PUBLIC
HEALTH
REPORTS

Public Health Reports
Vol. XX(X) 1-5

DOI: 10.1177/0033354919879727
journals.sagepub.com/home/phr
SAGE

Five-Year Follow-up of a Severe Case of Pertussis in Oregon, 2012

Juventila Liko, MD, MPH[1]; William J. Koenig, DO[2]; and Paul R. Cieslak, MD[3]

Abstract

Oregon continues to face epidemics of pertussis, and infants younger than 2 months of age have the highest incidence and rates of hospitalization and complications. We describe the medical course and sequelae of an infant's severe pertussis illness through age 5½ years. The child has failed to meet developmental milestones, requires substantial medical care, and bears the burdens of chronic lung disease, stroke, epilepsy, impaired neurodevelopment, and problems with vision. The medical and social burden of pertussis among infants too young to be vaccinated underscores the importance of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccination during pregnancy.

Keywords

pertussis, severity, vaccination, complications, infants and long-term sequelae

We previously described a severe case of pertussis in an Oregon neonate born in 2012 at 35 weeks' gestational age.[1] The patient was admitted to the hospital with pertussis at age 3 weeks and remained there for 90 days, including 75 days in a pediatric intensive care unit (PICU). Her hospital course was characterized by severe complications, including pneumonia, severe pulmonary hypertension, medically treated necrotizing enterocolitis, a left middle cerebral artery stroke, seizures, hyperbilirubinemia, dysphagia, encephalopathy, renal failure, benzodiazepine dependence, and bronchiolitis obliterans. She was mechanically ventilated for 72 days and supported by extracorporeal membrane oxygenation (ECMO) for 43 days. She received hemodialysis for 31 days. After 90 days in the hospital, she was discharged on 0.25 L/min oxygen via nasal cannula and with a feeding tube. Charges for that hospitalization totaled $1.5 million.[1]

The case was part of an outbreak of pertussis that occurred in Oregon in 2012. In that year, the state reported 910 cases of pertussis, the largest number of pertussis cases since 1953, when 942 pertussis cases were reported (unpublished data, Oregon Health Authority, 2019). This child had the most severe case of pertussis reported during the 2012 epidemic and the longest hospital stay of any pertussis patient in Oregon during 2012-2018 (unpublished data, Oregon Health Authority, 2019).

In this brief report, we describe the follow-up of this severely ill patient for 5 years after her hospital discharge to highlight the prolonged medical and social burden of pertussis in an infant who was too young to be vaccinated. It underscores the importance of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination during pregnancy. These costs are in addition to those associated with the original hospitalization.[1]

Methods

One of us (W.J.K.), her primary pediatrician, assembled the list of her specialty care providers. We reviewed all primary care and specialty outpatient medical records, including provider notes, laboratory and other test results, and treatments, for the 5-year period after the patient's discharge from the hospital on day 114 of life, summarizing them by organ system.

Results

In addition to general pediatric care, her outpatient care comprised specialists in pulmonology, feeding and swallowing

[1] Oregon Immunization Program, Public Health Division, Oregon Health Authority, Portland, OR, USA
[2] Physicians Medical Center, McMinnville, OR, USA
[3] Communicable Diseases and Immunizations, Public Health Division, Oregon Health Authority, Portland, OR, USA

Corresponding Author:
Juventila Liko, MD, MPH, Oregon Health Authority, Public Health Division, Oregon Immunization Program, 800 NE Oregon St, Ste 370, Portland, OR 97232, USA.
Email: juventila.liko@state.or.us

disorders, ophthalmology, and neurology. She was also referred for occupational, physical, and speech therapy after discharge.

Her respiratory problems followed her after the hospital discharge. At age 5 months—2 months after discharge—a chest x-ray showed substantial lung scarring, thought to be secondary to her prolonged requirement for ECMO. Seven months after discharge, at age 10 months, she had a computed tomography (CT) scan of her chest that suggested bronchiolitis obliterans on the right lung and bronchiectasis and atelectasis in the left lower lobe. Her pulmonologist started her on azithromycin at age 1 year as an anti-inflammatory treatment and stopped it after 29 months because of constipation. Intermittent wheezing persisted. At age 31 months, exertional dyspnea was diagnosed. She has taken fluticasone continuously since she was 31 months of age and albuterol daily or as needed. At age 62 months (59 months after discharge), the child had chronic wet cough, bronchiectasis, and bronchiolitis obliterans (Figure 1).

