

# Clinical observation of generalized sarcoidosis with damage of bones

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## Abstract

Sarcoidosis is a multisystem disease of unknown etiology, at the basis of which there is an inflammatory granulation epithelioid process without a pronounced exudative reaction and without caseous necrosis. This disease has various manifestations.

The aim of the study was to investigate the clinical case of generalized sarcoidosis with bone lesion in a patient M., born in 1987. There were performed X-ray examinations, computed tomography (CT), fibrobronchoscopy, determination of calcium levels, angiotensin converting enzyme (ACE), soluble IL-2 receptor in the blood. Dynamic observation was performed for 10 months.

The patient started methylprednisolone therapy at a dose of 20 mg/day. Significant positive effect of this treatment was noted.

Thus, when patients complain of the bone and joint system problems, examination plan should include radiological examination of thoracic organs, which will allow us to avoid late diagnosis of sarcoidosis or other multisystem diseases that may have similar clinical manifestations.

## Keywords

clinical case, sarcoidosis, bones of hands, methylprednisolone

## Introduction

Sarcoidosis is a multisystem disease of unknown etiology, at the basis of which there is an inflammatory granulation epithelioid process without a pronounced exudative reaction and without caseous necrosis (Vizel 2009). In its history more than a century, sarcoidosis has undergone a complex journey from dermatological disease, atypical tuberculosis and tumors to systemic granulomatosis (Dzeman 2012). Sarcoidosis was first described by English dermatologist in a patient with skin lesion as “papillary psoriasis” and, for many years, was considered a rare dermatological disease. C.Boeck introduced the term “sarcoïd” in 1899, based on the similarity of histological changes in skin with sarcoma (Havrysiuk et al. 2014). J. Schaumann in 1919 described a

patient with lesions of the skin, lungs, bones, spleen, liver, and suggested that the signs previously attributed to various diseases, are to be included to one systemic pathology. He called it “benign lymphogranulomatosis”, that is, he first noted the systemic nature of the disease. In 1934, at the International Dermatologists’ Congress in Strasbourg, the term–“Bennier-Beck-Schauman’s Disease” was offered, and in 1948 the term “sarcoidosis”, now used in the international classification, was recommended instead of the that term at an international conference in Washington (Dzeman 2012; Sergienko 2014).

The incidence of sarcoidosis worldwide varies from 0.125 to 24.0 of new cases per 100.000 of population per year, with a prevalence of 1 to 64 per 100.000 of population. The climate factor has an undeniable influence on

the incidence – in Africa, Asia and Central America, sarcoidosis morbidity rates are the lowest and in temperate and cold climates the highest ones (Havrysiuk et al. 2014; Order of the Ministry of Health of Ukraine 2014).

The maximum incidence of sarcoidosis is observed in the age of between 35 and 55 years. People under 25 and over 75 years are rarely ill. In almost all epidemiological studies it is noted that women with sarcoidosis predominate (approximately 65%) (Havrysiuk et al. 2014).

This disease has various manifestations: from asymptomatic changes in thoracic organs' X-ray (Thoracic Organs) to severe multi-organ lesions (Panselinas and Judson 2014). According to modern ideas, the frequency of involvement of various organs and systems into the pathological process is determined approximately as follows: lymph nodes are affected in 100% of all cases, intra-thoracic lymph nodes and lungs – in 60–70%, spleen and liver – in 50–60%, skin –in 30–40%, eyes –in 10–20%. The nervous system, kidneys, salivary glands and bones – all together –constitute 10% of all lesion locations (Judson 2014; Veltkamp and Grutters 2014). Finally, some authors point to a 17–20% incidence of bone loss. For the first time in the world literature in 1908 N.V. Morozov described in detail radiographic changes in the bones of the hands' phalanges of the 42-year-old patient, and later, in 1920 Jüngling's work was published (Vizel 2009; Havrysiuk et al. 2018; X-ray picture URL: <https://auno.kz/rentgenodiagnostika-zabolevanij-kostej/380-rentgenologicheskaya-kartina-kostej-i-sustavov.html>).

