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САРКОИДОЗ ОРГАНОВ ДЫХАНИЯ

SARCOIDOSIS OF THE RESPIRATORY SYSTEM

Учебно-методическое пособие

Минск БГМУ 2024

УДК 616.2-002.582(075.8)
ББК 54.12я73
К82

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Рецензенты: канд. мед. наук, доц., зав. отделом пульмонологии и хирургических методов лечения болезней органов дыхания Республиканского научно-практического центра пульмонологии и фтизиатрии Е. И. Давидовская; каф. пульмонологии и фтизиатрии с курсом аллергологии, иммунологии и профпатологии Института повышения квалификации и переподготовки кадров здравоохранения Белорусского государственного медицинского университета

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Представлены современные данные о потенциальных этиологических факторах, патогенезе и патоморфологии саркоидоза, освещены вопросы диагностики, дифференциальной диагностики, принципы лечения, варианты клинических проявлений и осложнений заболевания.

Предназначено для студентов 4-го курса медицинского факультета иностранных учащихся, обучающихся на английском языке по специальности 1-79 01 01 «Лечебное дело» по учебной дисциплине «Фтизиопульмонология».

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MOTIVATIONAL CHARACTERISTICS OF THE TOPIC

The topics: «The topics covered in the sessions delve into the complexities of sarcoidosis of the respiratory organs, encompassing epidemiology, pathogenesis, pathomorphology, classification, clinical manifestations, diagnosis, and treatment».

Sarcoidosis of the respiratory system and extrapulmonary manifestations of sarcoidosis. Clinic, diagnostics, Differential diagnostics. Differential diagnosis of disseminated pulmonary processes.

Sarcoidosis is portrayed as a systemic inflammatory disease of unclear etiology, characterized by the formation of epithelioid-cell granulomas without caseous necrosis in lymph nodes, lungs, and other organs, presenting a variety of clinical manifestations. Its relevance stems from the fact that sarcoidosis is no longer a rare disease, with prevalence ranging from 2–5 to 70–80 cases per 100,000 population depending on the country and diagnostic capabilities of medical institutions. Clinical features of sarcoidosis are diverse, and the absence of specific diagnostic tests can complicate diagnosis. Recent advancements in immunology and molecular biology have enhanced understanding of sarcoidosis pathogenesis, improving diagnostic and treatment possibilities. However, sarcoidosis remains a disease with unknown etiology, unpredictable course, and characterized by diverse diagnostic and therapeutic approaches in patient management.

The aim of the sessions: Is to explore the pathogenesis, pathomorphology, clinical manifestations, diagnosis, differential diagnosis, and fundamental principles of treatment of sarcoidosis of the respiratory organs.

Tasks of the sessions:

1. Familiarize with contemporary perspectives on potential etiological factors and pathogenetic mechanisms of sarcoidosis.
2. Study the modern classification and clinical manifestations of sarcoidosis of the respiratory organs.
3. Examine the results of clinical, radiological, laboratory, and morphological studies in the context of differential diagnosis of sarcoidosis with other respiratory diseases.
4. Explore the clinical manifestations of extrapulmonary manifestations of the disease.
5. Internalize contemporary principles of diagnosis and treatment of sarcoidosis of the respiratory organs.

Requirements for the baseline level of knowledge: Review from the normal anatomy and histology course: structure of the lungs, respiratory tract structure; from the pathological anatomy course: pathomorphological characteristics of inflammation, interstitial lung diseases, their pathogenetic mechanisms; from the normal physiology course: gas exchange in the lungs, factors influencing gas diffusion between alveolar air and blood, spirometry (calculation of normal

parameters); from the pathological physiology course: respiratory system insufficiency, stages of chronic respiratory failure, its clinical manifestations, disorders of pulmonary ventilation (obstructive, restrictive, and mixed), main causes and manifestations; from the radiological diagnostics course: main radiological syndromes in respiratory diseases; from the propaedeutics course: examination of patients with lung diseases, pathological symptoms and syndromes; from the phthisiopulmonology course: disseminated tuberculosis, tuberculosis of intrathoracic lymph nodes.

Control questions from related disciplines:

1. Radiological syndromes of focal dissemination, expansion of lung roots and mediastinum, their manifestations on chest X-ray and computed tomography.
2. Features of interstitial inflammation.
3. Patient examination plan with respiratory diseases.
4. Signs of restrictive and obstructive disorders of external respiration according to spirometric examination data.

Control questions on the topic of the session:

1. Possible etiological factors and pathogenetic mechanisms of sarcoidosis, disease epidemiology.
2. Structure of sarcoid granuloma, its differences from tuberculosis.
3. Variants of clinical manifestations and course of sarcoidosis. Löfgren's syndrome, Heerfordt-Waldenström syndrome.
4. Main stages of diagnosis and methods of sarcoidosis diagnosis verification.
5. Radiological manifestations of sarcoidosis of the respiratory organs.
6. With which diseases should differential diagnosis of sarcoidosis of the respiratory organs be conducted?
7. Differential diagnosis of intrathoracic lymphadenopathy (tuberculosis, sarcoidosis, lymphoma, etc.).
8. Main principles and methods of sarcoidosis treatment.

Self-study assignments for students:

1. Develop a plan for examining a patient suspected of sarcoidosis of the respiratory organs.
2. Conduct a clinical examination of a patient suspected of sarcoidosis.
3. Interpret chest X-rays of patients with sarcoidosis of the respiratory organs.
4. Evaluate the results of laboratory and functional research methods of patients with sarcoidosis of the respiratory organs.
5. Formulate a clinical diagnosis of sarcoidosis of the respiratory organs.
6. Develop an approximate treatment plan for a patient with sarcoidosis.

EDUCATIONAL MATERIAL

Sarcoidosis is a multisystem disease of unspecified etiology, characterized by the accumulation of CD4+ lymphocytes in target organs due to the immune response of type 1 T-helper cells (Th1), the development of productive inflammation with the formation of epithelioid-cell granulomas without necrosis, and outcomes ranging from resolution to fibrosis. Sarcoidosis belongs to the group of granulomatous diseases and the group of interstitial lung diseases.

The history of studying sarcoidosis spans at least 150 years, yet the understanding of its etiology, pathogenesis, and rational therapy remains incomplete and requires clarification.

The first description of sarcoidosis as a distinct disease was made by the renowned British physician Jonathan Hutchinson, known not only as a dermatologist and venereologist but also as a surgeon, ophthalmologist, neurologist, and morphologist. In 1869, J. Hutchinson described a 58-year-old patient with large, symmetric, painless purple patches on the skin of the hands and feet, suffering from «gout» and dying from «kidney failure». In 1899, Cesare Beccar first introduced the term «sarcoidosis», which translates from Greek as «resembling flesh». For their contributions to the study of the new disease, the International Congress of Dermatologists in 1934 proposed to name sarcoidosis Benign Schaumann Beck disease after the surnames of the famous scientists. Research on the disease continued by Danish ophthalmologist Christian Frederik Heerfordt, who in 1937 described the highly specific Heerfordt syndrome associated with sarcoidosis, characterized by subacute onset often accompanied by cranial nerve palsy/paralysis. This syndrome was subsequently named after him.

Swedish researcher Sven Löfgren first described the most typical variant of acute sarcoidosis in 1941, named after him as Löfgren's syndrome (bilateral lymphadenopathy combined with nodular erythema on the shins). In 1948, at the International Congress of Dermatologists, the new name «Sarcoidosis» was officially recognized. In 1951, American physician and educator G. Israel, followed by L. Zilchbach, suggested using systemic corticosteroids for sarcoidosis treatment, which remains the cornerstone of therapy today. In 1958, K. Wurm developed a classification of sarcoidosis of the respiratory organs based on radiographic stages, which is still used worldwide with certain modifications. In the same year, the 1st International Conference on Sarcoidosis was held in London. In 1987, the World Association of Sarcoidosis and Other Granulomatous Diseases (WASOG) was established, with the first president being the famous therapist and medical historian Gerald James, who founded the sarcoidosis clinic in London.

