УДК 616.24:616-002.182-07 DOI: http://doi.org/10.30978/TB2024-3-40

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The Role of Video Thoracoscopy in the Diagnosis of Sarcoidosis

Sarcoidosis is a systemic autoimmune disease associated with the development of non-caseous granulomas. Early and accurate diagnosis of sarcoidosis is an important and difficult task, since the initial manifestations are diverse, nonspecific, and many patients are asymptomatic.

Objective — to study the role of video thoracoscopy and to present our own experience of invasive diagnosis of sarcoidosis.

Materials and methods. Patients included in the study were divided into 2 clinical groups depending on whether the diagnosis at admission coincided with the final diagnosis established after the morphological examination of lung biopsies or not. Group I — 74 patients with PDS and ML (41.6 %), whose diagnosis at admission coincided with the final clinical diagnosis (established on the basis of morphological examination of lung biopsies). Group II — 104 patients with PDS and ML (58.4 %), whose diagnosis upon admission did not coincide with the final clinical diagnosis.

Results and discussion. Insufficient diagnosis of lung cancer (lung carcinomatosis) — 3 (2.9 %) cases at admission and 31 (29.8 %) cases after lung biopsy. The small percentage of diagnosis of interstitial, granulomatous lesions of the lungs or pneumonitis with systemic connective tissue pathology is also noteworthy - 3 (2.9 %) cases before lung biopsy and 19 (18.3 %) after. In patients who were diagnosed with pulmonary sarcoidosis without histological confirmation, such a pathology as tuberculosis was found in 14 (13.5 %), oncological lesion — 23 (22.1 %), interstitial or granulomatous lesion together with pneumonia in systemic pathology — 17 (16.3 %) and «other» — 20 (19.2 %) cases. We performed 178 VATS biopsies, among which lung biopsy prevailed — 67 (37.6 %) cases, pleural biopsy was the least performed — 18 (10.1 %) cases. Intraoperative complications were recorded in 2 (1.1 %) cases, in the form of bleeding from a lymph node, the elimination of which required the use of electrocoagulation, the use of local and systemic hemostatic agents. Postoperative complications were observed in 5 (2.8 %) cases and were caused by the lack of lung tightness and the resulting long-term discharge of air through the drainage.

Conclusions. Manifestations of sarcoidosis often simulate other disseminated processes, so its invasive diagnosis is an effective and safe way of establishing the diagnosis, especially in complex cases and atypical clinical and radiological picture. Among invasive methods, preference should be given to mini-invasive methods, therefore, the optimal choice is VATS, which has high informativeness and a low percentage of postoperative complications and allows to evaluate a wide range of tissues such as the pleura, lymph nodes and lungs.

Keywords

Sarcoidosis, VATS, lung biopsy, biopsy of mediastinal lymph nodes.

Sarcoidosis is a systemic autoimmune disease associated with the development of non-caseous granulomas. The disease more often affects the lymph nodes, lungs, skin and eyes [10]. It is common in Northern Europe, the United States, and India, and is also common in Sweden, Denmark, and among the African-Caribbean population. The exact cause of sarcoidosis has not yet been established, but many believe that the essence of the disease is a certain genetic predisposition combined with environmental factors, especially occupational exposure [7]. The most common symptoms are cough, shortness of

breath, fatigue, but there may be chest pain, weakness, fever, arthralgia or arthritis, erythema nodosum, peripheral lymphadenopathy. About a third of people with the corresponding X-ray picture are asymptomatic [12]. The pathological process is more often observed in people aged 20 to 50 [5].

Early and accurate diagnosis of sarcoidosis is an important and difficult task, since the initial manifestations are diverse, nonspecific, and many patients are asymptomatic. Radiological diagnosis of pulmonary sarcoidosis includes the use of chest X-ray and spiral computed tomography (SCT) in which pulmonary dissemination syndrome (PDS) and bilateral basal lymphadenopathy are detected. Biopsy makes it possible to morphologically determine the nature of the disease, differential diagnosis, and makes it possible to rule out the presence of other pathologies. Preference is given to the use of minimally invasive methods such as fibrobronchoscopy (FBS), mediastinoscopy, video thoracoscopy (VATS) [3].

The diagnosis of sarcoidosis is based on:

1) comparison of clinical and radiological picture;
2) morphological confirmation of the non-caseous origin of the granuloma;
3) exclusion of other diseases with similar manifestations, such as infections or malignant neoplasms [6, 9 13].