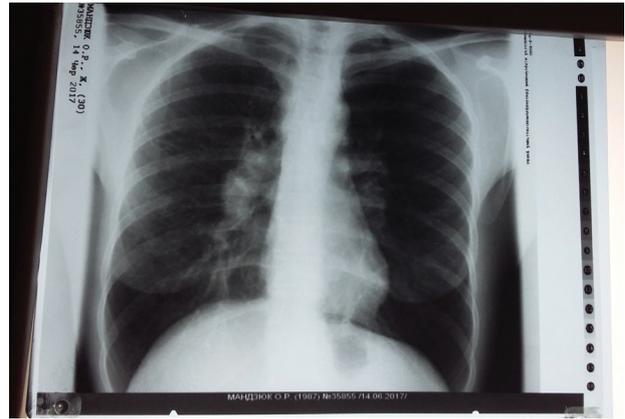
The **objective** of the work – is to study the clinical case of generalized sarcoidosis with bone damage.

## Material and methods

The case of sarcoidosis in the patient M., born 1987, was studied. There were performed clinical, laboratory, instrumental methods of the research according to the “Unified clinical protocol of primary, secondary (specialized), tertiary (highly specialized) medical care “Sarcoidosis” (Order of the Ministry of Health of Ukraine №634 dated 08 September 2014) (Order of the Ministry of Health of Ukraine 2014). These included radiographic examinations of thoracic organs, hands; computed tomography (CT) of thoracic organs and fingers of the right hand; fibrobronchoscopy; determination of calcium levels, angiotensin-converting enzyme (ACE), soluble IL-2 receptor in the blood. Dynamic observation was performed for 10 months.

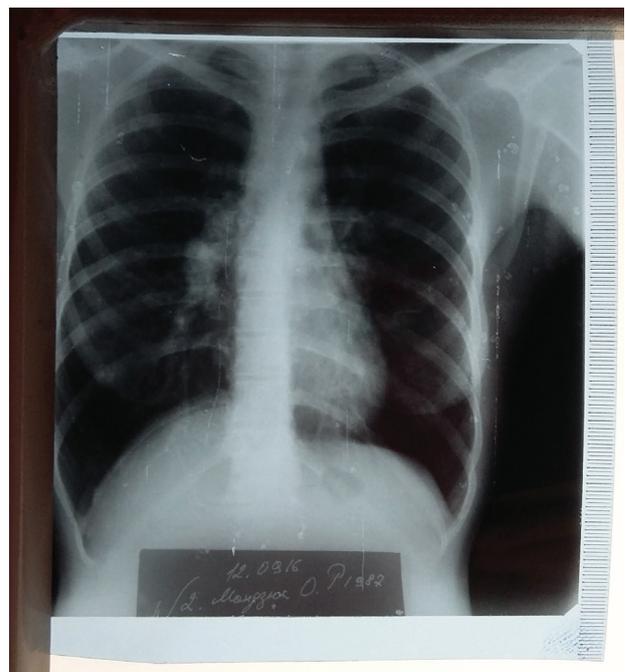
## Results and discussion

Patient M., a pharmacist, was hospitalized at the Department of Differential Diagnostics of the Regional Clinical Phthysiopulmonology Center (RCPC) in June 19, 2017, as the results of thoracic organs radiography in June 14, 2017 (Figure 1) revealed enlarged intra-thoracic lymph nodes (ITLN). Analyzing the radiological archive, it was found



