

Measles outbreak in adults in Italy

Epidemia di morbillo in Italia in pazienti adulti

Matteo Bassetti¹, Eva Schenone¹, Anna Calzi¹, Marco Camera², Laura Valle³, Filippo Ansaldi³, Gabriella Pagano², Claudio Viscoli¹

¹Infectious Diseases Division, San Martino Hospital and University of Genoa, School of Medicine, Genoa, Italy;

²Infectious Diseases Division, San Martino Hospital, Genoa, Italy;

³Hygiene Unit, San Martino Hospital and University of Genoa, Genoa, Italy

INTRODUCTION

The World Health Organization Regional Office for Europe has set 2010 as the target for elimination of measles in the region [1, 2]. This objective has already been achieved in some States through routine immunization programs which maintain high coverage [3]. In Italy, measles vaccination is currently offered free of charge as combined measles-mumps-rubella (MMR) vaccine.

Although childhood vaccination coverage has increased in recent years, reaching the national average of 88% in 2006 (source: Ministry of Health), it is still below the target of 95% set by the National Measles Elimination Plan (MEP) launched in 2003 and after 2007 outbreaks continue to occur in various Italian regions [4-6]. In the last six-year period (2001-2006) an average of approximately 5400 cases were reported annually, ranging from 215 cases in 2005 to 18020 cases in 2002 [7].

A new large outbreak began in Italy in September 2007, among a group of unvaccinated young and in the following weeks spread from Piemonte to neighbors regions. Since September, clusters of cases and important outbreaks have been detected in several Italian regions.

The objective of this study is to analyze characteristics of cases of measles who were hospitalized in Genoa (Italy) from January 2008 to April 2009.

METHODS

All suspected cases of measles hospitalized at San Martino Hospital from January 2008 to

April 2009 were analyzed. A suspected case of measles was defined according to EUVAC.net definition (http://www.euvac.net/graphics/euvac/cd_measles.html). Laboratory confirmation was attained by determination of measles-specific IgM antibodies by enzyme immunoassay and/or detection of measles virus genome in throat swab or urine by nested polymerase chain reaction (PCR).

A subset of positive samples, constituted by 75% of detected viruses, underwent to genetic characterization by entire sequence analysis of Haemagglutinin-coding region (H) and 450 nucleotides encoding the COOH-terminal 150 aminoacids of the Nucleoprotein (N), in accordance with the international standards [6, 8].

A standardized form including demographic data, underlying medical conditions, clinical signs and symptoms, selected laboratory tests, radiographic findings, treatment course, and outcome, was used for data collection. Vaccination status, potential source of measles, length of hospitalization (LOS) were also included.

The review was approved by the local institutional review board, and patient consent was not required.

RESULTS

In the study period, 114 patients with suspected measles were observed and laboratory confirmation were obtained in 83 cases: 34 (34/83; 41%) by MV genome PCR; 5 (5/83; 6%) only by MV IgM antibodies and 44 (44/83, 53%) by both methods. Forty-three (52%) of the 83 patients were female. The median age was 25 years (range 15-66) (Table 1).

Table 1 - Characteristics of hospitalized patients (n=83) with measles.

Characteristic	No. patients (%)
Female sex	43 (52)
Age, median (range), years	25 (15-66)
Age group	
15-18 yr	20 (24)
19-25 yr	24 (29)
26-30 yr	16 (19)
31-40 yr	20 (24)
>40 yr	3 (4)
Race or ethnic group	
Caucasian	76 (92)
Hispanic (South America)	7 (8)

Table 2 - Clinical characteristics of measles cases (n=83) at admission in the hospital.

Signs and Symptoms	No. patients (%)
Fever	83 (100)
Rash	83 (100)
Conjunctivitis	61 (73)
Cough	70 (84)
Koplik's spot	30 (36)
Nausea/Vomiting	28 (34)
Joint pain	7 (8)
Lymphadenopathy	69 (83)
Hepatosplenomegaly	73 (88)

Table 3 - Laboratory data of measles cases (n=83) at admission in the hospital.

Laboratory data	No. patients (%)
Leucopenia (<4,5 x10 ³ /L)	19 (22.9)
Neutropenia (<1,8x10 ³ /L)	16 (19.3)
AST elevation (>40 UI)*	53 (63.9)
ALT elevation (>40 UI)**	58 (69.9)
AST/ALT elevation	47 (57)
Bilirubin elevation (>1,20 mg/dL)	3 (4.2)
GGT elevation (>50 UI)***	43 (54.4)
*Median value: 81 UI; range: 18-492; **Median value: 120 UI; range: 16-546; ***Median value: 95 UI; range: 6-644.	

Clinical characteristics of cases are reported in Table 2. At the first physical examination all patients presented fever and the classical generalized maculopapular rash.

