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CLINICAL CASE OF PURULENT PLEURAL EFFUSION IN FEMALE PATIENT RECEIVING MULPTIPLE SCLEROSIS THERAPY

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Abstract

Objective. To demonstrate the case history of purulent pleural effusion in a female patient suffering from multiple sclerosis receiving corticosteroid pulse-treatment and her positive outcome.

Methods. The authors described a clinical case of a female patient with multiple sclerosis receiving pathogenetic corticosteroid pulse-treatment complicated with purulent pleural effusion and her positive beneficial outcome. An analysis of clinical information on possible infectious complications of multiple sclerosis therapies in Russian and foreign references was performed.

Results. A positive beneficial outcome after the treatment of left purulent pleural effusion revealed in thoracic surgery department in case of 67-years old female patient with multiple sclerosis was provided by early verification by means of X-ray examination and consequent spiral computer chest tomography as well as its optimal medical treatment.

Conclusion. At multidisciplinary therapeutic hospitals, the possibility of the occurrence of nosocomial opportunistic respiratory tract infectious complications in immunocompromised patients receiving hormonal treatment should be considered.

Keywords: multiple sclerosis, autoimmune disease, purulent pleural effusion, case history

КЛИНИЧЕСКИЙ СЛУЧАЙ ЭМПИЕМЫ ПЛЕВРЫ У БОЛЬНОЙ ПРИ ЛЕЧЕНИИ РАССЕЯННОГО СКЛЕРОЗА

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Резюме

Цель. Представить клинический случай возникновения эмпиемы плевры у больной рассеянным склерозом, получавшей кортикостероидную пульс-терапию, с положительным прогнозом.

Методика. Представлен наблюдаемый авторами клинический случай гнойного экссудативного плеврита при гормональном лечении обострения рассеянного склероза с положительным прогнозом. Проведен анализ клинической информации отечественных и зарубежных источников о возможных инфекционных осложнениях при лечении рассеянного склероза.

Результаты. В клинических условиях торакального хирургического отделения достигнут положительный результат лечения эмпиемы левой плевральной полости у пациентки, страдающей ремитирующей формой рассеянного склероза при своевременной компьютерной рентгенодиагностике и оптимальной медикаментозной терапии.

Заключение. В условиях многопрофильных терапевтических стационаров следует помнить о возможности появления нозокомиальных оппортунистических респираторных инфекционных осложнений у иммунокомпрометированных больных, получающих гормональную терапию.

Ключевые слова: рассеянный склероз, аутоиммунное заболевание, эмпиема плевры, клинический случай

Introduction

Multiple sclerosis (multiple disseminated sclerosis, MS) is a chronic disease of the central nervous system of an autoimmune origin, characterized by the formation of multiple demyelinated foci in the brain tissue and in the spinal cord. Recently there is a significant increase in MS prevalence worldwide. This is due to both the very increase in MS incidence and the improvement of diagnostic methods with widespread introduction of modern neuroimaging methods into neurological practice, allowing to detect the disease at its early stages [1-3].

Autoimmune lesions in MS may be complicated with some infectious diseases, which are also caused by adverse events of pathogenetic treatment. We observed a hospitalized female patient suffering from MS, whose poor condition was complicated with purulent pleural effusion during the treatment of the underlying disease. This case is presented below.

Methods

The authors described a clinical case history of a female patient with multiple sclerosis receiving pathogenetic corticosteroid pulse-treatment complicated with purulent pleural effusion and her positive beneficial outcome. An analysis of clinical information on possible infectious complications of multiple sclerosis therapies in Russian and foreign references was performed..

Clinical case history

A female patient named G.I.S., 67 years old, 2-nd group of disability, was admitted to the neurological department of Smolensk Railway Station Clinical Hospital on 6th of September 2019 (case report form N6947/522).

Clinical diagnosis: underlying condition: central nervous system (CNS) demyelinating disease (multiple sclerosis), remittent course, exacerbation, vestibular ataxia, 2.5 points of Expanded Disability Status Scale (EDSS). Competing conditions: subtotal left destructive pneumonia. Left pleural effusion. Respiratory insufficiency, grade I. Concomitant diseases: coronary artery disease (cardiosclerosis). Complex (arteriosclerotic, hypoxic) dyscirculatory encephalopathy, 2A stage, cerebral asthenia, moderate cognitive disorders. Remission of duodenal peptic ulcer.

The patient complained of dizziness, loss of coordination while walking, weakness and fatigue.

