Pediatr Pol 2019; 94 (4): 276–282
DOI: https://doi.org/10.5114/polp.2019.88047
Submitted: 31.03.2019; Accepted: 11.06.2019; Published: 30.08.2019

PEDIATRIA Polska
PISMO POLSKIEGO TOWARZYSTWA PEDIATRYCZNEGO
Polish Journal of PAEDIATRICS
OFFICIAL JOURNAL OF POLISH SOCIETY OF PAEDIATRICS

CASE REPORT

Clinical peculiarities of measles in children from the Ternopil region, Ukraine

Halyna Pavlyshyn, Ivanna Horishna

Department of Pediatrics, Ivan Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

ABSTRACT

The medical cards of children hospitalised in the Infectious Department of Ternopil Children's Hospital were analysed. Children, mainly unvaccinated or incompletely vaccinated, form the majority in the structure of measles morbidity in the Ternopil region of Ukraine. The disease has typical cyclic course with pathognomonic symptoms and is mainly moderate and uncomplicated. Complications are predominantly characterised by respiratory and digestive system involvement. Prolongation of the prodromal period with prodromal rash and shortening or prolongation of the exanthema period in some patients, characterised by specific rash staging, are the main clinical peculiarities in children of this region. Leukopaenia, thrombocytopaenia, eosinophilia, and leukocytic left shift are typical for the prodromal and exanthema period, and normocytosis or leukocytosis with lymphocytosis are typical for the pigmentation period. A biochemical blood test shows the impairment of the liver function in some cases. Chest X-ray shows strengthening of the pulmonary pattern in the base of the lungs in the case of complications with bronchitis and infiltrates in the lower lobes in case of pneumonia.

KEY WORDS:

measles, children, immunisation, clinical course, complications.

INTRODUCTION

Measles was one of the most frequent infectious diseases of childhood for many centuries. Immunisation, which was initiated in 1963, decreased the morbidity throughout the world. In Ukraine vaccinations were started in 1966 with booster vaccinations since 1986, which decreased the morbidity rate and prolonged epidemic intervals to 5–6 years. However, measles morbidity increased in 2016–2018 in many countries in the European region, and Ukraine held first place among them. A total of 53,218 Ukrainians were ill in 2018 according WHO data, and 16 cases were fatal. That is 64.67% of the diseased within the European region. The morbidity rate in that period was 1209.26 per million, which was higher than in Serbia, Georgia, or Albania [1]. Such high figures are not only because of vaccine shortages, but also because of many parents refusing to vaccinate their children. In the period 2006–2016 the percentage of measles vaccinated 12-month-old infants in Ukraine decreased from 98% to 42%, and booster vaccinated at six years fell from 98% to 31% [2]. A measles epidemic in the Ternopil region of Ukraine started in June 2017 and is ongoing. So far, 3,659 cases have been registered for this period, and 2,405 (65.73%) of them were children.

The aim of this work was to discover and analyse epidemiological, clinical, laboratory, and instrumental peculiarities of measles in children from the Ternopil region of Ukraine in 2018.

ADDRESS FOR CORRESPONDENCE:

Halyna Pavlyshyn, Department of Pediatrics, Ivan Horbachevsky Ternopil National Medical University, Maidan Voli 1, 46001 Ternopil, Ukraine, ORCID: 0000-0003-4106-2235, e-mail: halynapavlishin@gmail.com

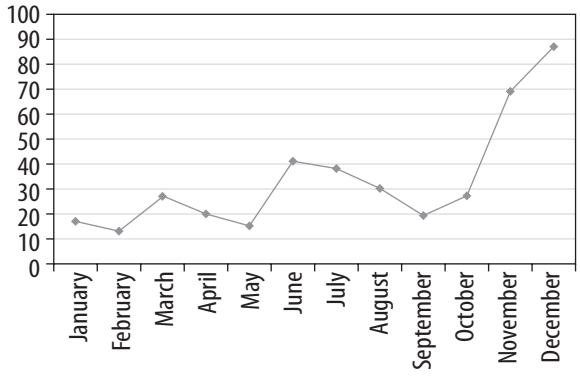

FIGURE 1. Measles morbidity among the patients of the Infectious Department, Ternopil City Hospital, 2018

