Report on three cases of pertussis in the Urbino area (Italy)

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SUMMARY

Pertussis is a contagious, infectious disease that affects mainly children and is caused by Bordetella pertussis. The pertussis vaccine has changed the epidemiology of the disease up to the point when it almost vanished, with a minimum number of cases recorded in Italy (2008) when vaccination coverage was 97%. For the same reason the natural history of the disease was also modified. Indeed, in high-income countries the lack of immunity acquired with the vaccine causes adolescents and adults to become an important source of infection for unvaccinated subjects, the newborn and children who have not completed their primary education. The reduction in the vaccinated pediatric population and the loss of acquired immunity could be the cause of the re-emergence of a disease which, in developing countries, has a 4% mortality rate among children under one year of age. In this work we describe three cases of pertussis that are apparently unrelated. They occurred in the area of Urbino in a period of slightly under a month. Italy is going through a historical moment of great suspicion regarding pediatric vaccination, despite scientific evidence that should allay such suspicion. To increase people’s awareness of vaccinations with a view to comments made regarding older children and adults it is our view that more effective intervention methods are needed.

Keywords: whooping cough, pertussis vaccine, Central Italy

INTRODUCTION

Pertussis is a contagious disease transmitted by air and affects mostly children. The causative agent is Bordetella pertussis, a Gram-negative pleomorphic bacillus, difficult to grow in vitro. B. parapertussis, B. bronchiseptica, Mycoplasma pneumoniae, Chlamydia trachomatis and C. pneumoniae and some Adenovirus can cause a whooping syndrome. Man is the only known reservoir, thus the transmission can occur only between humans [1]. Contrary to other childhood diseases, acquired immunity is not permanent, but over time it falls off. Moreover, pertussis may affect also infants born from an immune mother [2]. B. pertussis causes respiratory infections that may not be apparent or extremely serious, especially in newborns and in immune-compromised hosts. Pertussis is characterized by persistent cough attack with hypoxemia and cianosis. The first phase, called “catarrhal”, begins with a mild cough, accompanied by fever and nasal secretions. Then it could have “convulsive or paroxysmal” phase. The name is related to cough features and could manifest respiratory difficulty. Prolonged or repeated paroxysms episodes of apnea, cyanosis and vomiting could occur. [3] The inactivated vaccine is recommended but not mandatory in Italy, and it is generally associated with a diphtheria and tetanus vaccine [4]. The pertussis vaccine has changed not only the epidemiology of the disease (leading to a significant reduction of total and hospitalized cases and of lethality rate), but also the natural history (for the reduction of natural features during childhood), with the consequence of forming a more susceptible youth and adult population [5]. The immunity decay that occurs in vaccinated sub-
jects (4-12 years after inoculation) determines the fact that adolescents and adults become a greater source of infection for unvaccinated children and newborns. Moreover, pertussis is underestimated in the adolescent and adult population because of atypical clinical presentation and poor recourse to laboratory confirmation [6-8]. A recent population study conducted in the Netherlands has shown that the infection sources in young children are brothers, especially those between 9 and 13 years old (41%) and mothers (38%) [9].