**Figure 1.** Radiography of the thoracic organs of the patient M., born 1987, made 14.06.2017.

that in September 12, 2016 (fluorographic examination during the preventive medical examination) (Figure 2), ITLN had already been increased, but this was not stated in the radiologist's conclusion. There were no subjective symptoms of the bronchopulmonary system. Instead, she noted the pain and edema of the middle phalanx of the third finger of the right hand (Figure 3), general weakness, sweating, temperature rise up to 37–37.5 °C. The above-mentioned complaints have been a concern since April 2017. She sought medical help in a traumatologist. X-ray examination (Figure 4a) and CT scan of the hands (Figure 4b) were performed, the results of which showed the destructive changes of the middle phalanx of the third finger of the right hand. During April-May 2017, she was treated as an outpatient by a traumatologist (using lincomycin, doxycycline, metronidazole, ceftriaxone, meloxicam ) without improvement of her condition.



**Figure 2.** Fluorography of the thoracic organs of the patient M., born 1987, made 12.09.2016.

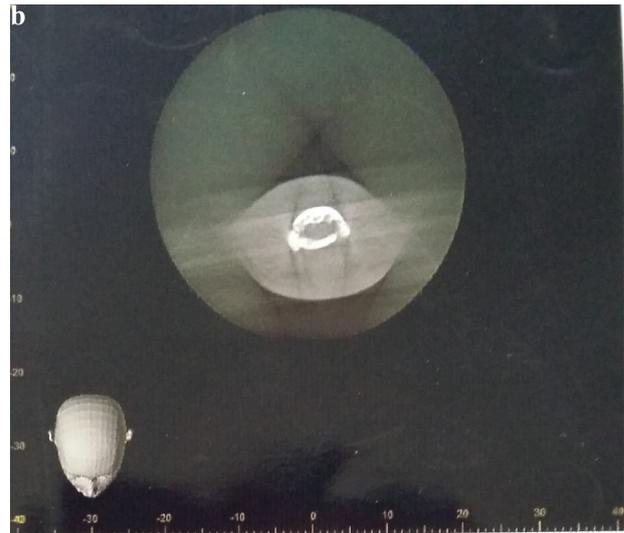


**Figure 3.** Swelling of the middle phalanx of the third finger of the right hand of the patient M., born 1987.

Having analyzed the anamnesis data, the results of radiological examination of the chest organs and hands in the Department of Differential Diagnosis, a series of additional examinations have been performed. In particular, a spiral CT scan of the thoracic organs was performed in 20 June 2017. It was determined that in both lungs, multiple dense foci of various size are chaotically located along the entire length (Figure 5a). All calcified and enlarged groups of lymph nodes of the mediastinum and the roots of the lungs are visualized (Figure 5b). The study concluded that CT signs may correspond to the sarcoidosis of ITLN and lungs, but they are not excluded – residual changes after tuberculosis of ITLN and lungs.

