ORIGINAL ARTICLE

PROBLEMS OF "CONTROLLED INFECTION": PECULIARITIES OF MEASLES IN ADULTS IN IVANO-FRANKIVSK REGION

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ABSTRACT

The aim: To study the clinical and epidemiological peculiarities of measles in adults according to the data of the Regional Clinical Infectious Disease Hospital in Ivano-Frankivsk, Ukraine.

Materials and methods: The article analyzes the epidemiological and clinical features of 113 cases of measles among adults who undergone inpatient treatment in 2017-2018. The diagnosis was confirmed by the detection of antiviral Ig M antibodies. Determination of the genotype of the virus was performed in Regional WHO Reference Laboratory in Luxembourg.

Results: The genotype of the measles virus was *MVs/Cambridge GBR/5.16 D8* is circulating through the region territory. In 98.3% of adult patients a typical clinical picture of moderate severity was observed. Measles was accompanied by complications such as acute bronchitis (23.9%), reactive hepatitis (13.3%), reactive pancreatitis (10.6%) and pneumonia (7.1%).

Conclusions: The following epidemiological peculiarities in adult patients with measles: young people are mostly ill, urban residents are not vaccinated, partly vaccinated or with an unknown vaccine status. There was a change in the genotype of the virus of measles circulating in the Ivano-Frankivsk region: in 2012 genotype *MVs/ManchesterGBR/10.09D4* was confirmed, now the genotype of the measles virus is *MVS/ CambridgeGBR/5.16D8*. In 98 (86.73%) patients was a typical clinical picture of the disease, of moderate severity. Among the complications of the disease were diagnosed: bronchitis and pneumonia (23.9% and 7.1% respectively), reactive hepatitis and reactive pancreatitis (13.3% and 10.6%).

KEY WORDS: measles, genotype, complications, pneumonia, hepatitis

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INTRODUCTION

At the present stage, measles remains an extremely important problem for public health. As WHO reported – now there is the largest outbreak of the measles over the past 20 years in the countries of the European region. The disease affected even those countries that, according to preliminary data, overcame measles (Greece, Albania, Israel and the United Kingdom), that is, interrupted its spread for 3 years [1]. The increase in the measles incidence rate is cyclic and is observed every 5-6 years. At the moment, Ukraine has headed the "alarmingly high" rate of measles in the world, says the UN Children's Fund (UNICEF). In addition to Ukraine, in the list of countries where measles spreads – there are 47 countries of the European region, which reported a ten-fold increase in the incidence of measles [2], as well as the United States, Philippines, Brazil, Yemen, Venezuela, Serbia, Madagascar, Sudan, Thailand, France. The international organizations call the main reason of the current situation an anti-vaccine campaign [3]. According to the latest WHO-UNICEF data on measurable coverage of measles vaccine by the first [4] and second [5] vaccine doses, only four countries (Hungary, Portugal, Slovakia and Sweden) reached 95% [6]. For the period of 2008-2016, the percentage of implementation of the vaccination plan in Ukraine by the MPR (MMR) vaccine of the children according to the scheduled calendar (at the age of 1 and 6 years) amounted an average 79.6% and 59.8% respectively, but the critical low numbers were observed in 2016 – only 45.5% of children aged 1 year of life and 30.2% of children at the age of 6 years received a MMR vaccine [7, 8]. The projected increase in measles morbidity in 2017-2018 is already more than just a high-profile indicator in Ukraine, which is stubbornly kept at a high level since the beginning of 2019. Among adults, the proportion of patients is about 40%. According to the Center for Public Health of the Ministry of Health of Ukraine in 2017, 1344 patients with measles were registered in Ivano-Frankivsk Oblast, which is 46.7 times higher than in 2016; in 2018 – 5617 patients; and in the four months of 2019 there were 1824 cases of measles, including 417 adult patients [9]. According to literature sources, measles in adults, like most "childhood infections", runs with severe course and a higher percentage of complications, in particular respiratory, digestive, nervous systems, and ENT-organs [10, 11]. The difficulty lies in the fact that complications can occur in any period of the disease and require an individual approach to therapy, taking into account the severity of the disease and already existing concomitant pathology.

THE AIM

To study the clinical and epidemiological peculiarities of the course of measles in adults according to the data of the Regional Clinical Infectious Disease Hospital in Ivano-Frankivsk, Ukraine.

MATERIALS AND METHODS

The analysis of 113 cases of measles in adults who undergone inpatient treatment in the Ivano-Frankivsk Regional Hospital in 2017-2018, was performed. The diagnosis was determined on the basis of data from an epidemiological history, complaints of patients, a characteristic clinical picture of the disease and specific laboratory methods for the study of Ig M antibodies in the blood serum by immunoassay analysis (ELISA). To determine the genotype of the virus, there was performed the selection and delivery of samples of urine and nasopharyngeal swabbing from patients with suspected measles to the Central (National) Virology Reference Laboratory of the Center for Public Health of the Ministry of Health of Ukraine for the diagnosis of poliomyelitis, measles, rubella, rotavirus and influenza. Subsequently, samples were tested in the Regional WHO Reference Laboratory for the diagnosis of measles and rubella in Luxembourg.

