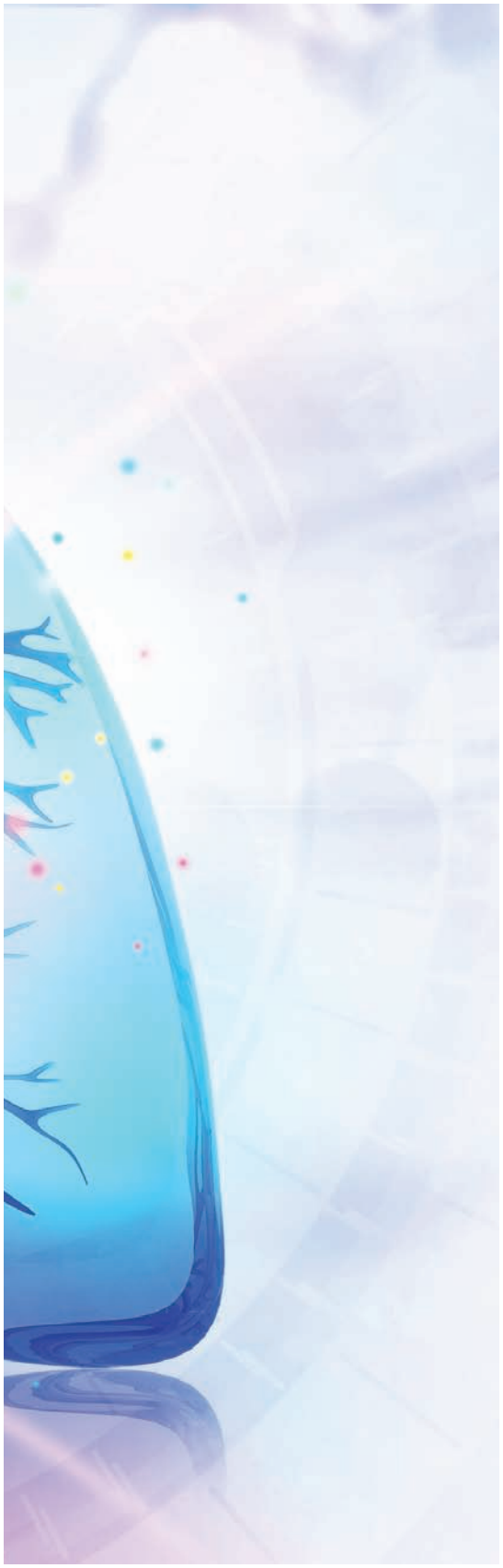

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Sarcoidosis: What nurses need to know

BY ANNA CRAWFORD AND LISA RUTH-SAHD, DEd, RN, CCRN, CEN, CNE, CCFP, ANEF

Abstract: Pulmonary sarcoidosis is a multisystem disease characterized by sarcoid granulomas, vasculitis, and degrees of necrosis with unknown etiology. This article discusses the pathophysiology of sarcoidosis and its medical and nursing management. A case presentation highlights some long-term concerns with this chronic disease.

Keywords: granulomas, inflammatory lung disease, pulmonary, sarcoidosis

Case presentation: *CS is a 22-year-old White female with a history of asthma who presented to the ED with severe stabbing right lateral chest pain and shortness of breath. CS also reported extreme fatigue for several months after a viral upper respiratory infection and pneumonia. CS denied recent weight loss. She was adopted from Russia and is not aware of her family history.*

She reported waking up early in the morning due to a "constant stabbing pain" that increased with deep inspiration and expiration. She rated the pain as a 9/0-10 on the numerical pain rating scale, and said that it aggravated with exertion and would not go away.

