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International Journal of Clinical Reports and Studies

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Review Article

Sarcoidosis of the Urogenital Tract

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Received Date: December 03, 2024 | Accepted Date: February 25, 2025 | Published Date: March 07, 2025

Citation: Grey Venyo AK, (2025), Sarcoidosis of the Urogenital Tract, *International Journal of Clinical Reports and Studies*, 4(1); **DOI:**10.31579/2835-8295/110

Abstract

Although the sarcoidosis is a multisystemic disease that theoretically can affect almost any organ, the presence of sarcoidosis in the male urethra had apparently not been described in the medical literature until 2022. The first case of sarcoidosis in the male urethra was only apparently in 2022, and very few cases of sarcoidosis of the female sarcoidosis had been reported in the global literature. In view of the rarity of sarcoidosis of the urethra throughout the world, it would be assumed that the majority of clinicians in the entire world would not have ever encountered a case of sarcoidosis of the urethra before and they would therefore not be familiar with the diagnostic features of sarcoidosis of the urethra in both males and females. Sarcoidosis of the urethra has not been covered extensively in the majority of test books of surgery, medicine, and urology. Sarcoidosis of the urethra manifests with non-specific symptoms which simulates the manifestations of more common conditions of the urethra including urethral stenosis, urethral stricture, urethral tumour, and paraurethral tumours and para-urethral cysts and abscesses. Sarcoidosis of the urethral may present as a symptomatic or asymptomatic mass within the urethral region, haematuria, lower urinary tract symptoms and or urethral discharge which may or may not be associated with non-specific general symptoms. A high index of suspicion is required in order not to miss the diagnosis of sarcoidosis of the urethra. The diagnosis of sarcoidosis of the urethra can be confirmed based upon the characteristic histopathology examination features of biopsy / excised specimens of the urethral which demonstrates among other features presence of non-specific non-caseous granuloma and thorough assessment of each patient to exclude other causes of non-caseating granuloma. The ensuing chapter contains an update of sarcoidosis as well as sarcoidosis of the urethra.

Keywords: sarcoidosis; urethra; urethral stenosis; urethral stricture; biopsy

Introduction

It has been iterated that sarcoidosis had traditionally been considered to be a pulmonary disease, which primarily affects young African-American females. [1] It has also been iterated that contemporary epidemiology evidence had indicated that, in fact, African-Americans have 3 to 4 times increased risk of developing sarcoidosis, which is considerably <10–17 times increased risk found in the older literature. [1] [2] Furthermore, it has been stated that extra-pulmonary presentations of sarcoidosis impact up to 25–30% of patients, which is significantly higher than was previously thought.[1] [3] [4] It has been pointed out that whilst genitourinary (GU) tract involvement of sarcoidosis had traditionally been considered not to be common, it has been documented that the literature had indicated that the incidence of sarcoidosis of the GU tract organs may actually be considerably higher, often going undetected or manifesting with symptoms that are not immediately referable to the urinary tract. [1] [5] Sarcoidosis of the urethral may present as a symptomatic or asymptomatic mass within the urethral region, haematuria, lower urinary tract symptoms and or urethral discharge which may or may not be associated with non-specific general symptoms. A high index of suspicion is required in order not to miss the diagnosis of sarcoidosis of the urethra. The diagnosis of sarcoidosis of the urethra can be confirmed based upon the characteristic histopathology examination features of biopsy / excised specimens of the urethral which demonstrates among other features presence of non-specific non-caseous granuloma and thorough assessment of each patient to exclude other causes of non-caseating granuloma. The ensuing chapter contains an update of sarcoidosis as well as sarcoidosis of the urethra.

Aim

To provide an update on sarcoidosis of the urethra.

Methods

Internet databases were searched including: Google; Google Scholar; Yahoo; and PUBMED. The search words that were used included: Sarcoidosis of urethra and urethral sarcoidosis. Twenty-six (26) references were identified which were used in writing the chapter which has been divided into two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to sarcoidosis of the urethra.

