Abstract
We present a case of cardio-pulmonary sarcoidosis in a 68-year-old African American male that was diagnosed when he presented to dermatology for treatment of an itchy scalp. Skin examination revealed male pattern hair loss without scarring or scale but with an annular pattern of mildly hyperpigmented indurated papules arranged in 2 cm to 3 cm plaques on his frontal and parietal scalp. A 3 mm punch biopsy was taken from the right parietal scalp lesion active edge, which revealed non-caseating granulomas, characteristic of sarcoidosis. This case stresses the need for a thorough history, biopsy and medical evaluation in order to diagnose and manage sarcoidosis effectively. Often, cutaneous lesions are the primary presenting sign of sarcoidosis, making the dermatologist the first physician called upon to make the diagnosis. This case also demonstrates the importance of correlating systemic findings, such as this patient’s two-year history of third-degree AV block, with cutaneous lesions.

Introduction
In dermatology, sarcoidosis is known as the “great imitator” because of its diverse morphological manifestations.1 Sarcoidosis is an antigen-mediated disease of unknown origin characterized by systemic, non-caseating granulomas present within organs and tissue. Granulomas can be found in the skin, lungs, lymph nodes, eyes, joints, brain, kidneys and heart.2 Cutaneous lesions are sometimes the primary presenting sign of sarcoidosis.3

The lifetime risk of disease is 0.88% in Caucasians and 2.4% in African Americans. Sarcoidosis carries a mortality rate of 5% to 6% due to cardiac involvement.4 There is also a larger incidence of sudden cardiac death (SCD) in patients with sarcoidosis than the average population due to structural and functional alterations in the heart.4 SCD as an initial indication of undetected disease makes early intervention and diagnosis of sarcoidosis essentially life saving.4 Clinical manifestations of cardiac disease are present in 5% to 10% of patients, but the actual incidence is reported to be much higher.3 This case demonstrates the importance of a dermatologist’s role in identifying internal disease that manifests cutaneously and impacting a patient’s mortality and life expectancy.

Case Report
A 68-year-old, well-developed, well-nourished African American male presented to Dermatology with complaints of an itchy scalp that had not responded to topical flucinonide and ketoconazole shampoo prescribed by another physician for presumptive seborrheic dermatitis. His past medical history was remarkable for diagnosis of complete AV block two years prior, though the patient had refused pacemaker implantation and had not seen his cardiologist for further management. He did not have any history of heart failure, liver disease, renal disease/nephrolithiasis or neurological impairment. On review of symptoms, the patient denied complaints of syncope, arthritis, eye inflammation, fever, tender leg lesions or edema. He noted shortness of breath with exertion.

On physical exam, the patient did not appear to be in acute distress. Skin examination revealed male pattern hair loss without scarring or scale but with an annular pattern of mildly hyperpigmented, indurated papules arranged in 2 cm to 3 cm plaques on his frontal and parietal scalp. According to the patient, these lesions had been present for one year. No facial lesions were noted, and the remainder of his skin exam was unremarkable.

The patient’s lesions were concerning for granuloma annulare or sarcoidosis, so a punch biopsy and chest X-ray were ordered. A 3 mm punch biopsy was taken from the right parietal scalp lesion active edge (Figure 1), which revealed non-caseating granulomas, characteristic of sarcoidosis (Figures 2 and 3). A histiocytelymphocytic infiltrate within the superficial dermis, composed of mononuclear cells with a variable amount of foamy cytoplasm and scattered, occasionally frequent multinucleated giant cells and granuloma formation was visualized. In addition, interspersed lymphocytes, plasma cells, and patchy neutrophils were noted. Grocott’s methenamine silver (GMS) stain for fungus and Kinyoun stain for acid-fast bacilli were both negative. A chest X-ray revealed hilar changes and infiltrates in the lungs (Figure 4, p. 20), likely contributing to his ongoing complaints of dyspnea.
Results of the skin biopsy and chest X-ray were reviewed with the patient and his cardiologist. Although the patient had been reluctant to undergo the pacemaker insertion recommended by his cardiologist over a year ago, he decided to undergo the procedure after the cardiac and pulmonary work-up were completed and he was advised of potential risks and benefits of inserting the device because of his underlying sarcoidosis. The patient elected to receive a biventricular pacemaker with implantable cardioverter-defibrillator (ICD), which would ideally improve his cardiac output and correct for possible life-threatening arrhythmias. Absolute indications for pacemaker placement in this patient were: complete atrioventricular block (third-degree heart block) and cardiac resynchronization therapy with biventricular pacing.