RESULTS AND DISCUSSION

Among the patients there were 53 men (47%) and 60 women – (53%). The average age was 25.2±3.8 years (the oldest patient was 61 years old). Of these there were urban residents – 74 (65%), rural inhabitants – 39 (35%). According to anamnesis and medical documentation, 17 (15.1%) patients did not receive any dose of measles vaccine, 30 (26.5%) received 1 dose, 18 (15.9%) – 2 doses, and in 48 (42.5%) cases the number of injections is unknown. 10-14 days prior to the onset of the disease 46 (40.7%) patients indicated that they contacted with patients with measles, and in 7 cases (6,2%) patients suffered from this disease previously. Depending on the severity of the disease, the patients were distributed as follows: in 11 (9.73%) patients there was a severe degree, in 98 (86.73%) the disease was of moderate severity and in 4 (3.54%) there was a mild degree of illness. In 106 (93.8%) patients, measles had a typical form, in 7 (6.2%) – an atypical form.

The mild degree of severity was predominantly characterized by atypical mitigated form, which was manifested by slightly expressed symptoms of intoxication and catarrhal phenomena. Most patients were hospitalized for epidemiological indications. The catarrhal period of the disease lasted 2-3 days with slightly expressed rhinitis phenomena, conjunctivitis, coughing, elevation of body temperature to subfebrile digits. During the period of rash on the facial skin, an uneven spotted-papular rash was observed behind the ears, which lasted 2-3 days without a characteristic stage and did not leave the pigmentation and peeling. Koplik's spots, as a pathognomonic symptom of the disease, were not noted in any patient. However, all cases of the disease were confirmed by the laboratory tests with the detection of anti-measles Ig M antibodies in the blood serum by ELISA. The complications of the disease in patients with measles were not diagnosed. The average length of stay in the hospital was 4.3±1.1 days. Mean duration of stay in the hospital was 4.3±1.1 days.

Measles of the mild severity was diagnosed in 98 patients. The disease was typical in 95 (96.9%) patients, and 3 (3.1%) had an atypical form. In typical cases, the catarrhal period was characterized by a moderate intoxication syndrome, an increase of body temperature to febrile one, rhinitis phenomena, conjunctivitis, cough for 3-5 days. In 12 (12.6%) adult patients, prodromal papular rash on the face skin was observed, which occurred 1-2 days before the onset of the period of rash. Koplic's spots on the cheek mucus in the catarrhal period were detected in 70 (73.7%) patients. The period of rash was characterized by abundant spotted-papular rash with an inherent stage during 3-4 days and moderately severe intoxication. In 10 (10.5%) patients, a rash with a hemorrhagic component was noted.

In patients with an atypical measles of moderate severity after the prodromal period with moderate catarrhal and intoxication manifestations, febrile body temperature for 3-4 days, abortion was noted with the onset of papular rash on the face, shoulder girdle for 1-2 days, with a decrease in temperature body to subfebrile indicators.

In 39 (39.8%) patients with measles of moderate severity, the following complications developed: acute catarrhal non-obstructive bronchitis – 25 (25.5%) cases; acute reactive hepatitis – 10 (10.2%); reactive pancreatitis – 8 (8.2%). The average duration of stay in the hospital was 7.3±1.8 days.

Severe cases were diagnosed in 11 (9.73%) patients. The catarrhal period in such patients lasted 4-6 days. The marked phenomena of conjunctivitis (photophobia, tearing), cough with the phenomena of laryngotracheitis, temperature increase up to 39-40°C, were observed. In the period of rash there were observed: severe intoxication, increase of body temperature to 38-40°C, expressed dry cough, hoarse voice, conjunctivitis, vomiting, diarrhea. An abundant spot-papular rash with a hemorrhagic component was observed, drained on the face and trunk, with a characteristic stage and subsequent pigmentation, soft palate enanthema, which were present for 5-7 days. All patients had one or more complications: pneumonia in 8 (72.7%) patients; reactive hepatitis – in 5 (45.5%); reactive pancreatitis – in 4 (36.4%); acute catarrhal non-obstructive bronchitis – in 2 (18.2%); ITSh – in 1 (9.1%). The average duration of stay in a hospital – 10±2.7 days.

An interesting clinical peculiarity of the measles in adult patients was the preservation of Belsky-Filatov-Koplik's spots on mucous membrane of the cheeks until 2-3 days since the onset of rash in 37 (32.7%) patients. In addition to Koplik's spots, a large proportion of patients were observed a non-specific painless enanthema on the mucous membrane of the palate, which lasted throughout the period of rash. An aphthous stomatitis developed in 18 (15.9%) adult patients.