Blood examinations are reported in Table 3. The vaccination status was known for 80/83 patients and among them the proportion of unvaccinated was 90% (72/80). No severe complications were observed. Most common complications were nausea/vomiting in 28/83 (34%) and radiological documented interstitial pneumonia in 22/83 (26%) cases. The median length of hospitalization was 5 days (range 1-9 days).

Nucleoprotein nucleotide sequence comparison and phylogenetic reconstruction indicating that all Genoese strains were identical and belonged to genotype D4. The Genoese strains showed 100% homology with MV isolated in other Italian Regions and neighboring Local Health Units in Liguria.

This strain was detected during 2007 in the UK, Ireland and the U.S.A. and, during the following year, in several European countries, such as the Netherlands, Spain, France. Previous outbreaks in Liguria were due to viruses belonging to genotypes D7 and D8, while the D4 strains isolated during the 2006 outbreak in Tuscany fell into a clearly separate cluster compared with D4 viruses detected during the 2007/2008 season, excluding the re-circulation of strains circulating in Northern Italy during the previous seasons. Phylogenetic analysis of H gene confirmed the above information.

DISCUSSION

Measles cannot be regarded solely as a childhood disease. In fact in our experience almost 90% of patients were aged 20 years or older with median age of 25. It is interesting to notice that the most affected people were those that should have had immunity resulting from the vaccination. The subjects with more than 40 years were affected by the measles and this may be attributable to the low vaccination coverage that involves a shift to the most advanced ages [12]. In Italy the measles vaccination with attenuated virus is recommended since 1979 for all children from 12 to 15 months. In our country childhood vaccination coverage has increased in recent years; however, it is still below the target.

In fact, although in Italy measles vaccine is of-

ferred free of charge, the measles outbreak is not unexpected in the context of the still insufficient measles vaccination coverage allowing for silent accumulation of susceptible subjects. Indeed adolescent and young adults have been particularly affected and most reported cases were unvaccinated [9].

The vaccination coverage is important also because measles remains a risk factor for traveling young adults. In fact the outbreak described in our study began after the return of a girl from a travel in United Kingdom [10, 11]. Clinical diagnosis was confirmed by laboratory assays in almost 73% of the cases, but it needs to be considered that the positive predictive value of the clinical case definition is low in settings of low incidence. It demonstrates that the laboratory confirmation is essential to ensure an accurate diagnosis of measles when it is rare. It is important to accurately identify each case because one case may be the only evidence of measles transmission in the area and a misidentification of measles case results in misdirection of the outbreak response [12].

In this study, conducted in an adult hospital, we noticed that signs and symptoms observed are similar to those described for children [13]. The only exception has been the low observation of Koplik's spot observed only in 37% of cases. Although increased hepatic enzymes has been observed in 57% of patients, the elevation has been transitory. These data are comparable with those reported in literature, even if in our

population jaundice was not noticed. Involvement of the respiratory tract is part of the virus infection itself [14]. Roentgenographic evidence of pneumonia is common, even during apparently uncomplicated measles [15]. In our experience pneumonia has been identified in 26% of patients without respiratory complications.

Our study has some limitations. Vaccination status was obtained by tacking medical history in the hospital: only in few patients vaccination status could be documented. This might have led to an underestimate of vaccinated subjects. The study has been carried out in an adult hospital and this can lead to an underestimation of children population.

In conclusion, there is an urgent need to improve vaccination coverage with two doses of MMR in Italy, not only among children, but also among adolescents and young adults in order to prevent new outbreaks and hospitalizations in adult population.

Key words: measles, outbreak, hospital, unvaccinated, adults.

Transparency declarations

The authors declare that they have no competing interests.

Funding statement

The work was carried out as part of the regular work of our department.

SUMMARY

Several outbreaks of measles have been reported since 2007 both in Italy and elsewhere in Europe. The objective of this study was to analyze the characteristics of the cases of measles that were hospitalized at San Martino Hospital from January 2008 to April 2009. All suspected cases of measles from January 2008 to April 2009 were analyzed.

Laboratory confirmation was attained by determination of measles-specific IgM antibodies with enzyme immunoassay and/or detection of the measles virus genome in throat swab or urine by nested polymerase chain reaction (PCR). In all, 114 patients with clinically suspected measles were observed and laboratory confirmation was obtained in 83 cases: 34 (34/83; 41%) by specific genome PCR; five

(5/83; 6%) only by IgM antibodies and 44 (44/83; 53%) by both methods. The median age was 25 years (range 15-66). The vaccination status was known for 80/83 patients, amongst whom the proportion of unvaccinated was 90% (72/80). No severe complications were observed. The most common complications were nausea/vomiting in 28/83 (34%) and radiologically documented interstitial pneumonia in 22/83 (26%) cases. The median length of hospitalization was five days (range 1-9 days). Almost 90% of patients were aged 20 years and older and hence measles cannot be regarded solely as a childhood disease. Thus widespread high vaccination coverage would be required to prevent new outbreaks and hospitalizations in the adult population.