Cardiac MRI revealed mild myocardial enhancement, biventricular enlargement with biventricular dysfunction and cardiomyopathy (Figures 5 and 6). Cardiac ECHO revealed a left ventricular ejection fraction of 28%, diastolic dysfunction, and dilated left ventricle. Cardiac positron emission tomography (PET) scan showed infiltration of the basal to mid inferior wall and possible involvement in the basal anterior wall, indicating active sarcoidosis. The patient had an elevated angiotensin-converting enzyme (ACE) of 68 U/L and some other minor laboratory changes including decreased platelets (125 K/uL), elevated blood urea nitrogen (27 mg/dL) and elevated creatinine (1.45 mg/dL). Pulmonary function testing SPIRO/DLCO revealed impairment with an FVC of 82%, FEV 1 of 91%, and DLCO of 65% (not corrected for hemoglobin).

Currently, indications for primary prophylaxis

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical Findings</th>
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<tbody>
<tr>
<td>Papular(^{19})</td>
<td>Numerous, non-scaly, 1-10mm papules ranging in color from yellow to brown. Frequent on the face (eyelids, nasolabial folds).</td>
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<tr>
<td>Nodular(^{6,20})</td>
<td>Large collections of sarcoidal granulomas, each approximately 1-2cm in diameter. May resemble rhinophyma on the nose.</td>
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<tr>
<td>Subcutaneous (Darier-Roussy)(^{21})</td>
<td>Nodular sarcoidosis predominantly involving subcutaneous tissue that presents with erythematous, hyperpigmented, indurated nodules found on upper extremities. Often form linear bands.</td>
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<tr>
<td>Maculopapular(^{8})</td>
<td>Infiltrated, hyperpigmented, red-brown patches scattered with raised papules commonly found on the face, especially around eyelids and mouth.</td>
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<tr>
<td>Plaque(^{1})</td>
<td>Oval or annular, well-demarcated, red-brown plaques with occasional scale that often involve the shoulders, posterior arms, back and buttocks.</td>
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<tr>
<td>Lupus pernio(^{22,23})</td>
<td>Central facial distribution of violaceous, indurated papules, plaques and/or nodules. Usually found at the tip of the nose or cheeks. Greater risk of pulmonary involvement of sarcoidosis.</td>
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<tr>
<td>Hypopigmented(^{19})</td>
<td>Well-demarcated, hypopigmented patches or slightly raised plaques. Affects dark-skinned individuals almost exclusively.</td>
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<tr>
<td>Atrophic/Ulcerated(^{24})</td>
<td>Depressed, atrophic, hyperpigmented plaques that may become ulcerated. Three variants: morpheaform, necrobiosis-lipoidica-like, lipodermatosclerosis-like.</td>
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<tr>
<td>Angiolupoid (Brocq-Pautrier)(^{25})</td>
<td>Slightly raised plaques with prominent telangiectasias, often developing on the central face or scalp. Variant of plaque sarcoidosis. (Rare)</td>
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<tr>
<td>Ichthyosiform(^{26})</td>
<td>Asymmetrical, dry, polygonal gray-brown scales involving the pretibial lower extremities. (Rare)</td>
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<tr>
<td>Erythrodermic(^{27})</td>
<td>Large, geometric, erythematous yellow-brown plaques covering large areas of the skin. Potential for desquamation. (Rare)</td>
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account for most ICD implants. Class I indication in this patient was a left ventricular ejection fraction (LVEF) less than 35% (NYA class II or III), Class IIA indication (benefit outweighs the risk and is reasonable to administer the treatment) was cardiac sarcoidosis. Prednisone was started at 40 mg per day for one month and subsequently tapered by 10 mg every month. The patient has been maintained thereafter with a 10 mg daily dose indefinitely and follows closely with both cardiology and pulmonology. Due to this patient’s low ejection fraction (28%) indicating a poorer prognosis, biologic therapy was not instituted. The patient recently returned for a visit with dermatology and showed resolution of his cutaneous lesions. He displayed gratitude for the multi-disciplinary specialty approach led by the dermatologist and extension of his life expectancy.

