Sarcoidosis: A comprehensive review and update for the dermatologist

Part II. Extracutaneous disease

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After completing this learning activity, the participants should be able to recognize the various manifestations of systemic sarcoidosis; select the appropriate laboratory and imaging tests for the diagnosis and evaluation of systemic sarcoidosis; and monitor patients with skin sarcoidosis for the development of extracutaneous sarcoidosis.

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Sarcoidosis is a multisystemic, granulomatous disease with protean manifestations and variable prognosis. Because the skin can be the only organ in which the disease is recognized, dermatologists may be responsible for the care of sarcoidosis patients. Therefore, dermatologists should be cognizant of the disease's extracutaneous manifestations to assure appropriate evaluation and treatment. Part II of this review describes the diagnostic approach and management of the extracutaneous manifestations of sarcoidosis. (J Am Acad Dermatol 2012;66:719.e1-e10.)

Sarcoidosis is an inflammatory disorder that is characterized by noncaseating granulomas in one or more organ systems. Health practitioners caring for patients with sarcoidosis need to remain vigilant concerning progression of the disease and additional sarcoidosis organ involvement. The diagnosis of sarcoidosis may be problematic because there is no definitive diagnostic test for the disease. The establishment of a diagnosis requires histopathologic evidence of noncaseating granulomatous inflammation in the presence of characteristic clinical and/or radiographic findings. The manifestations of sarcoidosis are highly variable and depend on the organs involved. Disease severity may range from an asymptomatic state to a life-threatening condition. When the disease presents with skin lesions, the dermatologist may be the main health care provider for the patient. Consequentially, dermatologists should assure that their patients are assessed for extracutaneous disease and are referred to appropriate specialists when necessary.

CAPSULE SUMMARY

- Dermatologists play an important role in the diagnosis and initial evaluation of sarcoidosis because the skin is involved in 20% to 35% of all cases and is often the initially affected organ.
- Dermatologists need to initiate or arrange assessment for potential extracutaneous involvement at the time of diagnosis and ensure ongoing monitoring and treatment of extracutaneous disease.
- Awareness of the signs and symptoms associated with extracutaneous sarcoidosis by treating dermatologists enhances the care of patients with this challenging disease.

DIAGNOSIS AND MANAGEMENT OF SARCOIDOSIS

Key points

- **The diagnosis of sarcoidosis is strongly supported by the presence of noncaseating granulomas on histology**
- **The presence of granulomatous inflammation is insufficient for the diagnosis of sarcoidosis because there are many causes of granulomatous inflammation. Additional requirements for the diagnosis include characteristic clinical and/or radiologic findings and adequate exclusion of alternative granulomatous diseases**
- **Sarcoidosis is a systemic disease that may require a consultation from several specialists**

There is no diagnostic test for sarcoidosis. Clinical and radiographic data that support a diagnosis of sarcoidosis are listed in Table I.[1] An algorithm to establish a diagnosis of systemic sarcoidosis has been proposed (Fig 1).[1] Most cases of cutaneous sarcoidosis are diagnosed by a biopsy specimen of characteristic skin lesions with corroborative histology and exclusion of other causes of granulomatous inflammation. Infectious conditions that need to be excluded include tuberculosis, histoplasmosis, coccidiomycosis, leprosy, leishmaniasis, and syphilis. Noninfectious conditions that may cause granulomatous inflammation include beryllium, zirconium, and tattoo pigments.[2]

Angiotensin-converting enzyme (ACE) serum levels are increased in 60% of patients with sarcoidosis,[3] and serum ACE has therefore been considered a potential diagnostic test for sarcoidosis. Elevations of serum ACE higher than 50% of the upper limit of normal are highly suggestive of the disease.[4] Kruit et al[5] found that ACE levels are influenced by the insertion/deletion polymorphism in the ACE gene, and suggested that correcting serum ACE values according to genotype improve the diagnostic and prognostic values of the test.[5] However, even with correction for genotype, serum ACE levels are not

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Abbreviations used:

