Characteristics of serological profile in adult measles patients depending on the development of complications

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The aim – to determine the characteristics of serological profile in adult measles patients depending on the development of complications.

Material and methods. In total, 88 patients with measles aged between 21 and 53 years were followed-up (36 men and 52 women). Measles was diagnosed according to the WHO criteria (2013). All the patients were tested for measles virus IgM at the end of the first week of the disease to confirm the diagnosis. Measles virus IgG was measured using ELISA (Vircell Microbiologists, Spain) on hospital admission, on average the (4.8 ± 0.2) day of the disease, to determine probable post-vaccination immunity to measles.

Results. It was found that in most adult measles patients (75.0 %), the diagnosis was confirmed by the detection of IgM to measles virus at the end of the first week of the disease, while the other patients were diagnosed with measles by clinical and epidemiological criteria.

Most patients (71.6 %) were seropositive with the presence of measles virus IgG on the 4.8 ± 0.2 day of the disease, others had a negative IgG serologic result. Complications of measles were diagnosed in the majority of adult patients (76.1 %), the frequency of which was associated (χ² = 4.84, P < 0.01) with seropositivity in this follow-up period, namely complications were more common in the seronegative patients (92.0 %) against 69.8 % in the seropositive patients. Seronegative patients were more likely to have gastrointestinal complications as compared to seropositive individuals (68.0 % vs. 30.2 %, χ² = 10.60, P < 0.001) due to more frequent development of hepatitis (68.0 % vs. 28.6 %, χ² = 11.61, P < 0.001). The frequency of two or more complications combined was also clearly correlated with the presence of measles virus IgG in patients on day 4.8 ± 0.2 of the disease (χ² = 7.70, P < 0.01).

A comparison of the quantitative content of IgG against measles virus in seropositive adult measles patients showed an association with the development of complications: the highest level was detected in patients with uncomplicated measles amounting to 23.58 [21.87; 26.78] optical density units. In seropositive adult patients with measles-associated hepatitis, the measles virus IgG content was lower (P = 0.004) than in patients with uncomplicated measles. A similar pattern was observed in pneumonia development (P = 0.0002). There were correlations between measles virus IgG content and platelet count (r = +0.32, P < 0.05), relative number of lymphocytes (r = +0.46, P < 0.05), ALT activity (r = -0.45, P < 0.05), relative number of band neutrophils (r = -0.36, P < 0.05).

Conclusions. In adult measles patients on day 4.8 ± 0.2 of the disease, seropositivity with measles virus IgG presence was observed in 71.6 % of cases. Measles complications were recorded in 76.1 % of adult patients. The incidence of complications was correlated with the presence of IgG against measles virus. Complications were more common in seronegative patients than in seropositive ones (92.0 % vs. 69.8 %, P < 0.01). The development of pneumonia (P < 0.01) and hepatitis (P < 0.01) was associated with the lowest level of measles virus IgG.

Ключові слова: кір у дорослих, серологічний тест, ускладнення.

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Мета роботи – з’ясувати особливості серологічного профілю дорослих, які хворі на кір, залежно від розвитку ускладнень.

Матеріали та методи. Під спостереженням перебували 88 хворих на кір віком від 21 до 53 років: 36 чоловіків, 52 жінки. Діагноз кіру встановлювали за критеріями ВООЗ (2013). Усім хворим визначали IgG до вірусу кіру на 4.8 ± 0.2 день хвороби (Vircell Microbiologists, Spain) методом ІФА.

Результати. Встановлено, що в більшості дорослих, які хворі на кір (75.0%), діагноз підтверджено виявленням IgM до вірусу кіру наприкінці першого тижня захворювання для підтвердження діагнозу. Заголовка кіру встановлювали за критеріями ВООЗ (2013). Усім хворим визначали IgM до вірусу кіру на 4.8 ± 0.2 день. Серед серонегативних пацієнтів найбільша частка (χ² = 10.60, P < 0.001) хворих віком 25–44 років – 80,0 % в порівнянні з 71,6 % у хворих від 45 до 53 років.

