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Sarcoidosis: Pathogenesis, Diagnosis, and Clinical Management

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Abstract

Introduction: Sarcoidosis is a multisystem inflammatory disease of unknown etiology. It is more common in women and in people suffering from obesity. A characteristic feature is the formation of non-sarcomatous granulomas, which could occure important organs. It could also present as an asymptomatic form, and its diagnosis may be made incidentally on a routine chest X-ray.

Aim of the study: The aim of this study was to review the literature describing the disease sarcoidosis-its course, clinical forms, diagnosis and treatment.

Methods and materials: : We reviewed the literature available in the PubMed database, using the key words: "sarcoidosis"; "granulomatosis''; "cardiac sarcoidosis"; "neurosarcoidosis"; "pulmonary sarcoidosis''.

Results: The most common form of sarcoidosis is pulmonary, with enlargement of hilar lymph nodes and parenchymal lesions**.** The disease could manifest itself in the form of skin lesions-specifically and non-specifically, ocular lesions, where nay most often appears as uveitis, usually bilateral, and could also involve the heart. Patients with neurosarcoidosis usually have involvement of the pituitary, hypothalamus, meninges and cranial nerves.

Conclusion: The diagnosis of sarcoidosis is difficult because its symptoms are often nonspecific. Diagnosis is based on exclusion of other diseases and is confirmed through imaging, histopathological, and immunological tests. In most cases, the prognosis of sarcoidosis is positive, and the disease may resolve spontaneously or under treatment. Treatment of

sarcoidosis depends on the severity of the disease and the involvement of specific organs, the most common treatment is glucocorticoids.
Keywords: sarcoidosis; granulomatosis; cardiac sarcoidosis; neurosarcoidosis; pulmonary sarcoidosis

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown etiology, characterized by the formation of non-caseating granulomas. Although the exact mechanisms of the disease are not fully understood, both genetic and environmental factors—such as infections and immune reactions—are thought to contribute to its development [1, 2]. It is more common in women, the elderly, and individuals with obesity, being twice as frequent in those with a BMI > 30 [3, 4]. Sarcoidosis can affect various organs, but it most commonly presents as parenchymal changes in the lungs, accompanied by enlargement of the hilar lymph nodes. Other common forms include the cutaneous, ocular, and neurological forms, with the pituitary, hypothalamus, meninges, and cranial nerves most often involved in the neurological form. Early diagnosis and appropriate treatment can improve patients' prognosis and quality of life [5].

Pathogenesis

The exact pathogenesis of sarcoidosis is still unknown. It is believed that an excessive response of Th1 lymphocytes to an unknown antigen leads to granulomatous inflammation. Macrophages and other antigen-presenting cells in patients with sarcoidosis are characterized by an overreaction to antigens [6]. In areas of active disease, such as lymph nodes and tissues rich in lymphoid cells, Th1 lymphocytes and macrophages accumulate and transform into epithelioid cells, forming the non-caseating granulomas characteristic of sarcoidosis. In most patients, inflammation and granuloma formation are self-limiting [7]. Cytokines that play a major role in the pathophysiology of sarcoidosis include interleukins (IL)-1, IL-2, IL-12, IL-17, IL-18, IL-23, IFN-γ, and TNF-α. The genetic basis of sarcoidosis is not well understood, but it is believed that certain HLA (human leukocyte antigen) alleles may be associated with an

increased risk of developing sarcoidosis, particularly HLA-DQB1. HLA-DRB1 may also be associated with the development of Löfgren's syndrome [8, 9].

Clinical Forms

Sarcoidosis can affect multiple organs and may also be asymptomatic, often being detected incidentally on a chest X-ray performed for another reason. Some patients may experience systemic symptoms such as fatigue, weakness, loss of appetite, weight loss, and elevated body temperature.