In modern Russia and Belarus, sarcoidosis as a lung disease also began to be considered relatively late, in the 1950s-1960s, mainly by phthisiologists.

RISK FACTORS FOR SARCOIDOSIS DEVELOPMENT AND POTENTIAL ETIOLOGICAL FACTORS

The definitive risk factors for sarcoidosis development have not been established. The crucial role in the disease's development is played by the environmental factors' influence on a genetically predisposed organism.

Probable external factors (triggers) for sarcoidosis development include the presence of certain bacteria — tuberculosis mycobacteria with altered properties (reverts) that do not cause tuberculosis, Propionibacterium acnes, Propionibacterium granulosum, Borrelia burgdorferi, fungi. Some authors' data on the mycoplasma and viral origin of sarcoidosis have not found significant confirmation. The significance of the trigger theory is confirmed by the possibility of transmitting sarcoidosis from animal to animal in experiments and during organ transplantation in humans.

Among researchers, there are proponents of hypotheses related to harmful environmental factors. American researchers believe that agricultural dust and mold, work in fires and military service associated with contact with mixed dust and smoke, may be risk factors for sarcoidosis development. A high risk of sarcoidosis development was found among individuals engaged in industries involving organic dust exposure, especially among people with fair skin, and among those working with construction and garden materials. The risk of sarcoidosis was also higher among individuals working with children. There have been separate studies linking sarcoidosis with toner dust inhalation. Many observations show that sarcoidosis onset was preceded by stressful events.

The use of interferons and interferon-inducing agents is a factor in the development of sarcoid reaction or sarcoidosis. Interferons are immunomodulators used in various diseases, including infection with certain hepatitis viruses, multiple sclerosis, and neoplastic diseases.

Genomic association studies have identified genetic factors influencing the likelihood of developing sarcoidosis and its clinical manifestations diversity. The role of genetic factors is confirmed by cases of familial sarcoidosis. Familial sarcoidosis occurs with an average frequency of 9.5 % (from 4.6 to 16.1 %), most commonly among French, African Americans, Dutch, and Irish.

EPIDEMIOLOGY

Sarcoidosis occurs worldwide, affecting individuals of both sexes, all races, and ages. Women are slightly more commonly affected than men.

The detection of sarcoidosis is closely related to the level of knowledge among physicians about the signs of this disease, as sarcoidosis is often referred to as the «great imitator». Intrathoracic forms of the disease are most commonly

detected during fluorographic and radiographic examinations, after which the patient is immediately referred to a phthisiologist (to exclude tuberculosis) and/or a pulmonologist for further examination and observation.

The prevalence of sarcoidosis depends on the racial background and the population under study. It has been established that in the United States, the incidence and prevalence of sarcoidosis are significantly higher among African Americans (17.8 and 178.5 per 100,000, respectively) than among whites (8.1 and 49.8), Hispanics (4.3 and 21.7), or individuals of Asian descent (3.2 and 18.9). High prevalence of sarcoidosis is observed in Scandinavian countries, ranging from 40–70 per 100,000 population. Sarcoidosis is rare in Korea, China, African countries, and Australia. There are ethnic peculiarities in the manifestation of the disease — frequent skin involvement among black patients, high prevalence of cardiac sarcoidosis and neurosarcoidosis in Japan. Sarcoidosis is much less common in children. For example, in Denmark, the incidence was 0.22–0.27 per 100,000 pediatric population.

In the Russian Federation, depending on the region, the prevalence of sarcoidosis ranges from 22 to 64 per 100,000 population, with a male-to-female ratio of approximately 1:2.

In the Republic of Belarus, the prevalence of sarcoidosis is 36–38 cases per 100,000 population, and the incidence of sarcoidosis is 3.9 per 100,000. The overall mortality from sarcoidosis ranges from 1 to 5 % in different countries.

PATHOGENESIS AND PATHOMORPHOLOGY

The main pathomorphological substrate of sarcoidosis is epithelioid-cell granuloma, which consists almost exclusively of epithelioid cells, occasional Langhans giant cells and foreign body giant cells, with a narrow rim of lymphocytes around the mound, without foci of caseous necrosis in the center and perifocal inflammation around. A characteristic feature of sarcoid granuloma is the presence of sinusoidal or capillary-type blood vessels in it, distinguishing it from tuberculous granuloma.

Each sarcoid granuloma has stages of development. They include:

1) Early or macrophage granuloma, sometimes mixed with histiocytes, lymphocytes, neutrophils.

2) Granuloma with accumulation of epithelioid cells in the center and macrophages at the periphery.

3) Epithelioid-lymphocytic granuloma.

4) Appearance of giant multinucleated cells (initially foreign body cells, subsequently Langhans giant cells).

5) Early cellular necrosis in the center of the granuloma due to nuclear pyknosis, appearance of apoptotic bodies, necrosis of epithelial cells.

6) Central fibrinoid, granular, coagulative necrosis.

7) Granuloma with partial fibrosis.

8) Hyalinized granuloma.

Russian authors also distinguish three stages of granuloma formation: proliferative, granulomatous, and fibrous-hyalinotic. Sarcoid granulomas are usually smaller in size than tuberculosis granulomas and do not tend to merge. Central necrosis may occur in sarcoidosis; however, it is usually punctate and poorly visualized. There is no correlation between the radiological stages of sarcoidosis as a disease and the stages of granuloma formation.

Sarcoid granulomas heal either by characteristic concentric fibrosis or by forming homogeneous hyaline bodies. In contrast to sarcoidosis, tuberculosis granulomas heal in the form of linear or stellate scars, or lymphohistiocytic aggregates remain in their place.

The pathogenesis of sarcoidosis involves both innate and adaptive immune systems. NOD-like receptors, Toll-like receptors, cell factors such as dendritic cells and macrophages, as well as T helper 1 (Th1), Th17, regulatory T (Treg) cells, and B cells of the adaptive immune system, play important roles in the pathogenesis of sarcoidosis. Sarcoidosis is characterized by an immune paradox: signs of local inflammation involving type 1 helper T cells coexist with peripheral anergy induced by regulatory T cells. A distinguishing feature of active sarcoidosis is the predominant expression of interferon-gamma in affected organs with the participation of such active cytokines as interleukins (IL) - IL-2, IL-12, and tumor necrosis factor-alpha.

Typical clonal amplification (copying) of CD4+ T cells in sarcoidosis indicates that the development of the disease is facilitated by a certain pathogenic antigen. Developing T-cell alveolitis serves as a biomarker reflecting the enhancement or reduction of disease activity. The immune reaction continues even after the potential triggering antigen disappears. In typical cases, compact, non-caseating epithelioid cell granulomas are formed, which are sterile and predominantly located in the lungs along lymphatic pathways.

Recent clinical studies on the etiology and pathogenesis of sarcoidosis have been confirmed by modeling sarcoidosis in animals. Heat shock proteins in humans, which can induce the formation of sarcoid granuloma under the influence of both infectious and non-infectious factors in genetically predisposed individuals, are involved in the pathogenesis of the immune response in sarcoidosis. Oxidative stress — cell damage due to oxidation of its components, plays a role in these events. The role of oxidative stress has been demonstrated in cardiac sarcoidosis. In addition, activated macrophages and granuloma cells can produce 1,25-(OH)2-D3 (calcitriol), leading to hypercalcemia (in 2–10 % of patients) and/or hypercalciuria (in 6–30 % of patients) and to urolithiasis and renal failure.

Granulomas can be found not only in intrathoracic lymph nodes and lungs but also in the skin, liver, spleen, nervous system, heart, muscles, and other tissues.