Results

[A] Overview

Definition, General statements, Practice Essentials. [6] Medscape kamanga

- Sarcoidosis has been defined as a multi-system inflammatory disease of unknown aetiology which predominantly affects the lungs and intrathoracic lymph nodes and is manifested by the presence of non-caseating granulomas (NCGs) within afflicted organ tissues of the body. [6]
- It has been iterated that Sarcoidosis is characterized by a seemingly exaggerated immune response against a difficult–to-discern antigen. [6] [7]
- The age-adjusted incidence of sarcoidosis has been stated to be 11 cases per 100,000 population in whites but 34 cases per 100,000 population in African Americans. [6] [7]

Signs and symptoms

The presenting signs and symptoms in sarcoidosis are stated to vary depending upon the extent and severity of the organ which is involved by sarcoidosis as follows: [6]

- Sometimes sarcoidosis may be asymptomatic, and incidentally identified upon chest radiography images in about 5% of cases. [6]
- It has been stated that in 45% of cases, sarcoidosis may present with systemic complaints including: fever, and anorexia in 45% of cases. [6]
- It has been documented that sarcoidosis in 50% of cases does manifest with pulmonary complaints including: dyspnoea on exertion, cough, chest pain, and haemoptysis on rare occasions. [6]
- It has been stated that at times, sarcoidosis may present as neuro-sarcoidosis including: cranial neuropathies, leptomeningeal disease, intraparenchymal lesions, and myelitis, which does occur in between 5% to 10% of cases. [8]
- It has additionally been stated that in sarcoidosis, Löfgren syndrome which manifests with fever, bilateral hilar lymphadenopathy, and poly-arthralgias does occur and this sarcoidosis affliction is common in Scandinavian patients, but it is not common in African-American and Japanese patients. [6]

The pulmonary findings on physical examination of patients affected by sarcoidosis had been summarized as follows: [6]

- Usually there has tended to be normal pulmonary examination of patients afflicted by sarcoidosis. [6]
- In some cases of sarcoidosis, clinical respiratory tract examination of affected individuals might demonstrate audible crackles. [6]
- In some individuals affected by sarcoidosis, their clinical examination may demonstrate exertional oxygen desaturation. [6]

It has been stated that dermatology manifestations of sarcoidosis may include the following: [6]

- Erythema nodosum. [6]
- A lower-extremity panniculitis with painful, erythematous nodules that often tend to be seen in association with Löfgren syndrome. [6]
- Lupus pernio, which is documented to be the most specific associated cutaneous lesion of sarcoidosis. [6]
- Violaceous rash on the cheeks or nose tend to be common in cases of sarcoidosis. [6]
- Maculopapular plaques tend to be visualised in some cases of sarcoidosis which has been stated to be an uncommon feature of sarcoidosis. [6]

It has been iterated that ocular involvement, in cases of sarcoidosis which may lead to blindness if untreated, may present as follows: [6]

- Anterior or posterior granulomatous uveitis, which is most frequently seen. [6]
- Conjunctival lesions as well as scleral plaques. [6]

Other possible presentations of sarcoidosis do include the ensuing: [6]

- Osseous involvement. [6]
- Heart failure from cardiomyopathy may be encountered on rare occasions. [6]
- Heart block and sudden death of the sarcoidosis affected individual. [6]
- On rare occasions lymphocytic meningitis of the sarcoidosis afflicted individual. [6]
- On rare occasions, individuals who are affected by sarcoidosis may manifest with stroke, seizure, intracranial mass, hypopituitarism, neuropsychiatric symptoms, and encephalopathy and all these manifestations are stated to be rare. [6]

Diagnosis

The radiology-image studies for sarcoidosis had been summarized as follows: [6]

- Chest radiography: It has been iterated that chest radiograph is central to the evaluation of sarcoidosis. [6]
- Routine chest computed tomography (CT): It has been iterated that the undertaking of computed tomography of the thorax adds little to radiography findings. [6]
- High-resolution CT (HRCT) scanning of the chest: It has been iterated that high-resolution CT (HRCT) scan may be helpful, in that it does identify active alveolitis versus fibrosis, and findings correlate with biopsy yield. [6]
- Gallium scans: It has been pointed out that Gallium scans are undertaken infrequently and that Gallium scan has a-low sensitivity and specificity, but may be helpful when the clinical picture remains confusing despite histology examination evidence of non-caseating granulomas, for example in differentiating chronic hypersensitivity pneumonitis from sarcoidosis. [6]

Staging of sarcoidosis had been summated as follows: [6]

- Stage 0: Normal chest radiographic findings
- Stage I: Bilateral hilar lymphadenopathy
- Stage II: Bilateral hilar lymphadenopathy and infiltrates
- Stage III: Infiltrates alone

- Stage IV: Fibrosis

It has been stated that pulmonary function tests and a carbon monoxide diffusion capacity test of the lungs for carbon monoxide (DLCO) are used routinely in evaluation and follow-up of individuals afflicted by sarcoidosis. [6] and that some of the possible findings of the tests do include the following: [6]