Pulmonary Form

Pulmonary involvement in sarcoidosis is highly variable and unpredictable, ranging from asymptomatic cases with spontaneous remission to chronic progressive disease, including pulmonary fibrosis and respiratory failure [10]. Respiratory symptoms occur in 30-53% of patients, with the most common being shortness of breath, cough, and chest pain. The cough is usually chronic, can be either productive or non-productive, and rarely occurs during sleep. The most common mechanisms causing cough in pulmonary sarcoidosis are thought to be airway irritation and damage caused directly by granulomatous inflammation. Chest pain associated with pulmonary sarcoidosis is typically pleuritic in nature and most often occurs in the subcostal and subscapular regions, often associated with coughing but unrelated to exertion. The pleuritic nature of the pain and its association with coughing suggest that it may result from musculoskeletal irritation of the chest wall due to coughing. No correlation has been found between chest pain and disease stage [11, 12, 13]. The diagnosis of pulmonary sarcoidosis requires a compatible clinical picture, supported by radiologic and pathologic studies. Based on the chest X-ray, the different stages of the disease can be distinguished:

- **Stage 0**: Normal image.
- **Stage I**: Isolated enlargement of hilar and mediastinal lymph nodes.
- **Stage II**: Enlargement of hilar and mediastinal lymph nodes with associated changes in the lung parenchyma.
- **Stage III**: Changes in the lung parenchyma, without bilateral lymphadenopathy.
- **Stage IV**: Pulmonary fibrosis.

Chest CT is much more sensitive than X-ray in detecting lung nodules and subtle fibrosis. Pulmonary nodules are usually small, ranging from 2-5 mm in diameter, and are most often located along the bronchovascular bundles, interlobular septa, and subpleural areas. Pulmonary fibrotic changes may be the predominant feature, with typical signs including obliterated

architecture, volume loss, and bronchial dilatation, usually predominating in the middle and upper lung fields [14]. The "galaxy sign," which can be observed on chest CT, is highly characteristic of sarcoidosis. It consists of a central thickening (up to several cm in diameter), usually with irregular borders, resulting from the confluence of microgranulomas. Numerous smaller granulomas (up to 3 mm) may be present around the periphery of the lesion [5]. Positron emission tomography (PET) with 18F-fluorodeoxyglucose is used to assess disease activity. Bronchoscopy, enabling lymph node biopsy, is also applicable in the diagnosis of the pulmonary form [15]. The three main complications that occur in advanced pulmonary sarcoidosis are pulmonary fibrosis, pulmonary hypertension, and respiratory infections. These can result from structural changes in the lungs and impaired immunity due to both the disease itself and its treatment [10]. Indications for drug therapy include stage II and III sarcoidosis with progression of lung parenchymal changes or worsening pulmonary dysfunction. The drugs of choice are corticosteroids. If corticosteroids are ineffective, other options such as methotrexate, azathioprine, or leflunomide should be considered. In cases of ongoing disease progression, anti-TNFα antibodies, particularly infliximab and adalimumab, may also be considered. In cases of advanced disease with severe respiratory failure, lung transplantation should be considered [14, 16].

Cardiac Form

Approximately 5% of patients with sarcoidosis have clinical cardiac involvement. In these patients, cardiac symptoms are usually more pronounced than non-cardiac symptoms. An additional 20-25% of patients have asymptomatic cardiac involvement (i.e., clinically silent), which is often detected through autopsy studies [17, 18]. The main symptoms of sarcoidosis involving the heart include atrioventricular conduction abnormalities, ventricular arrhythmias (including sudden cardiac death due to complete block), and heart failure—most commonly congestive heart failure resulting from the infiltration of the ventricular myocardium [17, 19]. In patients with suspected cardiac involvement, cardiac MRI is recommended, as its diagnostic and prognostic value is greater than that of PET (positron emission tomography) and transthoracic echocardiography [20]. The most typical features of cardiac sarcoidosis seen on echocardiography (ECHO) are interventricular thinning and segmental contractile abnormalities. However, in most patients, echocardiography is either normal or reveals nonspecific and variable abnormalities [21]. Fluorodeoxyglucose (FDG-PET) is useful in differentiating inflammatory lesions, as activated pro-inflammatory macrophages show a higher rate of glucose metabolism. A focal or focal-diffuse pattern of FDG uptake suggests an