Three stages of lung sarcoidosis development are distinguished: pregranulomatous (alveolitis), granulomatous, and fibrotic. In the alveolitis stage, inflammatory changes are characterized by interstitial thickening due to microcirculation disturbances, appearance of edema, and lymphocyte-macrophage infiltration. The granulomatous stage is characterized by the appearance of Langhans giant cells and epithelioid cells formed from macrophages in the center of the inflammatory focus. A favorable course of the disease is accompanied by granuloma resolution. In other cases, a fibrotic stage develops, manifested by focal lesions in the granuloma zone and diffuse lesions in the interstitial tissue. The process of fibrosis begins at the periphery of the granuloma, after which fragmentation occurs in the central part, deposition of hyaline, and scar formation. Therefore, sarcoid granulomas have a «stamped» appearance. The wave-like course of sarcoidosis during exacerbations is morphologically manifested by polymorphism — granulomatous changes of varying degrees of maturity.

The pathogenesis of lung function disorders in sarcoidosis has various mechanisms. Bronchoobstructive syndrome and increased resistance can result from sarcoid involvement of bronchial and bronchiolar walls or their compression by enlarged lymph nodes. Restrictive changes in sarcoidosis are associated with the formation of pulmonary fibrosis and «cellular lung». The pathogenesis of pulmonary hypertension in sarcoidosis is associated with granulomatous infiltration of pulmonary vessels, including capillaries and veins (leading to the development of occlusive venopathy), or with increased sensitivity to vasoactive drugs and compression of the pulmonary artery by enlarged mediastinal lymph nodes. In the terminal stage of sarcoidosis, pulmonary hypertension is associated with hypoxic vasoconstriction and reduction of the vascular lumen due to fibrotic changes.

Localization of granulomas in the myocardium, less commonly in the peri-, epi-, endocardium, in the interventricular septum, papillary muscles leads to rhythm disturbances, reduction of myocardial contractility, and sudden death. Localization of granulomas in the brain, meninges, brainstem leads to a wide range of neurological disorders: from minor to severe, which can lead to patient disability.

CD-10 CODING

D50-D89 CLASS III. Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism

D86 Sarcoidosis

D86.0 Pulmonary sarcoidosis

D86.1 Sarcoidosis of lymph nodes

D86.2 Pulmonary sarcoidosis with sarcoidosis of lymph nodes

D86.3 Cutaneous sarcoidosis

D86.8 Sarcoidosis of other specified and combined sites
Iridocyclitis in sarcoidosis +(H22.1*)
Multiple cranial nerve palsies in sarcoidosis +(G53.2*)
Sarcoidosis (specifier):
Arthropathy +(M14.8*)
Myocarditis +(I41.8*)
Myositis +(M63.3*)
D86.9 Sarcoidosis, unspecified.
In the presented ICD-11 project, sarcoidosis belongs to the class:
Immune system disorders / Specific immune system disorders
4B20.0 Pulmonary sarcoidosis
4B20.1 Sarcoidosis of lymph nodes
4B20.2 Sarcoidosis of the digestive system
4B20.3 Neurosarcoidosis
4B20.4 Ocular sarcoidosis
4B20.5 Cutaneous sarcoidosis
4B20.Y Other specified sarcoidosis
4B20.Z Sarcoidosis, unspecified

CLASSIFICATION OF SARCOIDOSIS

Currently, sarcoidosis of the thoracic organs is divided into 5 stages (from 0 to IV).

0. Sarcoidosis of extrapulmonary localization in the absence of changes in the thoracic organs;

I. Sarcoidosis of intrathoracic lymph nodes (mediastinal form);

II. Sarcoidosis of the lungs and intrathoracic lymph nodes (pulmonary-mediastinal form);

III. Pulmonary sarcoidosis (pulmonary form);

IV. Pulmonary fibrosis.

The widespread use of computer tomography has significantly changed the distribution of patients by stages. Since the capabilities of computer tomography in diagnosing lung lesions are significantly higher compared to X-ray, the proportion of patients with stage II–III sarcoidosis has noticeably increased.

Sarcoidosis Phenotypes:

1. By Localization:
   a. Classic, with predominance of intrathoracic (pulmonary) lesions.
   b. With predominance of extrathoracic lesions.
   c. Generalized.

2. By Clinical Course:

a. With acute onset (Löfgren's syndrome, Heerfordt-Waldenström syndrome).

b. With initially chronic course.

c. Recurrence.

d. Sarcoidosis in children under 5 years of age.

e. Sarcoidosis refractory to systemic steroid treatment.

Exacerbation — reactivation of the process within a year after completion of the main course of treatment, which ended with complete disappearance of activity signs and process regression.

Recurrence — resumption of sarcoidosis manifestations one year after completion of the main course of treatment, which ended with process resolution, or after spontaneous process regression.

Clinical diagnosis of sarcoidosis includes:

1. Localization (listing organs and systems affected during examination).

2. Activity: 0 degree (inactive) — asymptomatic course, absence of inflammatory laboratory signs; 1 degree (active) — presence of clinico-laboratory signs of inflammation, in the presence of a complete clinical picture, «Löfgren's syndrome» or «Heerfordt-Waldenström syndrome» may be indicated instead of activity.

3. Course: stable, progressive, regressive, exacerbation, recurrence.

4. Complications: functional insufficiency (affected organ specified) and/or persistent structural changes (fibrosis, calcification, cysts, etc.).

CLINICAL PRESENTATION

Clinical manifestations of sarcoidosis and the degree of their severity are diverse, depending on the organ or system affected. The onset of the disease can be asymptomatic, gradual, or acute. Complaints depend on the predominant localization of the lesion and the course variant — acute or primary-chronic. Intrathoracic sarcoidosis is most common (about 96 % of all cases of sarcoidosis in Europeans).

In the absence of clinical manifestations, intrathoracic sarcoidosis is usually detected during radiographic examination of the thoracic organs. The gradual onset of sarcoidosis is characterized by sparse clinical symptoms: pain and pressure behind the sternum, between the shoulder blades, dry cough, dyspnea with physical exertion, general malaise, weakness, fatigue, sweating. Weakness and fatigue are the most common complaints and independent signs of sarcoidosis, may not have a direct correlation with granulomatous organ involvement.

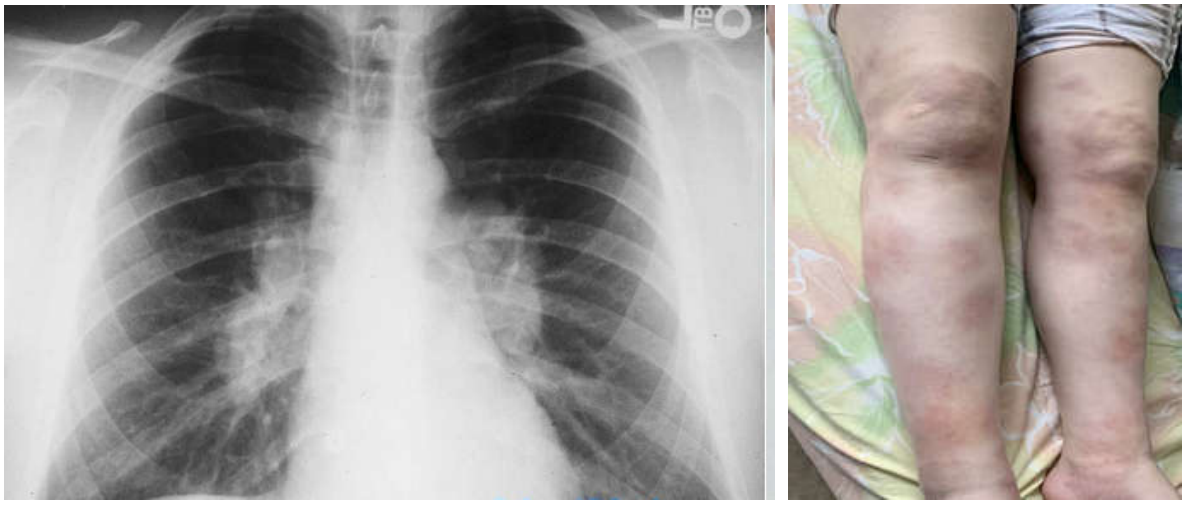
Cough in sarcoidosis is usually dry and is caused by enlargement of intrathoracic lymph nodes, which is accompanied by increased pressure on the

bronchial wall or irritation of nerve endings in the walls of the respiratory tract by sarcoid granules. In later stages, cough is a consequence of extensive interstitial changes in the lungs and relatively rarely a consequence of pleural involvement. Dyspnea is usually inspiratory and is a sign of decreased diffusing capacity of the lungs with increasing inflammatory or fibrotic changes in the lungs.

