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PECULIARITIES OF THE CLINICAL COURSE OF INFLUENZA-ASSOCIATED PNEUMONIA

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It was found that in 2017, compared to 2016, in the Poltava region there were 6 times fewer cases of influenza, as indirectly indicated by the number of hospitalized patients due to this pathology in PRCIH. But despite this, the incidence of pneumonia, which complicated the course of influenza according to the data of PRCIH, remained at a consistently high level (20.84% in 2016 and 20.19% in 2017). It was demonstrated that the clinical course of pneumonia as a complication of influenza had some peculiarities.These peculiarities were observed as early as in the initial period of the disease with a predominance of the symptoms of toxic syndrome. This can mask the symptoms of early development of pneumonia and cause hospitalization of patients at a later date. Substantially half of patients had a bilateral inflammatory process, wherein physical changes (auscultatory pattern of pneumonia and a decrease in pulse oxygen saturation) preceded the radiological changes. The course of pneumonia in a significant number of patients was severe with the need for oxygen therapy. Sputum culture in patients with a pneumonia as a complication of influenza more often demonstrated the pathogens such as Stretococcus pneumonia and Staphylococcus aureus.

Key words: influenza-associated pneumonia, prevalence, risk factors, clinical features.

The present study is a fragment of the research scientific work performed by the of Infectious Diseases and Epidemiology Department of HSEE "Ukrainian Medical Stomatological Academy", MOH of Ukraine: "Determination of the Toll-like receptors polymorphism role in the pathogenesis of infectious diseases", state registration number 0113U005006.

Influenza is the most common and mass infectious disease on the globe. Thus, according to estimates, annually from 4 to 15% of the world's population are infected with influenza and acute respiratory diseases, and 250-450 thousand people die of influenza and its complications [3]. Incidence of disease increases to 50-70% of the population during the influenza pandemics, which in the human population are associated with shifted changes in the pathogen [4]. At the same time, the mortality from the flu and its complications ranks first among all infectious diseases [1, 2, 8]

It has been shown that influenza-associated pneumonia remains the main cause of morbidity, hospitalization and mortality in a flu, and therefore it is a very complicated health problem worldwide, including in developed countries. It is known that the influenza is complicated by pneumonia in 10-20% of all patients with flu, and in about half of the hospitalized patients [5, 6].

Thus, the problem of influenza-associated pneumonia remains relevant, which makes the need for further study of the features of their clinical course, generalization of the results of laboratory and instrumental and radiological studies to optimize diagnostic and therapeutic tactics.

The purpose of the study was to analyze the prevalence and to describe the clinical course of pneumonia as a complication of influenza in the Poltava region.

Materials and methods. To achieve this purpose we have analyzed the data of the official reporting documentation provided by the State Institution "Poltava Regional Laboratory Center of the Ministry of Health of Ukraine" and the chart of patients with a laboratory confirmed diagnosis of influenza who were in inpatient treatment at the Poltava Regional Clinical Infectious Hospital (PRCIH) in 2016-2017. In more detail, we examined 68 patients with pneumonia as a complication of influenza. Female patients were 27 (39.71%) persons, male patients were 41 (60.29%) persons, aged 18 to 80 years.

Influenza was diagnosed based on epidemiological, clinical data, serological findings with the determination of the increasing of specific antibody titers in the hemagglutination inhibition reaction with influenza diagnostic agent A/H1N1, A/H2N2, A/H3N2, B and the detection of Influenza virus A/H1N1/California in polymerase chain reaction (PCR). Among the factors that complicated the course of the disease, we considered obesity, chronic pathology of the cardiovascular and respiratory systems, diabetes mellitus, immunodeficiency of various etiology and neoplasms.