Figure 1. Chest radiograph showing airway thickening and bilateral ground glass opacities in a 5-year-old Oregon patient in 2017, 5 years after she had been admitted at age 3 weeks for severe pertussis that required extracorporeal membrane oxygenation.

Her neurodevelopmental problems persisted through 2017, when we discontinued follow-up (Figure 2). At age 4 months, 1 month after discharge, a neurologic examination showed poor overall muscle tone and poor eye contact with the examiner. She was enrolled in an early intervention program for children with developmental delays and disabilities. She required supplemental feeding via nasogastric tube until age 5 months, when she began feeding by mouth. At age 9 months, she was introduced to pureed food. At age 1 year, an examination showed continuing poor muscle tone and mild difficulty with gross motor skills including crawling and walking. She could sit unassisted for only a few seconds and was unable to crawl or pull to stand. She was unable to use her right hand, and strength and coordination were diminished in her left hand. At age 2 years, she began to speak, and by age 3 years she could speak in 2-word combinations. At age 3 years, she started receiving school-based neurodevelopmental services, and at age 3.5 years, she began to walk. At age 5 years, she could run, jump, and gallop, but she could not ride a tricycle; she was not yet potty trained; and she knew colors but did not recognize letters.

By age 5 years, she had had a series of vision and ophthalmological problems and had undergone 2 corrective eye surgeries. The first eye surgery was undertaken at age 14 months for left esotropia (thought to be a sequela of left sixth nerve palsy after her in-hospital stroke). Right-eye patching for 6 hours per day was recommended from 6-22 months of age and then reduced to 1 or 2 hours per day. Glasses were recommended at age 18 months. A second eye surgery was performed at age 28 months for left exotropia. At age 5 years, she continued to require corrective lenses, although she wanted to remove them, so wearing time had been limited. Eye patching was again being considered.

After the patient's onset of seizure disorder during her 2012 hospitalization, she remained free of seizures until age 4 years, when the seizures recurred. An electroencephalogram at that time showed sharp and slow discharges in the left parasagittal region. Complex partial seizures were diagnosed, and she received treatment with oxcarbazepine, which controlled the seizures from that time until the end of follow-up in 2017.

A neurodevelopmental evaluation at age 5 years indicated that her function was equivalent to that of a typical 1- to 3-year-old child. A neurologic examination revealed diffuse hypotonia, hyperextensibility of the joints superimposed upon mild right spasticity, mild right foot drop, and decreased selective motor control with the right hand. Her gait remained abnormal. Her neurologists described her as pathologically left-handed, with spastic right hemiparesis and impaired cognition, all attributable to the left middle cerebral artery stroke she had during the initial hospitalization. At the end of follow-up, at age 5 years, she continued to require physical, occupational, and speech therapy and was being followed by a pediatric neurologist.

The patient had many visits to providers and medical procedures. Through age 5.5 years, she had 6 well-child visits; 26 outpatient primary care clinic visits; 3 visits to the emergency department for upper respiratory symptoms, seizures, and ear infections; and 47 specialty care visits. The reasons for the outpatient primary care clinic visits included routine follow-up after hospitalization, medication checks, preoperative physical examinations, constipation, strabismus, ear infection, cough, rash, respiratory symptoms, and administration during her first 2 consecutive respiratory syncytial virus (RSV) seasons of palivizumab, a monoclonal antibody to prevent RSV infection, for which her chronic lung disease was thought to pose a high risk. She had undergone 4 chest x-rays (at ages 5, 10, 31, and 62 months), 1 chest CT scan without contrast (at age 10 months), and a sleep study (at age 38 months) to rule out obstructive sleep apnea; it was negative.