Indications for invasive diagnostics:

- suspicion of a lymphoproliferative process;
- unilateral lymphadenopathy;
- compression syndrome (signs of compression or displacement of the superior vena cava, esophagus, trachea, bronchi);
- differential diagnosis with other disseminated processes (Langerhans cell histiocytosis, hypersensitivity pneumonitis, disseminated pulmonary tuberculosis [2].

Treatment is based on the use of corticosteroids as a first-line option and the use of immunosuppressants as second-line therapy and anti-TNF agents in severe and/or refractory cases [8].

Objective — to study the role of video thoracoscopy and to present our own experience of invasive diagnosis of sarcoidosis.

Materials and methods

Since PDS and mediastinal lymphadenopathy (ML) are among the significant manifestations of sarcoidosis, an analysis of 178 case histories of inpatients with PDS and ML who underwent VATS biopsy of the lung, mediastinal lymph nodes, and pleura was performed. The criteria for the inclusion of patients in the study were their performance of a pathohistological examination of lung biopsies with the mandatory establishment of the etiology of PDS and the receipt by these patients of conservative therapy until the morphological verification of the diagnosis is performed. The criteria for the exclusion of patients in the study were non-compliance with the treatment regimen, lack of informed consent of the patient, refusal to participate in the research at any stage. Parametric statistics methods were used in data analysis. The check was performed using a special function NORMSAMP_1 developed for the Excel program. In our research, we used methods of descriptive statistics. To estimate how much the sample arithmetic mean differed from the general mean, the mean squared deviation was calculated.

$$\sigma = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - \bar{x})^2}.$$

The capabilities of Microsoft Excel were used for evaluation.

Patients included in the study were divided into 2 clinical groups depending on whether the diagnosis at admission coincided with the final diagnosis established after the morphological examination of lung biopsies or not.

Group I — 74 patients with PDS and ML (41.6 %), whose diagnosis at admission (established on the basis of laboratory and clinical and radiological examination methods) coincided with the final clinical diagnosis (established on the basis of morphological examination of lung biopsies).

Group II — 104 patients with PDS and ML (58.4 %), whose diagnosis upon admission did not coincide with the final clinical diagnosis (established on the basis of the morphological study of lung biopsies).

Results and discussion

All studied patients underwent general clinical, instrumental X-ray research methods, as well as histological examination of lung biopsies and mediastinal lymph nodes.

Distribution of patients by gender is presented in Table 1.

The analysis of the data presented in Table 1 allows us to conclude that in both groups there was a slight predominance of men — 39 (52.7) % in Group I and 57 (54.8) % in Group II.

Data on the average age of the studied patients are presented in Table 2.

Analyzing the data presented in Table 2, it can be concluded that the lung biopsy was performed on persons of working age.

Data on the distribution of patients in the studied groups depending on the diagnosis before and after histological examination of lung biopsies are presented in Table 3.

The data presented in Table 3 suggest that 74 (71.2 %) patients from Group II had a diagnosis of

Table 1. **Distribution of patients by gender**

Groups of patients	Number of patients	Men		Women	
		n	%	n	%
I	74	39	52.7	35	47.3
II	104	57	54.8	47	45.2
Total	178	96	53.9	82	46.1

Table 2. **Average age of the studied patients (M ± m), %**

Groups of patients	Number of patients	Age of the studied patients (years)		
		Average age		Total average age (years)
		Men	Women	
I	74	43.7 ± 1.7	46.9 ± 2.0	45.3 ± 1.4
II	104	44.6 ± 2.9	51.5 ± 3.4	47.5 ± 2.2

Table 3. **Distribution of patients in groups by diagnosis before and after histological verification**

Nosological form of diseases	Terms of diagnosis verification	Groups of patients			
		I (n = 74)		II (n = 104)	
		n	%	n	%
Sarcoidosis	Upon admission	33	44.6	74	71.2
	Upon discharge	33	44.6	9	8.7
Tuberculosis	Upon admission	17	23.0	10	9.6
	Upon discharge	17	23.0	15	14.4
Oncological lesion	Upon admission	4	5.4	3	2.9
	Upon discharge	4	5.4	31	29.8
Interstitial or granulomatous lesions and pneumonia in systemic pathology	Upon admission	6	8.1	3	2.9
	Upon discharge	6	8.1	19	18.3
Others	Upon admission	14	18.9	14	13.5
	Upon discharge	14	18.9	30	28.8