active cardiac sarcoidosis process [22]. Endomyocardial biopsy has high specificity but low sensitivity for diagnosing cardiac sarcoidosis. Additionally, since it is an invasive procedure, it is not recommended as a first-line diagnostic test [20, 22]. Granulomatous infiltrates in the heart should be differentiated from those found in conditions such as idiopathic myocarditis, infective endocarditis, rheumatoid arthritis, Takayasu disease, or granulomatosis with vasculitis, among others [23].

Cutaneous Form

Skin lesions occur in approximately 25% of patients with sarcoidosis, more commonly in women. These lesions may precede or accompany systemic involvement [24]. Lesions are classified as:

- **Specific**: Biopsy reveals non-serous granulomas. The most common types include maculopapular lesions, subcutaneous nodules, plaques, infiltrative scars, and lupus pernio (lupus erythematosus).
- **Nonspecific**: These include erythema nodosum, and less frequently, erythema multiforme.

Skin biopsy can facilitate the early diagnosis of sarcoidosis [25, 26]. Löfgren's syndrome (LS) is one of the clinical forms of sarcoidosis that includes a cutaneous component, typically with an acute course and relatively good prognosis. The characteristic triad of this syndrome includes:

1. Symmetrical enlargement of the hilar lymph nodes
2. Joint pain accompanied by swelling of the periarticular tissues (the ankle, knee, elbow, wrist, and metacarpophalangeal joints are most often involved)
3. Erythema nodosum [27].

Löfgren's syndrome (LS) typically occurs between the ages of 25 and 40, with a second peak between the ages of 40 and 60. It is more common in women (70%). The symptoms of LS vary by gender: nodular erythema is more common in women, while joint symptoms are more frequently seen in men [28]. Whenever skin lesions typical of sarcoidosis are diagnosed, a diagnostic workup for systemic sarcoidosis is necessary. In most patients with skin lesions, organ involvement coexists, which influences the course of the disease, treatment, and prognosis [5, 29].

Ocular Form

Ocular sarcoidosis can affect all parts of the eye, but it most commonly presents as uveitis, typically bilateral, occurring in about 30-50% of patients with sarcoidosis. If not treated in time, this form can lead to blindness [5, 30]. The course is usually chronic, though acute or recurrent exacerbations are much rarer [5].

Uveitis can be classified into four types, depending on the primary site of inflammation:

- **Primary uveitis**: Affects the iris and part of the ciliary body.
- **Intermediate uveitis**: Affects the so-called flat part of the ciliary body.
- **Posterior uveitis**: Involves the choroid and retina due to their significant integration.
- **Panuveitis**: Inflammation of the entire uvea of the eye [5, 31].

Anterior uveitis is associated with a better visual prognosis than posterior uveitis, where ocular complications and central nervous system involvement are more common [30]. Topical corticosteroids are the first-line treatment. Systemic corticosteroids are indicated when uveitis does not respond to topical corticosteroids or when there is bilateral involvement of the posterior segment of the eye, especially in cases of macular edema [32]. In cases that respond poorly to corticosteroids, additional immunosuppressive therapy may be needed to maintain remission. Methotrexate is commonly used, and in special cases, monoclonal antibodies targeting tumor necrosis factor (TNF) α—such as adalimumab -can also be used [33, 34]. However, very rarely, sarcoid uveitis does not respond to combination therapy with corticosteroids and methotrexate, which may indicate either poor treatment adherence or the presence of another granulomatous disease [32, 35]. The differential diagnosis should specifically exclude ocular tuberculosis, syphilis, and viral infections [36].

