Review Article

Genitourinary sarcoidosis: An essential review for the practicing clinician

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ABSTRACT

Introduction: Sarcoidosis is a multisystem disease that commonly involves the lungs, but may also present with extrapulmonary manifestations. Genitourinary (GU) tract involvement has been traditionally thought to be rare, but that view may underestimate the true prevalence of the disease due to the often, silent presentation thereof.
Methods: The literature pertaining to sarcoidosis from the general systemic point of view, etiology and therapy and with regard to specific organs was reviewed by identifying key words in a PubMed search. That material with special relevance to the Indian experience was emphasized.
Results: There are a number of isolated case reports in the literature describing symptomatic and asymptomatic GU tract sarcoidosis. The world literature associated with the generalized syndrome was reviewed and summarized. Specific aspects of GU involvement are presented for each organ of the GU tract.
Conclusions: It is critical for the practicing clinician to have a working knowledge of the clinical manifestations of this disease as it involves the GU tract, as well as to be able to distinguish it from tuberculosis and the various malignancies that affect this organ system.

INTRODUCTION

Sarcoidosis has traditionally been thought of as a pulmonary disease, which primarily affects young African-American females. Contemporary epidemiologic evidence suggests that, in fact, African-Americans have 3–4 times increased risk of developing sarcoidosis, which is considerably <10–17 times increased risk found in the older literature.[1] In addition, extrapulmonary manifestations of sarcoidosis impact up to 25–30% of patients, which is significantly higher than previously thought.[2,3] While genitourinary (GU) tract involvement has traditionally been considered rare, the literature suggests that the incidence may actually be considerably higher, often going undetected or presenting with symptoms that are not immediately referable to the urinary tract.[4]

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INCIDENCE AND PATHOGENESIS

Sarcoidosis was first described and named by Boeck in 1899; the name was chosen because of its close appearance, both on a gross and histologic level, to that of sarcoma.[5] Since its early description, concepts of the disease have broadened from those of a primary dermatologic disorder to those of a systemic disease involving all organ systems. One review revealed that 16.6% of patients had extrapulmonary presentations of the disease.[6] In another review, evaluating 1254 cases of histologically-proven sarcoidosis, Mayock *et al.*[7] found one case of adrenal involvement, 54 (4.3%) cases of renal involvement, and six (1%) cases of epididymal involvement. Other involved GU organs were not delineated. They also found that patients were 37% male and 63% female; 30% were described as "white" and 70%

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as "black." The US prevalence is currently estimated to be 10–14/100,000 for Caucasians and 34–65/100,000 for African-Americans. African-American females between 30 and 39 comprise the largest group of people with sarcoidosis, accounting for an estimated prevalence of 107/100,000.[7,8]

The etiology of sarcoidosis remains poorly understood, but it is widely believed to be a disease of activated T-cell lymphocytes. Granulomatous inflammation is predominantly a T-helper 1 response mediated by a complex network of lymphocytes, macrophages, and cytokines. The pathogenesis of progression to chronic, potentially fibrotic forms, is unclear but may involve apoptotic mechanisms, loss of regulatory responses, or a persistent, uncleared antigen.[7] Hypercalcemia, thought to be due to its influence on 1, 25 hydroxy-vitamin D, is present in 5–10% of all cases.[7] Familial clusters support some level of genetic involvement, possibly related to T-cell function regulation. Patients with particular human leukocyte antigen alleles may have increased susceptibility.[7] There has also been some evidence, based on the presence of mycobacterial DNA sequences within tissue specimens, of an infectious etiology, as well.[7]

SARCOIDOSIS, THE GREAT IMITATOR

In addition to the direct tissue-related effects of GU organ involvement, sarcoidosis is significant for its ability to mimic other diseases, such as cancer, often making definite diagnosis difficult or confusing. It has truly taken the role of Grand Imitator from syphilis and tuberculosis in the 21st century, and in fact, may be associated with several cancers, such as carcinoma of lung, pancreas, liver, colon, breast, cervix, ovary, skin, and non-Hodgkin's lymphoma. One report suggests a 30% increase in cancer incidence in patients with sarcoidosis.[9]

Sarcoidosis often coexists with other auto-immune conditions. Specifically, sarcoidosis has been found in association with the following: Malakoplakia, coeliac disease, multiple sclerosis, systemic lupus erythematosus, autoimmune chronic hepatitis, myxedema, thyrotoxicosis, chronic ulcerative colitis, and neurogenic bladder.[10] Many of these disorders have urologic manifestations, and as such have relevance to the practicing urologist.[11]

