УДК 616.13-002.7-06:616.24
https://doi.org/10.20538/1682-0363-2021-3-219-224

A clinical case of lung damage in granulomatosis with polyangiitis

Kraposhina A.Yu.[1, 2], Demko I.V.[1, 2], Sobko E.A.[1, 2], Gordeeva N.V.[1, 2], Soloveva I.A.[1, 2], Matveeva I.V.[2], Kazmerchuk O.V.[1], Katser A.B.[1], Abramov Yu.I.[1], Malchik N.V.[1]

[1] *V.F. Voino-Yasenetsky Krasnoyarsk State Medical University*
1, Partizana Zheleznyaka Str., Krasnoyarsk, 660022, Russian Federation

[2] *Krasnoyarsk Regional Clinical Hospital*
3A, Partizana Zheleznyaka Str., Krasnoyarsk, 660022, Russian Federation

ABSTRACT

The article presents a case of granulomatosis with polyangiitis, which is difficult for clinical diagnosis. Recently, the incidence of systemic vasculitis has increased, and given the similarity of clinical symptoms with other pathologies, a doctor of any specialty should carry out differential diagnosis. Granulomatosis with polyangiitis is characterized mainly by damage to the upper respiratory tract, lungs, and kidneys. The main method for diagnosing granulomatosis with polyangiitis is biopsy with histological examination, which allows to detect inflammation in the affected tissues. A feature of granulomatosis with polyangiitis is detection of antineutrophil cytoplasmic antibodies in the blood serum. However, these antibodies are recorded only in 80% of patients and are not detected in the remission phase, which makes diagnosis much more difficult.

Key words: granulomatosis with polyangiitis, lung damage, system vasculitis.

Conflict of interest. The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

For citation: Kraposhina A.Yu., Demko I.V., Sobko E.A., Gordeeva N.V., Soloveva I.A., Matveeva I.V., Kazmerchuk O.V., Katser A.B., Abramov Yu.I., Malchik N.V. A clinical case of lung damage in granulomatosis with polyangiitis. *Bulletin of Siberian Medicine.* 2021; 20 (3): 219–224. https://doi.org/10.20538/1682-0363-2021-3-219-224.

Клинический случай: поражение легких при гранулематозе с полиангиитом

Крапошина А.Ю.[1, 2], Демко И.В.[1, 2], Собко Е.А.[1, 2], Гордеева Н.В.[1, 2], Соловьева И.А.[1,2], Матвеева И.В.[2], Казмерчук О.В.[1], Кацер А.Б.[1], Абрамов Ю.И.[1], Мальчик Н.В.[1]

[1] *Красноярский государственный медицинский университет (КрасГМУ) имени профессора В.Ф. Войно-Ясенецкого*
Россия, 660022, г. Красноярск, ул. Партизана Железняка, 1

[2] *Краевая клиническая больница (ККБ)*
Россия, 660022, г. Красноярск, ул. Партизана Железняка, 3а

РЕЗЮМЕ

Представлен сложный для клинической диагностики случай заболевания гранулематозом с полиангиитом. В последнее время увеличилась заболеваемость системными васкулитами, а учитывая схожесть

✉ *Kraposhina Angelina Yu.,* e-mail: angelina-maria@inbox.ru

клинических симптомов с другими патологиями, врачу любой специальности следует проводить дифференциальную диагностику. Гранулематоз с полиангиитом характеризуется преимущественно поражением верхних дыхательных путей, легких и почек. Ключевым методом диагностики гранулематоза с полиангиитом является биопсия с гистологическим исследованием, позволяющим выявить воспалительный процесс в пораженных тканях. Особенностью гранулематоза с полиангиитом является регистрация антинейтрофильных цитоплазматических антител в сыворотке крови, однако данные антитела регистрируются лишь у 80% больных и не выявляются в фазе ремиссии, что значительно затрудняет диагностику.

Ключевые слова: гранулематоз с полиангиитом, поражение легких, системные васкулиты.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Для цитирования: Крапошина А.Ю., Демко И.В., Собко Е.А., Гордеева Н.В., Соловьева И.А., Матвеева И.В., Казмерчук О.В., Кацер А.Б., Абрамов Ю.И., Мальчик Н.В. Клинический случай: поражение легких при гранулематозе с полиангиитом. *Бюллетень сибирской медицины.* 2021; 20 (3): 219–224. https://doi.org/10.20538/1682-0363-2021-3-219-224.