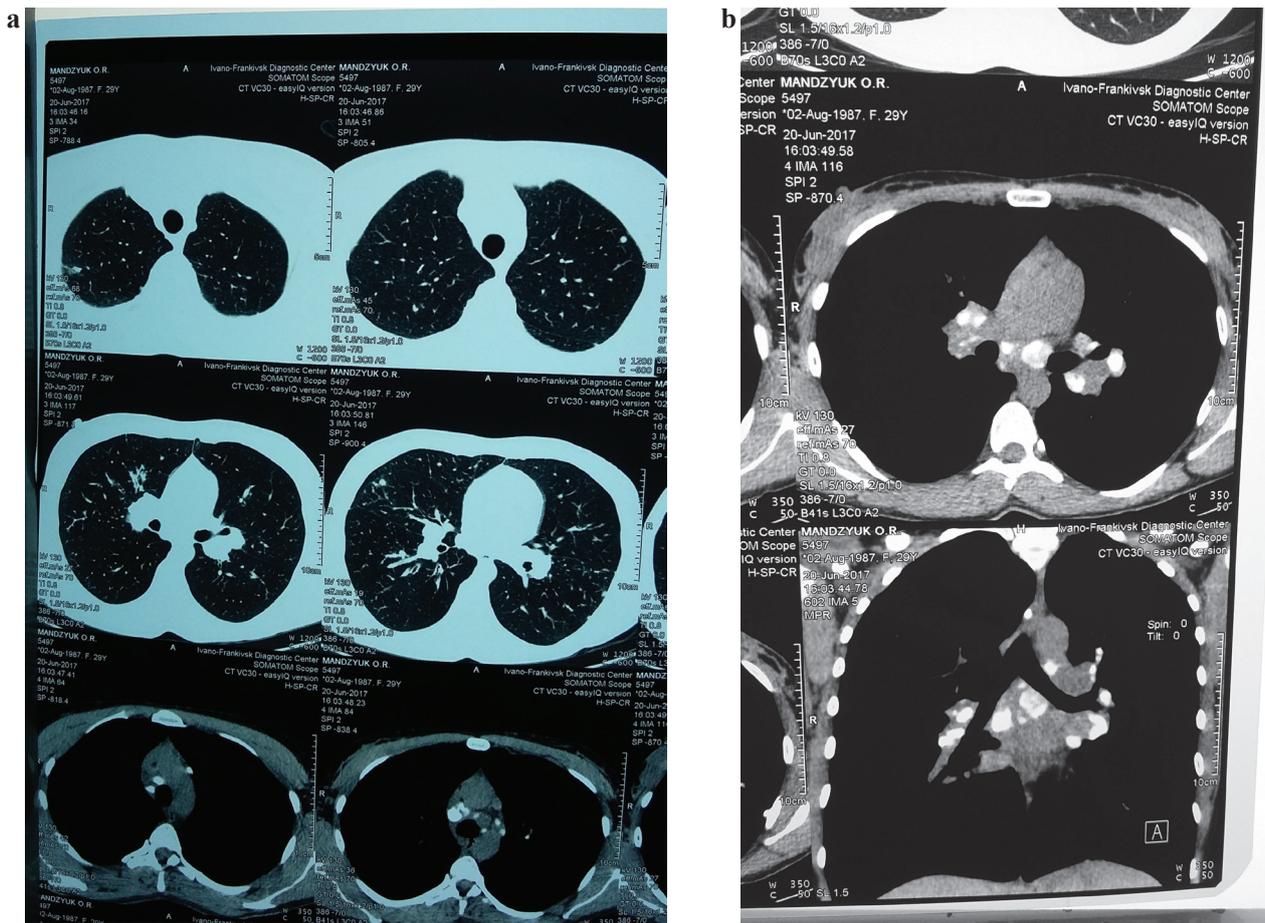
According to ultrasound examination in June 20, 2017, an enlargement of the supraclavicular lymph nodes was observed: on the right, a lymph node was  $1.4 \times 1.0$  cm and  $1.5 \times 0.8$  cm, on the left –  $2.0 \times 1.2$  cm with preserved structure. No pathological changes of the abdominal organs were detected.

Fibrobronchoscopy (FBS) (21 June 2017) was performed; it was found that the mucous membrane of the bronchial tree on the right and left is hyperemic due to the spread of the vascular pattern throughout, bronchial lumens are somewhat narrowed. Cytologically, in the bronchial washings (№10 dated 21 June 2017) against the inflammatory background there were accumulations of alveolar macrophages, a group of cells of the bronchial epithelium. Atypical cells and acid-resistant bacteria were not found.



**Figure 4.** Destructive changes in the middle phalanx of the third finger of the right hand on radiograph (a) and computed tomography of the right hand.

A series of laboratory examinations was performed. In the complete blood count analysis (CBC), only erythrocyte sedimentation rate (ESR) elevation of up to 17 mm/h was found. The level of calcium, angiotensin converting enzyme (ACE) and soluble receptor for IL-2 in the blood were normal, Mantoux reaction with 2 TO – was negative. Such methods as bacterioscopy and Gi-



**Figure 5.** Spiral computed tomography of the thoracic organs of patient M., born 1987, made on 20.06.2017: **a** – chaotically located, multiple of different size dense foci in both lungs; **b** – calcified and enlarged all groups of lymph nodes of the mediastinum and the roots of the lungs.

neXpert did not find the *Mycobacterium tuberculosis* (MTB) in the sputum.

