38th day of hospital stay.

CASE 2: A 16 year-old-patient who was diagnosed with condroblastic osteosarcoma of right iliac bone 3 months ago, admitted to Van Yüzüncü Yıl Hospital Emergency Department due to fever and mouth sores at the third month of chemotherapy. She received last chemotherapy protocol 20 days ago. On physical examination; she was febrile (tympanic temperature was 39.1°C). Paleless and oral mucositis were detected. The laboratory investigations revealed a hemoglobin of 6.7 g/dL, platelet count of 11.000/μL and a white blood cell count of 1100/μL (neutrophils 8%, lymphocytes 80%, monocytes 1%, eosinophile 1%), with normal liver enzymes, kidney function tests. Her eritrocyte sedimentation rate was 85 mm/h and C-reactive protein was 17.5 mg/dL (normal: 0–0.8 mg/dL). The patient was hospitalized to the pediatric inpatient clinic due to neutropenic fever. Ceftazidime (150 mg/kg/day) was started. *S. pneumonia* (penicilline sensitive) was isolated from blood culture which was taken from the peripheral vein on admission Serotype 15A was detected. Urine culture on admission and the blood cultures in second and third day of the treatment were sterile. Teicoplanin (10 mg/kg/day) was added on the third day of treatment because of *S. pneumonia* and persistence of the fever. The forth day of treatment the fever reduced and clinic improvement was observed on the follow-up. The ceftazidime stopped at the 10th day of hospital stay and teicoplanin treatment was completed on the 13th day of hospital stay. The patient received for 10 days treatment of each antibiotic with no complication.

Discussion

PCVs are incorporated into pediatric vaccination schedules in more than 120 countries.[3] After PCV7, PCV13 was introduced into the NIP of Turkey and many countries as there has also been a relative increase of the infections due to non-vaccine serotypes such as 19A.[1,4] The widespread use of pneumococcus vaccines has significantly decreased the incidence of serious IPD and carriage in children due to the coverage of PCV13 serotypes.[2] The reduction in nasopharyngeal carriage of vaccine serotypes has also led to a substantial herd effect (indirect protection) in the older children and adults similarly in Turkey.[1] However IPD continues to occur with the serotype replacement due to an increase circulation of new pneumococcal serotypes not included in the PCV recently. In particular, increases of non-vaccine serotypes, such as 6C, 15A, 23A, and 35B, have been reported in the United States and European countries.[3,5] The clinical importance of serotype 15A is arising. In Germany, Canada, Denmark, France and Japan serotype 15A was found to be one of the sharply increasing serotypes in IPD with mostly non-susceptible to penicilin.[2,5-7] In the study of Nakano et al. six mortality cases were observed in a nationwide surveillance program of IPD and non-IPD cases from 2012 (PCV7 era) to 2014 (PCV13 era) in Japan and three of them (50%) included serotype 15A.[8] Serotype 15A was significantly found more prevalent in isolates of patients with meningitis than other illnesses e.g. pneumonia in the study of Ubukata et al.[3]

Approximately 97% of the target population (the first 5 y of age) was vaccinated with PCV between 2010–2013 in Turkey (see http://www.who.int/immunization/monitoring_surveillance/Immunization_Summary_2013.pdf?ua=1,http://www.sgk.gov.tr). Nevertheless the potential serotype coverage ranged from 57.5% to 36.8%, from 65% to 44.7%, and from 77.4% to 60.5% for PCV7, PCV10, and PCV13 during the first 5 y of age in 2008–2014, respectively in Turkey, and there was a significant increase (37.6%) in non-vaccine as result of serotype replacement.[1] Our patients seem like to threaten of the future cases of serotype 15A in Turkey. So it is essential to monitor own local seroepidemiological information.

Pneumococcal colonization is important for the IPD. Children's nasopharynx is a reservoir for colonization for strains covered by in IPD and non-IPD. Colonization helps to transmission of the pathogen and surrounding tissue or the bloodstream. The changes in the serotype distribution of IPD are associated with serotype distribution of colonization and geographic locations.[2,4,7] Serotype replacement in IPD may suggest simultaneous replacement of PCV serotypes with non-PCV serotypes among pneumococci that colonize the nasopharynx of children.[3]

Nazofarengeal carriage of serotype 15 was detected after the implementation of PVC13. The study of Soysal et al. has shown that the prevelance of pneumococcal carriage was 6.4%, with 45% non-vaccine type among isolated *S. pneumoniae* strains and the most common non-serotype was serotype 15A/F in Turkey.[4] Our patients might take serotype 15A from nasopharynx flora of carriers.

