Case report

Central Eur J Paed 2017;13(1):73-77.
DOI 10.5457/p2005-114.173

PERTUSSIS-LIKE SYNDROME IN PRIMARY CARE PRACTICE

Amra JUNUZOVIĆ[1], Sanjin MUSA[2], Aida PILAV[3]

[1]The Public Institution Health Centre of Sarajevo Canton, Sarajevo, BA
[2]Institute of Public Health of the Federation of BA, Sarajevo, BA, [3]Clinical Centre University of Sarajevo, Sarajevo, BA

Correspondence:
amra.Junuzovic@gmail.com
Tel.: +387 61 194 888
Fax.: +387 33 278 676

Received: December 11, 2016
Accepted: February 9, 2017

Key words: Pertussis ▪ Vaccine hesitancy ▪ Primary care.

Objective – The aim of the paper is to describe the complexity of pertussis-like syndrome in primary health care practice, and to highlight consequences of vaccine hesitancy. **Case reports** – We described five cases of pertussis-like syndrome in pediatric practice. Patients were unvaccinated or not fully vaccinated against pertussis due to parental refusal. There was intrafamilial and interfamilial spread of infection. **Conclusion** – Evaluation and treatment of pertussis-like syndrome remain challenging in primary health care practice. Dealing with vaccine hesitancy requires an adequate understanding and answer. Vaccine refusal increases the individual risk of disease but also increases the risk for outbreaks of vaccine-preventable diseases.

Introduction

Pertussis is a highly contagious disease, endemic in all countries (1). In the Federation of Bosnia and Herzegovina, pertussis is a notifiable disease with a low incidence. The disease is caused by *Bordetella pertussis*, a gram-negative, pleomorphic bacillus. Pertussis is transmitted from infected to susceptible individuals by droplets. Pertussis begins with mild upper respiratory tract symptoms similar to the common cold (catarrhal stage) and progresses to cough and then usually to paroxysms of cough (paroxysmal stage), characterized by inspiratory whoop and commonly followed by vomiting. Fever is absent or minimal. Symptoms wane gradually over weeks to months (convalescent stage) (2).

Pertussis is most severe when it occurs during the first 6 months of life. Complications among infants include pneumonia (22%), seizures (2%), encephalopathy (less than 0.5%), hernia, subdural bleeding, conjunctival bleeding, and death (2). Initial diagnosis is based on symptomatology. Varieties of laboratory tests are used for the diagnosis of pertussis (culture, polymerase chain reaction - PCR, and serology). Although, *Bordetella pertussis* is a fastidious organism and requires special media for isolation (3). An elevated white blood cell count with a lymphocytosis is usually present in classical disease of infants. The absolute lymphocyte count often reaches 20000 or greater. In some infants and children or in persons with mild or modified cases of pertussis, there may be no lymphocytosis (3). Other causes of sporadic prolonged cough illness include *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia tracho-*

matis, *Chlamydophila pneumoniae*, *Bordetella bronchiseptica*, and certain respiratory tract viruses, particularly adenoviruses and respiratory syncytial viruses (2).

The medical management of pertussis cases is primarily supportive. Antibiotics eradicate the organism from secretions, thereby decreasing communicability and, if administered in early stage, may modify the course of the illness. Recommended antibiotics are azithromycin, clarithromycin, and erythromycin. Trimethoprim-sulfamethoxasole can also be used (3). Penicillins and first- and second-generation cephalosporins are not effective against *Bordetella pertussis* (2). Antimicrobial agents for infants younger than 6 months of age require special consideration. An association between orally administered erythromycin and infantile hypertrophic pyloric stenosis has been reported in infants younger than 1 month of age (2). The introduction of effective infant immunization programs was associated with a steep decline in the number of pertussis cases and deaths in children. Unfortunately, in the last decades, health systems in the numerous countries are faced with vaccine hesitancy and anti-vaccine activists with possible serious consequences on the health status of children and youth.

The aim of the paper is to describe the complexity of pertussis-like syndrome evaluation and treatment in primary health care practice, and to highlight consequences of vaccine hesitancy.