ACE:	angiotensin-converting enzyme
MRI:	magnetic resonance imaging
67Ga:	gallium 67 scintigraphy
18F-FDG PET:	fluorine-18-fluorodeoxyglucose positron emission tomography

specific enough for use as a diagnostic test.[4] Because ACE is produced by epithelioid cells in granulomas, it has been proposed that elevated serum levels in sarcoidosis correlate with the granuloma burden.[6] However, serum ACE levels have not been shown to be valuable in predicting prognosis or determining the need for treatment.[7] In addition, baseline ACE levels vary between individuals.[8,9]

Because patients with cutaneous sarcoidosis often have systemic involvement at the time of diagnosis or a few years after,[10,11] all patients with skin sarcoidosis should be initially evaluated for extracutaneous disease. Table II outlines the recommended assessment for patients diagnosed with sarcoidosis.[12]

Over the course of the disease, previously uninvolved organs may develop sarcoidosis, whereas affected organs may heal or become impaired.[13] There are currently no established guidelines for monitoring patients for the development of extracutaneous sarcoidosis who have disease limited to the skin. However, we propose an approach to monitoring for the development of extracutaneous disease in Table III. If new or worsening extracutaneous involvement is suspected on the basis of symptoms, the physical examination, or laboratory abnormalities, referral to an appropriate specialist for further evaluation and management may be required.

Several imaging modalities, including chest radiographs, high-resolution computed tomography, magnetic resonance imaging (MRI), gallium 67 scintigraphy (67Ga), and fluorodeoxyglucose positron emission tomography (18F-FDG PET), may be used to indicate organ involvement. However, in most cases, a diagnostic biopsy specimen is preferred because it is more specific. Two exceptions are with cardiac sarcoidosis and neurosarcoidosis, whereby biopsy is highly invasive and imaging studies are relatively specific in the proper clinical context.

ORGAN INVOLVEMENT

Pulmonary disease

Key points

- **The lung is the most commonly affected organ in sarcoidosis**
- **All patients, even those without respiratory symptoms, should be evaluated with a chest radiograph and pulmonary function tests**

Table I. Clinicoradiographic data supporting or weakening the likelihood of sarcoidosis*

	Strengthens	Weakens
Demographics	• US African American • Northern European	• Age <18 y • Age >50 y (male)
Medical history	• Asymptomatic (in patients with CXR findings) • Symptoms involving >2 organs frequently effected in sarcoidosis • No history of smoking • Family history of sarcoidosis	• Exposure to tuberculosis • Exposure to beryllium • Exposure to organic bioaerosol • Intravenous drug use
Laboratory data	• Elevated serum ACE levels	
Radiographic findings	• Bilateral hilar adenopathy (especially if asymptomatic) • Disease along the bronchovascular bundle on HRCT	

ACE, Angiotensin-converting enzyme; *CXR*, chest radiograph; *HRCT*, high-resolution computed tomography.
*Modified from Judson.[1]

Common respiratory symptoms of pulmonary sarcoidosis include dyspnea, cough, wheezing, chest pain, and tightness.[3] Chest radiographs show abnormalities at some point in the disease course in more than 90% of cases of sarcoidosis.[14,15] Common pulmonary radiographic findings include bilateral hilar adenopathy, mediastinal adenopathy, and parenchymal infiltrates, especially in the upper lobes.[16]

The chest radiographic findings of pulmonary sarcoidosis are classified into five stages (Table IV).[17] A Danish study[18] evaluating the radiographic stages of sarcoidosis over time reported that about 85% had stability, improvement, or resolution of radiographic abnormalities in the first 2 years. More than half of patients with sarcoidosis are initially asymptomatic and have bilateral hilar lymphadenopathy (stage I) on the primary chest radiograph.[17] Patients with stage IV chest radiographs usually have chronic, symptomatic pulmonary disease with irreversible fibrosis on chest radiograph,[17,19] and may develop complications such as pneumothorax, cor pulmonale, mycetomas, or respiratory failure.[17,19] Pulmonary function tests are abnormal in 20% of patients with stage I chest