She was suffering for about 15 years. At first she noticed dizziness and double vision. The patient was treated with nonspecific neurotrophic medications. However, due to the repeated episodes of persistent dizziness she had to see a doctor for a consequent examination that resulted in revealing of focal changes in her brain tissue while MRI which were characteristic for demyelinating CNS disease (MS). The patient was consulted at the department of neurology and neurosurgery of Smolensk State Medical Academy (currently named Smolensk State Medical University, SSMU for short), and the diagnosis was confirmed i.e., demyelinating central nervous system disease (MS), remittent course and the disease modifying preparation was prescribed (low dose beta-1a interferon). The female patient was observed consequently at the local polyclinic as well as at the department of neurology and neurosurgery of SSMU. She was prescribed corticosteroid methylprednisone pulse-treatment at a dose of 3.0-5.0 g in relapses of MS. The patient noticed deterioration of her general state and well-being for one month and she attributed it to severe emotional stress while working. She was treated on her own with neurotrophic drugs. Due to the lack of improvement she came unscheduled to the department of neurology and neurosurgery of SSMU, where the patient's condition was diagnosed as MS relapse, and she was referred to the hospital for glucocorticosteroidal pulse-treatment.

Neurological condition. Cranial nerves: the pupils were equal in size, the light reaction was retained. There were moderate weak convergence and slight deterioration of eyes movements in both sides. No pathology was found in the rest of cranial nerves. Reflexes were within normal ranges too. The patient's muscle strength was reduced diffusely due to asthenia. Neither sensitive disorders nor any meningeal signs were revealed. Romberg's sign was negative but after the treatment the coordination finger-nose tests improved and became more precise. Blood pressure was 120/80 mm Hg.

Paraclinic examination results: slight anemia was revealed in her blood tests with red blood cells (RBC) from 3.88 to 3.43 $\times 10^{12}$/L, hemoglobin level 115-102 g/L, neutrophilic leukocytosis up to 87.9% with the total amount of white blood cells (WBC) 16.7 $\times 10^{9}$/L and relative lymphopenia 11.2-18.2%. ESR was

very fast, 58-67 mm/h. Blood chemistry revealed the following changes: fibrinogen increase up to 6 g/L (normal upper limit 4 g/L), C-reactive protein was 86.2-198 mg/L (normal range is 0-6 mg/L), hypoproteinemia 57.6 g/L (lower limit is 65 g/L), moderate increase of alanine transaminase (ALT, or SGPT) activity 62.1 U/L (normal upper level of SGPT is 31 IU/L), significant decrease in serum iron to 3.3 mkmol/l (more than 12 mkmol/L is normal). Microprecipitation reaction, HBs antigen and anti-HCV tests were negative. No HIV antibodies were detected. No pathological changes were revealed in urine tests.

The following results were revealed on the electrocardiogram taken on admission to the hospital: sinus rhythm, 88 per min., cardiac electric axis was deflected slightly to the left. Diffuse reduction of myocardial depolarization processes was obtained.

The oculist diagnosed an initial cataract and retinal angiopathy in both eyes of the patient.

On the sixth day of hospitalization the patient's general condition worsened. She produced severe moist cough with mucus, and she had subfebrile body temperature. Discomfort occurred in the left half of her chest while breathing.

The patient was examined by a therapist who suspected moderate nosocomial pneumonia in the left lung complicated by an abscess and parapneumonic pleural effusion. The clinical pharmacologist clarified some peculiarities in the patient's history: in May 2019 she took a good rest on the Black Sea beach and unfortunately suffered from an episode of drowning with the emergency resuscitation.

There was no acid-resistant mycobacteria of tuberculosis in the patient’s sputum. High power field microscoping of sputum helped to reveal large amounts of white blood cells and few plain epithelium cells.

Thoracic radiography and ultrasound examination of pleural cavities identified left-sided encysted pleurisy. Multispiral computer chest tomography obtained data of left-sided subtotal destructive pneumonia complicated by an abscess, severe pneumosclerosis, aortic calcification and sclerosis of coronary arteries.

On the 12th day of hospitalization the patient was consulted by a thoracic surgeon who recommended the treatment of the left-sided destructive pneumonia with pleurisy at the specialized thoracic surgery department in Smolensk Regional Clinical Hospital (SRCH).