Case reports

Case 1

A four-year-old female child was brought to a doctor because she had a cough, described as being paroxysmal, frequent during night. In the last two nights before the visit, sometimes the patient stopped breathing after a severe bout of coughing and turned blue. In emergency medical service, she was treated with fluticasone propionate inhalations and received an herb based cough syrup. She was born premature, with a birth weight of 2800 grams. She had received BCG and hepatitis B vaccine at birth. Parents, of high education level, refused further immunization. Upon admission to the doctor's office, the child looked exhausted, occasionally coughing. A sore throat was found, pulmonary examination results were normal. A WBC was $19x10^9$/L with a lymphocytosis of 67.3%. Sideropenic anemia was also found. She was referred to an infectious disease specialist for evaluation. Parents refused hospitalization but changed their minds two days later. The child stayed in hospital for 10 days. The parents demanded an earlier discharge, against the doctors' advice. Discharge letter was not picked up and shown to the primary care service.

Case 2

A two-year-eight-month-old female child has been receiving treatment for repeated attacks of wheeze, triggered by infections of the upper air passages. She had received BCG at birth and hepatitis B vaccine at birth, and at one month of age. Parents, medical technicians, refused further immunization. She was brought to a doctor because of intense cough and a weak appetite. She was subfebrile. Clinical pulmonary examination showed bronchial obstruction. A WBC was $47.5x10^9$/L, with 61.3% lymphocytes, neutrophils 31.9%; a RBC was $5.22x10^{12}$/L, HGB 13.2g/L, HCT 40.5%, CRP 40.7mg/L. She was referred to an infectious disease specialist and a pediatric pulmonologist, with a diagnosis of pertussis-like syndrome. Azithromycin, monelukast and ipratropium bromide inhalations were prescribed. Her chest radiograph showed perihilar irregular bronchovascular markings in both lungs. Three weeks later, she had a cough of the same intensity. Pulmonary examination-auscultation showed weaker breath sounds with prolonged expiration.

Repeated inhalation treatment was given. Six weeks later, she had a productive cough, intermittent fever up to 38°C. The diagnoses were confirmed by a pulmonologist: obstructive bronchitis and resolved lung infiltration bilaterally in basal regions. A WBC was $9.6x10^9$/L, lymphocytes 46.2%, neutrophils 39.4%, monocytes 14.4%, CRP 1.7 mg/L. Therapy given by pulmonologist included ampicillin, ipratropium bromide inhalations and expectorants bromhexin. Cough decreased gradually and the child's condition improved. Case 1 and case 2 are connected (family relationships), and met each other during the acute phase of illness of the case 1. Case 2 started coughing eight days later.

Case 3

A five-month-old female infant was born with a gestational age of 39 weeks, a birth weight of 3350 grams and Apgar score 10/10. During pregnancy the mother was treated with oseltamivir due to flu. The child had received BCG at birth and hepatitis B vaccine at birth, and at one month of age. She was brought to the doctor because of cough that was frequent during night. She was diagnosed with a tracheobronchitis, and initially treated with ampicillin and inhalations of normal saline. The child was reevaluated seven days later in the doctors' office for intense coughing and refusing to eat. She was referred to a pediatric clinic, where she was diagnosed with bronchitis and treated with inhalations of salbutamol in normal saline. Two weeks later she had a cough, described as paroxysmal and productive, with a shortness of breath. A WBC was $19.8x10^9$/L, with 64.4% lymphocytes and CRP 0.3 mg/L. She was referred to an infectious disease specialist for a suspected pertussis-like syndrome and received ampicillin for two weeks. *Bordetella pertussis* IgG and IgM by ELISA test were negative. During follow-up care, mother mentioned persistent cough. The child was treated with ipratropium bromide and montelukast by pulmonologist. Six weeks later the cough was declining.

Case 4

A five-year-ten-month male infant (brother of a case 3) was brought to a doctor because of cough, ten days after the beginning of his sister's illness. He was diagnosed with acute tonsillitis and treated with antibiotic and a cough syrup. *Bordetella pertussis* antibody IgG was positive and IgM was negative by ELISA test. A nasopharyngeal swab from the patient was negative. A sedimentation rate was 20 mm/h, a WBC was $5.9x10^9$/L. After 7 days, the boy's condition improved. He had received BCG, three doses of hepatitis B vaccine, 3 doses of oral polio, and 3 doses of DTP.