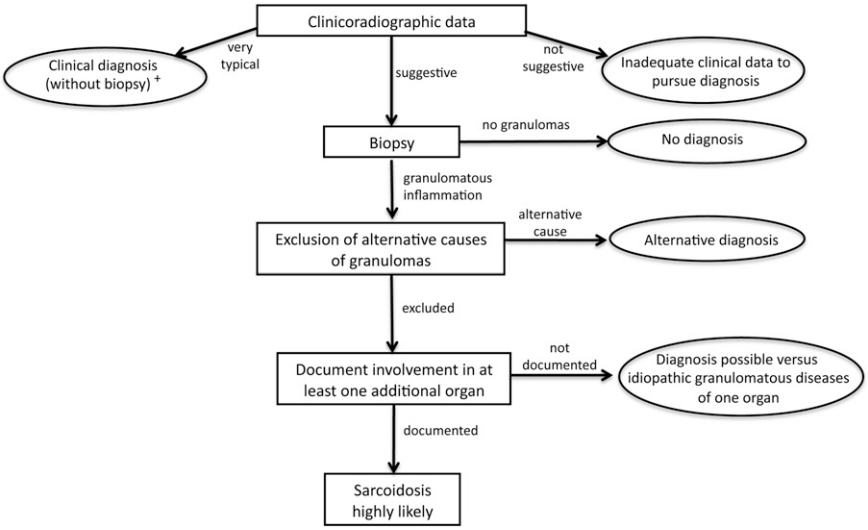

Fig 1. A stepwise approach for the diagnosis of systemic sarcoidosis. †There are particular clinical presentations that are so typical of sarcoidosis that only exclusion of other diseases is required for the diagnosis; no biopsy specimen is needed. Some of these presentations include Löfgren syndrome, Heerfordt syndrome, and asymptomatic bilateral hilar adenopathy on chest radiography. (Modified from Judson.[1])

Table II. Recommended initial screening for all suspected or diagnosed cases of sarcoidosis*

Detailed history: symptoms that may suggest sarcoidosis organ involvement (eg, cough, eye symptoms) and occupational/environmental exposure history that may suggest an alternative diagnosis (eg, beryllium exposure suggesting chronic beryllium disease, bird exposure suggesting hypersensitivity pneumonitis)
Physical examination: may reveal additional organ involvement (neurologic deficits, cardiac rhythm disturbances, or red eyes)
Posteroanterior chest radiograph
Pulmonary function test: spirometry, diffusion capacity, and total lung capacity
Electrocardiogram and echocardiogram
Serum chemistries: calcium, creatinine, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase to examine liver and renal function
Urine analysis to evaluate for nephrolithiasis
Complete blood cell count
Routine ophthalmologic examination: slit-lamp and fundoscopic eye examination
Tuberculin skin test or interferon release assay to exclude the diagnosis of tuberculosis and as a precaution should immunosuppressive therapies be required

*Modified from Hunninghake et al.[12]

radiographs and in 40% to 70% of patients with higher stages.[4] Although pulmonary function and prognosis tend to worsen in groups of pulmonary sarcoidosis patients with higher radiographic stages,[18,20] this staging scheme cannot be used in individual patients to assess pulmonary dysfunction, disease activity, the need for treatment, or to reliably predict prognosis.[17]

Sarcoidosis is an interstitial lung disease that causes restrictive lung abnormalities (reduced total lung capacity and forced vital capacity). However, sarcoidosis may cause significant airway obstruction from granulomatous involvement of the airways or distortion of airways from pulmonary fibrosis. Therefore, pulmonary sarcoidosis may mimic other obstructive lung diseases.[21] Pulmonary hypertension may occur with sarcoidosis by a number of mechanisms. Such patients typically present with dyspnea and increased oxygen requirements. Sarcoidosis-associated pulmonary hypertension is potentially life threatening and portends a poor prognosis.[22,23]

OCULAR SARCOIDOSIS

Key points

- **All sarcoidosis patients should have routine ophthalmologic examinations even if they have no ocular symptoms**
- **Ocular sarcoidosis should always be treated, even in patients without eye symptoms, because such patients may develop permanent vision impairment**
- **Anterior uveitis is the most common manifestation of ocular sarcoidosis**
- **Optic neuritis, presenting with partial or total loss of vision or color acuity, is an emergency that can cause blindness if not treated immediately**

Table III. Monitoring recommendations for cutaneous sarcoidosis

Interval of evaluation
- Treated patients should be examined at least once every 6 months
- Patients with stable disease that do not require therapy may be followed annually
- Patients should be followed for at least 3 years after therapy has been discontinued