- An isolated decrease in DLCO is the most common abnormality found in cases of sarcoidosis. [6]
- A restrictive pattern is seen in patients with more advanced pulmonary sarcoidosis disease. [6]
- About 15% to 20% of sarcoidosis patients are iterated to have obstruction. [6]
- It has been iterated that cardiopulmonary exercise testing is a sensitive test for the identification and quantification of the extent of pulmonary involvement. [6]
- Cardiopulmonary exercise testing also may indicate cardiac involvement that otherwise is not evident. [6]
- Impaired heart rate recovery during the first minute ensuing exercise had been demonstrated to be an independent predictor for cardiovascular and all-cause mortality, [9] and it might identify patients who are at high risk for the development of arrhythmias and sudden death.[10]
- It had been advised that all patients with sarcoidosis should have an annual electrocardiogram, and that patients who report palpitations should have a thorough evaluation with at least Holter monitoring. [6]
- Diagnosis of sarcoidosis requires biopsy in most cases. [6]
- Endobronchial biopsy via bronchoscopy is often undertaken. [6] The yield is stated to be high; and it has been iterated that results of the biopsy may be positive even in patients with normal chest radiographs. [6] The central histopathology examination finding is the presence of non-caseating granulomas with special stains negative for fungus and mycobacteria. [6]

Routine laboratory evaluation is stated to be often unrevealing, but possible abnormalities include the following: [6]

- Hypercalcemia (about 10-13% of patients)
- Hypercalciuria (about a third of patients)
- Elevated alkaline phosphatase level
- Elevated angiotensin-converting enzyme (ACE) levels.

Management

The management of sarcoidosis has been summarized as follows: [6]

It has been iterated that non-steroidal anti-inflammatory drugs (NSAIDs) are indicated for the treatment of arthralgias and other rheumatic complaints. [6] It has also been stated that patients with stage I sarcoidosis often do require only occasional treatment with NSAIDs. [6]

Treatment in sarcoidosis patients with pulmonary involvement has been summated as follows:

- Asymptomatic patients may not require treatment at all and would need to be observed.
- In sarcoidosis patients with minimal symptoms, serial re-evaluation is important. [6]
- Treatment is indicated for sarcoidosis patients with significant respiratory symptoms. [6]
- Corticosteroids can produce small improvements in the functional vital capacity and in the radiographic appearance in sarcoidosis patients with more severe stage II and III disease. [6]

For extrapulmonary sarcoidosis involving such critical organs such as the heart, liver, eyes, kidneys, or central nervous system, corticosteroid therapy is stated to be indicated. [6] It has been iterated that topical corticosteroids are effective for ocular disease. [6] For pulmonary sarcoidosis disease, it has been iterated that prednisone is generally given daily and then tapered over a 6-month course. It has also been stated that high-dose inhaled corticosteroids could be an option, particularly in sarcoidosis patients with endobronchial disease.

Common indications for non-corticosteroid agents in cases of sarcoidosis had been stated to include the ensuing: [6]

- Steroid-resistant disease
- Intolerable adverse effects of steroids
- Patient desire not to take corticosteroids

Non-corticosteroid agents that tend to be used in sarcoidosis include the ensuing: [6]

- Methotrexate (MTX) had been a successful alternative to prednisone. [6]
- Chloroquine and hydroxychloroquine had been used for cutaneous lesions, hypercalcemia, neurologic sarcoidosis, and bone lesions. [6]
- Chloroquine had been found to be effective for acute and maintenance treatment of chronic pulmonary sarcoidosis. [11] [12]
- Cyclophosphamide had been rarely used with modest success as a steroid-sparing treatment in patients with refractory sarcoidosis. [13] [14]
- It has been iterated that Azathioprine is best used as a steroid-sparing agent. [6] [15]
- It has been iterated that Chlorambucil might be beneficial in patients with progressive disease unresponsive to corticosteroids or when corticosteroids are contraindicated. [6] [16]
- It had been stated that cyclosporine might be of limited benefit in skin sarcoidosis or in progressive sarcoid resistant to conventional therapy. [6] [17]
- It has been documented that Infliximab, [18] [19] and thalidomide, [20] [21] had been utilised for the treatment of refractory sarcoidosis, particularly for cutaneous disease, as well as for the long-term management of extrapulmonary sarcoidosis. [22]
- It had furthermore, ben stated that Infliximab appeared to be an effective treatment for patients with systemic manifestations such as lupus pernio, uveitis, hepatic sarcoidosis, and neuro-sarcoidosis. [6]