Discussion

Long-term respiratory sequelae and developmental impairment have been associated with pertussis, but to our

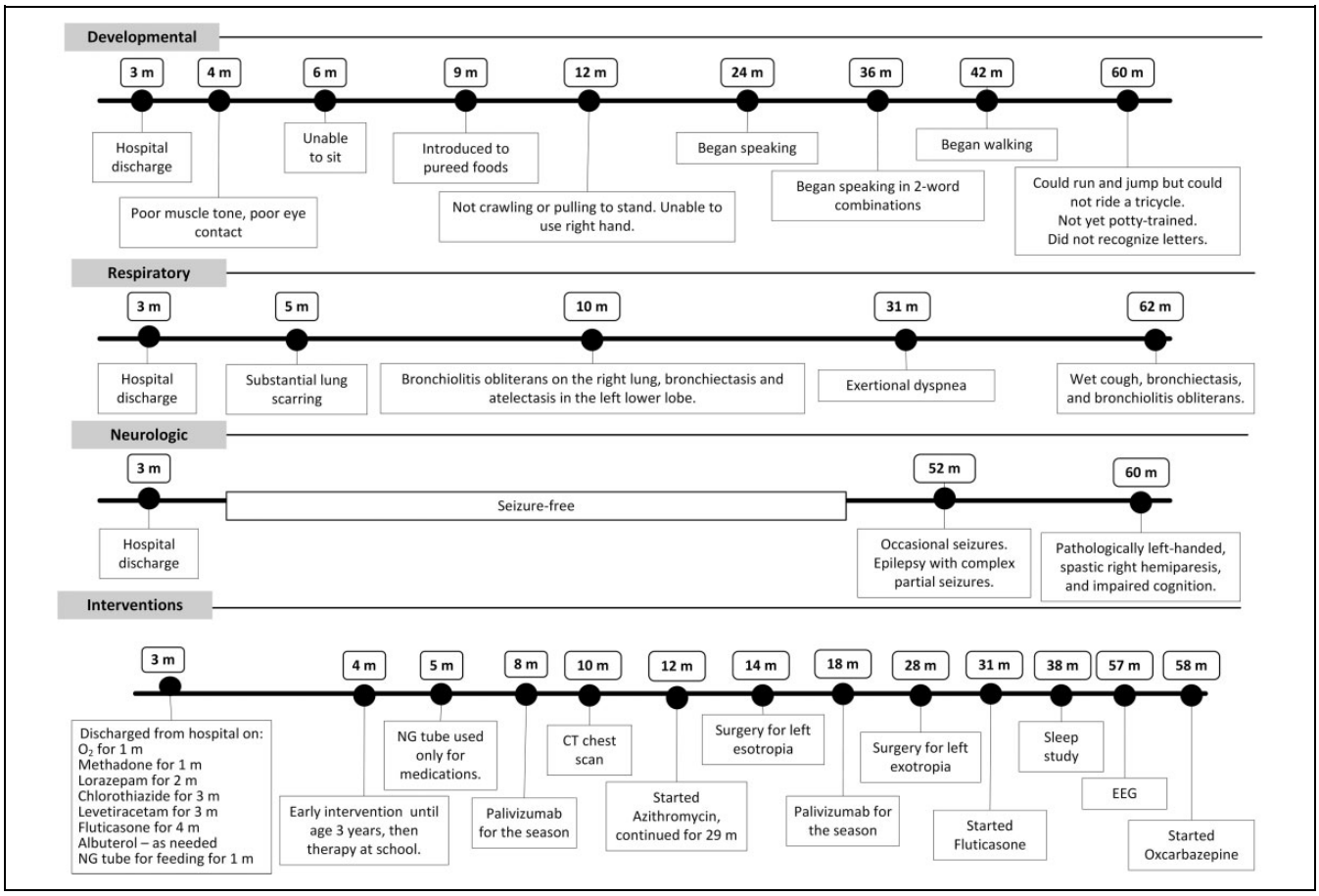

Figure 2. Posthospitalization observations and interventions in a severe case of pertussis in an infant, by age and organ system, Oregon, 2012-2017. Abbreviations: CT, computed tomography; EEG, electroencephalogram; m, month; NG, nasogastric.

knowledge, this brief report is the first in the era of ECMO and the 2012 maternal Tdap recommendation to sketch the long-term sequelae and the associated health care burden of all organ systems involved in a severe case of pertussis in an infant.[2-6] When we ended follow-up in 2017, when the child was aged 5½ years, she had failed to meet developmental milestones, continued to require substantial medical care, and bore the burdens of chronic lung disease, stroke, epilepsy, impaired neurodevelopment, and vision problems. The intensity of her care is an indicator of the severity of the sequelae and their high cost, both in dollars and in burden on her family.