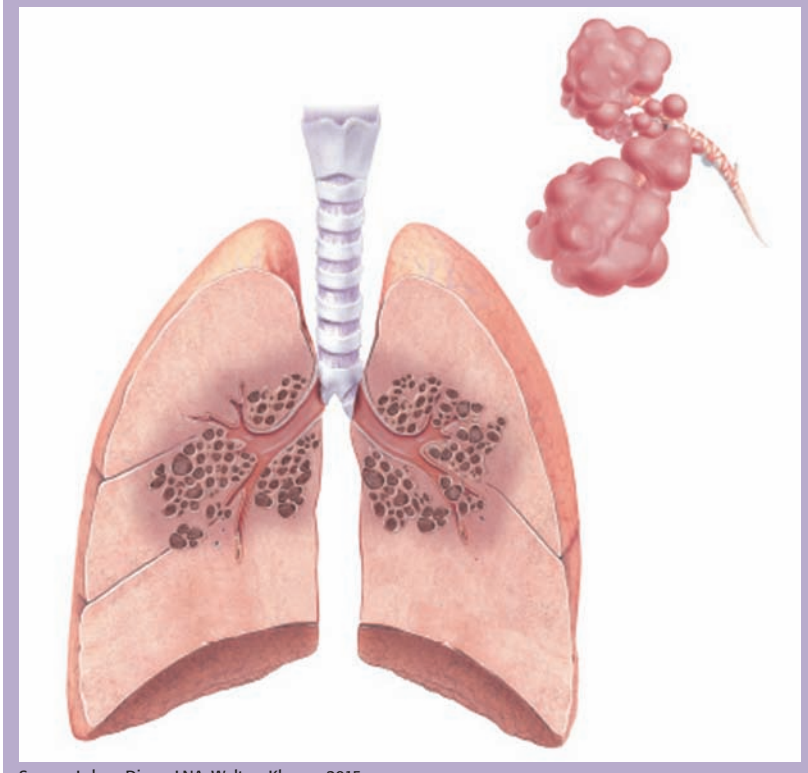
Upon arrival in the ED, CS was tachycardic (HR: 120/minute) and tachypneic (RR: 22/minute). SpO2 was 91% on room air. Temperature and BP were within the normal range. CS received a combination of the beta2-adrenergic bronchodilator, and the anticholinergic bronchodilator, ipratropium bromide, via nebulizer.

Lab data revealed a positive D-dimer, and consequently, CS was initially thought to have a pulmonary embolism.[1] *Her serum C-reactive protein concentration was elevated at 7.0 mg/dL (normal, <1 mg/dL).*[1] *Other lab values, including HIV testing, liver panel, cyclic citrullinated peptide antibody, and rheumatoid factor, were all negative.*

Electrocardiography showed sinus tachycardia with nonspecific T-wave abnormalities. A chest radiograph demonstrated abnormalities that necessitated high-resolution computed tomography (HRCT) of the chest with contrast. The HRCT report showed pulmonary masses that may be malignant, so CS was admitted to the hospital for further diagnostic testing. CS was subsequently diagnosed with sarcoidosis.

Sarcoidosis is a multisystem inflammatory disease that leads to the formation of abnormal masses or nodules called granulomas in various organs.[2,3] This article discusses a case study on sarcoidosis to help nurses have a better understanding of the overall disorder, recognize diagnosis and treatment options, and provide holistic care to patients with this diagnosis.

Granulomatous tissue formation in sarcoidosis



Source: Labus, Diane. LNA. Wolters Kluwer; 2015.

Epidemiology

In the US, the incidence of sarcoidosis is less than 200,000 cases per year.[4] New evidence indicates that the disease is much more prevalent than previously estimated as it is often misdiagnosed as tuberculosis (TB).[4] Black Americans are three times more likely to develop sarcoidosis than White Americans.[4] Compounding this greater incidence is that Black Americans also seem to have more severe and chronic diseases.[4] The male-to-female ratio is 1:2. The morbidity, mortality, and extrapulmonary involvement are also higher in females.[5] The peak incidence is 25 to 35 years, with a second peak occurring in women between 45 and 65 years old.[5] The overall mortality is less than 5%, with the cause of death being the result of progressive cardiac and neurologic involvement and pulmonary fibrosis.[4]

Risk factors

Environmental exposure to dust, beryllium metals, and certain microbacteria (such as *Propionibacterium acnes*) are considered risk factors for the development of sarcoidosis.[5] Environmental exposure to dust was identified after the attack on the World Trade Center in 2001.[4] Genetic factors may also increase the risk of developing sarcoidosis as many patients report having a family member with sarcoidosis.[5,6] Viral infections, another possible risk factor, are thought to trigger an exaggerated immune response.[6]

Pathophysiology

Both excessive immune and inflammatory responses are involved in the pathology of sarcoidosis.[6] The pathology triggers macrophages and T cells to propagate an immune response, leading to the accumulation of neutrophils and CD4 cells; the release of interleukin (IL) at disease locations, mainly the lungs, skin, and eyes; and increased cytokine (such as interferon) production.[6-8] The heterogeneous multisystem inflammatory response is the result of tumor necrosis factor (TNF), glycoprotein KL-6, and surfactant protein D (SP-D) release. This inflammatory response is classically characterized by the development and accumulation of noncaseating granulomas in many organ systems, which then change the normal structure of the organ and affect the organ function. (See *Granulomatous tissue formation in sarcoidosis*.[7]) Half of patients with sarcoidosis have elevated angiotensin-converting enzyme (ACE) levels.[6-10] In the giant cells of both infectious and noninfectious granulomas, spiderlike cytoplasmic inclusions may be present.[11] Although nonspecific, these inclusions should raise a concern for the diagnosis of sarcoidosis.