While staying in bed at the neurological department the patient received the following treatment: total dose 5 g of methylprednisone, omeprazole, potassium and magnesium asparaginate, intramuscular injections of B_1, B_6 and B_{12} vitamins with lidocaine, mexidol, actovegin, nootropil, azithromycin 1500 mg/day, ceftriaxone 2 g/day, metronidazole 500 mg/day, sulperacef 2 g/day, vancomycin 1 g/day, ambroxol and theophyllin.

On 19th of September 2019 the patient was transferred to the thoracic surgery department in Smolensk regional clinical hospital, where she was given treatment for the following 22 days up to 10.10.2019 (case report form N26552/40). The patient’s condition was regarded of moderate severity, she complained of moderate pain in the left half of her chest, weakness, palpitations, high body temperature with fluctuations of fever from 38.4 to 37.2ºC during the week. Pulmonary auscultation revealed weakened vesicular respiration along the left posterior axillary line. The patient underwent thoracocentesis in the left half of her chest and Bülau drainage was installed.

On 27.09.2019 on the control chest X-ray examination pronounced favourable dynamics was observed: pleural effusion decreased. Right lung pattern was normal. On the contrary, left lower lobe lung pattern was deformed and increased due to the peribronchial component. Pleural overlays and a small amount of effusion were preserved in the anterior sinus, above the diaphragm and along the interlobular pleura.

Blood tests revealed normochromic anemia with RBC 3.23-3.44 $\times$ 10^{12}/L, hemoglobin 100-103 g/L, leukemoid shift up to 1% of meta - and myelocytes with 11-5% band cells predominance, high ESR of 66-62 mm/h. WBC varied from 5.9 to 9.6 $\times$ 10^9/L. There were hyperfibrinogenemia 5.2 g/L with slight hypoproteinemia up to 64 g/L in blood chemistry. Urinalysis revealed severe toxic proteinuria up to 0.3 g/L.

The patient was on the adjusted antibacterial treatment with cefoperazone and sulbactam 2 g intravenously then cefepim intramuscularly 2 g b.i.d., co-trimoxazole 960 mg b.i.d. and metronidazole 1.5 g/day.

Microbiological examination of the patient’s pleurisy fluid was performed in the laboratory at Smolensk Scientific Research Institute of Antimicrobial Chemotherapy (case report N1928381). It revealed Streptococcus intermedius, and its microscopy revealed a large number of segmental neutrophils more than 25 in the high power field and clusters of Gram-positive cocci.

Sinus tachycardia 100 per min. and diffuse repolarization decrease of the hypertrophic left ventricle were registered on the patient's electrocardiogram.

The control multispiral computer chest tomography was performed on 08.10.2019. There were no focal and infiltrative shadows in the right patient's lung. There was a residual air cavity in the upper parts of the left lung. Moderate fibrous deformation of the left lung was seen and there was a small amount of fluid (23 × 52 × 52 mm) in its posterior-lateral sinus. Mediastinum was in median location and there were no additional formations in it. The large bronchial openings could be viewed. The intrathoracic lymph nodes were not enlarged. The heart was aortic configuration. No bone-destructive changes were detected.

The female patient was discharged from the hospital for out-patient follow-up. Neurotrophic medications were indicated and she took advice to avoid hypothermia.

Discussion of results

MS was firstly identified and described by a French neurologist J.-M. Charcot in 1886 as a nosological form of disease. This disease is characterized by its undulating course with periods of exacerbation or relapses and partial or full remission. MS affects mainly young people aged 20 to 40 years, rarely it starts in childhood and in people aged over 50 years.

Currently, there are about 3 million MS patients in the world. Women get sick 1.5-2 times more often as compared to men [3-5]. We also observed a remitting course of MS in the female patient that is consistent with epidemiological data.

The medical and social significance of MS is determined by the fact that this disease is characterized by the development of persistent disability. During the first 5 years from the MS onset about 43% of patients lose their working ability and when the disease is persistent up to 10 years 72% of patients become disabled [3]. Our patient was examined for 2-nd disability group for the last 11 years. According to MS morbidity prevalence there are zones with high, moderate and low incidence. The disease is especially common in North America and North-Western Europe. The number of MS patients in the North-Western regions of the European part of Russia, in Siberia and in the Far East has significantly increased. MS morbidity rate varies 2-70 per 100,000 people in different regions of our country. There are more than 150,000 patients with MS in Russia, and there are about 7000 patients only in Moscow. In recent years, this disease has been noticed in those regions where it was not observed previously (Central Asia, Transcaucasia) [1, 2].