The most common complications of sarcoid uveitis are cataracts, glaucoma, and macular edema-where cataracts and glaucoma are often side effects of corticosteroid use [30, 37]. Ocular inflammation associated with sarcoidosis can have a smoldering course, and patients may remain asymptomatic for long periods. Therefore, ophthalmic screening is recommended for all patients with newly diagnosed sarcoidosis, even in the absence of symptomatic ocular involvement [5, 38]. Involvement of the lacrimal glands and conjunctiva is also common, presenting clinically as dry eyes or remaining asymptomatic with a generally good visual prognosis [5].

Neurosarcoidosis Form

Neurosarcoidosis (NS) is a rare but severe manifestation of sarcoidosis, associated with significant morbidity and mortality, although it can also undergo spontaneous remission. The disease can affect both the central and peripheral nervous systems. Patients with neurosarcoidosis typically develop involvement of the pituitary gland, hypothalamus, meninges, and cranial nerves. Sarcoidosis can affect the spinal cord through several mechanisms, including infiltration of the spinal cord parenchyma, meninges, epidural space, or extradural tissues, which may lead to spinal cord compression. Meningitis occurs in 3-26% of cases and can present as either acute or chronic. Hypothalamic or pituitary involvement, resulting in subsequent endocrine dysfunction, is seen in 10-25% of cases. Endocrine disorders most commonly include anterior hypopituitarism (affecting LH, FSH, TSH, GH, ACTH), hyperprolactinemia, and simple uremia [5, 39]. A characteristic symptom of hydrocephalus (HF) may be increased intracranial pressure, resulting from impaired cerebrospinal fluid (CSF) flow due to granuloma presence. This can lead to hydrocephalus. Lesions localized within the central nervous system can cause focal neurological deficits and generalized tonic-clonic seizures [40]. Granulomatous infiltration of cranial nerve nuclei or nerves can lead to cranial neuropathy, one of the most common symptoms of neurosarcoidosis (NS). The condition typically follows a subacute, progressive course. The optic nerve, facial nerve, and vestibulocochlear nerve are most commonly affected, with unilateral localization being much more frequent [41]. Some patients may develop peripheral neuropathy, with a particular form being fine fiber neuropathy, which is accompanied by severe pain and autonomic symptoms. Less commonly, expansive lesions in the spinal canal may cause myelopathy. In some cases, patients may also develop depression or psychosis [42]. The study of choice for diagnosing neurosarcoidosis is contrast-enhanced brain MRI. On MRI, enhancement of the soft meninges and white matter lesions are observed, often resembling a demyelinating process. Cerebrospinal fluid (CSF) analysis may reveal elevated protein concentration, pleocytosis (an increase in lymphocytes and neutrophils), and the presence of oligoclonal bands. For a definitive diagnosis of neurosarcoidosis, biopsy of the lesions with histopathological examination can be helpful, but due to the invasive nature of the procedure, biopsy should be considered a last resort [39, 43].

Summary

The diagnosis of sarcoidosis can be challenging due to its nonspecific symptoms. It is primarily based on the exclusion of other diseases, as well as imaging, histopathological, and immunological studies. In most cases, the prognosis is favorable, and the disease may resolve

either spontaneously or with treatment. However, patients with sarcoidosis require long-term medical care and ongoing monitoring of organ function, particularly when the lungs, heart, or nervous system are involved. Early diagnosis and appropriate treatment can significantly improve the patient's quality of life and reduce the risk of complications.

Author's contribution

Conceptualization M.K. , supervision, project administration: M.K., M.S. J.S., methodology, software M.M., J.S., D.F. , check D.Z., M.S., formal analysis D.S. , M.B., Jadwiga I., investigation Julia I., resources D.F. D.S., data curation, writing - rough preparation, writing - review and editing,visualization, - M.B., Jadwiga I., Julia I., D.Z. and M.M.