S. pneumoniae was the most common pathogen associated with head injury with basilar skull fracture and cerebrospinal fluid leakage. Pneumococcal vaccine should be received to these patients that haven't received appropriate vaccine dose[9] but sometimes appropriate vaccination cannot be enough due to non-vaccine types as so our first patient. Additionaly we should pay attention to the patients with severe underlying disease for the prevention and treatment of IPD with non-vaccine serotypes as well as our second patient.[8]

The distribution of serotype replacement looks like different in USA and European countries as well as the coverage of the PCVs among countries are different according to various factors not only seroepidemiologic differences. Therefore more studies are needed to investigate the other external and internal factors for understanding the diversity of serotype replacements.[1,6,10]

In conclusion, every country must have a surveillance of invasive pneumococcal infections and carriage. It is the key factor for monitoring the selective pressure of serotype replacement besides impact of PCVs for treatment of PID and preventation.

Disclosure of potential conflicts of interest

The authors certify that they have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript (e.g., employment, consultancies, stock ownership, honoraria).

References

[1] Ceyhan M, Ozsurekci Y, Gurler N, Oksuz L, Aydemir S, Ozkan S, Aydemir S, Ozkan S, Yuksekkaya S, Keser Emiroglu M, et al. Serotype distribution of Streptococcus pneumoniae in children with invasive diseases in Turkey: 2008-2014. Hum Vaccin Immunother 2016; 12(2):308-13; PMID:26325175

[2] Chan KC, Subramanian R, Chong P, Nelson EA, Lam HS, Li AM, Ip M. Pneumococcal carriage in young children after introduction of PCV13 in Hong Kong. Vaccine 2016; 34(33):3867-74; PMID:27265449

[3] Ubukata K, Chiba N, Hanada S, Morozumi M, Wajima T, Shouji M, Iwata S; Invasive Pneumococcal Diseases Surveillance Study Group. Serotype changes and drug resistance in invasive pneumococcal diseases in adults after vaccinations in children, Japan, 2010-2013. Emerg Infect Dis 2015. 21(11):1956-65; PMID:26485679

[4] Soysal A, Karabag-Yilmaz E, Kepenekliv E, Karaaslan A, Cagan E, Atici S, Atınkanat-Gelmez G, Boran P, Merdan S, Hasdemir U, et al., The impact of a pneumococcal conjugate vaccination program on the nasopharyngeal carriage, serotype distribution and antimicrobial resistance of Streptococcus pneumoniae among healthy children in Turkey. Vaccine 2016; 34(33):3894-900; PMID:27269059

[5] Tin Tin Htar M, Christopoulou D, Schmitt HJ. Pneumococcal serotype evolution in Western Europe. BMC Infect Dis 2015; 15:419; PMID:26468008

[6] Slotved HC, Dalby T, Hoffmann S. The effect of pneumococcal conjugate vaccines on the incidence of invasive pneumococcal disease caused by ten non-vaccine serotypes in Denmark. Vaccine 2016; 34(6):769-74; PMID:26772630

[7] Varon E, Cohen R, Bechet S, Doit C, Levy C. Invasive disease potential of pneumococci before and after the 13-valent pneumococcal conjugate vaccine implementation in children. Vaccine 2015; 33 (46):6178-85; PMID:26476365

[8] Nakano S, Fujisawa T, Ito Y, Chang B, Suga S, Noguchi T, Yamamoto M, Matsumura Y, Nagao M, Takakura S, et al. Serotypes, antimicrobial susceptibility, and molecular epidemiology of invasive and non-invasive Streptococcus pneumoniae isolates in paediatric patients after the introduction of 13-valent conjugate vaccine in a nationwide surveillance study conducted in Japan in 2012-2014. Vaccine 2016; 34(1):67-76; PMID:26602268

[9] Santos SF, Rodrigues F, Dias A, Costa JA, Correia A, Oliveira G. [Post-traumatic meningitis in children: eleven years' analysis]. Acta Med Port 2011; 24(3):391-8; PMID:22015025

[10] Alari A, Chaussade H, Domenech De Celles M, Le Fouler L, Varon E, Opatowski L, Guillemot D, Watier L. Impact of pneumococcal conjugate vaccines on pneumococcal meningitis cases in France between 2001 and 2014: a time series analysis. BMC Med 2016; 14(1):211; PMID:27998266; https://doi.org/10.1186/s12916-016-0755-710.1186/s12916-016-0755-7