With the development of peribronchial fibrosis, persistent obstructive respiratory function disorders may occur. Pain and discomfort in the chest are not always clearly explained by the nature and volume of changes detected by computed tomography of the thoracic organs (CT of the thoracic organs). Discomfort in the back area, burning sensation between the shoulder blades, heaviness in the chest, inability to «take a full breath» are noted. Pain can also be localized in the bones, muscles, joints and have no characteristic features.

Acute onset of sarcoidosis is observed in approximately 20 % of patients and is characterized by specific Löfgren's or Heerfordt-Waldenström syndromes. Löfgren's syndrome is characterized by fever, erythema nodosum, arthritis predominantly affecting the ankle and/or knee joints, bilateral hilar lymphadenopathy, elevated ESR in the general blood test.

Incomplete variants of this syndrome are also possible — only erythema with intrathoracic lymphadenopathy, lymphadenopathy with arthritis (fig. 1). Histopathologically, erythema nodosum is a vasculitis with primary destructive-proliferative lesions of arterioles, capillaries, venules.



a ***b***

Fig. 1. Symptoms of Löfgren's syndrome:
a — bilateral intrathoracic lymphadenopathy; *b* — nodular erythema in Löfgren's syndrome

The appearance of nodular erythema requires exclusion of sarcoidosis but is not a specific manifestation of this disease. Changes usually occur bilaterally, with the lower extremities in the area of the shins being more frequently affected. The nodes range in size from one to several centimeters in diameter, they are firm, slightly raised above the skin surface. Initially, the nodes may be bright red, but after several days they acquire a bluish-purple hue, and ultimately become yellow or greenish, sometimes leaving pigmentation at the site of the nodes. Nodular erythema does not contain sarcoid granulomas, and biopsy of its elements is not diagnostically significant.

Heerfordt-Waldenström Syndrome (Heerfordt-Waldenström) — a combination of fever, intrathoracic lymphadenopathy, involvement of the parotid salivary glands, eyes (anterior uveitis), and facial nerve (Bell's palsy). The parotid glands are enlarged, painless on chewing and touch. In uveitis, patients note redness of the conjunctiva, tearing, deterioration of vision, appearance of «floating opacities» before the eyes. Bell's palsy may develop — this is unilateral paralysis of the facial nerve, initially there is pain behind the ear, then weakness or paralysis of half of the face appears, the patient stops feeling the taste with the anterior part of the tongue on the affected side. With unilateral paralysis, it seems to a person that the face is twisted, with bilateral paralysis it becomes like a mask and expresses nothing. Some patients find it difficult to furrow their forehead or blink (fig. 2).

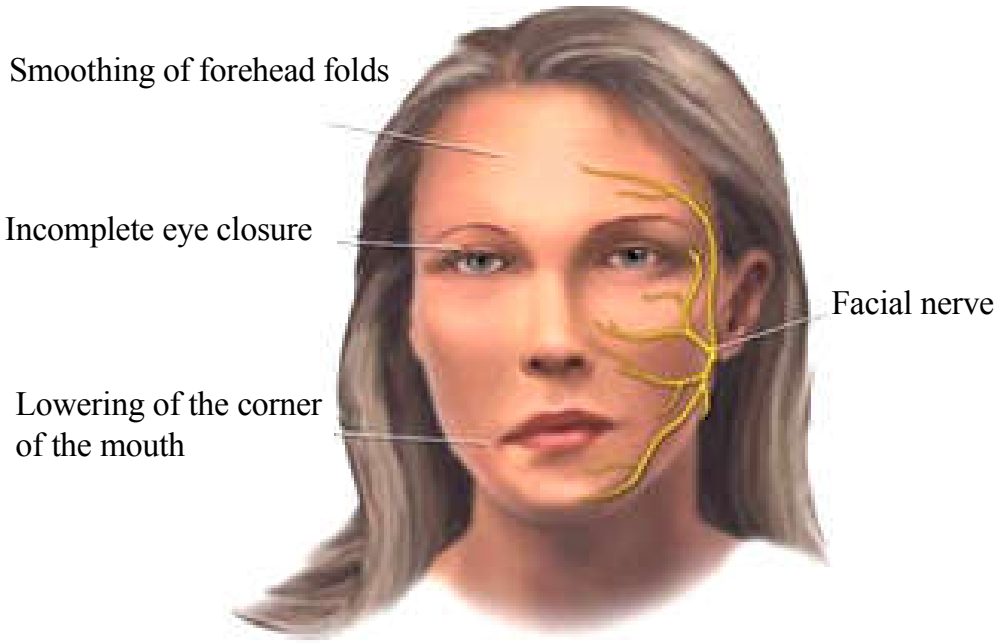


Fig. 2. Facial nerve paralysis

The acute onset of sarcoidosis is not a prognostically unfavorable sign; for such cases, rapid and complete resolution of changes in affected organs is characteristic, and pronounced symptoms allow timely diagnosis and treatment.

Intrathoracic sarcoidosis is combined with extrapulmonary lesions in almost 20 % of patients.

Extrathoracic localizations of sarcoidosis usually have a multifocal nature, and their presence usually predisposes to a recurrent course of the disease. The incidence of the most common extrathoracic localizations of sarcoidosis is presented in the table above.

Table

Most Common Extrathoracic Localizations of Sarcoidosis

№	Extrapulmonary sarcoidosis	Frequency of occurrence, %
1	Sarcoidosis of the skin	10–56
2	Sarcoidosis of the organ of vision	5–25
3	Sarcoidosis of peripheral lymph nodes	10–25
4	Sarcoidosis of the spleen	10–40
5	Sarcoidosis of the kidneys	5–30
6	Sarcoidosis of bones	1–39
7	Sarcoidosis of the heart	2–18
8	Neurosarcoidosis	5–10

In cutaneous sarcoidosis (most often frequency 10–30 %), perivascular histiocytic infiltration is observed in the dermis, signs of septal panniculitis. Specific manifestations include nodules, plaques, maculopapular changes, lupus pernio («frozen lupus»), scar sarcoidosis. Lupus pernio manifests as indurative plaques with color change on the nose, cheeks, lips, and ears, often coexists simultaneously with pulmonary manifestations.

Other skin changes in sarcoidosis include Brocq-Potrie angiolupoid; Darier-Roussy subcutaneous sarcoids, macular, lichenoid, psoriasiform sarcoids, fine-nodular and coarse-nodular forms, rarely psoriasiform and ulcerative forms, ichthyosis, alopecia, hyper- and hypopigmented spots, nail involvement. Typically, chronic sarcoid skin changes are not accompanied by pain or itching, do not ulcerate (fig. 3).

Eye involvement in sarcoidosis is considered one of the most dangerous manifestations as it can lead to significant vision impairment and loss. It occurs in approximately 5–25 % of cases of sarcoidosis, with 70–75 % involving anterior uveitis and 25–30 % involving posterior uveitis, less frequently affecting the conjunctiva, sclera, and iris. Uveitis is a component of Heerfordt-Waldenström syndrome. Sarcoidosis involvement of the optic nerve is rare but warrants prolonged corticosteroid treatment.