The patient was offered to perform a biopsy of the supraclavicular lymph node and a bone marrow biopsy of the middle phalanx of the third finger of the right hand for histological verification of the pathological process. The patient categorically refused from these examinations.

Summarizing the anamnesis data, all laboratory and instrumental studies performed in the RCPC it was concluded that the patient M. has sarcoidosis of ITLN, lungs, peripheral lymph nodes, bones of the right hand. In order to clarify the diagnosis and to decide further therapeutic tactics, the patient was referred for consultation to the State Institution “National Institute of Phthisiology and Pulmonology named after F.H. Yanovsky of the Academy of Medical Sciences of Ukraine” in Kyiv. Specialists of leading institutions in the field of Phthisiology and Pulmonology, Traumatology, Oncology in Kyiv examined the patient. The diagnosis was confirmed and formulated as “Sarcoidosis of the respiratory system, peripheral lymph nodes (supraclavicular on the right), bones (middle phalanx of the third finger of the right hand), II degree, first detected, process progression”.

The issue of treating patients with sarcoidosis has been debated since the definition of sarcoidosis as an indepen-

dent nosological form. At the same time, they express extreme points of view regarding both the treatment of sarcoidosis in general and considering the use of different medicines. In recent years, most of the cases of the initially revealed sarcoidosis of the respiratory organs with an acute or subacute course, including those with Löfgren syndrome without extrapulmonary lesions, have not been treated early with medicines. It is considered favorable in the prognostic plan, there is only symptomatic therapy with non-steroidal anti-inflammatory drugs and the waiting tactics with repeated clinical, radiological, functional and laboratory examinations every 3 months has been chosen. Generally recognized and absolute indications prior to the start of systemic treatment of sarcoidosis are all stages of it with extracorporeal manifestations, as in the case of our patient. Glucocorticoids continue to be the main means of therapy, like half a century ago. They have anti-proliferative, anti-inflammatory effects, inhibit granuloma formation, inhibit the release of cytokines from lymphocytes and macrophages (Baughman and Drent 2014; Havrysiuk et al. 2018).

The patient started methylprednisolone therapy at a dose of 20 mg/day. Significant positive effect of this treatment was noted: swelling of the third finger of the right hand has disappeared on the 3<sup>rd</sup> day, a significant reducti-

on of destructive changes of the middle phalanx and partial resorption of foci in the lungs were recorded on radiographs and CT after 4 months, normalization of the size of the lymph nodes in the supraclavicular regions occurred after 7 months. During the course of treatment, the side effects of GC-therapy were corrected with the inclusion of hepatoprotectors, antifungal medicines, proton pump inhibitors, and antacids.

During the outpatient phase of the examination and treatment of the patient, there was made an error in the diagnosis of this pathology due to its asymptomatic course in September 2016 and atypical – in April-May-June 2017. Increased lymph nodes of the mediastinum, determined since September 2016, most of them with calcifications, which indicate the **prescription of the process** (*it means "time of duration, recentness, long standing, age"*) (4–5 years). Bone lesions in sarcoidosis indicate chronic course, disease progression.

At the phase of diagnosis of this clinical case in the RCPC one can talk about incomplete examination of the patient, because there was no morphological confirmation of the diagnosis in the presence of changes that could make it possible. The patient refused biopsy of the supraclavicular lymph node and bone tissue of the middle phalanx of the third finger of the right hand.

However, in a short period of time, a positive clinical effect after the use of systemic steroid therapy, especially of the bone tissue, was observed. This demonstrates both the benefit of correct diagnosis and the adequacy of the glucocorticoid doses selected.