Pneumonia was diagnosed on the basis of a comprehensive analysis of epidemiological and clinical and laboratory data with mandatory X-ray/tomographic confirmation. The course of pneumonia and the need for hospitalization to the intensive care unit was determined on the IDSA/ATS (American Thoracic Society and Infectious Diseases Society of America), wherein we were guided by the order of the Ministry of Health of Ukraine from March 19, 2007 No. 128, and classified the patients into one of five groups, depending on the severity and the presence of concomitant pathology. Treatment of patients with pneumonia of Groups I-III was conducted in the diagnostic department of PRCIH; pneumonia of Group IV was treated in the intensive care unit. All patients received antiviral therapy (oseltamivir 150

mg/day in the case of pneumonia of Group II-III, and 300 mg/day in the case of pneumonia of Group IV), antibiotic therapy in accordance with the Protocol of treatment (orders of the Ministry of Health of Ukraine from May 20, 2009, No. 189, and from November 18, 2009, No. 832), oxygen therapy for indications. We have conducted a comprehensive survey of all patients with determination of pulse oxygen saturation (SpO_2), bacteriological examination of sputum, laboratory and additional research depending on concomitant and diagnosed pathology with the involvement of consultants of the corresponding profile.

Results of the study and their discussion. The conducted studies showed that 1344 cases of influenza were registered in 2016 according to the official reporting documentation provided by the State Institution "Poltava Regional Laboratory Center of the Ministry of Health of Ukraine", in Poltava Region, which amounted to 93.91 cases per 100000 population, and 305892 cases of acute infections of the upper respiratory tract of multiple or uncertain localizations (21374.46 cases per 100000 population). In 2017, the flu has been diagnosed in 216 patients in the Poltava region (15.22 cases per 100000 population), and acute upper respiratory infections of multiple or uncertain localizations have been diagnosed in 232050 patients (16353.32 cases per 100000 population). We also observed a similar tendency to reduce the incidence of influenza in 2017, also according to the data of PRCIHL; the number of hospitalized patients with this pathology indirectly indicated this. In 2016, 499 patients with flu diagnosis were treated in PRCIHL (influenza A was diagnosed for 65 patients, influenza B - for 2 patients, and the flu diagnosis was clinically established based on clear clinical and epidemiological data for 432 patients). In 2017, the number or patients with influenza was only 104 (influenza A - 25 , influenza B - 3, influenza (clinical) - 76). It should be noted that although the incidence of influenza substantially decreased in 2017, as compared to 2016, the frequency of pneumonia, which complicated the flu according to the data of the PRCIHL, remained at a stable high level (20.84% in 2016 and 20.19% in 2017).

Among patients with pneumonia, as a complication of the flu, most individual (n = 39; 57.35%) were over 40 years old. We identified the risk factors for the severe flu and accordingly the development of pneumonia, with the following frequency: chronic diseases of the cardiovascular system – 22.06%, chronic diseases of th respiratory system – 20.59%, obesity – 5.88%, diabetes mellitus – 7.35%, HIV infection - 1.47%, tumors - 1.47% (Tab. 1).

Table 1

Demographic indicators and the frequency of the risk factors of the complicated course of influenza in the examined patients with pneumonia

Indicators		**abs.**	**%**
Gender	male	41	60.29
	female	27	39.71
Age	18-30	13	19.12
	31–40	23	33.82
	41–50	8	11.76
	51–60	11	16, 17
	61 and older	13	19.12
Risk Factors	pathology of the respiratory system	14	20.59
	cardiovascular pathology	15	22.06
	obesity	4	5.88
	diabetes	5	7.35
	immunodeficiency	1	1.47
	neoplasm	1	1.47

The analysis of terms of hospitalization of patients to a hospital showed that early treatment for medical aid was prevalent among patients. This fact indirectly pointed to the severe course of the disease and the possible early development of complications. Thus, almost half the patients (n = 32; 47.06%) were hospitalized on the 1-3 day, the same number of patients (n = 32; 47.06%) on 4-6 day; 3 (4.41%) patients were hospitalized after 6 days from the onset of the disease.

At the prehospital stage, 40 (58.82%) patients were treated; among these patients 23 individuals received antibiotic therapy, 17 individuals received preparations of antiviral therapy, which is usually combined with symptomatic drugs.