TABLE 2. Patients' complaints in admission to the Infectious Department, Ternopil City Hospital, 2018

Complaints	Number of cases	Percent of cases
High fever	350	86.8
Cough	398	98.8
Nasal congestion	204	50.6
Rhinorrhoea	148	36.7
Conjunctivitis	305	75.7
Rash	326	80.9
Appetite loss	348	86,4
Nausea and vomiting	12	3.0
Stomach ache	28	6.9
Diarrhoea	108	26.8
Hoarseness	24	6.0
Dyspnoea	74	18.4
Fatigue, sleepiness	228	56.6
Total amount	403	100

MATERIAL AND METHODS

Medical charts of patients treated in the Infectious Department of Ternopil Children's Hospital in 2018 were analysed. Diagnosis of measles was verified by the presence of measles-specific IgM antibodies, detected in the blood serum after three days of exanthema by ELISA. 2017 statistics were taken from the Infectious Department annual report.

RESULTS

In total 403 children were treated in 2018 in comparison with 67 in 2017; the monthly rate is shown in Figure 1. Boys comprised 49.4% (n = 199) and girls 50.6% (n = 204). By age, they were represented as follows: infants 14.4% (n = 58), toddlers 15.1% (n = 61), pre-schoolers 20.3% (n = 82), and schoolchildren 50.1% (n = 202). The disease was moderate in 94.5% (n = 381) (complicated in 33.6% of them) and severe in 5.5% (n = 22); in all severe cases measles had complicated course. 185 complications were seen in 37.2% (n = 150) of patients generally because some children had more than one. The range of complications is demonstrated in Table 1.

TABLE 1. Measles complications in the patients of the Infectious Department, Ternopil City Hospital, 2018

Complications	Number of cases	Percent from all the complications
Obstructive bronchitis	65	35.1
Pneumonia	33	18.0
Laryngotracheitis	24	13.0
Otitis media	11	6.0
Tubo-otitis	3	1.6
Sinusitis	2	1.1
Aphthous stomatitis	11	6.0
Gastroenteritis	10	5.4
Hepatitis	8	4.3
Pancreatitis	1	0.5
Acute appendicitis	1	0.5
Urinary tract infection	7	3.8
Encephalitic reaction	3	1.6
Encephalitis	1	0.5
Subconjunctival bleeding	3	1.6
Nasal bleeding	1	0.5
Metrorrhagia	1	0.5
Total amount	185	100

The complaints, present on admission, are shown in Table 2.

The percentage of children hospitalised during the prodromal period of measles was 15.4% (n = 62), during the period of exanthema – 83.4% (n = 336), and during the pigmentation period – 1.2% (n = 5). 48.6% (n = 196) of children were not vaccinated by measles vaccine, 25.6% (n = 103) were vaccinated only once, and 25.8% (n = 104) were completely vaccinated. The high percentage of vaccinated children among the diseased can be explained by unsatisfactory documentation of vaccination (fictitious records), which is one of the main problems of primary healthcare in our country.

The prodromal period of measles lasted 2–6 days (mainly 3 to 4) in 71.0% (n = 286). The disease had an acute beginning from high-grade fever in 52.6% (n = 212) or moderate in 44.7% (n = 180), which decreased to low-grade in 60.8% (n = 245) or normal in 6.2% (n = 25) in the last 1–2 days of this period.

Catarrhal syndrome, initially manifested with mild non-productive cough, started mainly on the second day in 59.1% (n = 238). Rarely cough was a single first sign

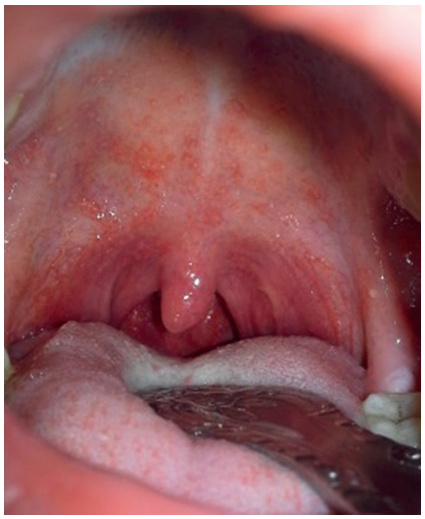

FIGURE 2. Enanthema on the palate

FIGURE 3. Koplik's spots on the 3rd day of the prodromal period

FIGURE 4. Koplik's spots on the 5th day of the disease

FIGURE 5. Aphthae on the 5th day of the disease

of the disease – 3.0% (n = 12), or it appeared at the end of the prodromal period – 17.9% (n = 72). Coryza and conjunctivitis manifested on the 3rd or on the 4th day in 56.1% (n = 226), rarely together with the cough on the second day in 15.6% (n = 63), or at the beginning of the exanthema period – 9.4% (n = 38).