Особливості серологічного профілю в дорослих, які хворі на кір, залежно від розвитку ускладнень

Zaporozhye medical journal. 2020; 22 (6), 823-827

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UDC 616.915-036.1-053.8
DOI: 10.14739/2310-1210.2020.6.218457

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Цель работы – выяснить особенности серологического профиля у взрослых больных корью в зависимости от развития осложнений.

Материалы и методы. Под наблюдением были 88 больных корью в возрасте от 21 до 53 лет: 36 мужчин, 52 женщины. Диагноз кори устанавливали по критериям ВОЗ (2013). Всем больным определяли IgM к вирусу кори в конце первой недели заболевания для подтверждения диагноза. Для выяснения наличия вероятно поствакцинальных антител при поступлении в стационар определяли IgG к вирусу кори в среднем на 4,8 ± 0,2 дня болезни (Vircell Microbiologists, Spain) методом ИФА. Большинство больных (71,6 %) серопозитивны с наличием IgG к вирусу кори, среди них преобладали пациенты молодого возраста (63,6 %). Среди серонегативных пациентов больше всего (χ² = 4,04, p < 0,01) больных в возрасте 25–44 лет – 80,0 % против 57,1 % серопозитивных.

Результаты. Установлено, что у большинства взрослых больных корью (75,0 %) диагноз подтвержден обнаружением IgM к вирусу кори в конце 1 недели заболевания, у других диагноз кори утвержден по клинико-эпидемиологическим критериям. Большинство больных (71,6 %) на 4,8 ± 0,2 дня болезни серопозитивны с наличием IgG к вирусу кори, другие имели отрицательный результат. Осложнения кори диагностированы у большинства взрослых больных (76,1 %), частота развития которых имела связь (χ² = 4,84, p < 0,01) с серопозитивностью в эти сроки наблюдения: осложнения чаще зафиксированы у серонегативных больных (92,0 %) по сравнению с серопозитивными (69,8 %). У серонегативных пациентов чаще, чем у серопозитивных отмечены осложнения со стороны желудочно-кишечного тракта (68,0 % против 30,2 %, χ² = 10,60, p < 0,001) за счет более частого развития гепатита (68,0 % против 28,6 %, χ² = 11,61, p < 0,001). Частота развития двух и более осложнений также четко зависела от наличия IgG к вирусу кори у пациентов на 4,8 ± 0,2 дня болезни (χ² = 7,70, p < 0,01).

Сравнение количественного содержания IgG к вирусу кори у серопозитивных взрослых больных корью показало связь с развитием осложнений. Самый высокий их уровень зафиксирован у пациентов с неосложненным течением кори, составивший 23,58 [21,87; 26,78] опт.ед. У серопозитивных взрослых больных корью, которая осложнилась гепатитом, содержание IgG к вирусу кори было ниже (p = 0,004), чем у пациентов с неосложненным течением кори. Аналогичная закономерность отмечена и при развитии пневмоний (p = 0,002). Установлены корреляции содержания IgG к вирусу кори с содержанием тромбоцитов (r = 0,32, p < 0,05), относительным количеством лимфоцитов (r = +0,46, p < 0,05), активностью АЛТ (r = -0,45, p < 0,05), относительным количеством палочкоядерных лейкоцитов (r = -0,36, p < 0,05).

Выводы. У взрослых больных корью при поступлении на 4,8 ± 0,2 дня заболевания серопозитивность с наличием IgG к вирусу кори отмечена в 71,6 % случаях. Осложнения кори зафиксированы у 76,1 % взрослых больных. Частота развития осложнений имеет связь с наличием IgG к вирусу кори на момент госпитализации. Осложнения чаще зафиксированы у серонегативных, чем у серопозитивных пациентов (92,0 % против 68,8 %, p < 0,01). Развитие пневмоний (p < 0,01) и гепатита (p < 0,01) ассоциируется с низким уровнем IgG к вирусу кори.

According to the WHO, in European countries, including Ukraine, there was a significant increase in measles patients in 2017–2019. In the first six months of 2019, almost 90 thousand cases of measles were detected, which was more than the number of reported cases for the whole of 2018, when 84 thousand cases of this infection were registered. Ukraine headed the list of the top ten countries with the highest number of measles cases in 2018 [1].