pulmonary sarcoidosis upon admission and received certain courses of specific treatment, whereas 9 (8.7 %) patients had this diagnosis only after lung biopsy. Such a significant difference in the final diagnosis is explained by the fact that an asymptomatic course is possible in the presence of radiological changes. Therefore, such patients are often prescribed therapy using cytostatics or glucocorticosteroids, and only in case of negative clinical and radiological dynamics, the issue of lung biopsy is decided. From Table 1, we can draw a conclusion about insufficient diagnosis of lung cancer (lung carcinomatosis) — 3 (2.9 %) cases at admission and 31 (29.8 %) cases after lung biopsy. In this case, we are talking mainly about patients whose primary tumor was not detected before the lung biopsy, and only after histological verification of the diagnosis, a diagnostic search was carried out to establish the primary tumor site. Special attention is paid to the differential diagnosis of mediastinal lymphadenopathy for patients with an oncological anamnesis and chemotherapy, and in the presence of foci in the lungs. In addition, check point inhibitors can also lead to a granulomatous reaction which can be misdiagnosed as sarcoidosis. These issues must be considered when investigating the relationship between sarcoidosis and malignant tumors [7]. The small percentage of diagnoses of interstitial, granulomatous lesions of the lungs or pneumonitis with systemic connective tissue pathology is also noteworthy — 3 (2.9 %) cases before lung biopsy and 19 (18.3 %) after. The group «Others» includes various variants of pneumoconicosis, invasive aspergillosis, pneumocystis pneumonia, lymphangioleiomyomatosis, etc. In this nosological group of patients, signs of hypodiagnosis are also observed — 14 (13.5 %) cases before biopsy and 30 (28.8 %) after. Since the group «Others» contains different etiology and

Table 4. **Change of diagnosis for Group II patients after lung biopsy**

Diagnosis on admission	Number of cases	%	Diagnosis at discharge	Number of cases	%
Sarcoidosis	74	71.2	Tuberculosis	14	13.5
			Oncological lesion	23	22.1
			Interstitial or granulomatous lesions and pneumonia in systemic pathology	17	16.3
			Others	20	19.2
Tuberculosis	10	9.86	Sarcoidosis	8	7.7
			Others	2	1.9
Oncological lesion	3	2.9	Interstitial or granulomatous lesions and pneumonia in systemic pathology	2	1.9
			Others	1	1.0
Interstitial or granulomatous lesions and pneumonia in systemic pathology	3	2.9	Oncological lesion	2	1.9
			Others	1	1.0
Others	14	13.5	Sarcoidosis	1	1.0
			Tuberculosis	2	1.9
			Oncological lesion	6	5.8
			Others	5	4.8

pathogenesis of the disease, it does not make it possible to draw a correct conclusion regarding the possible reasons for such a discrepancy in the diagnoses before and after the morphological verification of PDS and ML.

After morphological verification, the main diagnosis was established. Data on the change in diagnosis among patients of Group II are presented in Table 4.

The data presented in Table 4 suggest that the patients who were diagnosed with pulmonary sarcoidosis without histological confirmation, had such a pathology as tuberculosis in 14 (13.5 %) cases, oncological lesion in 23 (22.1 %) cases, interstitial or granulomatous lesions together with pneumonitis in systemic pathology in 17 (16.3 %) cases and «Others» in 20 (19.2 %) cases. The similarity of the clinical and radiological manifestations of sarcoidosis and pulmonary tuberculosis is explained by common points in the pathogenesis of these diseases. Oncological and interstitial or granulomatous lesions of the lungs together and pneumonitis with systemic lung pathology in the initial stages of the disease can be asymptomatic, which is the main factor in establishing a false diagnosis of sarcoidosis. Nosologies classified as «Others» also have a long period of asymptomatic course. Although sarcoidosis was most often unjustifiably diagnosed for patients with oncology — 23 (22.1 %) cases, even timely diagnosis of lung carcinoma and the appointment of chemotherapy do not significantly affect the prognosis of the disease. The prescription of cytostatics or glucocorticoids for pulmonary tuberculosis most often leads to the progression of the disease (in the study, this accounted for 16 (13.0 %) cases).

We used the VATS method for invasive diagnostics. It requires the use of an operating room and the use of anesthesia with postoperative analgesia, but allows obtaining a larger amount of material, simultaneously performing a biopsy of mediastinal lymph nodes, lungs, pleura, depending on the manifestations of the disease and the clinical task. VATS ends with drainage of the pleural cavity, which is a prevention of postoperative pneumothorax.

Data on types of VATS are presented in the Table 5.

We performed 178 VATS biopsies, among which lung biopsy prevailed — 67 (37.6 %) cases, pleural biopsy was the least performed — 18 (10.1 %) cases, since pleurisy in sarcoidosis is relatively rare.