Infants have the highest incidence of pertussis and are the most likely to have severe consequences, including death. A comprehensive analysis of nationwide pertussis data reported from 2000 through 2016 showed that infants had the highest incidence (75.3 per 100 000 population) and proportion (49.9%) of hospitalized cases and accounted for 88.8% of deaths.[7] Oregon continues to face periodic epidemics of pertussis; the last was the one described here, in 2012. In that year, >900 cases were reported, and the incidence was highest (253 per 100 000 population) among infants. All 5 fatal cases in Oregon since 2003 have been among infants.[8-10]

Data published in 2018 on severe pertussis in 100 California infants aged ≤120 days affirmed that pertussis among infants can be severe and require PICU admission and sometimes mechanical ventilation and ECMO, among other complex medical treatments. Among infants who were admitted to the PICU during October 1, 2013, through April 25, 2015, and ultimately died, the median age at pertussis onset was 23 days. Three of 4 children treated with ECMO died, and the lone survivor was left deaf and blind.[11]

Severe pertussis among young infants and its associated treatments can lead to long-term sequelae. A study among infants hospitalized in the PICU with pertussis in multiple sites across the United States identified neurodevelopmental deficits among more than one-third of survivors 1 year after PICU discharge.[12] The patient in our study had severe but typical consequences of pediatric stroke, including hemiparesis, substantial disability, and epilepsy, and subsequently required rehabilitation.[13-15] Another study among infants aged <6 months hospitalized with pertussis found a 3-fold risk of respiratory infections (pneumonia, bronchitis, or >6 episodes of influenza, pharyngitis, otitis media, or sinusitis) and episodes of wheezing or dyspnea at age 13-45 months.[16] The risk of epilepsy was 70% higher among Danish children

with a previous hospital diagnosis of pertussis and born between 1978 and 2011 than among the general population of children matched by sex and year of birth.[17]

Strategies have been proposed to prevent infant pertussis. Studies in the United Kingdom and the United States showed that vaccination of expectant mothers with Tdap prevents pertussis in infants aged younger than 2 months.[18-20] A case-control study of infants younger than age 2 months with cough onset during 2011-2014 in several US states (including Oregon) that participate in the Centers for Disease Control and Prevention's Emerging Infections Program surveillance showed that the receipt of Tdap vaccine by the mother during the third trimester of pregnancy was 78% effective in preventing pertussis and 91% effective in preventing pertussis hospitalization.[20] Another study from California conducted among infants born during 2011-2015 also found the maternal Tdap vaccine to be 72% effective in preventing hospitalizations of infants for pertussis.[21]

This follow-up report highlights the toll that severe pertussis in an infant can exact in the ensuing years of life and punctuates the importance of administering Tdap during pregnancy to protect these vulnerable infants. Pregnant women should be strongly advised to be vaccinated with Tdap.

Acknowledgments

The authors thank Anne M. VanCuren, BA, Oregon Immunization Program, for her assistance with Visio for the timelines.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by cooperative agreement No. 6 NH23IP000767-05-01 and Emerging Infections Program cooperative agreement No. CK000484 from the Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC or the US Department of Health and Human Services.