There is a benign form of MS with its remitting course and this case we discuss here. Remissions and relapses are observed but each deterioration ends with a fairly complete restoration of the disturbed neural functions. There is almost always a complete recovery after the first relapse, usually up to 4-8 weeks from the onset. Then the disease becomes progressive in about 60% of patients and this illness has progressive course from the first its symptoms in 30% of persons [1-3].

Treatment of MS consists of measures aimed to decrease demyelination of the central nervous system, and symptomatic therapy exists too. Methods against demyelination are divided into treatment of relapses and treatment of chronic progressive disease [4, 5].

It is impossible to predict the effectiveness of corticosteroids in each individual patient. Equally it is impossible to predict the result of the corticotrophin (ACTH) action to produce endogenous corticosteroids. As a response to ACTH administration in some patients, there is an increase of corticosteroids activity; a similar reaction is not observed in other patients. Probably it explains the differences of efficacy of ACTH treatment in clinical conditions. The mechanisms of action of glucocorticosteroids in demyelinating diseases are understood poorly. Although immunosuppression is most important in steroids action, its therapeutic effects may result to the reduction of edema and beneficial changes in the electrophysiological properties of nervous tissue. There are two groups of patients: treatment-responsive and irresponsive ones. The authors consider that ACTH or corticosteroids are indicated especially in acute episodes, in frequent relapses and in patients with optic neuritis [3-5].

In recent years, very high doses of methylprednisolone (10-15 mg/kg per day) have been used successfully in exacerbations of remitting course of MS. It is administered intravenously for 3-5 days then the patient takes medications orally (1 mg/kg per day) with gradually decreasing doses according to the above mentioned scheme. Many authors note greater effectiveness of methylprednisone compared to that of ACTH. Since ACTH and corticosteroids may activate tuberculosis, chest radiography is absolutely necessary before treatment [4, 5].

Unfortunately, in our patient X-ray chest examination was performed with some delay, only on the sixth day of her stay at the hospital. Probably, this may be explained by the lack of respiratory symptoms at patient's admission to the clinic.

An event of patient's drowning in spring sea water with successful resuscitation measurements may aggravate the immunosuppressive effect of subsequent pulse-treatment with glucocorticoid methylprednisone. It is possible to assume that the occurrence of bullous pulmonary foci with subsequent valve pneumothorax was due to artificial lung ventilation, which also resulted to an opportunistic infection in the left pleural cavity of our patient.

Due to its relative advantages and indications for immunosuppressive therapy in most clinical trials of disease modifying treatment of MS, patients were examined for HIV infection and hepatitis C virus (HCV), which is extremely necessary in clinical practice. Opportunistic infections were rare even in HIV-positive patients receiving MS disease modifying treatment. Most drugs affected the movement or decrease of total amount of T-lymphocytes, for example, natalizumab, fingolimod and alemtuzumab, respectively [6, 7]. Cases of Kaposi's sarcoma, cutaneous histoplasmosis and central nervous system toxoplasmosis have been reported in HIV-negative MS patients treated with fingolimod [6]. Similarly, there are rare cases of pneumocystic pneumonia, nocardiosis and listeriosis in MS patients which were given treatment with alemtuzumab, as well as Legionella pneumonia when dimethyl fumarate was administered [7, 8]. In our case, the patient did not receive any drugs that may modify the course of the underlying disease, for example, monoclonal antibodies and/or fingolimod, but only glucocorticosteroid immunosuppressive and symptomatic treatment. According to the references results, clinical X-ray observation or preventive measures are not strictly indicated in such patients, but clinicians should always be aware of the possibility of such unusual opportunistic infections. The use of disease modifying drugs for MS, including alemtuzumab, ocrelizumab and mitoxantrone, was accompanied by a statistically significant risk of infectious complications, in most cases with moderate nasopharyngitis, upper respiratory tract and urinary tract infections, although preventive measures in these cases were not indicated [9].

As far as it concerned for the opportunistic infection with Streptococcus intermedius strains isolated from the purulent pleural fluid of our patient named G.I.S., according to the available data of recent publications, these strains of Streptococcus intermedius were the most pathogenic among "Streptococcus milleri group", causing the development of deep abscesses of different localization [6].

Conclusions

1. When planning the glucocorticoid pulse-treatment in immunocompromised patients, for example, suffering from multiple sclerosis, first of all it is necessary to perform chest radiography.
2. Patients with multiple sclerosis taking treatment with corticosteroids should undergo thorough clinical and X-ray screening to exclude the possibility of opportunistic nosocomial infections and in suchcases they are to be treated with timely optimal drugs and/or preventive measures.

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