Table 5. **Types of VATS**

Type of VATS	Number	%	Number of complications
Lung biopsy	67	37.6	3
Biopsy of mediastinal lymph nodes	55	30.1	1
Biopsy of lung and mediastinal lymph nodes	38	21.3	1
Pleura biopsy	18	10.1	0
Total	178	100.0	5

Intraoperative complications were recorded in 2 (1.1 %) cases, in the form of bleeding from a lymph node, the elimination of which required the use of electrocoagulation, the use of local and systemic hemostatic agents. Postoperative complications were observed in 5 (2.8 %) cases and were caused by the lack of lung tightness and the resulting long-term discharge of air through the drainage. This complication was observed at the junction of endoscopic sutures and did not require additional drainage. The complication was eliminated by temporarily switching the drainage of the pleural cavity to passive mode according to Bülau, with subsequent return to active mode after elimination of air discharge.

Clinical case

Patient T., 35 years old, turned to the doctor during the preventive chest X-ray, where it was found: «In the right lung, more in the projection of the upper lobe, there is a moderate small focal dissemination. Trachea, main bronchi are open, enlarged mediastinal lymph nodes on the right». The SCT has been performed. He did not make any complaints. At the pre-hospital stage, he was consulted by a pulmonologist, received a course of antibacterial therapy, after which a repeated SCT, radiologically without dynamics, a diagnosis of Sacroidosis of the lungs and mediastinal lymph nodes was made. Objectively: normosthenic physique, general condition is satisfactory, skin and mucous membranes are clean, breathing is vesicular, there is no peripheral lymphadenopathy. Blood and urine analysis without deviations. Examination of sputum by bacterioscopic, molecular genetic and cultural methods - mycobacterium tuberculosis was not detected. Taking into account the atypical radiological picture (predominantly unilateral nature of the impression of the lung and mediastinal lymph nodes, absence of complaints), it was decided to conduct a morphological verification of the disease. Radiologically, the disseminated process was more pronounced in the peripheral parts of the lungs, therefore, the VATS method was chosen as the most optimal.

Under anesthesia with one-lung ventilation, a biopsy of the second segment of the right lung with foci was performed using a suture device, a biopsy of medistinal lymph nodes was performed, and 2 drains were installed in the pleural cavity. The postoperative period was uneventful, the drains were removed on the 3rd day. Morphological examination: The biopsy material contains the tissue of the mediastinal lymph node and lung tissue with morphological signs of relatively long-term development of granulomatous epithelioid cell inflammatory process without obvious necrotic changes. In the lung tissue, focal growths of connective tissue with its partial

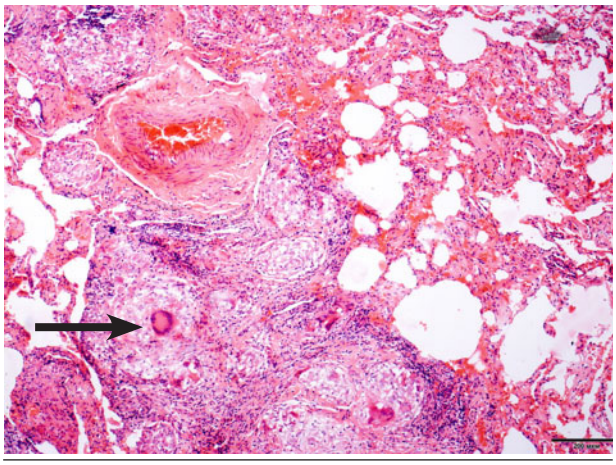

Figure. **Perivascular sarcoid nodule**

At low magnification, a cluster of small epithelioid cell granulomas is observed among the slightly changed lung tissue. Growth of connective tissue between them with moderate lymphoid cell infiltration can be seen. Giant multinucleated cells (arrow) are found in some granulomas. On the periphery of the node there is focal lymphoid cellular infiltration. Staining with hematoxylin and eosin.

hyalinosis are determined, in which there are multiple monomorphic epithelioid cell granulomas with numerous giant multinucleated cells of both types, with a tendency to their fibrosis. A predominantly perivascular location of nodules with granulomas is noted. The structure of the lymph node is partially disturbed due to the existing chronic granulomatous inflammatory process. Among the preserved small lymphocytes, sarcoid-type epithelioid cell granulomas with numerous giant multinucleated cells of both types are determined. Granulomas are surrounded by a thin connective tissue capsule. Conclusion: This morphological pattern corresponds to sarcoidosis of the respiratory organs of long-term development (nodular form of sarcoidosis of the lungs and mediastinal lymph nodes). Indirect morphological signs of its slow progression are presented in Figure.