As mentioned above, primary GU tract organ involvement by sarcoidosis is rare, yet the practicing urologist needs to be aware of the various sites that it may involve. In males, reproductive system involvement is estimated at <0.2% in life and 5% in autopsy series. In a group of 60 men with reproductive organ involvement, the epididymis was involved in 73%, the testis in 47%, and the spermatic cord and prostate in 3%. The disease may also cause scrotal or penile dermatologic lesions.[4] GU organ involvement in females is even more unusual, but once again may primarily affect the reproductive organs.[12]

SPECIFIC ORGAN INVOLVEMENT AND CLINICAL MANIFESTATIONS

Adrenal

Involvement of the adrenal gland is rare. In Mayock's series,[7] one of the 145 patients had adrenal involvement and died as a result of Addisonian crisis. Adrenal insufficiency and adrenal crisis are the possible manifestations of adrenal sarcoidosis and are usually caused by direct involvement of the adrenal gland, via an autoimmune mechanism.[7] Secondary adrenal insufficiency may also be caused by sarcoidosis, primarily as a result of hypothalamic-pituitary infiltration by sarcoid granulomata.[13]

Kidney

Involvement of the kidneys by sarcoidosis was suggested in 1915 by Kuznitsky and Bittoff.[14] In 1933, noncaseating granulomata were documented in renal parenchyma.[15] Despite the presence of sarcoid granulomata in up to 22% of kidneys studied, the granulomata are limited in number and extent and rarely suspected to cause significant impairment of renal function.

Other patterns of renal involvement have also been found in association with renal sarcoidosis. In a series by Bergner *et al.*,[16] 15 of 46 (33%) patients with sarcoidosis were found to have renal abnormalities. Ten patients underwent renal biopsy, of which six had nephrocalcinosis, two had granulomatous interstitial nephritis, one had interstitial nephritis without granulomata, and one had IgA-glomerulonephritis. Two patients had granulomatous interstitial nephritis combined with either nephrocalcinosis or IgA-glomerulonephritis.[16]

The relationship between renal insufficiency and hypercalcemia in sarcoidosis was first described in 1948.[17] It was noted that hypercalcemia is associated with hypercalciuria, nephrolithiasis, and nephrocalcinosis in a sarcoidosis patient. In 1953, it was suggested that the renal insufficiency of sarcoidosis was secondary to nephrocalcinosis rather than granulomatous infiltration.[18] This association was subsequently confirmed. The hypercalcemia is absorptive and is related to the increase of or sensitivity to Vitamin D. One report showed increasing serum concentrations of 1, 25 dihydroxycholecalciferol occurring concurrently with episodic hypercalcemia in a sarcoidosis patient. The disturbances in calcium metabolism are thought due to enzymatic activation of 1, 25 dihydroxycholecalciferol by the disease.[19] Activated macrophages in sarcoid granulomata express 1-alpha-hydroxylase. This leads to excessive circulation of 1, 25 dihydroxycholecalciferol resulting in enhanced intestinal calcium absorption.[16]

Muther *et al*.[19] listed multiple types of renal involvement for sarcoidosis. As noted, abnormalities in calcium metabolism may lead to hypercalcemia, hypercalciuria, nephrocalcinosis, and nephrolithiasis. These are the most common manifestations. In addition, glomerulonephritis, nephrotic syndrome (sometimes with renal vein thrombosis), renal insufficiency, hypertension, and several tubular defects (concentrating defects, acidification defects, inappropriate glucosuria, diabetes insipidus) may occur.[19]

Hypercalcemia occurs in 10–20% of patients with sarcoidosis. Hypercalciuria occurs in over 60%. Nephrocalcinosis occurs in <5% of sarcoidosis patients but in >50% of sarcoidosis patients with renal insufficiency. If nephrocalcinosis may occur in the absence of elevated serum or urinary calcium levels is not known. In most cases of such calcium metabolic dysfunction, nephrolithiasis or nephrocalcinosis may manifest.[19] Even patients with sarcoidosis and normal calcium concentrations apparently regulate 1, 25 dihydroxy-vitamin D abnormally, placing them at greater risk for nephrolithiasis and renal insufficiency.[20]

Several cases of sarcoidosis in association with renal carcinoma have been reported.[21-25] At least one case of carcinoma of the renal pelvis and bladder in association with sarcoidosis also has been reported.[26] The presence of sarcoidosis may simulate metastatic renal cell carcinoma in the lung and mediastinal nodes thus complicating management thereof.