Evaluation at every visit
- Medical history: skin lesions, weight loss, fever, fatigue, dyspnea, shortness of breath, cough, ocular problems, upper airway complaints, symptoms of nephrolithiasis, palpitations, syncope, symptoms of congestive heart failure, and neurologic complaints*
- Physical examination: lung, cardiac, abdomen, and skin examinations, palpation of lymph nodes, and neurologic examination*

Tests ordered annually
- Ophthalmologic examination: slit-lamp and fundoscopic eye examination
- Electrocardiogram (controversial)
- Chest radiograph
- Pulmonary function tests
- Complete blood count
- Serum chemistries

*Perform appropriate additional testing if the medical history or physical examination suggests potential specific organ involvement.

Table IV. Radiographic stages of thoracic sarcoidosis*

Stage	Bilateral hilar adenopathy	Parenchymal infiltrates	Fibrosis
0	Absent	Absent	Absent
1	Present	Absent	Absent
2	Present	Present	Absent
3	Absent	Present	Absent
4	Variable	Variable	Present

*Modified from Judson et al.[17]

Table V. Manifestations of ocular sarcoidosis

Opthalmologic feature	Prevalence*	Symptoms
Anterior uveitis	66-70%	Asymptomatic, blurry vision, red eyes, painful eyes, and photophobia
Intermediate uveitis	Unknown	Painless blurry vision and floaters
Posterior uveitis	14-28%	Floaters, blurry vision, and photophobia
Lids and orbit	26%	Lids: dry eyes and lid granulomas; orbit: diplopia, pain with movement, and eye entrapment[28]
Optic neuropathy	<1-7%	Rapid loss of vision or color vision

*Prevalence of ophthalmologic findings in patients with ocular sarcoidosis.

Ocular sarcoidosis is present in 10% to 50% of American and European patients and in 50% to 90% of Japanese patients with sarcoidosis.[24] African Americans are more likely than whites to have eye involvement.[25] All patients should be regularly followed with ophthalmologic examinations because permanent ocular damage may result from initial asymptomatic eye involvement (Table V).[24,26]

Anterior uveitis, the most common ocular manifestation, occurs in approximately two thirds of ocular sarcoidosis cases.[26] Symptoms of anterior uveitis include blurry vision, red eye, photophobia, and eye pain. Notably, one third of the time, acute sarcoid anterior uveitis may cause no symptoms.[27] However, it still has the potential to permanently impair vision; therefore, all newly diagnosed sarcoidosis patients should be evaluated by an ophthalmologist even if they have no ocular symptoms. The prognosis of acute anterior uveitis is better than chronic uveitis, which often causes secondary complications, such as glaucoma, band keratopathy, and cataracts.[26,28] It may be difficult to distinguish sarcoidosis complications from those caused by corticosteroid therapy. Posterior uveitis may lead to permanent retinal damage and requires aggressive therapy. Posterior uveitis is associated with an increased risk of central nervous system involvement.[26] Uveitis has been associated with specific skin manifestations, such as maculopapular eruptions,[29] infiltrative scar sarcoidosis,[29] and lupus pernio.[10] Optic neuritis usually presents with blurring and partial loss of vision or color acuity and is an emergency that requires immediate treatment to prevent permanent blindness in the affected eye.

CARDIAC SARCOIDOSIS

Key points

- **All patients with sarcoidosis should be evaluated for cardiac sarcoidosis. At a minimum, this evaluation should include a medical history directed at symptoms of left ventricular dysfunction and cardiac arrhythmia and an electrocardiogram**
- **Manifestations range from asymptomatic electrocardiographic abnormalities to fatal arrhythmias and heart failure**

Table VI. Frequency of cardiac sarcoidosis symptoms*

Presentation	Frequency†
Atrioventricular block	26-62%
Bundle branch block	12-61%
Ventricular tachycardia	2-42%
Congestive heart failure	10-30%
Sudden death	12-65%

*Modified from Kim et al.[34]
†Frequency of cardiac presentations in patients with cardiac sarcoidosis.