INTRODUCTION

In recent years, there has been an increase in the incidence of systemic vasculitis. Lesions are characterized by non-specific symptoms in the onset and similarity of clinical symptoms with other pathologies, which makes differential diagnosis difficult, despite continuously developing diagnostic methods in rheumatology. One of the types of systemic vasculitis is granulomatosis with polyangiitis (Wegener's granulomatosis) – giant cell necrotizing granulomatous vasculitis of small caliber vessels associated with the production of antineutrophil cytoplasmic antibodies (ANCA) and characterized by a damage predominantly to the upper respiratory tract, lungs, and kidneys [1–3]. The disease is multi-organ in nature and is characterized by a variety of symptoms. The onset of the disease most often occurs at the age of over 40 years; its incidence is 1.5 times higher in the European population [2].

Despite many years of study, the etiology of granulomatosis with polyangiitis remains unknown. However, most often, the manifestation of the disease is preceded by infections caused by Staphylococcus aureus, pneumocystis, as well as acute respiratory viral infection (ARVI), vaccination, and antibiotic prophylaxis, which trigger the formation of autoantigens [4]. The autoimmune process activates a cascade of cellular reactions that reproduce polymorphic-cellular granulomatous inflammation, which leads to the activation of macrophages, antigen-presenting cells, and then effector memory T cells and plasmacytes capable of producing not only IL-6, IL-10, TNF-α, but also ANCA [5].

During these processes, polymorphonuclear leukocytes penetrate into the bloodstream, disrupt the vascular permeability, and produce lysosomal enzymes, which results in necrosis of the vessel wall and its occlusion. Most often, the first foci that reflect autoimmune granulomatous inflammation are the upper respiratory tract, lungs, and kidneys. Biopsy with histological examination is considered to be the key method for diagnosing granulomatosis with polyangiitis, since only these results can confirm the nature of the inflammatory process in the affected tissues. Undoubtedly, the hallmark of Wegener's granulomatosis is detection of ANCA in the blood serum, but it should be taken into account that the studied antibodies are usually recorded only in 80% of patients and cannot be detected in remission [6].

We present a case of granulomatosis with polyangiitis that is difficult for clinical diagnosis.

CLINICAL CASE

Patient K, female, 40 years old, was admitted to the Department of Otorhinolaryngology at the Krasnoyarsk Regional Clinical Hospital in July 2019 with complaints of severe headaches, pain behind the ear, purulent drainage from the right ear, periodic rise in the body temperature to 37.5–37.8^0 C, and balance problems (staggering) when walking.

From the anamnesis: acute onset of the disease (2 weeks ago) – earache and purulent drainage from the right ear occurred. The patient went to a private clinic to see an ENT doctor, where she was prescribed with antibacterial and antifungal treatment, which turned out to be ineffective. The patient was sent to the outpatient clinic of the Regional Clinical Hospital.

Upon admission: clear consciousness, moderate severity of illness (SOI), the skin was clean and of normal moisture, the musculoskeletal system was without abnormalities. *Status localis:* the nasal septum was deviated. The inferior turbinates were edematous. Upon percussion of the right mastoid process, sharp tenderness was noted. The right external auditory canal was filled with purulent drainage; the left external auditory canal was free. The tympanic membrane was not visualized. Otoscopy: in the right external auditory canal, there was profusely purulent discharge; after sanation, in the projection of the tympanic membrane, there was pink tissue with a bumpy surface (polyp?), when touched with the instrument, it was tender but did not bleed. Vesicular respiration was observed. Respiratory rate (RR) was 14 per min. The heart tones were clear. The blood pressure was 110 / 70 mm Hg., the heart rate – 56 beats per minute. The abdomen was soft and painless and participated in the act of breathing. Urination was free and painless. A preliminary diagnosis was made: acute suppurative otitis media, right ear, perforation stage; acute mastoiditis, right side. Meningitis?

The blood test showed relative leukocytosis (9.16×10^9 / l), hypochromic anemia (erythropenia 3.55×10^{12} / l, HB – 113 g / l), an increase in C-reactive protein (132.5 mg / l) and fibrinogen (5.1 g / l), as well as an increase in the erythrocyte sedimentation rate (ESR) (61 mm / h). To exclude otogenic neuroinfection, a cerebrospinal fluid (CSF) analysis was conducted, which did not reveal meningitis. A CT scan of the temporal bones showed data corresponding to right-sided acute otitis media. Chest X-ray showed that the lungs were without visible infiltrative darkening. The pleural cavities were free, pleurodiaphragmatic adhesions on the right side were detected. Endoscopic electrosurgical removal of the middle ear tumor was performed. The diagnosis after the surgery was the following: chronic purulent epimesotympanitis with a polyp in the right external auditory canal and symptoms of otitis externa, subtotal tympanic membrane defect. The surgical material was taken for histopathological examination, which registered squamous cell papilloma with diffuse chronic inflammation.