The patient was diagnosed with respiratory sarcoidosis, stage II, detected for the first time, histologically verified. Condition after VATS biopsy in/lobe of the right lung, mediastinal lymph nodes on the right. Taking into account the absence of pulmonary insufficiency, glucocorticosteroid therapy was not prescribed, it was recommended to observe without treatment with control of chest X-ray, spirometry 1 time in 3 months. as the probability of spontaneous regression of the disease remained.

Conclusions

Manifestations of sarcoidosis often simulate other disseminated processes, so its invasive diagnosis is an effective and safe way of establishing the diagnosis, especially in complex cases and atypical clinical

and radiological picture. Early diagnosis of sarcoidosis allows you to avoid prescribing unnecessary drugs, prevent the progression of the disease and improve the results of treatment. Among invasive methods, preference should be given to mini-invasive methods, therefore, the optimal choice is VATS, which has high informativeness and a low percentage of postoperative complications and allows to evaluate a wide range of tissues such as the pleura, lymph nodes and lungs.

There is no conflict of interest.
Participation of the authors: research concept and design — M.S. Opanasenko, S.M. Shalahai; collection of material — S.M. Shalahai, O.V. Tereshkovych, B.M. Konik; material processing — L.I. Levanda, I.V. Liskina, L.M. Zagaba, S.M. Shalahai; writing the text — S.M. Shalahai; statistical processing of data — O.V. Tereshkovych, B.M. Konik, L.I. Levanda; editing of the text — S.M. Shalahai.

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Роль відеоторакоскопії в діагностиці саркоїдозу

Саркоїдоз — це системне автоімунне захворювання, пов'язане з розвитком неказеозних гранульом. Рання і точна діагностика саркоїдозу є важливим та непростим завданням, оскільки початкові вияви різноманітні, неспецифічні, у багатьох пацієнтів перебігають безсимптомно.

Мета роботи — вивчити роль відеоторакоскопії та представити власний досвід інвазивної діагностики саркоїдозу.

Матеріали та методи. Пацієнтів, залучених у дослідження, розподілили на дві клінічні групи: I група — 74 (41,6 %) хворих, у яких діагноз при госпіталізації (установлений за даними лабораторних і клініко-рентгенологічних методів обстеження) збігався з остаточним клінічним діагнозом (установленим за результатом морфологічного дослідження біоптатів легені); II група — 104 (58,4 %) хворих, у яких діагноз відрізнявся.

Результати та обговорення. Виявлено недостатню діагностику онкологічного ураження легень (канцероматозу легень) — 3 (2,9 %) випадки при госпіталізації та 31 (29,8 %) випадок після біопсії легені. Невеликою була частота діагностики інтерстиційних гранулематозних уражень легень або пневмонітів при системній патології сполучної тканини — 3 (2,9 %) випадки до біопсії легені та 19 (18,3 %) після. У хворих, яким без гістологічного підтвердження встановлений діагноз саркоїдозу легень, траплялися такі патології, як туберкульоз (14 (13,5 %) випадків), онкологічне ураження (23 (22,1 %)), інтерстиційне або гранулематозне ураження разом з пульмонітами при системній патології (7 (16,3 %)) та «інші» (20 (19,2 %)). Нами виконано 178 VATS-біопсій, серед яких переважала біопсія легені — 67 (37,6 %) випадків, найменше виконували біопсію плеври — 18 (10,1 %), оскільки плеврит при саркоїдозі трапляється відносно рідко. Інтраопераційні ускладнення зафіксовано

в 2 (1,1 %) випадках у вигляді геморагії з ложа лімфатичного вузла, ліквідація якої потребувала застосування електрокоагуляції, місцевих і системних гемостатичних засобів. Післяопераційні ускладнення, зареєстровані в 5 (2,8 %) випадках, були спричинені відсутністю герметизму легені.

Висновки. Вияви саркоїдозу часто симулюють інші дисеміновані процеси, тому його інвазивна діагностика є ефективним безпечним способом установлення діагнозу, особливо в складних випадках і при нетиповій клінічній і рентгенологічній картині. З інвазивних методів перевагу слід віддавати малоінвазивним методам, тому оптимальним є вибір VATS, що характеризується високою інформативністю, малою частотою післяопераційних ускладнень і дає змогу оцінити широкий спектр тканин, таких як плевра, лімфатичні вузли та легеня.

Ключові слова: саркоїдоз, VATS, біопсія легені, біопсія внутрішньогрудних лімфатичних вузлів.

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Стаття надійшла до редакції/Received 11.03.2024.
Стаття рекомендована до опублікування/Accepted 20.05.2024.

ДЛЯ ЦИТУВАННЯ

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