Table VII. Frequency of neurologic manifestations in patients with neurosarcoidosis*

Neurologic features	Frequency
Cranial neuropathy	50-75%
Parenchymal brain lesions	50%
Cognitive/behavioral manifestations	20%
Meningeal disease	10-20%
Peripheral neuropathy	15%
Spinal lesions	5-10%
Seizure	5-10%
Myopathy	1.4-2.3%

*Modified from Terushkin et al.[53]

- **Positron emission tomographic and gadolinium-enhanced cardiac magnetic resonance imaging scans are useful diagnostic imaging techniques for assessing cardiac sarcoidosis**

Cardiac sarcoidosis often remains clinically undetected throughout the patient's lifetime. Although only 5% of sarcoidosis cases have clinical manifestations of cardiac disease,[30] an autopsy study of 84 patients revealed that 27% of patients with sarcoidosis had granulomatous infiltration of the heart.[31] Cardiac involvement accounts for 13% to 25% of sarcoidosis-related deaths in the United States[31] compared with 58% to 85% in Japan.[32,33]

While cardiac sarcoidosis is often asymptomatic, the initial disease presentation may be sudden death (Table VI).[34] The clinical course is dependent on the extent of myocardial involvement and the location of the granulomas.[34] The disease can cause conduction abnormalities, arrhythmias, heart failure, and pericardial effusions. Associated symptoms include dyspnea, palpitations, syncope, dizziness, chest pain, orthopnea, and peripheral edema. Cardiac sarcoidosis should be considered in any individual, especially a young person, with impairment of the conducting system or heart failure without apparent cause.[35] In support of this contention, an observational study from Helsinki University Central Hospital revealed that 19% of patients under 55 years of age with a pacemaker for unexplained atrioventricular block had biopsy-proven cardiac sarcoidosis.[36]

It has been suggested that all patients with sarcoidosis should be evaluated with an electrocardiogram.[34] However, the presence of cardiac symptoms, such as palpitations, presyncope, or syncope, and Holter monitoring, appears to be more sensitive than electrocardiography for the detection of cardiac sarcoidosis.[37] Some have recommended echocardiography as a screening test for cardiac sarcoidosis, despite a low sensitivity and variable specificity.[34]

In terms of the diagnosis of cardiac sarcoidosis, endomyocardial biopsy is a specific test, but it is not routinely performed because the diagnostic yield is extremely low. In one study, the diagnostic yield of endomyocardial biopsy for cardiac sarcoidosis was only 36% from patients with ventricular dysfunction and 7% in those with conduction disturbances.[38]

Because of the poor diagnostic yield and invasiveness of endomyocardial biopsy, the diagnosis of cardiac sarcoidosis is often established using noninvasive imaging studies such as 67Ga scanning, MRI, or cardiac PET scanning.[39] PET scanning with 18F-FDG detects active disease and fibrosis in the myocardium,[40,41] and its sensitivity ranges from 82% to 100%.[42,43] Along with PET, gadolinium-enhanced cardiac MRI is favored as a diagnostic test for cardiac sarcoidosis.[44,45] Smedema et al[46] reported a sensitivity of 100% and specificity of 78% for cardiac MRI, and concluded that this type of imaging is both a useful and cost-effective tool to determine cardiac involvement.[46]

In terms of monitoring cardiac sarcoidosis, ejection fraction determination to assess myocardial function and 24-hour Holter monitoring to detect impairment of the conducting system have also been used.[39] The frequency of monitoring and the choice of test depend on the clinical signs and symptoms. All patients with evidence of left ventricular dysfunction require regular assessment of ejection fraction, segmental wall motion, and left ventricular volume. All cases of left ventricular dysfunction should also be monitored for heart block and arrhythmias. Evaluation for cardiac arrhythmias should be considered in any patient with cardiac sarcoidosis, because the initial presentation may be sudden death.[34]

CENTRAL NERVOUS SYSTEM DISEASE

Key points

- **Sarcoidosis may affect all portions of the nervous system. There is a predilection for the base of the brain**

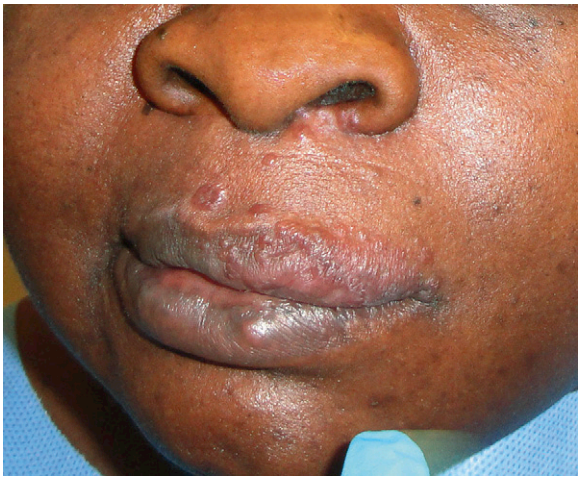

Fig 2. Facial nerve palsy with granulomatous papules.