According to World Health Organization (WHO) data since the global vaccination with acellular vaccine (1980), cases of pertussis have dropped from approximately 2 million to about 200 thousand a year; despite this, in 2008 (last available data) there were 195 thousand deaths estimated (with 16 million cases in total). In 2015 global coverage was 82% [10]. As regards the European situation, in 2012 more than 42,000 cases were notified (39,000 confirmed) with an incidence rate of 10.93 per 100,000 inhabitants, which was double respect to previous years [11]. The epidemiology of pertussis in Italy as well as in other countries is also changing with high vaccination coverage. In an article published in Euro Surveillance in 2014, Gonfiantini and colleagues signaled a reduction in mortality rate from 42.5 per 100,000 inhabitants in 1890 to zero cases in the period 2002-2012. The incidence was reduced from 86.3 cases to 1 case per 100,000 inhabitants from 1927 to 2008. These results were obtained especially thanks to a vaccination coverage that in our country increased from 32.8% in 1993 to 96% in 2006 [12]. The Italian Institute of Health data confirm that in Italy the cases of pertussis doubled in 2002-2012. The incidence was reduced from 86.3 cases to 1 case per 100,000 inhabitants from 1927 to 2008. These results were obtained especially thanks to a vaccination coverage that in our country increased from 32.8% in 1993 to 96% in 2006 [12]. The Italian Institute of Health data confirm that in Italy the cases of pertussis doubled in 2002-2012. The incidence was reduced from 86.3 cases to 1 case per 100,000 inhabitants from 1927 to 2008. These results were obtained especially thanks to a vaccination coverage that in our country increased from 32.8% in 1993 to 96% in 2006 [12]. The Italian Institute of Health data confirm that in Italy the cases of pertussis doubled in 2002-2012. The incidence was reduced from 86.3 cases to 1 case per 100,000 inhabitants from 1927 to 2008. These results were obtained especially thanks to a vaccination coverage that in our country increased from 32.8% in 1993 to 96% in 2006 [12]. The Italian Institute of Health data confirm that in Italy the cases of pertussis doubled in 2002-2012. The incidence was reduced from 86.3 cases to 1 case per 100,000 inhabitants from 1927 to 2008. These results were obtained especially thanks to a vaccination coverage that in our country increased from 32.8% in 1993 to 96% in 2006 [12].

CASE REPORTS

Reported cases involve three Italian children with an average age of 4.8 years, two males, all born in Urbino and residents in the Pesaro-Urbino province in an area no larger than about 40 km². Two of them (the youngest were 25 days and 16 months respectively) needed hospitalization c/o our unit while for the latter there was no need of hospitalization and the patient was treated at home by a general pediatric practitioner. The serology for B. pertussis tested positive for IgM class antibodies. **CASE 1.** The patient was a 16-month-old girl residing in Vallefoglia. She was hospitalized at the end of June 2016 after about two weeks of suffering from the cough. She was unresponsive to common antibiotics and anti-inflammatory treatment. On admission, she presented low-grade fever (37.5°C), with an oxygen saturation (SpO₂) level of 97%. The weight was 8.820 kg, blood pressure (BP) 90/60 mmHg and heart rate (HR) 120 beats/minute (bpm). The mother reported a similar episode in the 6-year-old brother, who had not yet had the vaccine booster dose of pertussis but was not particularly associated with cough episodes. On admission, cardiorespiratory and neurological examination resulted normal. Blood tests showed a moderate leukocytosis (WBC 18200 with an absolute lymphocytosis 65.6%). The child had not been vaccinated for the high frequency of febrile episodes that occurred in the first year of life. A gradual clinical improvement was observed after initiation of antibiotic therapy with clarithromycin.

**CASE 2.** The second case is referred to a 25-day old male resident in Fermignano. He was admitted in early July 2016 to our department at the onset of a persistent cough for about a week. At admission, he weighed 3.460 Kg and appeared asthenic but reactive. The vital parameters were normal, skin refill was higher than 2 seconds. Cardiovascular and neurological examination were normal. He presented cough attacks that ended with fits of apnea. There had been no cases either of flu syndrome and/or of cough in the family, or of the mother reporting ill health in previous weeks. The patient’s condition deteriorated rapidly, as did the frequency of coughing and duration of apnea, so on the second day it was necessary to transfer the patient to the Neonatal Intensive Care Unit. The chest X-ray was negative for pneumonia. The patient in intensive therapy performed high-flow oxygen therapy with no need for intubation and macrolide-antibiotic therapy and gradually improved.

**CASE 3.** The third patient was a child aged 13 days and living in Monte Grimano Terme. He
was the first born of a premature (twenty-ninth week) twin childbirth. The birth weight was 1.470 kg. He was affected by cerebral palsy. In late June 2016, the parents reported the onset of a productive cough in the absence of fever. Physical examination was normal. He presented pharyngeal hyperemia. For his persistent cough the child performed a standard chest radiography in two projections (negative for pneumonia). The family pediatrician prescribed treatment with macrolide to solve the disease. The patient did not finish the pertussis vaccination cycle.

DISCUSSION

Pertussis is a very contagious infectious disease and in children under the age of one or with severe comorbidities can be very dangerous, even lethal. The loss or reduction of immunity over the years increases the risk of contracting the disease, even in one’s family (in case 1 this possibility has not been excluded). In addition, it can show up (and obviously with greater severity) in infants who have not yet had the opportunity to be vaccinated (as the case 2) and do not acquire any maternal immunity and in general or in immunosuppressed patients with severe co-morbidity (case 3), which means it is even more important to make an effort to increase as much as possible the vaccine coverage of family members (adults and older children).