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References:

1. Brito-Zerón P, Pérez-Álvarez R, Ramos-Casals M. Sarcoidosis. Med Clin (Barc). 2022 Aug 26;159(4):195-204. English, Spanish. doi: 10.1016/j.medcli.2022.03.009. Epub 2022 Jun 6. PMID: 35680449.

2. Spagnolo P, Bernardinello N. Sarcoidosis. Immunol Allergy Clin North Am. 2023 May;43(2):259-272. doi: 10.1016/j.iac.2023.01.008. Epub 2023 Mar 3. PMID: 37055088.

3. Dumas O, Abramovitz L, Wiley AS, et al. Epidemiology of Sarcoidosis in a Prospective Cohort Study of U.S. Women. Ann Am Thorac Soc. 2016 Jan;13(1):67-71. doi: 10.1513/AnnalsATS.201508-568BC. PMID: 26501211; PMCID: PMC4722845.

4. Cozier YC, Govender P, Berman JS. Obesity and sarcoidosis: consequence or contributor? Curr Opin Pulm Med. 2018 Sep;24(5):487-494. doi: 10.1097/MCP.0000000000000503. PMID: 29979212.

5. Sève P, Pacheco Y, Durupt F, et al. Sarcoidosis: A Clinical Overview from Symptoms to Diagnosis. Cells. 2021 Mar 31;10(4):766. doi: 10.3390/cells10040766. PMID: 33807303; PMCID: PMC8066110.

6. Serei VD, Fyfe B. The Many Faces of Cardiac Sarcoidosis. Am J Clin Pathol. 2020 Feb 8;153(3):294-302. doi: 10.1093/ajcp/aqz169. PMID: 31769474.

7. Mortaz E, Rezayat F, Amani D, et al. The Roles of T Helper 1, T Helper 17 and Regulatory T Cells in the Pathogenesis of Sarcoidosis. Iran J Allergy Asthma Immunol. 2016 Aug;15(4):334-339. PMID: 27921415.

8. Abdelghaffar M, Hwang E, Damsky W. Cutaneous Sarcoidosis. Clin Chest Med. 2024 Mar;45(1):71-89. doi: 10.1016/j.ccm.2023.08.004. Epub 2023 Oct 28. PMID: 38245372.

9. Müller-Quernheim J, Prasse A, Zissel G. Pathogenesis of sarcoidosis. Presse Med. 2012 Jun;41(6 Pt 2):e275-87. doi: 10.1016/j.lpm.2012.03.018. Epub 2012 May 15. PMID: 22595775.

10. Gupta R, Baughman RP. Advanced Pulmonary Sarcoidosis. Semin Respir Crit Care Med. 2020 Oct;41(5):700-715. doi: 10.1055/s-0040-1709495. Epub 2020 Aug 10. PMID: 32777853

11. Judson MA. The Symptoms of Pulmonary Sarcoidosis. J Clin Med. 2023 Sep 20;12(18):6088. doi: 10.3390/jcm12186088. PMID: 37763028; PMCID: PMC10532418.

12. Judson, M.A. Chopra, A. Conuel, et al. The Assessment of Cough in a Sarcoidosis Clinic Using a Validated instrument and a Visual Analog Scale. Lung 2017, 195, 587–594.

13. Sinha, A.; Lee, K.K.; Rafferty, G.F.; et al. Predictors of Objective Cough Frequency in Pulmonary Sarcoidosis. Eur. Respir. J. 2016, 47, 1461–1471.

14. Ramachandraiah V, Aronow W, Chandy D. Pulmonary sarcoidosis: an update. Postgrad Med. 2017 Jan;129(1):149-158. doi: 10.1080/00325481.2017.1251818. Epub 2016 Nov 2. PMID: 27766929.

15. Iranmanesh AM, Washington L. Pulmonary Sarcoidosis: A Pictorial Review. Semin Ultrasound CT MR. 2019 Jun;40(3):200-212. doi: 10.1053/j.sult.2018.12.001. Epub 2019 Jan 4. PMID: 31200869.