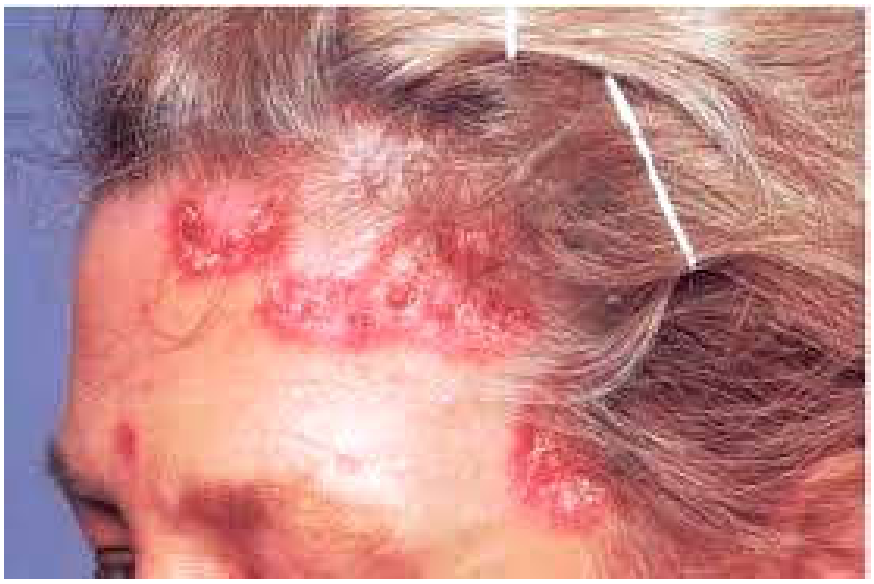


Fig. 3. Cutaneous Sarcoidosis

For children under 5 years old, a clinical triad of uveitis, skin lesions, and arthritis without lung involvement is characteristic.

In sarcoidosis of peripheral lymph nodes (10–25 % of cases), the process often involves the posterior and anterior cervical lymph nodes, supraclavicular, cubital, axillary, and inguinal lymph nodes. The lymph nodes are firm-elastic in consistency, do not soften, and do not form fistulas.

Splenomegaly is common in sarcoidosis (10–40 %) and may rarely develop hypersplenism — enlargement of the spleen combined with an increase in the number of cellular elements in the bone marrow and a decrease in formed elements in the peripheral blood (erythrocytes, leukocytes, and/or platelets).

Kidney involvement in sarcoidosis occurs in 5–30 % of cases, ranging from subclinical proteinuria to severe nephrotic syndrome, tubulointerstitial disorders, and renal failure, which may be due to granuloma formation and nonspecific inflammatory processes (microcirculation disorders, edema, vasculitis), as well as electrolyte balance disturbances. Granulomas in the kidneys are more often localized in the cortical layer. Calcium metabolism disorders, hypercalcemia, and hypercalciuria can be the cause of nephropathy in sarcoidosis. Calcium nephrolithiasis is found in 2–10 % of patients with sarcoidosis.

Musculoskeletal involvement in sarcoidosis often presents as joint syndrome, while bone and muscle involvement is much less common. Joint involvement (ankle, knee, elbow joints) in sarcoidosis most commonly occurs as part of Löfgren's syndrome and reaches 88 % in acute sarcoidosis. Along with arthritis, sarcoidosis has been described as periarticular swelling (swelling of soft tissues adjacent to the joint), tenosynovitis, dactylitis, bone involvement, and myopathy. Acute arthritis in sarcoidosis often resolves spontaneously without consequences.

Chronic arthritis, although less typical, can progress and cause joint deformities. Sarcoidosis of the bones often manifests as asymptomatic cystoid osteitis of the small bones of the hands and feet. Involvement of the finger bones manifests as bone cysts of the terminal phalanges and nail dystrophy, which is a sign of chronic sarcoidosis.

Cardiac sarcoidosis (2–18 %) is one of the life-threatening manifestations of sarcoidosis; it is characterized by a certain autonomy, not coinciding with the phases of the process in the lungs and intrathoracic lymph nodes. Three main syndromes are distinguished by clinical manifestations: painful (cardialgic), arrhythmic (manifestations of rhythm and conduction disturbances), and circulatory insufficiency syndrome. Patients may complain of discomfort in the heart area, palpitations or bradycardia, sensation of heart palpitations.

Any sections of the central and peripheral nervous system can be involved in the granulomatous process in sarcoidosis individually or in various combinations (5–10 % of cases). Complaints typically include chronic dull headaches, much less commonly acute or migraine-like, moderate, rarely intense, dizziness, usually in the vertical position of the body, swaying when walking, constant daytime sleepiness, sensory disturbances: vestibular, taste, auditory, visual, olfactory; epileptiform seizures have been described. Sarcoidosis of the pituitary gland can manifest as disturbances in its function and impotence. The following clinical manifestations of neurosarcoidosis are distinguished: cranial nerve involvement, involvement of meninges, hypothalamic dysfunction, brain tissue lesions, spinal cord tissue lesions, convulsive syndrome, peripheral neuropathy, myopathy.

Rarely, the thyroid gland, pharynx, and mammary glands are affected by sarcoidosis. Adrenal glands remain intact in sarcoidosis.

DIAGNOSIS

The main objectives of diagnosing sarcoidosis are to identify the characteristic clinical and radiological symptom complex, histological verification of the diagnosis, and determination of disease activity.

Clinical diagnosis is based on the identification of the aforementioned symptoms and syndromes of the disease based on patient complaints. During examination, skin lesions are identified, and the joints of the hands and feet are carefully inspected. Inflammatory changes in the joints are transient, and deformity is atypical. Palpation of all groups of peripheral lymph nodes is necessary. Percussion and auscultation of the lungs are informative only in the later and more advanced stages of the disease, when weakened or harsh breathing is detected, and percussion reveals a box-like sound over bullous-altered areas of the lungs. The frequency and rhythm of the pulse should be carefully evaluated since cardiac

sarcoidosis is one of the fatal forms of the disease. Evaluation of the size and consistency of the liver and spleen may reveal hepatomegaly and splenomegaly, which can vary in severity and be dynamic over time.

Imaging methods play a crucial role in detecting and establishing a preliminary diagnosis of intrathoracic sarcoidosis (chest radiography and CT of the chest). The basis of the radiological symptom complex in sarcoidosis consists of intrathoracic lymphadenopathy, dissemination, and interstitial changes caused by phenomena of alveolitis and pneumosclerosis.

Symptoms of intrathoracic lymphadenopathy are observed either in isolation in sarcoidosis of intrathoracic lymph nodes (stage I) or in combination with changes in lung tissue in sarcoidosis of intrathoracic lymph nodes and lungs (stage II). Sarcoidosis is characterized by bilateral enlargement of intrathoracic lymph nodes, predominantly bronchopulmonary groups, although unilateral involvement is observed in 5–8 % of cases, which can cause diagnostic difficulties. Lymph nodes have a spherical or ovoid shape, homogeneous structure, smooth distinct contours, without perifocal infiltration and sclerosis (fig. 4).

Classic changes on chest CT in sarcoidosis include bilateral hilar lymphadenopathy (characterized by symmetrical bilateral enlargement of bronchopulmonary lymph nodes), enlargement of the lower paratracheal lymph nodes on the right, tracheobronchial lymph nodes, and aortopulmonary lymph nodes. Among atypical changes on CT in sarcoidosis are unilateral bronchopulmonary lymphadenopathy, involvement of mediastinal and pericardial lymph nodes.