Clinical manifestations of the disease and their frequency in patients are presented in Table 2 at the hospitalization. As can be seen from Table 2, in most patients the disease had an acute onset with a predominance of symptoms of general toxic syndrome with such frequency: hyperthermia (100.00%), headache (29.41%), muscle pain (32.35%). In addition, patients had symptoms of severe intoxication,

such as nausea and vomiting, in 11.76% of individuals. In the vast majority of patients we observed catarrhal syndrome of varying severity: scleritis and hyperemia of the oropharyngeal mucosa (57.35%), dry (57.35%) and productive (26.47%) cough. The high incidence of chest pain (27.94%) and breathlessness (27,94%) should be noted. The dry cough changed on productive in most patients in the dynamics. The type of sputum was mucoid – 20.59%, mucopurulent – 4.41% or bloody – 1.47%.

Table 2

The main clinical symptoms in patients with influenza, complicated with pneumonia

Symptoms		abs.	%
Onset	t 38-40C	37	54.41
	t to 38C	31	45.59
Headache		20	29.41
Myalgia		22	32.35
Rhinitis		14	20.59
Sore throat		25	36.76
Nausea, vomiting		8	11.76
Hyperemia of the oropharynx, scleritis		39	57.35
Pain in the chest		19	27.94
Caugh	dry	39	57.35
	productive	18	26.47
Bloody sputum		1	1.47
Breathlessness		19	27.94
Skin pallor, acrocyanosis		1	1.47
Auscultatory changes		66	97.06
Pneumonia	one-sided	38	55.88
	two-sided	30	44,12
Respiratory rate	up to 18	23	33.82
	19-25	38	55.88
	26-30	5	7.35
	More than 30	2	2.94
Sp O_2	100	1	1.47
	99-96	41	60.29
	95-92	19	27.94
	91 and less	6	8.82

Analysis of physical changes in the lungs in hospitalized patients showed that signs of pneumonia (dullness on percussion sound over the affected part of the lung, weakened or bronchial breathing, small bubbling rales, crepitations) were determined in 97.06% of subjects.

Of all patients, 6 (8.82%) were classified in Clinical Group IV . Among these patients, only 1 (1.47%) had a one-sided inflammatory process in the lungs, while in others inflammation was bilateral. 26 (38.24%) of patients were classified in Clinical Group III. Of these patients, 24 had bilateral pneumonia and 2 had one-sided pneumonia. 36 (52.94%) patients were classified in Clinical Group II, of which all except one had one-sided lung injury.

Radiographic picture of pneumonia in patients had certain features. One- or two-sided inflammatory process had essentially the same frequency - 55.88% and 44.12% respectively; the process started at the periphery and in the lower lobes, initially in the form of enhancement of the pulmonary pattern and inhomogeneous foci, which in severe cases subsequently spread and formed massive subtotal or total infiltrative changes in the lungs. The roots of the lungs were substantially expanded and infiltrated. By means of an estimation of the x-ray pattern in the dynamics, it was found that the resorption of infiltrates lasted more than 12 days, and residual pneumonia was preserved in the overwhelming majority (n = 60; 88,24%) of the persons discharged from the hospital.

The level of SpO_2 was significantly differed depending on the prevalence of inflammatory process in the lungs in patients. The levels of SpO_2 ranged from 100 to 92% (mean (95.1 ± 0.3%) in patients with pneumonia of Clinical Group II – III without inhalation of oxygen. In the case of pneumonia of Clinical Group IV with bilateral lung injury, blood oxygen saturation varied from 94 to 60% without inhalation of oxygen. All patients with pneumonia of Clinical Group IV received treatment in the intensive care unit to improve the condition from 3 to 13 days (on average – 6.1 ± 1.1 days).

Typical changes in the blood test of patients were: leukopenia – 30 (44.12%), lymphomonocytosis – 20 (29.41%). Also, patients had leukocytosis – 12 (17.65%), left shift – 52 (76.47%), ESR acceleration – 41 (60.29%).