16. Belperio JA, Shaikh F, Abtin FG, et al. Diagnosis and Treatment of Pulmonary Sarcoidosis: A Review. JAMA. 2022 Mar 1;327(9):856-867. doi: 10.1001/jama.2022.1570. PMID: 35230389.

17. Kandolin R, Lehtonen J, Airaksinen J, et al. Cardiac sarcoidosis:epidemiology, characteristics, and outcome over 25 years in anationwide study. Circulation 2015;131(07):624–632

18. Simonen P, Lehtonen J, Kandolin R, et al. F-18-fluorodeoxyglucose positron emission tomography-guided sampling of mediastinal lymph nodes in the diagnosis of cardiac sarcoidosis. Am J Cardiol. 2015 Nov 15;116(10):1581-5. doi: 10.1016/j.amjcard.2015.08.025. Epub 2015 Sep 3. PMID: 26411357.

19. Ribeiro Neto ML, Jellis CL, Cremer PC, et al. Cardiac Sarcoidosis. Clin Chest Med. 2024 Mar;45(1):105-118. doi: 10.1016/j.ccm.2023.08.006. Epub 2023 Sep 4. PMID: 38245360.

20. Kysperska K, Kuchynka P, Palecek T. Cardiac sarcoidosis: from diagnosis to treatment. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2021 Nov;165(4):347-359. doi: 10.5507/bp.2021.057. Epub 2021 Oct 14. PMID: 34671170.

21. Kouranos V, Tzelepis GE, Rapti A, et al. Complementary role of CMR to conventional screening in the diagnosis and prognosis of cardiac sarcoidosis. JACC Cardiovasc Imaging 2017;10(12): 1437–1447

22. Birnie DH. Cardiac Sarcoidosis. Semin Respir Crit Care Med. 2020 Oct;41(5):626-640. doi: 10.1055/s-0040-1712535. Epub 2020 Jun 27. PMID: 32593175.

23. Serei VD, Fyfe B. The Many Faces of Cardiac Sarcoidosis. Am J Clin Pathol. 2020 Feb 8;153(3):294-302. doi: 10.1093/ajcp/aqz169. PMID: 31769474.

24. Randhawa KS, Lee BW, Micali G, et al. Cutaneous sarcoidosis: Lupus pernio and more. Ital J Dermatol Venerol. 2022 Jun;157(3):220-227. doi: 10.23736/S2784-8671.21.07027-4. Epub 2022 Mar 11. PMID: 35274876.

25. Caplan A, Rosenbach M, Imadojemu S. Cutaneous Sarcoidosis. Semin Respir Crit Care Med. 2020 Oct;41(5):689-699. doi: 10.1055/s-0040-1713130. Epub 2020 Jun 27. PMID: 32593176.

26. Mañá J, Marcoval J. Skin manifestations of sarcoidosis. Presse Med. 2012 Jun;41(6 Pt 2):e355-74. doi: 10.1016/j.lpm.2012.02.046. Epub 2012 May 9. PMID: 22579238.

27. Karakaya B, Kaiser Y, van Moorsel CHM, Grunewald J. Löfgren's Syndrome: Diagnosis, Management, and Disease Pathogenesis. Semin Respir Crit Care Med. 2017 Aug;38(4):463-476. doi: 10.1055/s-0037-1602380. Epub 2017 Jul 27. PMID: 28750461.

28. Mendez Ezcurra LI, Castro HM. Löfgren syndrome. Med Clin (Barc). 2020 Apr 24;154(8):328-329. English, Spanish. doi: 10.1016/j.medcli.2019.05.039. Epub 2019 Aug 16. PMID: 31427151.

29. Błaszczyk M. Cutaneous sarcoidosis: clinical presentation and diagnostic difficulties. Dermatology Review/Przegląd Dermatologiczny. 2012;99(3):185-194.