These pathophysiologic alterations lead to pulmonary infiltrates, lymphadenopathy, and areas of necrosis.[8] Necrotizing pulmonary sarcoidosis, a rare subset of pulmonary sarcoidosis, occurs in 1.6% to 4% of patients and presents as areas of necrotizing sarcoid granulomas on the chest X-ray.[8] Prolonged inflammation and hypoxia of the pulmonary tissues lead to necrosis. Caseous necrosis or degeneration is a unique form of cell death. A distinctive form of coagulative necrosis, the dead tissue is a soft, white proteinaceous mass with a cheeselike appearance.[11] The areas of necrosis noted on CS' chest X-ray led to the possible diagnosis of sarcoidosis.

Sarcoidosis variants

Variants of sarcoidosis include Löfgren syndrome, an acute form of sarcoidosis characterized by a combination of erythema nodosum, bilateral hilar lymphadenopathy, fever,

and migratory polyarthritis that has remissions and exacerbations. Two other variants include lupus pernio and Heerfordt syndrome.[10] Lupus pernio is characterized by indurated skin lesions, often purplish in color, on the nose, ears, cheeks, lips, and forehead. Heerfordt syndrome is a rare manifestation of sarcoidosis characterized by the presence of facial nerve palsy, parotid gland enlargement, anterior uveitis, and low-grade fever. Some patients may have inactive forms of sarcoidosis wherein they exhibit no symptoms so they are thought to be in remission. Others may have flare-ups related to increased immune system activity.[5,6]

Prognosis

The prognosis for patients with sarcoidosis is good with complete resolution in 6 months to 2 years if it is diagnosed and treated early. Disease progression ranges from stage 0 with normal lung tissue to Stage IV which is an advanced disease with fibrosis. (See *Stages of sarcoidosis.*) Stage II and III often lead to pulmonary dysfunction.[5] Spontaneous remission occurs in 60%-90% of patients with stage I disease, 40%-70% with stage II disease, 10%-20% with stage III disease, and 0% with stage IV disease.[5] Death generally occurs due to complications of progressive pulmonary fibrosis, pulmonary hypertension, cryptogenic organizing pneumonia, pulmonary mucus buildup, or cardiac involvement, including sudden cardiac death secondary to dysrhythmias or heart failure related to myocarditis.[9,11,12] It must also be noted that a history of sarcoidosis puts the patient at an increased risk for melanoma; lymphoma; and cancers of the lung, liver, and stomach.[10,11]

The inflammation in sarcoidosis may resolve spontaneously even without treatment, but it becomes chronic in about one-third of patients.[10] Patients must be assessed and treated for complications, including pulmonary hypertension, which may occur in up to 25% of patients.[9] When tapering off medications, it is important to vigilantly monitor for relapse. One-third of patients relapse or have reoccurring/redeveloping of nodules and symptoms of the disease when tapering medications.[5,10]

Stages of sarcoidosis

Siltzbach Classification System Radiographic Stage	Chest Radiographic Findings
0	Normal chest radiography findings
I	Bilateral hilar lymphadenopathy (BHL)
II	BHL and basilar pulmonary infiltrates
III	Pulmonary infiltrates distributed throughout lung fields
IV (endstage)	Advanced pulmonary fibrosis with a "honeycombing" appearance and extensive damage leading to volume loss, traction bronchiectasis, extensive cavitation, calcifications, and/or cysts

Clinical presentation

Patients with sarcoidosis exhibit a broad spectrum of clinical manifestations ranging from an asymptomatic state to that of a progressive and relapsing disease, which causes a diagnostic dilemma.[9,10] While some patients have no symptoms or present with very vague signs and symptoms such as fever, malaise, generalized fatigue, nonproductive cough, visual changes, and weight loss, others can get severely ill with multiple organ system involvement.[2] (See *Systemic involvement of sarcoidosis.*[10,13])