Bacteriological study of sputum was performed for 24 (35.29%) patients. On the basis of the analysis of the obtained results it was established that the spectrum of isolated microorganisms in the subjects was wide. A total of 5 pathogens were identified. Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecium, Streecoccus agalacticae, Candida albicans were identified with the same frequency in patients with pneumonia as the complication of influenza.

According to the scientific literature, it is known that pneumonia caused by the combination of the influenza virus and S. aureus has the most severe course with high mortality [7, 9]. The association of these pathogens was identified in 2 (2.94%) patients. Clinical symptoms of pneumonia were characterized by severe course of these individuals. These patients were classified in Group IV and had bilateral subtotal or total lung injury. It should be noted that in other patients of Group IV with severe respiratory failure and bilateral lung subtotal lesion, various associations of pathogens were also identified on the basis of bacteriological study of sputum.

Conclusion

Thus, our studies have shown that the rate of development of pneumonia as a complication of the influenza remained at a stable high level (20.84% in 2016 and 20.19% in 2017), despite a significant decrease in the incidence of influenza in 2017 compared with 2016. Clinical course of pneumonia was characterized by some features. At the beginning of the disease, the symptoms of severe course of flu were dominated. This masked the early development of pneumonia and was often one of the reasons for late hospitalization. Physical changes (data of auscultation, percussion, decrease in pulse oxygenation) advanced the characteristic changes in the radiological pattern. Characteristic X-ray pattern of pneumonia as a complication of the influenza were: primary damage of the basal areas with the subsequent spread of the pathological process with the development of bilateral (44,12%) subtotal or total inflammation in the lungs. In a large number of patients (47,06%), pneumonia was severe and required oxygen support. The early administration of antibacterial therapy did not prevent the development of pneumonia and its progression, indicating a possible primary viral lesion. Most often, we identified Streptococcus pneumonia and Staphylococcus aureus on the basis of a bacteriological study of sputum in patients with pneumonia as a complication of the flu, wherein pneumonia had a severe course in cases of viral-bacterial microbial associations and the combination of several bacterial pathogens.

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Реферати

ОСОБЛИВОСТІ КЛІНІЧНОГО ПЕРЕБІГУ ГРИП-АСОЦІЙОВАНИХ ПНЕВМОНІЙ

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Встановлено, що в 2017 році в порівнянні з 2016 роком в Полтавській області зареєстровано в 6 разів менше випадків грипу, про що опосередковано свідчила і кількість госпіталізованих хворих з цією патологією в ПОКІЛ. Але незважаючи на це, частота розвитку пневмоній, які

ОСОБЕННОСТИ КЛИНИЧЕСКОГО ТЕЧЕНИЯ ГРИПП-АССОЦИИРОВАННЫХ ПНЕВМОНИЙ

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Установлено, что в 2017 году по сравнению с 2016 годом в Полтавской области зарегистрировано в 6 раз менше случав гриппа, о чем косвенно свидетельствовало и количество госпитализированных больных с этой патологией в ПОКИБ. Нонесмотря на это, частота развития пневмоний, которые

ускладнювали перебіг грипу за даними ПОКІЛ, залишалася на стабільно високому рівні (20,84% в 2016 році і 20,19% у 2017 році). Продемонстровано, що клінічний перебіг пневмонії, яка ускладнює грип, мало особливості, які проявляються вже в початковому періоді захворювання, з переважанням проявів загальноінтоксикаційного синдрому. Це могло маскувати симптоми раннього розвитку пневмонії і обумовлювати госпіталізацію хворих у більш пізні терміни. Практично у половини пацієнтів реєстрували двосторонній запальний процес, при цьому фізикальні зміни (аускультативна картина пневмонії і зниження пульсової сатурації кисню) передували рентгенологічним змінам. Перебіг пневмонії у значної кількості хворих був важким з необхідністю в кисневій терапії. При бактеріологічному дослідженні мокротиння у пацієнтів з пневмонією при грипі частіше ідентифікували такі патогени, як Stretococcus pneumonia і Staphylococcus aureus.