At the department, the patient received antibacterial (ceftazidime) and anti-inflammatory therapy. Despite the treatment, the patient complained of severe cough, deterioration of the condition, and a rise in the body temperature to 38.8 °C. To exclude pneumonia, chest X-ray was performed, which revealed a peripheral formation in the lower lobe of the right lung. The patient underwent chest multi-slice spiral computed tomography (MSCT) – the findings may correspond to those in destructive pneumonia, which should be differentiated from an abscess; bilateral pleural effusion. Blood tests revealed leukocytosis (10.9×10^9 / l), neutrophilia (74.3%), increased hypochromic anemia (107 g / l), and accelerated ESR (58 mm / h).

Having been examined by a thoracic surgeon, the patient was diagnosed with lung abscess with pneumonia in the lower lobe of the right lung. Antibacterial therapy (cefoperazone / sulbactam 2g 3 times a day) was prescribed. Sputum culture for acid-fast mycobacteria (AFB) was negative. Tracheobronchoscopy showed mild right-sided diffuse bronchitis with mild mucus hypersecretion.

Ultrasound of the pleural cavities revealed effusion ($V = 80$ cm³). Transthoracic puncture was performed, during which 200.0 ml of clear fluid of light straw color was obtained. A cytological examination of the pleural fluid identified red blood cells, eosinophilic substance, a pronounced number of neutrophilic leukocytes at the stage of degenerative changes, numerous fragments of destroyed cellular elements, and signs of dystrophic changes.

After the instrumental studies, it was decided to transfer the patient to the Department of Thoracic Surgery for further treatment and change the conservative treatment strategy – levofloxacin, meropenem, amikacin, and blood transfusion (erythromass) No. 6 were prescribed. Repeated chest MSCT showed negative dynamics due to an increase in the area of previously identified changes. The appearance of a rounded formation with a diameter of up to 12 mm was also noted nearby. There was a lucid area in the center, and a ground-glass opacity was determined around. The result may correspond to an abscess, with traces of pleural effusion on both sides. At the medial surface on the right, there was encysted pleurisy. In the blood test, signs of inflammation and hypochromic anemia were also detected. The acid-fast bacillus (AFB) test was negative.

Establishing a final diagnosis was difficult. Differential diagnosis was carried out with the following diseases: peripheral tumor in the lower lobe of the right

lung with decay, infiltrative pulmonary tuberculosis at the stage of decay, and lung abscess. Repeated chest MSCT showed negative dynamics due to an increase in the area of previously identified changes. The appearance of a rounded formation with a diameter of up to 12 mm was also noted nearby. There was a lucid area in the center, and a ground-glass opacity was determined around. The findings corresponded to an abscess, with traces of pleural effusion on both sides. At the medial surface on the right, there was encysted pleurisy.

It was decided to perform a right-sided thoracotomy and a lower lobectomy. During the surgical intervention, a palpable dense formation of about 10 cm in size was found in the basal segments of the right lung lower lobe, in the projection of which the lung was tightly attached to the diaphragm and the lateral costal surface of the chest wall. In S1, a focal formation of up to 0.5 cm was revealed. It was decided to resect the focal formation in the segment and remove the lower lobe. The main postoperative diagnosis was lung abscess. However, the pathohistological study of the surgical biopsy material showed morphological signs of granulomatous inflammation (single epithelioid cell granulomas and a large number of Langhans multinucleated giant cells).

In September 2019, the patient was transferred to the Krasnoyarsk Regional Tuberculosis Dispensary No.1 for further treatment with the following diagnosis: infiltrative tuberculosis in the lower lobe of the right lung in the phase of decay; *Mycobactérium tuberculósis* (–); exacerbation of chronic suppurative otitis media, right ear; acute suppurative otitis media, left ear; secondary (against the background of purulent epimesotimpanitis) peripheral neuritis of the facial nerve on the right side with slight paresis.

In the Krasnoyarsk Regional Tuberculosis Dispensary No.1, the patient had received anti-TB therapy for 22 days; no positive dynamics were observed. 17 sputum and ear content AFB tests were negative, and a polymerase chain reaction (PCR) was conducted twice – the results also did not reveal tuberculosis infection. It was noted that the disease progressed on the part of ENT organs: bilateral otitis media; mastoiditis on the right side, gingival fibromatosis, fibrotic changes in the nasal cavity with signs of mucosal bleeding.