It had also been iterated that for sarcoidosis patients with advanced pulmonary fibrosis from sarcoidosis, lung transplantation remains the only hope for long-term survival and that indications for transplantation include either or both of the following. [23] Forced vital capacity below 50% predicted [6]

- Forced expiratory volume in 1 second below 40% predicted. [6]

[B] Miscellaneius Narrations and Discussions from Some Case Reports, Case Series, And Studies Related to Sarcoidosis of The Urethra

Aizcorbe Gómez et al. [1] reported a 46 years old male, who was undergoing follow up due to lower urinary tract symptoms and who was diagnosed as having endobronchial sarcoidosis during the preoperative study preceding his undergoing of internal urethrotomy. After surgery, he presented clinical improvement for one year. Given the worsening, a new internal urethrotomy was undertaken. As it was impossible to undertake a successful optical urethrotomy due to complexity of his case, the urological surgeon took a biopsy of the urethra. Pathology examination of the biopsy specimen reported the finding of non-caseating granulomas, which had features that were compatible with sarcoidosis. After that, medical and endoscopic management of the urethral sarcoidosis was attempted. As it did not achieve an adequate control, the patient was referred to the "complex urethral unit" of the Cruces University Hospital. Once it was evaluated, it was decided to commence immunotherapy and subsequently a urethroplasty procedure with a double oral mucosa graft was undertaken. During his post-operative period, a urethral catheter was maintained for two weeks. The urethral catheter was removed after no urinary leakage was observed in de cystourethrography. After that the patient had remained with good evolution until the time of publication of the article. Aizcorbe Gómez et al. [1] made the ensuing conclusions:

- Urethral affliction by sarcoidosis is a therapeutic challenge itself.
- For a better symptom control and to reduce the recurrences, a dual approach utilising systemic treatment in combination with local surgical treatment seems necessary.

Ho and Hayden. [24] reported a case of sarcoidosis of the urethra, which was found during endometrial curettage in a thirty-nine-year-old woman with a history of menometrorrhagia and decreased urine stream. Ho and Hayden. [24] stated that sarcoidosis is known to occur in many parts of the body, but their extensive search of the literature in 1999, had failed to reveal any previous report of urethral involvement by sarcoidosis.

Droessler et al. [25] reported a 33-year-old African American female, a former smoker, who had presented in the emergency room (ER) with a 1-month history of recurrent urinary tract infections (UTI), severe dysuria, visible haematuria, a painful vagina, and increasing difficulty emptying her urinary bladder. She had been seen by an outpatient gynaecologist in the previous month and she was diagnosed with a UTI, which was confirmed by dipstick urinalysis and microanalysis, and treated with ciprofloxacin. It was noted at that visit that there was an abnormal palpable mass of the urethra, and she was referred to a urologist. She did not follow up with a urologist, and over the next month her periurethral pain gradually worsened, despite antibiotic treatment, which had prompted her to go to the ER. She had a history of sarcoidosis, which was diagnosed 4 months earlier through bronchoscopy and mediastinal lymph node biopsy, but she was not undergoing treatment and was being monitored by a respiratory physician and nephrologist. Her family history was significant for sarcoidosis in her sister and breast cancer in her maternal aunt.

Lesley et al. [26] in 1995, reported on a woman with urethral sarcoidosis with obstructive urinary symptoms and previously known systemic sarcoidosis.

Conclusions

- Extra-pulmonary manifestations of sarcoidosis might afflict up to 25–30% of patients with sarcoidosis.
- Whilst genitourinary (GU) involvement of sarcoidosis had traditionally been regarded to be occurring rarely, it could be envisaged that many cases go undiagnosed.
- Sarcoidosis may occur in any and all of the organs of the GU tract; its manifestations are protean, and sarcoidosis may simulate many other diseases, such as cancer.
- Urologists and pathologists need to have updated knowledge and understanding of the various manifestations of GU sarcoidosis, as well as to have a high index of suspicion for sarcoidosis of the urethra in order not to miss a diagnosis of sarcoidosis of the urethra.
- Direct involvement of the GU organs by sarcoidosis may cause direct or indirect clinical presentations.
- Furthermore, to be able to differentiate sarcoidosis affliction of the urinary tract from primary malignancies is critically important, in order to avoid the unnecessary removal of the organ.

Conflict of interest – none

Acknowledgements

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