In addition to actual malignancies, pseudotumors [Figure 1] may also occur with sarcoidosis. Renal infiltration by sarcoidosis may cause bilateral or unilateral renal enlargement or a mass lesion or lesions. Distinguishing these from a primary renal tumor may be difficult. All of the associated symptoms and signs associated with renal carcinoma may be present: Hematuria, fever, anorexia, and weight loss. Ultrasonography, computed tomography (CT) scan, and positron emission tomography imaging may all be nondiagnostic.[27] Rohatgi *et al*.[28] reported a renal pseudotumor simulating a renal cell carcinoma. If the suspicion is present, they can be distinguished from malignancy with percutaneous biopsy, prior to definitive treatment. This could save a renal unit in a patient at risk of renal insufficiency.[28,29]

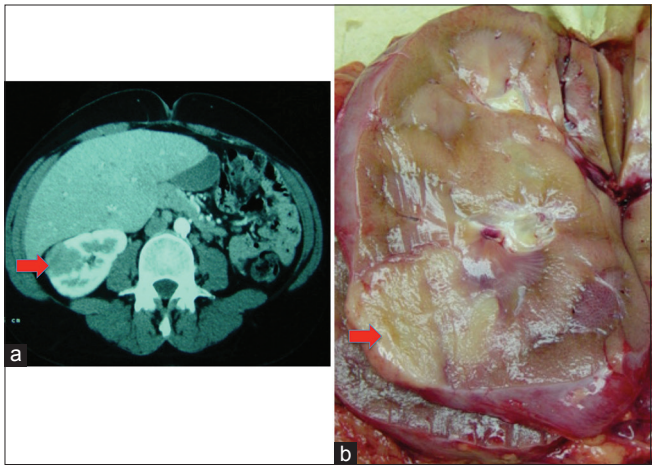

Figure 1: (a) Computerized axial tomography scan with contrast-early phase. Note intra-renal mass (arrow). (b) Gross view, kidney. Note intra-renal mass (arrow)

The final renal manifestation of sarcoidosis is the obstruction of renal pelvis or ureter from retroperitoneal lymphadenopathy or nonspecific retroperitoneal masses in association with sarcoidosis. Hydronephrosis has been reported, occasionally as a presenting sign of sarcoidosis.[30,31]

The first-line treatment for hypercalcemia and hypercalciuria in this disease is corticosteroids. These downregulate macrophage 1-alpha-hydroxylase activity and lead to normalization of calcium levels in serum and urine.[32] Moreover, as hypercalcemia can depress the glomerular filtration rate, the rapid improvement in creatinine in patients so treated can be explained.[19] Cessation or withdrawal of corticosteroid therapy may be associated with the recurrence of renal dysfunction but is reversible on reinstitution of steroid therapy.[33] Long-term low-dose treatment with steroids is usually required and must be balanced with the relevant side effects. Mycophenolate and azathioprine have also been used.[34] Infliximab may be effective in relapsing or steroid-resistant patients.[35] in very carefully selected cases, renal transplantation may be appropriate. Sarcoidosis may appear in the allografted organ.[36]

Ureter

There are only five reported cases of sarcoidosis involving the ureter. Flank pain, hydronephrosis, and hematuria were the presenting features in these cases. Of the patients who underwent surgery, two were treated by segmental resection of the ureter and one by total nephroureterectomy. In all of these cases, the diagnosis was pathologically verified.[37-39]

Sarcoidosis may also affect the ureter indirectly by means of extrinsic compression by peri-ureteral lymph nodes that are often seen in this condition. In addition, bladder wall involvement may cause secondary hydronephrosis, as well. These extrinsic causes of obstruction are much more common than direct ureteral involvement, but the actual incidence is difficult to quantitate from the literature.

Bladder

There are eight cases of sarcoidosis involving the urinary bladder.[40-46] Presenting features of bladder wall involvement include the following: Hematuria, irritative voiding symptoms, recurrent urinary tract infections, ureteral obstruction, and in two cases metachronous bladder cancers.

Redewill *et al*.[47] first pointed out the microscopic similarities between sarcoidosis and malakoplakia. There have been at least six cases of malakoplakia (occurring independently of sarcoid changes in bladder), in patients with generalized sarcoidosis.[45,47]

Indirect bladder involvement is another manifestation that can be seen in patients with sarcoidosis. Between 5% and 16% of patients with sarcoidosis have central nervous system involvement, which may secondarily manifest in the bladder. In fact, several cases of neurogenic bladder dysfunction derived from spinal cord sarcoidosis have been reported.[48] Finally, an intriguing case of sarcoidosis, which developed following intravesical instillation of mitomycin C, has been reported.[49]

Urethra

Two cases of sarcoidosis involving the urethra have been recorded. One case was symptomatic. The patient was a 60-year-old African-American female with progressive, irritative, and obstructive voiding symptoms. Transurethral biopsy confirmed the diagnosis and successful treatment involved oral steroids and urethral dilation. The second case was diagnosed during endometrial curettage for an unrelated problem. It was initially perceived as a mass in the urethra thought to be a urethral carcinoma. Instead, biopsy revealed it to be an inflammatory mass caused by sarcoidosis. Treatment was systemic steroids.[50,51]

Prostate

Sarcoidosis can directly involve the prostate gland [Figure 2]. There are 15 cases of sarcoidosis involving the prostate gland from the literature.[52-56] The majority of these cases have been documented to occur in African-American males, although six cases were in Caucasians. The average age at diagnosis was 58 years. Two patients were diagnosed at autopsy.