In October 2019, the patient was urgently hospitalized in the ENT Department of the Regional Clinical Hospital with complaints of earaches, more on the right side, hearing loss in both ears, purulent discharge from the ears, and numbness of the right cheek and zygomatic region. On the basis of complaints and anamnesis, the following diagnosis was made: chronic bilateral suppurative otitis media, exacerbation; acute mastoiditis, right side? An antromastoidotomy was performed on the right side: the antrum was small, slit-shaped, and expanded; in the antrum, granulations and altered mucosa with polyps were observed; single cells of the mastoid process were opened in the pathology-affected area, no purulent discharge was obtained, and the mucosa was hyperplastic. The bone was softened like a spongy bone and easily removed with a spoon. Pathohistological examination of the surgical material registered no findings for granulomatous inflammation and revealed signs of chronic inflammation of moderate intensity.

Given frequent exacerbations of chronic suppurative otitis media and the presence of an intensive destructive process in the lungs with a pronounced inflammatory response against the background of the ongoing anti-bacterial and anti-TB therapy, the doctor made a decision to hold a case conference with the involvement of a pulmonologist and a nephrologist.

During the patient's examination, leg swelling and swollen, painless axillary lymph nodes on the right side with the maximum size of no more than 2 cm were noted. On the anterior abdominal wall above the navel, there was a bluish induration covered with a crust from which purulent discharge periodically appeared. On the inner third of the right thigh and the lumbar area, indurations of 2.5–3 cm in diameter were palpated. They were painless; the skin above them was not altered. In the lungs, dry wheezing, mainly in the lower parts on the right, was noted. The data obtained, such as a lack of response to the therapy, systemic inflammatory response syndrome, respiratory syndrome, anemia, swelling, facial neuritis on the right, and lesions of the ENT organs, suggested the development of systemic vasculitis.

To confirm the diagnosis of the patient, chest MSCT was performed: two cavities with unevenly thickened walls were detected in the basal zone on the left. In the lower lobe of the right lung, rounded formations with clear, even contours, of 11.4 mm in diameter, were determined. These formations were located subpleurally. The MSCT data might correspond to Wegener's granulomatosis. Ultrasound of the pleural cavity registered fluid ($V = 100\ cm^3$) with a fibrinous component in the right pleural cavity. A pathohistological examination of the right bronchial mucosa revealed a pronounced diffuse polymorphic cellular inflammatory infiltrate among the fibrous tissue, which corresponds

to the picture of the inflammatory process. A pathomorphological examination of the gingival mucosa registered a productive granulomatous inflammation in the soft tissues of the gingival mucosa. Taking into account the anamnesis, the obtained data correspond to Wegener's granulomatosis.

It was decided to hold a repeated case conference, at which a conclusion was made. Taking into account the clinical features, such as damage to the upper and lower respiratory tract, hearing organs, and oral cavity, the data of the morphological studies, the productive granulomatous inflammation in the soft tissues of the gingival mucosa, negative AFB tests, unsuccessful anti-TB therapy, despite the negative ANCA, the following diagnosis was made: Granulomatosis with polyangiitis, high intensity, severe course, with damage to the lungs (multiple infiltrates with destruction) and hearing organs (bilateral otitis media, mastoiditis on the right side), gingival fibromatosis. Anemia, moderate severity.

After methylprednisolone (1,000 mg No. 3) and cyclophosphamide (1,000 mg No. 1) pulse therapy with subsequent oral administration of methylprednisolone (48 mg / day), positive clinical, laboratory, and radiological dynamics were observed. Follow-up chest MSCT from 14.11.2019 revealed a decrease in the amount of fluid in the right pleural cavity, as well as a decrease in the size of foci and infiltration in the upper segments of the right lung. By February 2020, the patient had received five courses cyclophosphamide pulse therapy at a dose of 1,000 mg. Currently, the patient continues to take methylprednisolone at a dose of 38 mg / day.

CONCLUSION

The presented clinical case demonstrates the complexity of differential diagnosis of systemic lesions. The diversity of the clinical course and the absence of specific symptom complexes cause a noticeable difficulty in the diagnosis and treatment of granulomatosis with polyangiitis. Despite this, a careful comparison of clinical manifestations and laboratory and instrumental data and immunological search for markers of the disease can lead to earlier and more accurate diagnosis of systemic vasculitis. It should be noted that late diagnosis may cause development of irreversible damage to vital organs, which can lead not only to deterioration of the quality of life, but also to a decrease in the five-year survival rate.