Throat inspection in children hospitalised in the first day of the catarrhal period showed anterior palatine arch and back pharyngeal hyperaemia (without special hallmarks). On the second day, maculous enanthema appeared on the soft palate near the uvula base (Fig. 2); on the 3rd day it transmitted all over the palate and Koplick's spots appeared on the cheeks of the mucosa with their typical localisation opposite the molars (Fig. 3). On the 4th day enanthema increased and formed total hyperaemia; Koplick's spots increased in amount, covered not only the cheeks, but also the lips, gums, and even the palate (Fig. 4). They were also present on the genital mucosa, which was accompanied with burning or itching in some cases. The tongue was coated throughout the prodromal period. Several patients (n = 11 [2.7%]) had aphthous stomatitis (Fig. 5), sometimes mimicked with Coxsackie stomatitis.

In some cases (n = 26 [6.5%]) a prodromal rash was noted in this period. On the 3rd–5th day, it was seen on the trunk, neck, and hands, appearing with fever and disappearing when the temperature became normal. Those children had a longer (5 to 6 days) prodromal period.

The period of exanthema manifested with rash in 99.8% (n = 402) (the rash was absent in one newborn child only), a second wave of a high grade fever ≥ 39°C in 60.0% (n = 242), and even ≥ 40°C in 11.2% (n = 45). Catarrhal signs became more severe. For 2–3 days the fever remained high, then decreased to low grade on the 3rd–4th day of the exanthema period in uncomplicated cases (n = 255 [63.3%]).

FIGURE 6. Initial localisation of the rash in measles, exanthema period

FIGURE 7. Typical morphology of the rash in measles

Typical rash primarily was located on the cheeks and nasal bridge was seen in 36.2% (n = 146), on the back of the ears in 35.7% (n = 144), on the forehead, near the hair line in 23.6% (n = 95) (Fig. 6). Rash had typical three days of staging in 66.5% (n = 268) of patients, was bright red and maculopapular (Fig. 7). In this case it covered the face, neck, and the upper part of the chest on the first day, spread to the whole trunk, arms, and upper part of the thighs on the second day, and all over the body on the 3rd day. Rarely the rash spread for two days (n = 78 [19.4%]), covering the face, neck, trunk, and the proximal parts of the arms on the first day and the rest of the body on the second day. In some patients (n = 36 [8.9%]), the rash had four days of staging, which on the 1st–2nd days was typical, appeared on the knees and feet on the 3rd day, and covered the whole body on the fourth day. In some cases (n = 18 [4.5%]) this variant of rash staging stopped in three days, so the thighs and shins remained free of rash. A considerable number of patients (n = 96 [23.8%]) complained of itching skin.

Koplick's spots in this period were present in 93.3% (n = 376) of children. They were absent only in infants younger than three months of age (n = 9 [2.2%]) and those hospitalised on the 3rd day of exanthema, or later. Throat hyperaemia decreased at the end of the exanthema period and the tongue lost its coating and became "strawberry" sometimes (n = 69 [17.1%]). Catarrhal signs stayed the same. Neck and occipital lymph nodes were palpable in 85.6% (n = 345), 0.5–0.8 cm in size, movable, elastic, and painless.

The pigmentation period started when the rash became purpuric, brownish, lost its papularity in the same way that it had appeared, frequently (n = 264 [65.5%]) with the haemorrhagic component of different severity (Fig. 8). In many cases (n = 252 [62.5%]) epidermis

FIGURE 8. Rash pigmentation with severe haemorrhagic component in measles

desquamation was present on the face and neck (Fig. 9). Conjunctivitis, rhinitis, and diarrhoea disappeared at the beginning of the pigmentation period (n = 348 [86.4%]). Cough became less frequent and more productive in 60.0% (n = 242) and disappeared without phlegm production in 38.7% (n = 156) of patients.