Recently, some regions have been trying to make mandatory the vaccination sine qua non on the institutional entry of babies into communities (nursing, nursery schools). This is very important because it seems evident from the three cases presented that pertussis is an insidious disease, for several reasons: it can manifest itself after several weeks during which the cardinal symptom of acute infectious disease (fever) may not be present; furthermore, the cough can be absolutely non-specific; a diagnosis, initially not easy, becomes so when the levels of service of a first-level hospital may not be sufficient (case 2); the transmission to a third party (secondary cases) may have already occurred; other viral infections could make the diagnosis and clinical course more difficult [17]. Recently Moore et al. have also reported that post-tussive vomiting in children has poor clinical diagnostic power (reaching a sensitivity and a specificity of just over 60%) [18]. Although, ultimately, molecular diagnostics (especially RT-PCR research on oropharyngeal secretion) can help in early diagnosis and is strongly recommended in certain categories of patients and at certain times of the year, as happened in our cases, hospitalization influenced late diagnosis [19].

The Italian National Health Institute data indicate that in our country, after the introduction of vaccination, pertussis cases decreased at a low record in 2008. Changes were also recorded between 2012 and 2014; in fact, the same data showed a downwards trend in vaccination coverage although there were no statistically-significant differences between the Italian regions, the relative decrease in the period 2012-2014 appears more serious in the following regions: the Marche, Abruzzo and Valle d’Aosta. Despite there being a considerable amount of clear-cut scientific data verified in all possible scenarios (high / low income countries, countries with immigration / emigration tendency) in Italy a strong wave of skepticism led to a general decline in having vaccinations. The vaccine coverage for pertussis decreased from over 97% in 2000 to less than 95% in 2014 (among children under 2 years of age).

The unwarranted distrust of vaccines is still a very current theme. The Health Ministry pointed out that the coverage decline was not a “temporary downturn but a trend which was being consolidated.” In fact, in 2015 the trend was confirmed by a further coverage reduction (93.3%). Lowering the vaccine coverage threshold to below 95% of the population results in the loss of the benefits of so-called “herd immunity”. According to WHO, this is the minimum population coverage value needed to prevent vaccine-preventable diseases. Italian data underlined the gravity of the situation in the Marche where only 91.74% of children under the age of two were vaccinated. The association of the pertussis vaccine to those of tetanus and diphtheria has made it easier to achieve a very high vaccine coverage that would be unthinkable for other diseases where vaccination is not mandatory (measles, chicken pox, rubella, for example, have a coverage of under 80% in the Marche). Despite this, the wave of distrust fueled by scientific studies was completely retracted by the authors and by a non-evidence-based intrusion by some mass media; indeed, it is above all the social networks that are likely to frus-
trate the efforts and results obtained in the past. Even if beneficial, vaccination of all those coming into close contact with of a newborn baby seems to be a less viable course of action. A mother’s vaccination in the third trimester of pregnancy and the development of new vaccine formulations that result in longer immune memory may be the most effective ways of preventing the onset of the disease [20]. As a final consideration, it is not surprising that all three children were Italian; according to data from the Health Authority Prevention Department of Pesaro-Urbino Province the level of coverage of immigrants (regarding childhood diseases) is higher than for Italians and this says a lot about the different risk perception towards diseases which, in many cases, still represents a scourge in most of the areas of origin of migrants (especially sub-Saharan Africa).

We are witnessing a delicate historical moment in the fight against preventable diseases. The results obtained in a recent past and the underestimation of what happened in a more remote past should help health workers providers not to let down their guard. It is probably the case that the perception of the general population is that pertussis, as with other childhood illnesses, is not such a serious illness, but we have to remember that the State of Washington pertussis outbreak in 2012 reached levels that had not been seen since 1942, with 2,520 cases recorded and an incidence of 37.5 cases per 100,000 inhabitants.

Conflicts of interest
None

ACKNOWLEDGMENTS
We would just like to thank dott. James Hart for proof-reading and translation checking.

REFERENCES