Today, countries with high measles immunization coverage are still at risk of epidemic outbreak because of a change in the measles epidemiology over a long period of routine immunization owing to an increase in the adult population [2,3]. In these countries, there is a decrease in the content of post-vaccination IgG in adults, and possible consequences of this phenomenon during the elimination period remain unclear [4]. According to a number of researchers, adults under the age of 30 attract special attention, because the largest number of measles virus seronegative individuals (more than 40 %) is observed in an age group of 18–30 years [5]. Serological epidemiological stud-
ies in Ukraine on the determining the most vulnerable age group of adults among population revealed persons aged 16 to 30 years, as only 78.1 % of examined people had immunity against measles, which coincides with the high proportion of this age group among measles patients [6].

**Aim**

The purpose of the work is to determine the characteristics of serological profile in adult measles patients depending on the development of complications.

**Material and methods**

In total, 88 measles patients aged 21 to 53 years, the average age was 30.9 ± 0.9 years, were examined. They were hospitalized to the Municipal Institution “Regional Infectious Diseases Clinical Hospital”, Zaporizhzhia Regional Council, during 2017–2019. There were 36 men and 52 women. The diagnosis of measles was made according to the WHO criteria (2013). All measles patients included in the study reported measles childhood vaccination, but without documented evidence. All the patients were tested for measles virus IgM at the end of the first week of the disease to confirm the diagnosis. Measles IgG was measured using ELISA (Vircell Microbiologists, Spain) on hospital admission to determine probable post-vaccination immunity to measles. Special studies were performed on the basis of the Training and Laboratory Center of ZSMU headed by Professor Abramov A.V. Statistical data processing was performed in the program Sntatistica 13 for Windows (StatSoft Inc., No. JPFZ604382130ARCN10-J).

On day 4.8 ± 0.2 of the disease, most patients (63.0–71.6 %) were seropositive with the presence of measles virus IgG, and 25 (28.4 %) patients had a negative IgG serologic result. Among adult measles patients, young patients predominated (n = 56; 63.6 %), only one of the three patients was middle-aged adult – 29 (33.0 %), late middle-aged adults were diagnosed with measles in isolated cases (n = 3; 3.4 %). The analysis of measles virus IgG presence showed the largest proportion (χ² = 4.04, P < 0.01) of patients aged 25 to 44 years among seronegative individuals amounting to 80.0 % (20 of 25) against 57.1 % (36 of 63) of seropositive ones (Fig. 1).

**Results**

According to the results of our study, in most adult measles patients (n = 66; 75.0 %), the diagnosis was confirmed by the detection of IgM to measles virus at the end of the first week of the disease, while 22 (25.0 %) patients were diagnosed with measles by clinical and epidemiological criteria.

An analysis of measles virus IgG presence showed that most patients (n = 63; 71.6 %) were seropositive on day 4.8 ± 0.2 of the disease, and 25 (28.4 %) patients had a negative result. At the same time, the majority of adult patients (n = 67; 76.1 %) developed complications of measles. A comparison of complication incidence in adult patients with measles showed dependence (χ² = 4.84, P < 0.01) on a serologic status, namely seronegative patients developed complications significantly more often – 23 (92.0 %) against 44 (69.8 %) seropositive patients. An analysis of a range of measles-related complications in adults showed that seronegative patients, unlike patients with measles virus IgG, were more likely to have gastrointestinal complications in the follow-up period (68.0 % vs. 30.2 %, χ² = 10.60, P < 0.001), primarily due to more frequent development of liver damage manifested as hepatitis (68.0 % vs. 28.6 %, χ² = 11.61, P < 0.001). Besides, a comparison of respiratory complications incidence did not reveal any statistically significant effect of measles virus IgG seropositivity at the time of hospital admission. However, the incidence of combination of two or more complications was clearly correlated with measles virus IgG presence in patients on day 4.8 ± 0.2 of the disease amounting to 64.0 % (16 of 25) in seronegative patients versus 31.7 % (20 of 63) in seropositive patients (χ² = 7.70, P < 0.01) (Table 1).