REFERENCES

1. Baranov A.A., Alekseeva E.I. Clinical guidelines for pediatricians. Rheumatic diseases in children. M.: Pediatr, 2016: 144 (in Russ.).
2. Petty R.E., Laxer R.M., Lindsley C.B., Wedderburn L. Textbook of pediatric rheumatology; 5th ed. Elsevier Saunders, Philadelphia, 2016: 736.
3. Gordeeva N.V., Demko I.V., Mamaeva M.G., Zeleny S.V., Guseva I.S., Sobko E.A., Kraposhina A.Yu., Soloveva I.A., Chubarova S.V. Hypersensitivity pneumonitis (difficult clinical case). *Siberian Medical Review.* 2015; 5: 92–95 (in Russ.).
4. Edmondson S.J., Attaran S., Rosendahl U.P. Complete resolution of Wegener"s granulomatosis lung granuloma after aortic root replacement. *Aorta (Stamford).* 2016; 4 (1): 25–28. DOI: 10.12945/j.aorta.2016.15.009.
5. Kubaisi B., Abu Samra K., Foster C.S. Granulomatosis with polyangiitis (Wegener"s disease): An updated review of ocular disease manifestations. *Intractable Rare Dis. Res*. 2016; 5 (2): 61–69. DOI: 10.5582/irdr.2016.01014.
6. Rosenbaum J.T., Choi D., Wilson D., Grossniklaus H.E., Harrington C.A., Sibley C.H., Dailey R.A., Ng J.D., Steele E.A., Czyz C.N., Foster J.A., Tse D., Alabiad C., Dubovy S., Parekh P.K., Harris G.J., Kazim M., Patel P.J., White V.A., Dolman P.J., Korn B.S., Kikkawa D.O., Edward D.P., Alkatan H.M., al-Hussain H., Yeatts R.P., Selva D., Stauffer P., Planck S.R. Orbital pseudotumor can be a localized form of granulomatosis with polyangiitis as revealed by gene expression profiling. *Exp. Mol. Pathol*. 2015; 99 (2): 271–278. DOI: 10.1016/j.yexmp.2015.07.002.

Authors contribution

Kraposhina A.Yu. – conception and design, substantiation of the manuscript, critical revision of the manuscript for important intellectual content. Demko I.V. – final approval of the manuscript for publication. Sobko E.A. – substantiation of the manuscript, critical revision of the manuscript for important intellectual content. Gordeeva N.V., Soloveva I.A., Matveeva I.V. – conception and design. Kazmerchuk O.V., Katser A.B., Abramov Yu.I., Malchik N.V. – analysis and interpretation of data.

Authors information

Kraposhina Angelina Yu., Cand. Sci. (Med.), Associate Professor, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Pulmonologist of the Medical and Diagnostic Department, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation. ORCID 0000-0001-6896-877X.

Demko Irina V., Dr. Sci. (Med.), Professor, Head of the Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Head of the Pulmonology and Allergy Center, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation. ORCID 0000-0001-8982-5292.

Sobko Elena A., Dr. Sci. (Med.), Associate Professor, Professor of the Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Head of the Department of Allergy, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation. ORCID 0000-0002-9377-5213.

Gordeeva Natalya V., Cand. Sci. (Med.), Associate Professor, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Pulmonologist of the Medical and Diagnostic Department, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation. ORCID 0000-0002-0586-8349.

Soloveva Irina A., Dr. Sci. (Med.), Associate Professor, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University; Pulmonologist of the Medical and Diagnostic Department, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation. ORCID 0000-0002-1999-9534.

Matveeva Irina V., Head of the Department of Nephrology and Rheumatology, Krasnoyarsk Regional Clinical Hospital, Krasnoyarsk, Russian Federation.

Kazmerchuk Olga V., Researcher, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation. ORCID 0000-0001-7999-4113.

Katser Anna B., Researcher, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation. ORCID 0000-0002-6649-8900.

Abramov Yury I., Researcher, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation. ORCID 0000-0002-9937-1025.

Malchik Natalya V., Researcher, Department of Internal Diseases and Immunology, V.F. Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation.

(✉) **Kraposhina Angelina Yu.,** e-mail: angelina-maria@inbox.ru

Received 03.06.2020
Accepted 29.09.2020