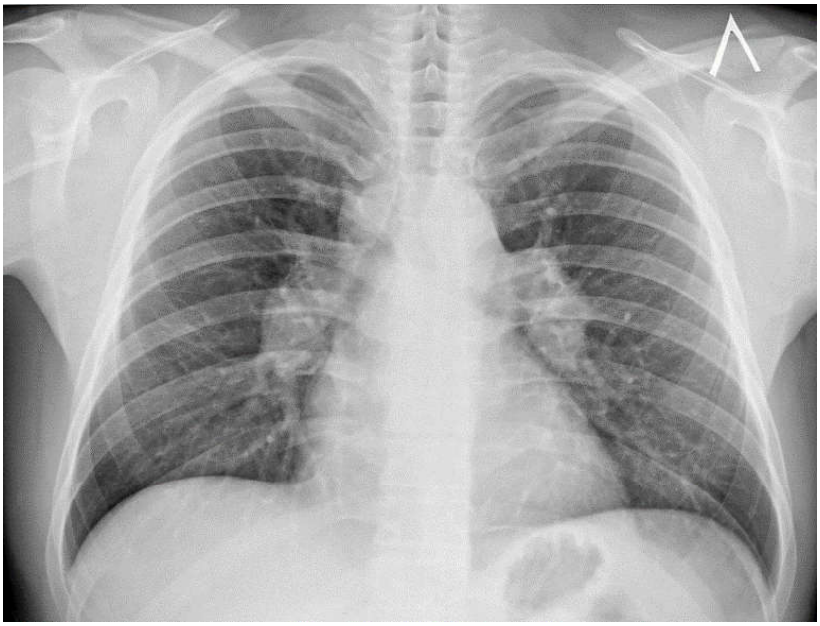


Fig. 4. Intrathoracic lymphadenopathy in respiratory organ sarcoidosis (chest X-ray)

In one-third of patients with long-standing sarcoidosis, calcifications appear in the structure of lymph nodes. Pulmonary dissemination in sarcoidosis is characterized by scattered focal shadows with diameters of 2–7 mm. Multiple small foci are located along bronchovascular bundles, interlobar fissures, costal pleura, and interlobular spaces (fig. 5, 6).

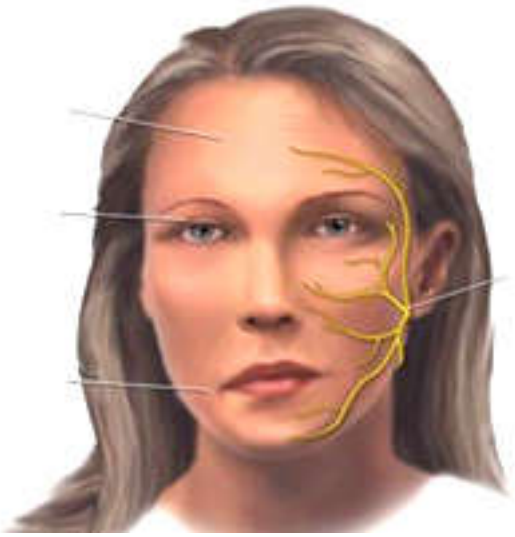


Fig. 5. Sarcoidosis of the lungs and intrathoracic lymph nodes (pulmonary-mediastinal form), stage II

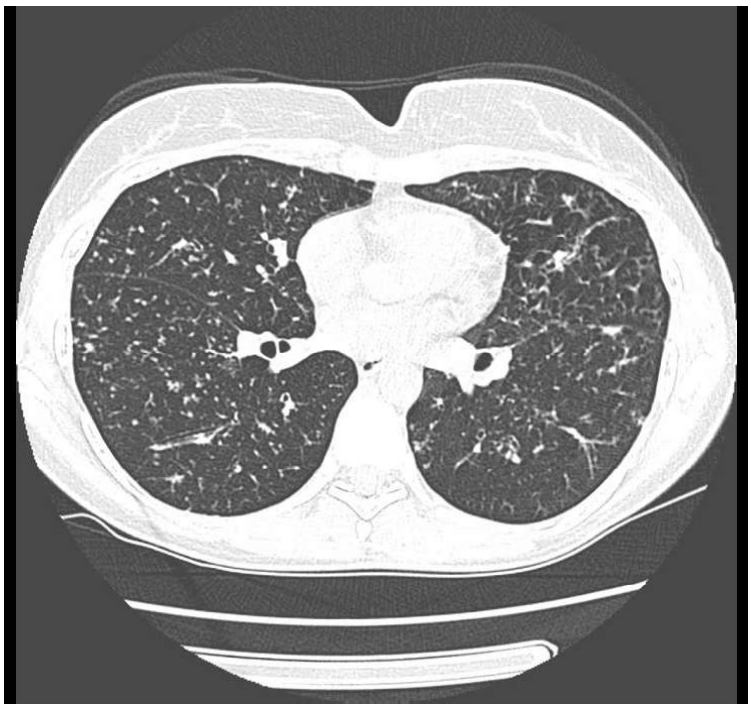


Fig. 6. CT image in sarcoidosis of the respiratory organs (focal dissemination)

Changes primarily in the middle lung fields, often in the perihilar region, and in combination with thickening of the walls of segmental bronchi. One of the rare manifestations of active sarcoidosis on chest CT can be the «ground glass» sign of varying extent and localization. In some patients, CT may show the merging of multiple small foci into larger nodules and small infiltrates. Such infiltrates have fuzzy contours, low density, and sometimes bronchial lumens are visible within them. This picture may resemble bacterial pneumonia or bronchioloalveolar carcinoma. Detection of enlarged mediastinal lymph nodes and lung roots provides certain assistance in diagnosis.

Among atypical changes on chest CT in sarcoidosis are the presence of conglomerate masses in the lung root area; clustered foci or merging foci surrounded by satellite foci («galaxy phenomenon»); presence of such small foci that they merge and appear as «ground glass» without nodules; in 2 % of cases, formation of lung cavities, pleural effusion, hilar effusion, and pneumothorax.

Reticular changes on chest CT in the form of uneven thickening of interlobular septa and intralobular structures in sarcoidosis may be associated with both inflammatory changes in the form of fine foci dissemination and the development of fibrotic changes. The key symptom of incipient fibrosis is the reduction of the volume of the posterior segments of the upper lobes of the lungs. Simultaneously, the cortical departments of the lungs expand, forming elements of cellular lung in subpleural zones. Reticular changes seem to be displaced from the periphery of the lung towards the root. At the same time, deformation and displacement of the leaflets of the interlobar pleura occur, and long linear shadows appear along the costal pleura.

Laboratory diagnostics. A complete blood count in acute sarcoidosis variants reveals an elevated erythrocyte sedimentation rate (ESR). Peripheral blood leukocytosis occurs in acute sarcoidosis and also in the background of glucocorticoid therapy. Signs of activity include lymphopenia and monocytosis, an increase in the neutrophil-to-lymphocyte ratio (Krebs index). C-reactive protein, an acute-phase reactant, is not very representative as an indicator of activity of epithelioid cell granulomatosis. Moderate elevation is typical for Lofgren's syndrome and other variants of acute sarcoidosis. Hypercalcemia (5 %) in sarcoidosis is considered by some researchers as a manifestation of active sarcoidosis. Hypercalciuria (25 %) is much more common and is a more accurate method of detecting calcium metabolism disorders.

The level of angiotensin-converting enzyme (ACE) is examined, which in the norm is 29–113 Units in the age range of 6–18 years and 20–70 Units in individuals older than 18 years. In the primary diagnosis of sarcoidosis, clinically significant is an increase in serum ACE activity by more than 150 % of the upper limit of normal. High ACE activity in serum should be interpreted as a marker of sarcoidosis activity rather than a significant differential diagnostic criterion.

The tuberculin test is included in the list of mandatory primary investigations in suspected sarcoidosis. The Mantoux test with 2 TU PPD-L in active sarcoidosis is negative in at least 80–85 % of patients who have not received systemic glucocorticoids (GCs). In patients with sarcoidosis treated with systemic GCs, previously infected with tuberculosis, the test may become positive. Tuberculin anergy in sarcoidosis is not related to tuberculin sensitivity in the general population. A positive Mantoux reaction (papule 5 mm or more) in case of suspected sarcoidosis requires very careful differential diagnosis and exclusion of tuberculosis. The significance of the test with a recombinant tuberculosis allergen (Diascintest, CPF10-ESAT6 protein) in sarcoidosis is not definitively established, but in most cases, its result is negative. In vitro interferon-gamma release tests (used to detect tuberculosis infection) usually yield a negative result in sarcoidosis.

Invasive diagnostic methods. A precise diagnosis of sarcoidosis is established when clinical and radiological data are supported by the detection of non-caseating epithelioid cell granulomas in biopsy specimens. Verification of sarcoidosis is carried out based on histological examination of biopsies from affected organs. Material for diagnosing intrathoracic sarcoidosis is obtained using bronchoscopic methods or during surgical diagnostic operations, most commonly video-assisted thoracoscopy (VATS) when a pathognomonic histological picture is detected: granulomas without caseation, consisting of epithelioid cells with an admixture of lymphoid cells and Langhans giant multinucleated cells.