- **The most common manifestation of neurosarcoidosis is a cranial neuropathy**
- **Magnetic resonance imaging is the imaging modality of choice for the diagnosis and management of neurosarcoidosis**

Involvement of the nervous system occurs in approximately 5% to 15% of patients with sarcoidosis.[47] Neurosarcoidosis usually presents within 2 years of the onset of sarcoidosis.[48,49] Cranial nerve involvement is a common presentation of neurosarcoidosis (Table VII), particularly a seventh cranial nerve palsy that causes facial paralysis in a lower motor neuron distribution (Bell's palsy; Fig 2).[50] Additional manifestations of neurosarcoidosis include central nervous system mass lesions, neuroendocrine abnormalities, encephalopathy, seizures, cognitive and behavioral symptoms, and spinal sarcoidosis.[51-54]

Neural tissue biopsy has a high risk of complications; therefore, the diagnosis of neurosarcoidosis is generally made by indirect methods.[53] In addition, because isolated neurologic disease is rarely the sole manifestation of sarcoidosis, most patients have extraneural disease from which a biopsy specimen can be obtained to establish a tissue diagnosis.[48] MRI imaging with and without intravenous gadolinium contrast is often used to confirm neurosarcoidosis.[53] However, MRI findings are not specific for sarcoidosis[55]; therefore, the presence of MRI findings requires correlation with the clinical features to ensure the diagnosis of neurosarcoidosis. In addition, the sensitivity of MRI scanning for neurosarcoidosis is not ideal, because it was reported at 85% in one study.[55] Abnormal cerebral spinal fluid findings include lymphocytic pleocytosis and decreased glucose and elevated protein levels. These findings have a low specificity and sensitivity,[53,56] but they support the diagnosis of neurosarcoidosis in the proper clinical context.[57]

OTHER ORGAN INVOLVEMENT

Key points

- **Sarcoidosis may involve other organs, including the liver, spleen, kidneys, and upper respiratory tract**
- **Calcium dysregulation, caused by the overproduction of active vitamin D, may result in hypercalcemia and hypercalciuria**
- **Peripheral lymphadenopathy and hematologic abnormalities may occur**

The reported frequency of hepatic sarcoidosis varies greatly depending on the method of detection. Hepatic granulomas are present in 50% to 65% of liver biopsy specimens from patients with sarcoidosis.[58] Elevated serum liver functions tests may be detected in up to 35% of patients.[59] However, signs or symptoms of liver involvement manifest in only 5% to 15% of patients.[60-62] Treatment is only necessary in symptomatic cases.[63] Significant hepatic dysfunction with severe hyperbilirubinemia or impaired synthetic ability is rare in hepatic sarcoidosis and, therefore, alternative causes should be excluded.[64] Splenic involvement occurs in 10% to 50% of sarcoidosis patients and requires no treatment in the absence of symptoms.[64] Sarcoidal lesions of the upper airways are underappreciated.[65] The nasal sinuses are the most likely affected portion of the upper airway, and typical symptoms include crusting, nasal congestion, and epistaxis.[64,65] Involvement of the thyroid gland,[66] breast,[67] reproductive tract, and other organs of the gastrointestinal tract[63] is rare.