Diagnosis

Carefully taking a patient's health history is crucial to making an accurate diagnosis of sarcoidosis. The history must include details regarding exposure to possible causative agents such as environmental chemicals like smoke (cigarettes or marijuana), metals, and illicit drugs (inhaled cocaine).[10] Healthcare providers must also inquire about a patient's home and work environment, allergies, and hobbies to identify potential chemical irritants. Further assessment must determine if the patient was exposed to viruses, fungi, or bacteria. Obtaining the patient's medication and family history is also pertinent.[11]

The early and timely diagnosis is important to improve patient outcomes. According to the American Thoracic Society, diagnosis of sarcoidosis is based on three major criteria: (1) compatible clinical presentation, (2) finding of nonnecrotizing granulomatous inflammation, and (3) exclusion of alternative causes of granulomatous disease.[10]

Clinical presentations that are highly suggestive of sarcoidosis include Löfgren syndrome, lupus pernio, and Heerfordt syndrome. Other features include bilateral hilar lymphadenopathy in patients with fever, night sweats, and weight loss. Diagnosis of sarcoidosis is greatly impacted by a collaborative approach among pulmonologists, advanced practice providers, rheumatologists, radiologists, and clinical pathologists who have a background

Systemic involvement of sarcoidosis[10,13]

Body System	Signs and Symptoms
Pulmonary	Pleuritic chest pain Hoarse voice Sinusitis, epistaxis, nasal polyposis
Neurologic	Hearing loss, meningitis, seizures, dementia, depression, psychosis Facial paralysis
Cardiac	Dysrhythmias. Heart block is common in younger patients. Pericarditis and/or heart failure
Immunologic	Enlarged and tender lymph nodes in the neck, axillae, and groin Enlarged lymph nodes in the chest and around the lungs
Gastrointestinal	Hepatomegaly Pancreatic sarcoidosis
Urologic	Decline in renal function Hypercalciuria Granulomatous interstitial nephritis Kidney stone formation
Musculoskeletal	Swollen and painful joints Acute and chronic arthritis Carpal tunnel is more common in patients with sarcoidosis Pain in the hands, feet, or other bony areas due to the formation of cysts
Ocular	Red and teary eyes or blurred vision Anterior and posterior uveitis, retinal vasculitis
Integumentary	Tender reddish lesions or patches on the skin or hypopigmented areas Papular and nodular sarcoidosis, nail changes, alopecia

in working with patients diagnosed with sarcoidosis.[10]

The 2020 clinical practice guidelines from the American Thoracic Society recommend that patients with suspected sarcoidosis be screened for differential diagnoses such as other infectious and noninfectious causes, including bacterial, fungal, parasitic, and viral infections; chronic granulomatous disease; lymphoma; drug-induced granulomas; foreign body granulomatosis; and chronic granulomatosis with polyangiitis.[10] It is also important to note that COVID-19 may mimic sarcoidosis and should be ruled out.[13] Other diseases that cause granulomatous necrosis should also be ruled out. These include granulomatosis with polyangiitis, rheumatoid nodule, TB, histoplasmosis, berylliosis, and parasitic and fungal infections.[10]

Fluor-18-deoxyglucose positron emission tomography (FDG-PET) and HRCT are sensitive for the diagnosis and prognosis of pulmonary and cardiac sarcoidosis.[12] These imaging studies provide detailed investigations of the lungs and surrounding lymph nodes and are the key to diagnosing sarcoidosis as well as identifying the locations of granulomas to stage the disease.[10] Radiographic findings of noncaseous granulomas surrounded by multinucleated giant cells and lymphocytes help confirm sarcoidosis. Bronchoscopy and tissue biopsy are necessary to confirm the diagnosis. Once noncaseating granulomas are found and no infection is present, sarcoidosis can be confirmed.[12]

Advanced cardiac imaging such as cardiac MRI and PET helps confirm cardiac involvement.[16]

Lab tests can reflect abnormal function of the involved organs such as the liver, kidney, and bone marrow. Hypercalcemia and hypercalciuria may be noted in patients with sarcoidosis secondary to the noncaseating granulomas producing 1,25-dihydroxyvitamin D.[14,15] Other helpful lab studies include serum ACE levels and T-cell counts. If these levels are high, they indicate an inflammatory state. Serum markers such as serum amyloid A, soluble IL-2 receptor, lysozyme, and the glycoprotein KL-6 have been reported to be markers of sarcoidosis. If the alkaline phosphatase level is elevated, it suggests hepatic involvement.[16] One study has shown that the severity of liver panel abnormalities is significantly related to the degree of fibrosis and extensiveness of the granulomatous inflammation in sarcoidosis.[17]