Case 5

A five-year-eight-month-old female child was brought to a doctor because of cough. Older brother and sister had a „cold". It was full term pregnancy, with birth weight of 2400 grams and Apgar score 9/9. She had received BCG and hepatitis B vaccine at birth. Parents refused further immunization. At 32 days of life, the baby had blood and mucus in stool, treated and diagnosed for cow's milk protein allergy, bilateral hip dysplasia, atopic dermatitis, and allergies to cefaclor and azithromycin. On examination, tonsil hypertrophy was found, pulmonary examination was normal. Symptomatic therapy was recommended. Two days later, the patient was brought in because of intense cough and fever. She was treated with amoxicillin-clavulanic acid, and salbutamol inhalations. For the next two weeks she had intense cough, with mucus expectoration produced during the paroxysmal stage. Laboratory tests were showed sedimentation rate of 30 mm/h, CRP 0.2 mg/L, WBC $10.5x10^9$/L, with lymphocytosis of

58%. Nasopharyngeal cultures were normal. She was sent to an infectious disease specialist for further evaluation, and subsequently she received azythromycin and inhalation therapy with normal saline. Eight days later, she showed improvement. During follow-up parents mentioned that a period of intense coughing lasted around five weeks.

Discussion

We described five cases of pertussis-like syndrome in pediatric practice. Children were unvaccinated or not fully vaccinated due to parental refusal. There was intrafamilial and interfamilial spread of infection. We believe that all these cases represent true pertussis, although the etiological diagnosis has not been thoroughly pursued. Parental vaccine hesitancy and underimmunization have been associated with identification of disease clusters (4). Vaccine hesitancy is a complex and rapidly changing global problem that requires ongoing monitoring. Reasons for vaccine hesitancy may include parental perceptions regarding the risk and severity of vaccine-preventable diseases, the safety and effectiveness of routine immunizations, and confidence in medical professionals, corporations, health care system and a government (5).

Estimated global DTP3 coverage among children aged <12 months in 2014 was 86%, ranging from 77% in the WHO African Region to 96% in the Western Pacific Region (6). In Federation of Bosnia and Herzegovina, due to shortage of acellular pertussis (aP) vaccine on the market in 2015, aP vaccine was temporary replaced with whole cell pertussis vaccine (wP), when DTP3 coverage by the age of one year decreased under 80% (7).

In addition to a vaccine refusal, waning immunity to pertussis has been evaluated and its association with disease resurgence has been established (8, 9). A shift in the age distribution of pertussis towards older age groups (adolescents and young adults) has been reported in some high income countries, in particular where aP vaccines have replaced wP vaccines for primary vaccination series.

Dealing with vaccine hesitancy requires an adequate answer. Primarily an understanding of the magnitude of the problem is needed and an insight into its roots, and then the identification and tailoring of evidence-based strategies to address the root causes is warranted (10).

Conclusion

Evaluation and treatment of pertussis-like syndrome remain challenging in primary health care practice. Dealing with vaccine hesitancy requires an adequate understanding and answer. Vaccine refusal increases the individual risk of disease but also increases the risk for outbreaks of vaccine-preventable diseases.

Authors' contributions: Conception and design: SM and AJ; Acquisition, analysis and interpretation of data: AJ; Drafting the article: AJ and SM; Revising the article critically for intellectual content: AP; Approved final version of the manuscript: AJ, SM and AP.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. World Health Organization. Pertussis vaccines: WHO position paper – August 2015. Wkly Epidemiol Rec. 2015;90(36):433-60.
2. American Academy of Pediatrics. Pertussis (Whooping Cough). In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics; 2012:553-66.
3. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015, pp. 261-78.

4. Lieu TA, Ray GT, Klein NP, Chung C, Kulldorff M. Geographic Clusters in Underimmunization and Vaccine Refusal. Pediatrics. 2015;135(2):280-9.

5. Salmon DA, Dudley MZ, Glanz JM, Omer SB. Vaccine hesitancy: causes, consequences, and a call to action. Am J Prev Med. 2015;49(6)(suppl 4): S391-S398.

6. World Health Organization. Global routine vaccination coverage, 2014. Wkly Epidemiol Rec. 2015;90(46):617-23.

7. Institute of Public Health of the Federation of Bosnia and Herzegovina. Epidemiological surveillance report on communicable disease in the Federation of Bosnia and Herzegovina, 2015. Institute of Public Health of the Federation of Bosnia and Herzegovina, Sarajevo/Mostar 2016.

8. Klein NP, Bartlett J, Rowhani-Rahbar A, Fireman B, Baxter R.Waning protection after fifth dose of acellular pertussis vaccine in children. N Engl J Med. 2012;367(11):1012-9.

9. Tartof SY, Lewis M, Kenyon C, et al.Waning immunity to pertussis following 5 doses of DTaP. Pediatrics. 2013;131(4):e1047-e1052.

10. Eskola J, Duclos P, Schuster M, MacDonald NE; SAGE Working Group on Vaccine Hesitancy. How to deal with vaccine hesitancy? Vaccine. 2015;33(34):4215-7.