ORCID iD

Juventila Liko, MD, MPH https://orcid.org/0000-0002-8632-4721

References

1. Liko J, Koenig WJ, Cieslak PR. Suffer the infants: a severe case of pertussis in Oregon, 2012. *Public Health Rep*. 2015;130(5):435-439. doi:10.1177/003335491513000505
2. Byers RK, Rizzo ND. A follow-up study of pertussis in infancy. *N Engl J Med*. 1950;242(23):887-891. doi:10.1056/NEJM195006082422301
3. Swansea Research Unit of the Royal College of General Practitioners. Respiratory sequelae of whooping cough. *Br Med J (Clin Res Ed)*. 1985;290(6486):1937-1940. doi:10.1136/bmj.290.6486.1937
4. Berg JM. Neurological sequelae of pertussis with particular reference to mental defect. *Arch Dis Child*. 1959;34:322-324. doi:10.1136/adc.34.176.322
5. Swansea Research Unit of the Royal College of General Practitioners. Study of intellectual performance of children in ordinary schools after certain serious complications of whooping cough. *Br Med J (Clin Res Ed)*. 1987;295(6605):1044-1047. doi:10.1136/bmj.295.6605.1044
6. Surridge J, Segedin ER, Grant CC. Pertussis requiring intensive care. *Arch Dis Child*. 2007;92(11):970-975. doi:10.1136/adc.2006.114082
7. Skoff TH, Hadler S, Hariri S. The epidemiology of nationally reported pertussis in the United States, 2000-2016. *Clin Infect Dis*. 2018;68(10):1634-1640. doi:10.1093/cid/ciy757
8. Liko J, Robison SG, Cieslak PR. Pertussis vaccine performance in an epidemic year—Oregon, 2012. *Clin Infect Dis*. 2014;59(2):261-263.
9. Oregon Health Authority. Pertussis vaccination: why bother. *CD Summary*. 2016;65(9):1-6. http://www.oregon.gov/oha/PH/DiseasesConditions/CommunicableDisease/CDSummaryNewsletter/Documents/2016/ohd6509.pdf. Accessed April 22, 2019.
10. Oregon Health Authority. Pertussis 2016. http://www.oregon.gov/OHA/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/DISEASESURVEILLANCEDATA/ANNUALREPORTS/Documents/2016/2016-Pertussis.pdf. Accessed April 22, 2019.
11. Cherry JD, Wendorf K, Bregman B, et al. An observational study of severe pertussis in 100 infants ≤120 days of age. *Pediatr Infect Dis J*. 2018;37(3):202-205. doi:10.1097/INF.0000000000001710
12. Berger JT, Villalobos ME, Clark AE, et al. Cognitive development one year after infantile critical pertussis. *Pediatr Crit Care Med*. 2018;19(2):89-97. doi:10.1097/PCC.0000000000001367
13. Felling RJ, Sun LR, Maxwell EC, Goldenberg N, Bernard T. Pediatric arterial ischemic stroke: epidemiology, risk factors, and management. *Blood Cells Mol Dis*. 2017;67:23-33.
14. Cole L, Dewey D, Letourneau N, et al. Clinical characteristics, risk factors, and outcomes associated with neonatal hemorrhagic stroke: a population-based case-control study [published erratum appears in *JAMA Pediatr*. 2017;171(6):602]. *JAMA Pediatr*. 2017;171(3):230-238. doi:10.1001/jamapediatrics.2016.4151
15. Porcari GS, Beslow LA, Ichord RN, Licht DJ, Kleinman JT, Jordan LC. Neurologic outcome predictors in pediatric intracerebral hemorrhage: a prospective study. *Stroke*. 2018;49(7):1755-1758. doi:10.1161/STROKEAHA.118.021845
16. De Greeff SC, van Buul LW, Westerhof A, et al. Pertussis in infancy and the association with respiratory and cognitive disorders at toddler age. *Vaccine*. 2011;29(46):8275-8278. doi:10.1016/j.vaccine.2011.08.112

17. Olsen M, Thygesen SK, Østergaard JR, et al. Hospital-diagnosed pertussis infection in children and long-term risk of epilepsy. *JAMA*. 2015;314(17):1844-1849. doi:10.1001/jama.2015.13971
18. Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. *Lancet*. 2014;384(9953):1521-1528. doi:10.1016/S0140-6736(14)60686-3
19. Dabrera G, Amirthalingam G, Andrews N, et al. A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012-2013. *Clin Infect Dis*. 2015;60(3):333-337. doi:10.1093/cid/ciu821
20. Skoff TH, Blain AE, Watt J, et al. Impact of the US maternal tetanus, diphtheria, and acellular pertussis vaccination program on preventing pertussis in infants <2 months of age: a case-control evaluation. *Clin Infect Dis*. 2017;65(12):1977-1983. doi:10.1093/cid/cix724
21. Winter K, Cherry JD, Harriman K. Effectiveness of prenatal tetanus, diphtheria, and acellular pertussis vaccination on pertussis severity in infants. *Clin Infect Dis*. 2017;64(1):9-14. doi:10.1093/cid/ciw633