Acute sarcoid arthritis is often associated with erythema nodosum and affects up to 40% of sarcoidosis patients.[68] It can precede other manifestations of sarcoidosis by months.[64] The ankles are the most commonly involved joints, followed by the knees.[68,69] Notably, acute arthritis usually has a benign course and resolves in 3 to 6 months.[70] Chronic sarcoid arthritis affects only 0.2% of sarcoid patients,[71] and if untreated can progress to permanent joint destruction.[72]

Osseous lesions are usually asymptomatic and rarely require treatment.[73] Musculoskeletal involvement in sarcoidosis is often subclinical.[53,68] Retrospective studies have reported that less than 2% of patients have symptomatic muscle disease.[68,74-76] Similar to hepatic sarcoidosis, biopsy specimens from muscles of asymptomatic patients have revealed noncaseating granulomas in 50% to 80% of patients.[74,77,78] It is important to differentiate sarcoid myopathy from steroid-induced myopathy.

Abnormal calcium metabolism commonly develops with sarcoidosis. The prevalence of hypercalciuria (40-62%) is much greater than the prevelance of hypercalcemia (5-10%).[79] Measurement of 24-hour urinary secretion of calcium has been recommended by some authors initially and on a routine basis.[3,80] This may be particularly prudent in white patients, who have a much higher frequency of disordered calcium metabolism in sarcoidosis than African Americans.[25] Impaired calcium regulation in sarcoidosis is primarily attributed to the increased production of 1,25 di-hydroxy vitamin D.[81] 1,25 di-hydroxy vitamin D promotes intestinal calcium absorption and urinary calcium excretion. 1,25 di-hydroxy vitamin D is overproduced in sarcoidosis because of increased conversion from 25-hydroxy vitamin D in activated macrophages. This is clinically important because 25-hydroxy vitamin D is routinely measured to determine vitamin D status in patients. A low 25-hydroxy vitamin D level in an active sarcoidosis patient may be the result of excessive conversion of 25-hydroxy vitamin D to 1,25-hydroxy vitamin D. Treatment of such patients for a "low vitamin D level" may have disastrous consequences, such as nephrolithiasis or renal failure.[82-84] To complicate matters further, vitamin D and calcium dysregulation, as well as chronic steroid use, may affect bone health.[83] For the reasons outlined above, a detailed analysis of vitamin D status is required before administering vitamin D to patients with sarcoidosis. Bisphosphonates may be recommended for sarcoidosis patients with osteoporosis or those subjected to chronic corticosteroids.[84]

Peripheral lymphadenopathy is present in approximately 10% of sarcoidosis cases.[85] Hematologic abnormalities, especially peripheral lymphopenia, anemia, and pancytopenia, eventually develop in 30% of patients.[86] The occurrence of thrombocytopenia in patients with sarcoidosis has been noted.[87,88]

Because of the heterogeneous manifestations of sarcoidosis, several syndromes with specific constellations of physical signs and symptoms have been recognized. Löfgren syndrome is characterized by the acute onset of arthritis, arthralgia, erythema nodosum, bilateral hilar lymphadenopathy, and fever.[89] This combination of findings is a very typical presentation of sarcoidosis; in the proper clinical context, the diagnosis of sarcoidosis can be assumed without a biopsy specimen of the affected tissue.[1] The same could be said for Heerfordt syndrome, also known as uveoparotid fever, which manifests as uveitis, parotid enlargement, facial nerve palsy, and fever.[90] Heerfordt syndrome accounts for a small percentage of sarcoidosis cases, but when present is strongly indicative of the disease. Mikulicz syndrome is characterized by bilateral enlargement of the parotid, sublingual, lacrimal, or submandibular glands.[91] Historically, Mikulicz syndrome has been considered a form of Sjögren syndrome, but it has also been associated with many different diseases, including lymphoma, lupus, and, rarely, sarcoidosis.[92]

SUMMARY

In nearly one third of cases, skin lesions are the presenting manifestation of sarcoidosis. Therefore, dermatologists often establish the diagnosis and may be the primary physician providing medical care. Without prompt recognition and early treatment, systemic sarcoidosis can cause significant morbidity. To that end, a general knowledge of the signs, symptoms, and proper evaluation of extracutaneous sarcoidosis is critical to the patient's overall care. The initial evaluation of all patients diagnosed with sarcoidosis should include a detailed history, physical examination, and laboratory studies aimed at excluding alternative causes of granulomatous inflammation and assessing sarcoidosis involvement of various organs. Additional studies may be warranted if this evaluation raises clinical suspicion for specific organ involvement. Because of the disease's variable clinical course, periodic evaluations of existing organ involvement and monitoring for new organ involvement should be undertaken.

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