Ключові слова: грип-асоційована пневмонія, поширеність, фактори ризику, клінічні особливості.

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осложняли течение гриппа по данным ПОКИБ, оставалась на стабильно высоком уровне (20,84% в 2016 году и 20,19% в 2017 году). Продемонстрировано, что клиническое течение пневмонии, осложняющей грипп, имело особенности, проявляющиеся уже в начальном периоде заболевания, с преобладанием проявлений общеинтоксикационного синдрома. Это могло маскировать симптомы раннего развития пневмонии и обуславливать госпитализацию больных в болем позднее сроки. Практически у половины пациентов регистрировали двухсторонний воспалительный процесс, при этом физикальные изменения (аускультативная картина пневмонии и снижение пульсовой сатурации кислорода) предшествовали рентгенологическим изменениям. Течение пневмонии у значительного количества больных было тяжелым с необходимостью в кислородной терапии. При бактериологическом исследовании мокроты у пациентов с пневмонией при гриппе чаще идентифицировали такие патогены, как Stretococcus pneumonia и Staphylococcus aureus.

Ключевые слова: грипп-ассоциированная пневмония, распространенность, факторы риска, клинические особенности.

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CHRONIC INFLAMMATION OF THE SCHNEIDERIAN MEMBRANE OF PATIENTS WITH STOMATOGENICAL MAXILLARY SINUSITIS ACCORDING TO THE RESULTS THE DATA OF THE LECTIN HISTOCHEMISTRY

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The differences of carbohydrate residues distribution in structures of the Schneiderian membrane of different groups was reliable between group of odontogenic maxillary sinusitis and the traumatic form of iatrogenic maxillary sinusitis. The differences of carbohydrate residues between the structures of the Schneiderian membrane was reliable in the group of odontogenic maxillary sinusitis and in the group of medicamentous form of iatrogenic maxillary sinusitis. The differences between saturation of the normal "lamina propria" of Schneiderian membrane and changed with fibrosis are reliable in the group of odontogenic maxillary sinusitis and in the group of medicamentous form of iatrogenic maxillary sinusitis. Distribution of carbohydrate residues differs in different groups of iatrogenic maxillary sinusitis.

Keywords: stomatologically maxillary sinusitis, ectinhistochemistry of the Schneider membrane.

The work is a part of the research project "Improvement of the bone plastics methods in removing defects and deformations of the face and jaws," state registration number 0116U004077.

The share of the maxillary sinusitis in the total number of inflammatory diseases of the paranasal sinuses is 56.0 - 73.0 %, and among the purulent - inflammatory processes of the maxillofacial region - up to 21.3 % [5]. According to various epidemiological studies, the incidence of maxillary sinusitis increases annually by 1,5 - 2,0 %. Over the past 10 years, the incidence has tripled [7]. The number of sinusitis associated with stomatological manipulation increased [6]. Our observations show, the presence of a direct relationship between the nature of stomatological manipulations preceding the development of inflammation in the sinus and the picture of the disease. Changes in the body of a local and general nature on the background of stomatological treatment, as well as the presence of concomitant diseases determine the manifestation of a certain type of symptoms of sinusitis and the degree of their severity. With a view to a more detailed study of the features of the formation and course of stomatogenical maxillary sinusitis, we proposed an etio-pathogenetic classification of its various forms [5]. In the frequency and nature of certain clinical, radiologic, morphological and ultrasound symptoms of these forms revealed statistically significant differences.

Since the glycosylation of glycoproteins in the inflammatory focus depends on the type and stage of a particular disease [10] there are fundamentally new approaches to differential diagnosis of diseases, which are based on the detection of glycoprotein. One way to identify the carbohydrate profile of the glycoprotein is the use of carbohydrate-binding proteins - lectins [1].