Invasive diagnosis of extrapulmonary sarcoidosis involves obtaining material from the affected organ (peripheral lymph nodes, skin, subcutaneous formations, liver, and others according to the affected organ).

Functional methods. For patients undergoing primary diagnosis and follow-up to assess the degree of lung involvement in sarcoidosis, spirometry is recommended, with the key indicator being forced vital capacity (FVC). Spirometry allows the detection of restrictive and obstructive disorders of lung function in some patients with sarcoidosis of the respiratory organs. The severity of changes may be minor and not correspond to the extent of lung involvement.

Body plethysmography with measurement of lung diffusion capacity using the single-breath carbon monoxide method (DLCO) is an important study for assessing dynamics and determining the management tactics of patients with sarcoidosis.

Respiratory gas exchange disturbances in sarcoidosis are assessed based on blood oxygen saturation (SpO_2) using pulse oximetry at rest and during the six-minute walking test (6MWT), as well as during arterial blood gas analysis. Changes may be associated with lung tissue involvement, respiratory regulation impairment.

Differential Diagnosis

Differential diagnostic range of sarcoidosis involving intrathoracic lymph nodes and lymphadenopathy of other origins:

– Tuberculosis;
– Mycobacteriosis (caused by nontuberculous mycobacteria);
– Brucellosis;
– Toxoplasmosis;
– Granulomatous histiocytic necrotizing lymphadenitis (Kikuchi's disease);
– Cat scratch disease;
– Sarcoid reaction of regional lymph nodes in carcinoma;
– Lymphogranulomatosis;
– Non-Hodgkin's lymphoma;
– Acute lymphoblastic leukemia;
– GLUS syndrome (Granulomatous lesions of unknown significance).

Differential diagnostic range of sarcoidosis involving respiratory organs and disseminations of other origins:

– Tuberculosis;
– Mycobacteriosis;
– Cryptococcosis;
– Aspergillosis;
– Dissemination of neoplastic nature;
– Histoplasmosis;
– Coccidioidomycosis;
– Blastomycosis;
– Pneumocystis carinii;
– Mycoplasma spp.;
– Hypersensitivity pneumonitis;
– Pneumoconioses: berylliosis (chronic beryllium disease), titanium, aluminum;
– Drug-induced lung damage;
– Langerhans cell histiocytosis (histiocytosis X);
– Granulomatosis with polyangiitis (Wegener's) (sarcoid granulomas are rare);
– Idiopathic interstitial pneumonias;
– Necrotizing sarcoid granuloma.

In addition to sarcoidosis, there is the so-called nonspecific sarcoid reaction in the form of epithelioid-cell granulomatosis. It is usually observed in regional lymph nodes but can also occur in lung tissue with pseudotumors, malignant neoplasms, parasitic diseases, hypersensitive pneumonitis, tuberculosis, etc.

Histologically, sarcoid reaction is characterized by limited and topical association with the specified pathological processes.

In children with early-onset sarcoidosis (under 5 years old), the differential diagnosis is conducted with uveitis, parotitis, arthritis, and skin lesions of various etiologies.

Treatment

Patients with sarcoidosis are recommended to lead an active lifestyle with moderate physical activity (as tolerated by the disease), avoid hyperinsolation, thermal physiotherapy procedures, intake of interferons, interferonogen inducers, and other immune stimulants (including dietary supplements). Limitation of dairy products and other foods with high calcium content is recommended for patients with hypercalcemia and/or hypercalciuria.

Sarcoidosis in most cases is not a contraindication to pregnancy and childbirth, but the treatment of sarcoidosis can adversely affect the mother's body and be dangerous for the fetus (methotrexate, leflunomide, mycophenolate, chloroquines, and several other drugs).

Since the frequency of spontaneous remissions of sarcoidosis is high, asymptomatic patients with stage I sarcoidosis do not require drug treatment. Also, asymptomatic patients with stage II and III sarcoidosis, in the absence of or with mild impairment of external respiration function and stable condition, may not receive drug treatment. The condition of about 70 % of these patients remains stable or spontaneous improvement is observed. An alternative is the prescription of vitamin E and/or pentoxifylline.

Systemic glucocorticoids (GCs) are considered first-line drugs for patients with sarcoidosis who require drug treatment (in patients with progressive sarcoidosis according to the results of radiological examination of the organs of the chest and functional examination of lung function, with pronounced symptoms or extrapulmonary manifestations impairing organ function). Oral GCs reduce systemic inflammation, thereby slowing down, stopping, and even preventing organ damage. GCs can be prescribed as monotherapy or in combination with other drugs.

Methotrexate is currently one of the most studied and frequently prescribed steroid-sparing agents for sarcoidosis. Compared to other cytotoxic agents used in sarcoidosis, this drug is characterized by high effectiveness, low toxicity, and low cost. Methotrexate in the treatment of sarcoidosis is considered a second-line drug:

- when refractory to steroids;
- when side effects caused by steroids occur;
- as a means of steroid dose reduction;
- or as a first-line agent in mono- or combination with GCs therapy.
- methotrexate is particularly often recommended in neurosarcoidosis.

Biological drugs produced by genetic engineering (infliximab and others). Tumor necrosis factor-alpha (TNF-α) plays a key role in maintaining granulomatous inflammation in sarcoidosis. TNF-α inhibitors (infliximab and adalimumab) are currently considered third-line agents in pulmonary sarcoidosis, mainly due to cost and presumed side effects. A small number of studies have shown that infliximab reduces sarcoidosis symptoms in patients refractory to other forms of treatment.

Hydroxychloroquine is most effective in the treatment of sarcoidosis when skin, musculoskeletal system, and hypercalcemia are involved.

Pentoxifylline reduces levels of TNF-α and C-reactive protein. It can be prescribed for sarcoidosis as both initial and steroid-sparing therapy.

Antioxidant therapy. An empirically selected dose of vitamin E at 200–400 mg per day has been shown to be an effective and safe method of treatment for newly diagnosed sarcoidosis without pronounced signs of progression.

Macrolides. Several studies have shown the effectiveness of azithromycin with long-term use (3 months or more). Research is underway on the combination of azithromycin, levofloxacin, rifampicin, and ethambutol («CLEAR regimen»), but studies are not yet complete.

Afferent methods. The most commonly used extracorporeal method is plasmapheresis. In addition to removing immune complexes and proinflammatory interleukins, plasmapheresis improves microcirculation, unblocks cell receptors, and stabilizes cell membranes during the procedure, leading to increased sensitivity of «target cells» to the action of pharmacological agents.

Respiratory failure in sarcoidosis is formed due to the replacement of lung tissue with fibrous tissue, deformation of the lungs, and airways. Oxygen therapy is indicated for chronic hypoxemia (PaO_2 < 55 mm Hg), with the dose titrated to achieve SpO_2 > 90 % when breathing through an oxygen concentrator.

Lung transplantation is performed at terminal stages of intrathoracic sarcoidosis, with a median survival of 69.7 months.

Treatment features of sarcoidosis in children. There is no evidence base for the features of sarcoidosis treatment in children and adolescents. Treatment is based on general therapy principles considering age restrictions and age-specific dosages of medications.

SELF-CONTROL OF MASTERING THE TOPIC

Test tasks

1. Which diseases belong to the group of granulomatosis:

a) sarcoidosis;
b) bronchiectasis;
c) alveolitis;
d) tuberculosis.

2. What is characteristic of sarcoid granuloma:

a) caseous necrosis;
b) epithelioid cells and Langhans giant cells;
c) Langerhans cells and eosinophils;
d) Berezovsky-Sternberg cells.

3. Affected by sarcoidosis:

a) adrenal glands;
b) spleen;
c) intrathoracic lymph nodes;
d) lungs.

4. Skin lesions in sarcoidosis:

a) erythema nodosum;
b) shivering lupus;
c) acute urticaria;
d) papilloma.