**Discussion**

Cutaneous manifestations of sarcoidosis are seen in greater than 25% of patients. Specific lesions can present as papules, nodules, plaques or infiltrated scars (Table 1). Nonspecific cutaneous eruptions, such as erythema nodosum, calcinosis cutis, Sweet syndrome and nail clubbing, can also present in patients with sarcoidosis. Erythema nodosum presents as inflammatory, tender nodules on the lower legs and was reported by one study to be found in 20% of patients with sarcoidosis and 62% of sarcoidosis patients with cutaneous lesions. Careful history and physical and skin examinations with biopsy are vital to early diagnosis and management of sarcoidosis. A biopsy was warranted in this patient to rule out a granulomatous process because of the annular morphology and the induration on palpation suggesting a dermal process. Absence of surface scale and erythema made the diagnosis of seborrheic dermatitis unlikely.

“Naked,” or non-caseating, granulomas characterize the histopathological findings of sarcoidosis and include aggregates of epithelioid histiocytes, giant cells and mature macrophages surrounded sporadically by CD4+ and CD8+ T-cell infiltrates. This arrangement differs from the dense, lymphocytic infiltrate classically seen in tuberculosis. Naked granulomas are estimated to be present in 71% to 89% of sarcoidosis lesions. What complicates this diagnostic picture is the fact that not all cutaneous lesions of sarcoidosis demonstrate classic histopathological findings. Other lesions may demonstrate elaborate lymphocytic infiltrates at the margin of granulomas, central caseating granulomas, vasculitis, or augmented dermal mucin.

The differential diagnosis for sarcoidosis includes foreign body reactions, tuberculosis, leprosy, and fungal and atypical mycobacterial infections. Special staining is done to exclude these conditions. Treatment is individualized, and various systemic therapies have been used including prednisone, methotrexate, hydroxychloroquine, minocycline, tumor necrosis factor-alpha inhibitors (infliximab and adalimumab) and, less often, thalidomide, isotretinoin and allopurinol. Corticosteroids in topical, intralesional or systemic form are the mainstay therapy for systemic sarcoidosis.

Sarcoidosis can involve multiple organ systems including the skin, lungs, lymph nodes, eyes, joints, brain, kidneys and heart. Endocrine (rarely diabetes insipidus) and exocrine dysfunction (< 10% parotid gland xerostomia) are also possible. Pulmonary involvement occurs in 90% of patients and ranges from alveolitis to granulomatous infiltration of the alveoli, blood vessels, bronchioles, pleura and fibrous septa. Routine chest films are frequently abnormal. Pulmonary function testing should be done initially and followed as symptoms warrant.

Sudden cardiac death may be the initial presentation in 40% of patients with cardiac sarcoidosis. Only 40% to 50% of patients with cardiac sarcoidosis identified on autopsy received this diagnosis during their lifetime. One study reported five cases of facial cutaneous sarcoidosis with concurrent cardiac involvement, with four out of the five patients displaying annular facial lesions. Complete heart block and bundle branch blocks are among the most common manifestations of cardiac sarcoidosis, occurring in 23% to 30% and 12% to 32% of patients, respectively. These statistics should encourage cardiac evaluation in any patient identified with cutaneous sarcoidosis.

**Conclusion**

Sarcoidosis can present in myriad ways, making careful history, physical and skin examinations with biopsy vital to early diagnosis and management. Biopsy confirmation of cutaneous sarcoidosis should prompt review of chest X-rays because of the very high incidence of associated pulmonary disease. Further systemic evaluation should include cardiac assessment with electrocardiogram, prolonged Holter monitoring, echocardiogram, MRI and PET scan. Arrhythmias due to undetected cardiac structural damage can lead to sudden cardiac death either prior to or after initiation of therapy. Laboratory testing and imaging are necessary to determine the extent of organ involvement and choose the best form of therapy. Underlying liver disease and cardiac disease might preclude use of certain modalities such as methotrexate, hydroxychloroquine and biologics. Treatment must be tailored to the patient. Finally, this case serves as a reminder of how a dermatologist’s role can extend beneath the skin and impact a patient’s mortality and life expectancy.