No significant dynamics in the lungs and ITLN should be expected, since the density of foci and the presence of calcifications in the roots of the lungs testify to the prescription and the irreversibility of the process.

## Conclusions

Patients with complaints of the bone-joint system should include a radiographic examination of Thoracic Organs into the examination plan, which will allow avoiding late diagnosis of sarcoidosis, tuberculosis, or other multisystem diseases that may have similar clinical manifestations. Accordingly, a multidisciplinary approach is recommended during the examination and treatment of patients with sarcoidosis. We emphasize the necessity for a balanced examination when determining the tactics of managing patients (treatment or active observation), taking into account the activity of the process, the impact of pharmacotherapy on the course of the disease and the possible development of undesirable side effects.

## Prospects for further research

Today, sarcoidosis, unfortunately, still belongs to diseases in the understanding of which there are more conjectures and hypotheses than real facts. Scientific researches of this disease are steadily continued, the signs of interstitial pulmonary fibrosis, the state of pulmonary ventilation and diffusion are being studied. Tests are being developed; they will be able to predict the progression of the disease. Genetic factors that can change the manifestations of the disease are being studied. Causes of sarcoidosis may be identified in the nearest future, and we will be able to effectively treat it. Each case of sarcoidosis is unique, and a personalized approach to the diagnosis and treatment of this disease should be used by the physician.

## References

- Baughman RP, Drent M (2014) The Treatment of Pulmonary Sarcoidosis. Humana Press, brand of Springer, 41–64. [https://doi.org/10.1007/978-1-4614-8927-6\\_3](https://doi.org/10.1007/978-1-4614-8927-6_3)
- Dzeman MI (2012) Sarcoidosis of the respiratory organs. *Praktykuyuchylar* 4: 23–28.
- Havrysiuk VK, Merenkova EM, Humeniuk HL, Shadrina OV, et al. (2014) Sarcoidosis of the respiratory organs: epidemiology, patient structure, treatment results. *Ukrainian therapeutic journal* 2: 95–100.
- Havrysiuk VK, et al. (2018) Treatment of patients with pulmonary sarcoidosis: methodical guidance. State Institution ‘National Institute of Phthysiology and Pulmonology’, Kyiv, 50 pp.
- Judson MA (2014) Pulmonary sarcoidosis: A Guide for the practicing clinician. Humana Press, brand of Springer, 22 pp.
- Order of the Ministry of Health of Ukraine (2014) Order of the Ministry of Health of Ukraine № 634, dated 08.09.2014 “Unified clinical protocol of primary, secondary (specialized), tertiary (highly specialized) medical care “Sarcoidosis”.
- Panselinas E, Judson MA (2014) Acute Pulmonary Exacerbation of Sarcoidosis. Humana Press, brand of Springer, 65–78. [https://doi.org/10.1007/978-1-4614-8927-6\\_4](https://doi.org/10.1007/978-1-4614-8927-6_4)
- Sergienko DV (2014) Respiratory organs sarcoidosis in clinical practice. *Rational pharmacotherapy* 1(30): 37–42.
- Veltkamp M, Grutters JC (2014) The pulmonary manifestations of sarcoidosis. Humana Press, brand of Springer, 19–40. [https://doi.org/10.1007/978-1-4614-8927-6\\_2](https://doi.org/10.1007/978-1-4614-8927-6_2)
- Vizel AA (2009) Sarcoidosis. *Pulmonology: National guidance* ed. by AG Chuchalin. GEOTAR-Media: 681–695.
- X-ray picture of bones and joints in various general infectious, fungal and parasitic diseases (2012) X-ray picture of bones and joints in various general infectious, fungal and parasitic diseases. <https://auno.kz/rentgenodiagnostika-zabolevanij-kostej/380-rentgenologicheskaya-kartina-kostej-i-sustavov.html>