A quantitative content of measles virus IgG in seropositive adult measles patients was found to be correlated with the development of complications. Thus, a content analysis showed the highest level of measles-specific IgG in patients with uncomplicated measles amounting to 23.58 [21.87; 26.78] optical density units. In seropositive adult patients with measles complicated by hepatitis, the content of measles virus IgG was statistically significantly lower (18.67 [15.02; 24.05] optical density units (P = 0.004)).

![Age structure among adult measles patients depending on the presence of measles virus IgG at hospital admission](image-url)
Patients with measles

Table 2. Measles-specific IgG content in seropositive adult measles patients depending on the development of complications, Me [Q1; Q3], n = 36

| Indicator                                      | Patients with measles without complications | Pneumonia (including combination with other complications) | Hepatitis (including combination with other complications) |
|------------------------------------------------|---------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Measles-specific IgG, optical density units   | 23.58 [21.87; 26.76]                        | 16.80 [14.66; 20.26]*                                     | 16.97 [15.02; 24.05]*                                     |

*: difference is significant compared to the corresponding indicators in patients without complications (P < 0.01).

The modern literature presents a large amount of study results demonstrating measles-associated pneumonia in individuals previously vaccinated for this infection [10, 14]. Today, a number of studies attempt to address the issue of pathogenetic features of focal pneumonia development in individuals previously vaccinated for measles. In particular, it is assumed that the measles virus can replicate in local lymphoid tissue, then spread through the blood stream in individuals with waning post-vaccination immunity over time [15]. The occurrence of lung inflammatory foci is explained by type III hypersensitivity, as previously vaccinated patients respond to measles virus dissemination by a rapid production of measles-specific IgG, which bind to the virus forming antigen-antibody complexes. As the measles virus is disseminated rapidly into many organs via viremia, similar foci of inflammation caused by immunocomplex mechanisms can be seen in other organs [16]. However, researchers believe that the mechanism of focal measles pneumonia in previously vaccinated individuals may differ from that in measles-associated lung infection in non-immune individuals [10]. It has been shown that foci of measles pneumonia in previously vaccinated individuals are common in the acute period of the disease, but the inflammatory foci show very long subsequent regression, usually within a few months [14]. Meanwhile, researchers have noted that in such patients, measles pneumonia is often focal and diagnosed better with computed tomography [10, 14]. According to researchers [10], measles-associated pneumonia was evident in such patients only with an IgG/IgM ratio >20, which may be useful to diagnose measles pneumonia during outbreaks of this infection [10].

The latest studies indicate a high incidence of liver damage in adult measles patients [17, 18]. The incidence of this complication in adult measles patients ranges from 45 % [18] to 81 % [17] against 1.4 % in children [7]. According to our study, the incidence of hepatitis in adult measles patients was 39.8 %, and it was proved to be much higher in the absence of serum measles-specific IgG at the time of hospital admission than in seropositive individuals (68.0 % vs. 28.6 %, P < 0.001). Recent data from the literature suggest that the risk of complications correlates with the severity of measles virus-induced immunosuppression in patients [19]. In conditions of secondary viremia, which is accompanied by clinical manifestations, the measles virus maximum amplification in the cells of lymphoid structures, respiratory system, gastrointestinal tract determines a number of complications. The process in these organs is serous-macrophage with lymphocytic infiltration and small-vessel vasculitis [20].

Conclusions

1. In adult measles patients on day 4.8 ± 0.2 of the disease, seropositivity with the presence of measles virus IgG was observed in 71.6 % of cases.
2. Measles complications were recorded in 76.1 % of adult patients. The incidence of complications was correlated with seropositivity and the presence of measles virus IgG on day 4.8 ± 0.2 of the disease, namely complications were more common in seronegative patients than in sero-positive ones (92.0 % vs. 69.8 %, \( \chi^2 = 4.84, P < 0.01 \)).

3. The development of measles complications such as pneumonia (\( P < 0.01 \)) and hepatitis (\( P < 0.01 \)) was associated with the lowest level of measles virus IgG.

Conflicts of interest: authors have no conflict of interest to declare.

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