In part of the patients – 23 (20.4%) during the period of rash, the moist small bubbling rales were heard in the lungs, which quickly disappeared within 1-2 days, they did not detect X-ray changes in the lungs. Such manifestations were considered as a violation of lymphatic- and blood circulation in the lungs caused by a measles virus. Pneumonia as a complication was diagnosed in cases confirmed radiologically and clinically (focal and infiltrative changes in the lower lung parts in chest radiography, changes in temperature curve, shortness of breath, decreased oxygen saturation in capillary blood with indirect pulse oximetry, auscultatory – small bubbling rales, leukocytosis of blood, culturing of bacterial flora from sputum) – in 8 (7.1%) patients.

Pancreas lesions were detected in part of the examined patients with moderate severity – in 8 (8.2%) patients and severe degree of measles – in 4 (36.4%) patients, which was often combined with other complications of the disease. Patients complained of nausea, vomiting, pain in the epigastric region, fluid excrement without pathological impurities 2-3 times a day. In the ultrasound examination of the abdominal organs (ultrasound examination), reactive changes in the pancreas were determined, and in the biochemical analysis of the blood, an increase in the level of α-amylase 1.5-2-fold ($p<0.05$).

Reactive hepatitis has developed in 10 (10.2%) patients with moderate severity and in 5 (45.5%) patients there was a severe illness. In the typical form of the measles in adult patients, no subicteritiousness of sclera, darkening of the urine, acholic stool, but hepatomegaly to + 1.5±0.3cm per l was noted. Medioclavicularis dextra was reported in 12 (10.6%) patients. Changes of laboratory parameters showed the disorders of the liver functioning, in particular, increased activity of aminotransferases in the blood, as well as during the ultrasound examination, revealed the phenomena of reactive hepatitis (elevated echogenicity of parenchyma, increased proportions in size). The activity of ALT varied from 43.8 units/l to 204.4 units/l, and on average it was – 125.0±8.3 units/l. The activity of AsAT increased from 47.3 units/l to 197.8 units/l, and on average it was 111.6±7.8 units/l.

In the general analysis of blood in adult patients with uncomplicated measles, normal or low leukopenia (from 4.0 to 2.8x109 g/l) with a pronounced shear-to-left shift (up to 10-18%) and an accelerated ESR (18-29 mm/hour) were registered. Laboratory confirmation of 40 (35.4%) cases of the disease with the detection of specific anti-blood antibodies of Ig M class in serum ELISA. The material from diagnostic patients and patients with an atypical form of the disease was sent for the study.

In determining the genotype of the measles virus in the nasopharyngeal swabbing and urine samples in the WHO Regional Reference Laboratory for the diagnosis of measles and rubella in Luxembourg, results were obtained indicating that the genotype of the measles virus *MVs/CambridgeGBR/5.16D8* (12 positive results from 14 tested samples – 85.7%). This genotype has been registered in recent years in Europe and the USA [3]. In 2012, in the Ivano-Frankivsk region, during the preliminary increase of measles morbidity, the circulation of the genotype *MVs/ManchesterGBR/10.09D4*, circulating at that time in European countries, was confirmed.

All adult patients with measles who were inpatient at the Regional Clinical Infectious Diseases Hospital in Ivano-Frankivsk in 2017-2018, received full pathogenetic and symptomatic therapy. The tactics of managing patients was individual and depended on the severity of the disease and the present complications. In the case of bacterial complications with appropriate changes in the laboratory blood index, the patient was referred to antibiotic therapy. Often a combination of several complications was observed in one patient, who probably depended on age-induced status and presence of comorbidity. Timely seeking for medical care and timely treatment contributed to faster recovery of patients and reduced the risk of serious complications. In particular, all patients who were under observation in the Regional Clinical Infectious Hospital, were observed completely recovered.

CONCLUSIONS

Consequently, the following epidemiological peculiarities can be distinguished in adult patients who were in the inpatient treatment at the Regional Clinical Infectious Diseases Hospital in Ivano-Frankivsk in 2017-2018 with a measles diagnosis: young people are mostly ill, urban residents are not vaccinated, partly vaccinated or with an unknown vaccine status. There was a change in the genotype of the virus of measles circulating in the Ivano-Frankivsk region: in 2012, during the previous increase in measles morbidity, the circulation of the genotype *MVs/ManchesterGBR/10.09D4* was confirmed, now the genotype of the measles virus *MVS/CambridgeGBR/5.16D8* circulates in the region.

In 98 (86.73%) patients during the 2017-2018 epidemiologic season there was a typical clinical picture of the disease, of moderate severity. The clinical peculiarities of the measles in adults include: the presence of prodromal papular rash on the skin of the face during the catarrhal period, the preservation of Koplik's spots on the mucous membrane of the cheeks for up to 2-3 days from the beginning of the period of rash, as well as the damage to the liver. Among the complications of the disease, the most frequently lesions of the respiratory system were diagnosed: bronchitis and pneumonia (23.9% and 7.1% respectively); and the lesions of the digestive system: reactive hepatitis and reactive pancreatitis (13.3% and 10.6% respectively). The timeliness of the seeking for medical assistance and the individually chosen treatment, depending on the severity of the disease and the present complications, contributed to the complete recovery of the patients.

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