30. Groen F, Rothova A. Ocular Involvement in Sarcoidosis. Semin Respir Crit Care Med. 2017 Aug;38(4):514-522. doi: 10.1055/s-0037-1602382. Epub 2017 Jul 27. PMID: 28750464.

31.Takase H. Characteristics and management of ocular sarcoidosis. Immunol Med. 2022 Mar;45(1):12-21. doi: 10.1080/25785826.2021.1940740. Epub 2021 Jul 2. PMID: 34214013.

32. Sève P, Jamilloux Y, Tilikete C, et al. Ocular Sarcoidosis. Semin Respir Crit Care Med. 2020 Oct;41(5):673-688. doi: 10.1055/s-0040-1710536. Epub 2020 Aug 10. PMID: 32777852.

33. Burek-Michalska A, Turno-Kręcicka A. Adalimumab in the treatment of non-infectious uveitis. Adv Clin Exp Med. 2020 Oct;29(10):1231-1236. doi: 10.17219/acem/125431. PMID: 33125196.

34. Al-Julandani DA, Bagri NK, Tsang N, et al. Outcome of adalimumab monotherapy in paediatric non-infectious uveitis. Pediatr Rheumatol Online J. 2023 Mar 2;21(1):21. doi: 10.1186/s12969-023-00794-y. PMID: 36864437; PMCID: PMC9983208.

35. Sève P, Jacquot R, El Jammal T, et al. Uvéites sarcoïdosiques : regards croisés de l'ophtalmologiste et de l'interniste Rev Med Interne. 2023 Mar;44(3):112-122. French. doi: 10.1016/j.revmed.2022.10.001. Epub 2023 Jan 13. PMID: 36642624.

36. Bazewicz M, Heissigerova J, Pavesio C, et al. Ocular sarcoidosis in adults and children: update on clinical manifestation and diagnosis. J Ophthalmic Inflamm Infect. 2023 Sep 18;13(1):41. doi: 10.1186/s12348-023-00364-z. PMID: 37721575; PMCID: PMC10507006.

37. Lobo A, Barton K, Minassian D, et al. Visual loss in sarcoid-related uveitis. Clin Exp Ophthalmol. 2003 Aug;31(4):310-6. doi: 10.1046/j.1442-9071.2003.00666.x. PMID: 12880455.

38. Rothova A. Ocular involvement in sarcoidosis. Br J Ophthalmol. 2000 Jan;84(1):110-6. doi: 10.1136/bjo.84.1.110. PMID: 10611110; PMCID: PMC1723211.

39. Bradshaw MJ, Pawate S, Koth LL, et al.. Neurosarcoidosis: Pathophysiology, Diagnosis, and Treatment. Neurol Neuroimmunol Neuroinflamm. 2021 Oct 4;8(6):e1084. doi: 10.1212/NXI.0000000000001084. PMID: 34607912; PMCID: PMC8495503.

40. Langrand C, Bihan H, Raverot G, et al. Hypothalamo-pituitary sarcoidosis: a multicenter study of 24 patients. QJM. 2012 Oct;105(10):981-95. doi: 10.1093/qjmed/hcs121. Epub 2012 Jun 30. PMID: 22753675.

41. Carlson ML, White JR Jr, Espahbodi M, et al. Cranial base manifestations of neurosarcoidosis: a review of 305 patients. Otol Neurotol. 2015 Jan;36(1):156-66. doi: 10.1097/MAO.0000000000000501. PMID: 25029595.

42. Krumholz A, Stern BJ. Neurologic manifestations of sarcoidosis. Handb Clin Neurol. 2014;119:305-33. doi: 10.1016/B978-0-7020-4086-3.00021-7. PMID: 24365304.

43. Rogoziewicz, M., Borkowska-Konieczna, A., & Kozubski, W. (2015). Neurosarkoidoza—patomechanizm, objawy kliniczne, diagnostyka i leczenie. *Polski Przegląd Neurologiczny*, *11*(1), 12-20.