Pulmonary function tests (PFTs) are necessary to gather baseline data and assess the progression of sarcoidosis as well as the response to treatment. While some patients will have normal PFTs, others will demonstrate reduced diffusing capacity and restrictive pattern which is the result of parenchymal involvement.[10]

Management

The management goal for patients with sarcoidosis is remission with no signs, symptoms, or complications.[10] While many patients may not require pharmacotherapy, they should be followed regularly by a pulmonologist, ophthalmologist, and other specialists as needed. Those requiring medications may be prescribed corticosteroids (prednisone), antimetabolites (methotrexate), biologics (infliximab), as well as TNF inhibitors to keep inflammation suppressed. Other medications that may be helpful in refractory sarcoidosis include cyclophosphamide, cyclosporine, tetracycline, and thalidomide. Medications may also be prescribed to treat pulmonary fibrosis and pulmonary hypertension if they develop. Some patients with stage IV sarcoidosis may qualify for a lung transplant, but this option can be difficult due to the selection criteria, availability of organs, and cost.[11-14]

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Back to CS

CS underwent an HRCT-guided biopsy of her right middle lobe via a right thoracostomy, which confirmed noninfectious, necrotic tissue, and was consequently scheduled for surgery. In preparation for surgery, CS underwent transthoracic echocardiography to rule out cardiac involvement which was normal. CS underwent surgery via a left thoracotomy to remove three nodules on the left lower lobe. The specimens contained granulomatous pale-tan, rubbery masses that had central areas of necrosis with inflammatory tissue and giant cells.

Postoperatively, CS was started on prednisone and scheduled for outpatient follow-up and monitoring, including PFTs and chest radiographs every 6-12 months, annual slit-lamp eye exams, and ECGs.

Nursing considerations

In the immediate postoperative period, nurses must manage the chest tube, encourage hourly use of incentive spirometry, and assess pulmonary status to prevent pulmonary complications. Pain management and early ambulation are also crucial. A comprehensive physical assessment is also needed since sarcoidosis affects many organ systems.

Patient education must include information about prescribed medications, such as steroids, and their potential adverse reactions, including hypertension, weight gain, thinning of the skin, osteoporosis, and hyperglycemia.

Associated conditions such as fatigue, depression, hypercalcemia, kidney stones, and pulmonary hypertension, which can adversely affect cardiopulmonary function, may require further intervention. Patient teaching must also include the need for follow-up testing including chest X-rays, HRCT, and blood work.[12] Patients must be encouraged to report any changes in their health to their healthcare provider.

Nursing care for patients like CS must include educating patients and and families about the disease process, management of signs and symptoms, and the need for follow-up with a pulmonologist. Patients must be informed to avoid respiratory irritants including dust, animal dander, mold, and chemicals known to exacerbate the pulmonary symptoms. Patients should also be taught infection prevention strategies, such as practicing oral and hand hygiene as well as getting vaccinated against annual seasonal influenza, pneumococcal disease, and COVID-19.

Nurses must collaborate with ophthalmologists to coordinate detailed eye exams, and with dermatologists for detailed assessments of the skin, hair, and nails, and other testing required to assess for involvement of organs besides the lungs.[10,12,15]

With increased awareness of sarcoidosis and the appropriate medical and nursing interventions, nurses and other healthcare providers may become familiar with sarcoidosis and the current treatment regimens. Informed providers will identify extrapulmonary areas that may become affected by sarcoidosis, and begin screening and treatment early to improve patient outcomes.

Future directions

At present, sarcoidosis is difficult to diagnose. Specific biomarkers such as the JAK/STAT and mTOR are being investigated because of their role in granulomatous formation.[12] The initiation of these signaling pathways may also provide information on the prognosis of sarcoidosis.

Sarcoidosis has no known etiology, but it is very treatable. Understanding its management enables nurses to meet the challenges of

patient care, conduct comprehensive assessments, provide compassionate care, advocate for their patients, and educate the public about sarcoidosis. ■

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Anna Crawford is a nursing student at York College. Lisa A. Ruth-Sahd is a professor of nursing at York College in York, Pa., and an adjunct professor at Georgetown University in Washington, D.C. She is a fellow in the American Academy of Nurse Educators.

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