5. Lofgren's syndrome is:

a) erythema nodosum;
b) fever;
c) polyarthritis;
d) facial nerve involvement.

6. Heerfordt-Waldenstrom syndrome is:

a) bilateral lymphadenopathy;
b) polyarthritis;
c) salivary gland involvement;
d) facial nerve involvement.

7. Stage I sarcoidosis is:

a) involvement of intrathoracic lymph nodes and lungs;
b) involvement of intrathoracic lymph nodes;
c) involvement of lungs only.

8. Stage II sarcoidosis is:

a) involvement of intrathoracic lymph nodes and lungs;
b) involvement of intrathoracic lymph nodes;
c) involvement of lungs only.

9. Sarcoidosis is characterized by:

a) hypercalcemia;
b) hypercholesterolemia;
c) hypocalcemia;
d) hyponatremia.

10. Skin biopsy in sarcoidosis is indicated from:

a) areas of erythema nodosum;
b) areas of shivering lupus;
c) unchanged areas.

11. Used in the treatment of sarcoidosis:

a) glucocorticoids;
b) interferon preparations;
c) TNF-alpha inhibitors;
d) antiviral drugs.

12. Not used in the treatment of sarcoidosis:

a) isoniazid
b) hydroxychloroquine
c) pentoxifylline
d) clofazimine

13. Tuberculin tests in sarcoidosis are more often:

a) negative;
b) positive;
c) hyperergic.

14. Radiological changes in pulmonary sarcoidosis occur more often:

a) symmetrically in both lungs in the middle sections;
b) in the upper parts of both lungs;
c) predominantly — on the right;
d) predominantly in the upper parts of the right lung.

15. The most informative research method for verifying the diagnosis of sarcoidosis of the respiratory organs:

a) biochemical blood analysis;
b) chest X-ray;
c) PCR diagnostics;
d) videothoracoscopy with intrathoracic lymph node biopsy.

16. The pathology in which biopsies contain epithelioid and giant-cell granulomas with Langhans cells:

a) tuberculosis;
b) berylliosis;
c) sarcoidosis;
d) lymphogranulomatosis.

Answers:

1 — a, d; **2** — b; **3** — b, c, d; **4** — a, b; **5** — a, b, c; **6** — a, c, d; **7** — b; **8** — a; **9** — a; **10** — b; **11** — a, c; **12** — a, d; **13** — a; **14** — a; **15** — d; **16** — a, c.

Situational tasks

Case 1. A 26-year-old man, a car parts salesman, presented to a doctor due to interstitial changes detected for the first time in both lungs during an annual chest X-ray examination. He denies any complaints. His medical history is notable for common colds. He has been smoking half a pack of cigarettes daily for 10 years. He denies alcohol abuse. There is no family history of acute infectious diseases among close relatives. On examination, he appears well with clear consciousness. His body temperature is 36.8 °C, skin is normal, BMI is 26.1 kg/m², blood pressure is 125/85 mmHg, pulse rate is 88 beats per minute, and respiratory rate is 18 breaths per minute. No crackles are heard on auscultation. No deviations are found in other organs or systems.

In the complete blood count, leukocytes are 7.7 × 10^9 /L, hemoglobin is 145 g/L, platelets are 213 × 10^9/L, segmented neutrophils are 47 %, monocytes are 2 %, and ESR is 14 mm/hour. The chest X-ray shows diffuse intensification and enhancement of the pulmonary pattern due to interstitial infiltration in the middle and lower lobes of both lungs, with signs of increased hilar lymph node shadow.

Triple induced sputum examination for acid-fast bacilli is negative, and Mantoux test with 2 TU PPD-L is negative.

Questions for Case 1:

1. What disease might be characterized by this clinical presentation?
2. What is the further diagnostic plan?
3. What changes in the complete and biochemical blood analyses can occur in sarcoidosis?
4. Name typical radiological changes in the lungs in stage 1 sarcoidosis.

Case 2. A 28-year-old man, a nuclear power plant engineer, presented to a doctor with complaints of severe weakness, decreased tolerance to usual physical exertion, dry cough, and shortness of breath. He has felt unwell for 2 months since having a respiratory infection. He has a history of common colds and undergoes annual medical check-ups. He does not smoke or abuse alcohol. He lives in a separate apartment with his wife. On examination, he appears closer to satisfactory, with clear consciousness. His body temperature is 36.9 °C, skin is normal, BMI is 28 kg/m², blood pressure is 135/85 mmHg, pulse rate is 82 beats per minute, and respiratory rate is 20 breaths per minute. No crackles are heard on auscultation. No deviations are found in other organs or systems.

In the complete blood count, leukocytes are 8.7 × 10^9/L, hemoglobin is 136 g/L, platelets are 203 × 10^9/L, segmented neutrophils are 47 %, monocytes are 3 %, and ESR is 16 mm/hour. A computer tomogram of the chest shows symmetric bilateral lung involvement with multiple small foci along vessels, bronchi, and pleural leaflets, and intrathoracic lymphadenopathy. No abnormalities are found in lung function testing. Abdominal ultrasound reveals diffuse liver enlargement and gallbladder polyps. Induced sputum examination for acid-fast bacilli is negative.

Questions for Case 2:

1. Can tuberculosis be excluded based on the results of the conducted examinations? Why?
2. What additional investigations are necessary for the patient?
3. Name typical radiological changes in the lungs in stage 2 sarcoidosis.
4. Name characteristic complaints of patients with sarcoidosis.

Case 3. A 30-year-old woman presents with complaints of intermittent fever up to 38 °C and changes on chest X-ray. She recently received treatment in the rheumatology department for nodular erythema on both shins and right-

sided gonarthritis. A chest X-ray reveals bilateral enlargement of lung roots and widening of the mediastinal shadow. On examination, painless enlarged lymph nodes are found, not adhered to surrounding tissues. In the complete blood count, leukocytes are 12.7×10^9/L, with left shift, hemoglobin is 117 g/L, and ESR is 38 mm/hour. CRP in the blood biochemistry is 20 mg/L. CT of the chest reveals small foci in both lungs and bilateral intrathoracic lymphadenopathy. A biopsy of the cervical lymph node reveals epithelioid and multinucleated Langhans cells without caseous necrosis.

Questions for Case 3:

1. What is the likely clinical diagnosis?
2. Name a syndrome characterized by such a clinical picture.
3. How does the pathological picture of this disease differ from tuberculosis pathology?
4. Name typical radiological changes in the lungs in stage 3 sarcoidosis.

Case 4. A 53-year-old woman, an elementary school teacher, was brought to the emergency department with complaints of fever up to 39–40 °C, eye pain and redness, numbness and a feeling of heaviness in the face, and swelling around the right ear. From the history, it is known that she became acutely ill when her temperature suddenly began to rise, followed by the appearance of the above-mentioned symptoms. The day before, she worked in the garden.

On examination, pronounced facial asymmetry is noted, and palpation around the ear area is painful.

In the complete blood count, leukocytes are 11.7×10^9 /L, hemoglobin is 107 g/L, and ESR is 31 mm/hour. Examination by an ENT doctor resulted in a diagnosis of acute exacerbation of chronic pharyngitis. Examination by an ophthalmologist resulted in a diagnosis of anterior uveitis. Examination by a neurologist resulted in a diagnosis of right facial nerve palsy.

A chest X-ray reveals diffuse intensification and enhancement of the pulmonary pattern in the middle and lower parts of both lungs, bilateral enlargement of lung roots, and widening of the mediastinal shadow.

Questions for Case 4:

1. What disease may present with these clinical and radiological symptoms?
2. Name the syndrome (by authors) characterized by the above-mentioned clinical manifestations of sarcoidosis.
3. Develop a diagnostic plan for the patient.
4. Name possible clinical manifestations in patients with sarcoidosis of the respiratory organs.

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САРКОИДОЗ ОРГАНОВ ДЫХАНИЯ

SARCOIDOSIS OF THE RESPIRATORY SYSTEM

Учебно-методическое пособие

На английском языке

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