RIASSUNTO

Numerose epidemie di morbillo sono state descritte in Europa e in Italia dopo il 2007. Lo scopo di questo studio è stato quello di analizzare le caratteristiche cliniche e microbiologiche dei casi ospedalizzati nella nostra Unità tra gennaio 2008 ed aprile 2009.

Sono stati considerati tutti i casi sospetti ricoverati presso l'Ospedale S. Martino di Genova dal gennaio 2008 all'aprile 2009. La diagnosi di certezza è stata ottenuta tramite la ricerca di IgM specifiche e/o attraverso l'isolamento del genoma del virus del morbillo (MV) tramite PCR (polymerase chain reaction) su urine o tampone faringeo.

La conferma laboratoristica è stata ottenuta in 83 dei 114 casi sospetti (72,8%): attraverso PCR in 34 (34/83; 41%) soggetti, in 5 (5/83; 6%) tramite posi-

tività per IgM specifiche e in 44 (44/83; 53%) con entrambe le metodiche. L'età media era di 25 anni (range 15-66). Lo stato vaccinale era noto in 80/83 pazienti (96%) con una percentuale del 91% di non vaccinati (73/80).

Non si sono manifestate complicanze gravi. Le complicanze più comuni sono state nausea/vomito (28/83; 34%) e polmonite interstiziale documentata radiologicamente (22/83; 26%). Il tempo medio di degenza è stato di 5 giorni (1-9).

Il fatto che il 90% dei pazienti inclusi nella nostra casistica avesse un'età superiore ai 20 anni, ci porta a non dover più considerare il morbillo come una mera patologia pediatrica. Sarebbe pertanto auspicabile una copertura vaccinale molto più ampia.

REFERENCES

- [1] World Health Organization Regional Office for Europe. Strategic plan for measles and congenital rubella infection in the European region of WHO. Copenhagen: WHO Regional Office for Europe; 2003.
- [2] World Health Organization Regional Office for Europe. Eliminating measles and rubella and preventing congenital rubella infection. WHO European Region strategic plan 2005-2010. Copenhagen, WHO Regional Office for Europe; 2005.
- [3] World Health Organization. Progress towards elimination of measles and prevention of congenital rubella infection in the European Region, 1990-2004. *Wkly Epidemiol. Rec.* 80, 65-71, 2005.
- [4] Presidenza del Consiglio dei Ministri. Repertorio Atti n. 1857 del 13 novembre 2003. Piano Nazionale per l'Eliminazione del Morbillo e della Rosolia Congenita (in Italian) Available from: <http://www.governo.it/backoffice/allegati/20894-1712.pdf>
- [5] Filia A., De Crescenzo M., Seyler T. et al. Measles resurges in Italy: preliminary data from September 2007 to May 2008. *Euro Surveill.* 13, 29, pii=18928, 2008.
- [6] Ansaldi F., Orsi A., Altomonte F. et al. Syndrome surveillance and molecular epidemiology for early detection and tracing of an outbreak of measles in Liguria, Italy. *J. Med. Virol.* 81, 1807-13, 2009.
- [7] Italian Ministry of Health. Circular no. DG-PREV.V/10606/P/I.4.c.a.9 of 20 April 2007
- [8] Featherstone D., Brown D., Sanders R. Development of the global measles laboratory network. *J. Infect. Dis.* 187, 264-269, 2003.
- [9] Ciofi Degli Atti M.L., D'Argenio P., Di Giorgio G. Measles in Italy 2002: studies show correlation between vaccine coverage and incidence. *Euro Surveill.* 6, 49, pii=1981, 2002.
- [10] Bray C., Williamson N., Morris J. A re-emerging infection? *South Med. J.* 102, 299-300, 2009.
- [11] van Binnendijk R.S., Hahné S., Timen A., et al. Air travel as risk factor for introduction of measles in a highly vaccinated population. *Vaccine* 26, 5775-5777, 2008.
- [12] Hutchins S.S., Papania M.J., Amler R., et al. Evaluation of the measles clinical case definition. *J. Infect. Dis.* 189, S153-S159, 2004.
- [13] Arenz S., Fischer R., Wildner M. Measles outbreak in Germany: clinical presentation and outcome of children hospitalized for measles in 2006. *Pediatr. Infect. Dis. J.* 28, 1030-1032, 2009.
- [14] Gavish D., Kleinman Y., Morag A., Chajek-Shaul T. Hepatitis and jaundice associated with measles in young adults. *Arch. Intern. Med.* 14, 674-677, 1983.
- [15] Kempe C.H., Fulginiti V.A. The pathogenesis of measles virus infection. *Arch. Gesamte Virusforsch* 16, 103-128, 1965.