Chest percussion in uncomplicated cases (254) revealed resonant sound. Chest auscultation of the same patients revealed harsh breathing in 89.0% of them (n = 226) in prodromal period or in the beginning of exanthema period, inconstant diffuse tiny rales in 58.7% of cases (n = 149) in the end of exanthema period or in the beginning of pigmentation period.

FIGURE 9. Epidermis desquamation on the face in measles, pigmentation period

Complete blood count (CBC) revealed leucopaenia 1.8–3.9 G/l (n = 176 [43.7%]), rarely – leukocytosis (n = 68 [16.9%]) or leukemic reaction by lymphocytic type (n = 8 [2.0%]), eosinophilia (n = 268 [66.5%]), neutrophilic left shift up to 42% of immature neutrophils (n = 345 [85.6%]), thrombocytopaenia 32–150 G/l (n = 198 [49.1%]), and lymphocytosis (n = 376 [93.3%]). Leucopaenia, thrombocytopaenia, eosinophilia, and neutrophilic left shift were mainly seen in the prodromal period or period of exanthema (n = 278 [69.0%]), and normocytosis or leukocytosis with lymphocytosis in the pigmentation period (n = 376 [93.3%]). Biochemical blood test revealed liver function impairment (cytolysis syndrome) in 7.9% (n = 32). Chest X-ray showed strengthening of the pulmonary pattern in the basal parts of the lungs (n = 65 [16.1%]) in the case of bronchitis and infiltrates in the lower lobes (n = 33 [8.2%]) in the case of pneumonia.

DISCUSSION

The WHO experts state that any person with fever, maculopapular rash and cough, coryza, or conjunctivitis is considered to be a clinical case of measles [3].

Epidemiological anamnesis (contact with an ill person, air-droplet transmission, and autumn-winter seasonality) is one of the diagnostic criteria of measles. 52.6% (n = 212) of our patients had proven direct contact with an ill person (in the family, in the child's collective, or in a hospital). The percentage of proven direct contact was not very high because of possible infection in out-hospital or nonspecialised hospital departments, where patients with measles in the prodromal period were examined or hospitalised. Grammens *et al.* (2017) reported low vaccination coverage of patients, high percentage of household or nosocomial measles infection in the period 2016–2017 in Belgium [4].

More than 50% of ill children in the Ternopil region of Ukraine were younger than six years old, as opposed to 73% of those older than 15 years in Italy in 2017 or 73.3% 12–29 years old in Shri-Lanka in 2013 [5, 6]. These statistics could be explained by the low immunisation coverage of children in Ukraine [7].

The average course of hospital treatment was 6.32 days. Patients with moderate measles (94.5%) or severe measles (5.5%) were hospitalised. Absence of mild cases among those treated in hospital could be explained by the fact that they did not need hospitalisation because their disease had an uncomplicated course, as Filia *et al.* considered, or because the typical course of measles is rarely mild in children [8].

The cyclic course of measles is the next diagnostic criterion of measles. The incubation period in our patients was mainly short (9–11 days) in 82.1%. This could be explained by close contact in families or in hospital. 15.4% of patients were hospitalised in the prodromal period, which lasted for 2–6 days. It is usually longer in unvaccinated persons [9]. Intoxication and a high fever are the first signs in this period. Catarrhal syndrome is the next: dry, rare than frequent cough accompanied by sore throat, and hoarseness in some patients; rhinitis (nasal congestion or coryza); and conjunctivitis (eyes reddening, photophobia, foreign body sensation, oedema of the eyelids). Vomiting, diarrhoea, and abdominal pain in this period develop because of gastrointestinal mucosa inflammation. Enanthema (rash on palate) and Koplick's spots that appear on the 2nd–3rd day of illness and increase the next day are specific signs of this period. Premaratna *et al.* described the presence of Koplick's spots from the 3rd–4th day of measles [10].

The exanthema period begins with a pinkish maculous rash on the face and backs of the ears, changing to reddish maculopapular and spreading downwards for 2–4 days on the background of high fever (second wave) and catarrh intensification. Typical rash with staging was seen in 99.8% of our patients. It was absent only in one newborn (two weeks old) (among three), who had contact with an ill mother after birth, presented catarrh and low-grade fever, and had a positive ELISA test with measles-specific IgM antibodies.

The rash usually begins on the 3rd–5th day of illness and spreads to the 5th–7th day [9]; it is itchy in some patients [11]. Some of our patients had prodromal rash in the prodromal period that lasted 1–3 days, located on different parts of the body, appeared on the 3rd–5th day of illness when the body temperature increased, and disappeared when it decreased. Our patients had mainly three-day typical rash staging (66.5%). Another variant was seen in 19.4% patients (two stages were passed on the first day), and sometimes four-day staging was present (8.9%). Koplick's spots were present in 93.3% of our

patients in the period of exanthema and could be seen for no longer than three days of this period. Other authors describe them in 24.2–42% of patients hospitalised in the period of exanthema [10, 11].

Pigmentation period usually begins on the 3rd–5th day after the rash appears, together with the body temperature normalisation. The rash becomes brownish, and loses its papularity in the same order as it appeared. Some patients have epidermis desquamation on the face and neck. Catarrh gradually disappears for 3–4 days in uncomplicated cases; cough stays longer and becomes less frequent or productive in patients, when they are usually discharged. Lung auscultation shows harsh breathing or unstable bubbling rales in lower lobes of the lungs in the case of productive cough.

In 33.6% of our patients, measles was complicated. Respiratory complications included laryngotracheitis, obstructive bronchitis, and pneumonia, as could be seen in many publications [4, 6, 8, 9, 12–17]. ENT complications included otitis media and sinusitis, as described in other publications [8, 12, 15, 18]. Also, digestive system complications were present, such as gastroenteritis, stomatitis, hepatitis, pancreatitis, and acute appendicitis. The same complications were described by many other authors [4, 6, 8, 11, 12, 15, 19, 20]. Neurological complications in our patients included one case of encephalitis and febrile seizures in three patients (1.0%); the same complicated course was described in the literature [4–6, 8, 21, 22]. Some cases of haematological complications (nasal bleeding, subconjunctival haemorrhages, metrorrhagia) were caused by thrombocytopaenia. Other authors describe such complications in 3.2–13% of cases [8, 22].

CBC revealed leucopaenia, thrombocytopaenia, eosinophilia, and leukocytic left shift in the prodromal and the exanthema period; normocytosis or leukocytosis (hyperleukocytosis sometimes) with lymphocytosis in the pigmentation period. Similar haematological signs were described by others [10, 11]. Biochemical blood test revealed liver function impairment and hyperamylasaemia in some cases, as seen in many publications [8, 10–12, 14, 15].

Chest X-ray showed basal pulmonary pattern intensification in the case of bronchitis, focal or segmental, mainly unilateral, and infiltration with pulmonary pattern intensification in the case of pneumonia. Bilateral pneumonia on X-ray was described by Premaratna *et al.* [10].

CONCLUSIONS

Children formed the majority of patients (65.73%) in the structure of measles morbidity in 2018 in the Ternopil region of Ukraine. This and the high percentage of vaccinal record falsification explains the necessity for primary care reorganisation in Ukraine.

Despite typical moderate measles in 94.5% of patients, 37.2% of cases were complicated – respiratory or digestive complications form the vast majority (82.7%) among them.

Prolongation of the prodromal period of measles up to six days with prodromal rash on the trunk or extremities, shortening of the exanthema period up to two days in 19.4%, or its prolongation up to four days in 8.9% of patients, characterised by a specific rash staging, and itchy rash in 23.8% were the main peculiarities of measles, in the 2018 season, among children. We did not investigate clinical peculiarities of measles in vaccinated and unvaccinated children separately. This could be the next step in our work.

Peripheral blood test in the prodromal period of measles and in the period of exanthema is characterised by leukopaenia, thrombocytopaenia, eosinophilia, and a left shift of the leukocytic formula, while in the pigmentation period it is characterised by normocytosis or leukocytosis with lymphocytosis.

Cytolytic syndrome is typical for measles in children.

Intensification of the lung pattern in the base of the lungs on chest X-ray is characteristic for bronchitis and infiltrates in the lower lobes – for pneumonia, as complications of measles in children.

DISCLOSURE

The authors declare no conflict of interest.

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