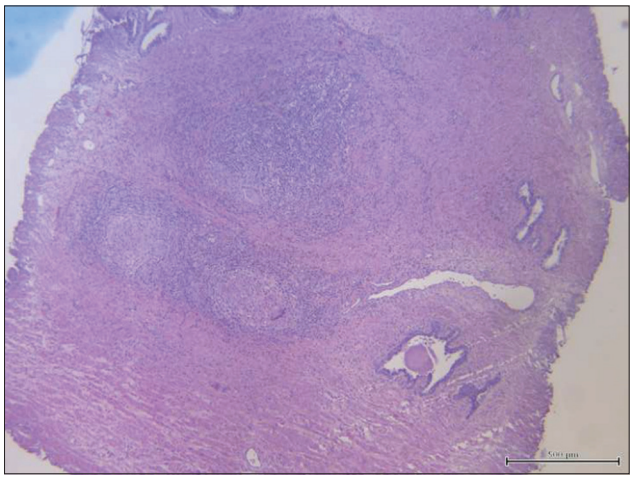

Figure 2: High power, H and E stain. Sarcoid granuloma in prostate chip. Note multinucleated giant cell

Histologically, the disease affects the periphery of the prostate; granulomata are not usually found within the parenchyma. Six patients had incidental sarcoid granulomata found at the time of radical prostatectomy for adenocarcinoma of the prostate.[56] Two patients had biopsies for prostate-specific antigen elevation in which the biopsy cores showed sarcoid involvement with no cancer being present.[52] Another patient presented with penile pain and diminished ejaculatory volume.[52] The ejaculatory difficulty and pain were attributed to the presumed rigidity of the bladder neck.

Penis

At least six cases of sarcoidosis involving the penis have been recorded.[54,57-61] The first report was in 1941 and describes a lesion on the skin of the penis.[62] Two of the cases occurred at the urethral meatus (they may have been urethral) and presented with urethral bleeding and dysuria.[58,59] Both of these were ulcerating lesions, atypical for sarcoid. One case appeared so much like an ulcerating carcinoma that several biopsies were done. After a short, initial response to steroids, recurrence occurred and partial penectomy was performed. A further recurrence, at 1 month following surgery, then appeared at the resection margin. A course of radiation therapy (3200 rads) was given. At 1 year, the lesion had not recurred. Radiation therapy is not normally effective for sarcoid lesions.[63,64]

Sarcoidosis may also affect potency through the mechanisms of hypothalamic-pituitary infiltration causing diminished androgenic hormone levels.[65]

SCROTUM, TESTICULAR, AND PARATESTICULAR STRUCTURES

The skin of the scrotum has been reported to be involved by sarcoidosis (the lesions are described as pruritic, eczematous eruptions of skin with pink-to-violaceous annular plaques and papules with edema and tenderness). There are three cases in the literature although, given that sarcoid frequently affects the skin, there are probably many more, unreported cases. The three cases were as follows: A 29-year-old African-American, who improved with steroid treatment, a 37-year-old African-American treated with steroids but lost to follow-up, a 5-year-old Caucasian male treated by surgical excision without recurrence.[66-68]

The scrotal contents are the most common site of involvement of the GU tract by sarcoidosis.[69] There have been dozens of case reports of testicular, epididymal, or combined involvement, frequently bilateral, and occurring in all age groups. Epididymal sarcoid usually presents as a painless mass. Although the masses may regress with treatment, they may also begin or advance during steroid treatment.

Testicular sarcoidosis occurs more frequently in African-American men between 20 and 40, which encompasses the same age range in which testicular cancer is more common. Testicular sarcoidosis as the presenting feature of the systemic disease is rare and was first reported by Schaumann in 1936.[70] Although testicular sarcoidosis is usually associated with epididymal sarcoidosis, it also may occur without any epididymal involvement.[71]

One of the most relevant and important traps for urologists is mistaking a sarcoid mass for a testicular tumor requiring excision. The reverse also occurs, and biopsy should, therefore, be considered in appropriate situations. On ultrasound, these lesions may be hypo- or hyper-echoic.[72] With magnetic resonance imaging, they may enhance with contrast on T1 images and/or show high signal intensity with T2-weighted images.[72] Gross *et al*. report two cases of testicular sarcoidosis, one diagnosed at radical orchiectomy and one diagnosed by testicular biopsy, thus preserving the testis.[73] Knowledge of a past or current history of sarcoidosis may therefore allow some form of testicular-sparing surgery.

Sixty-six cases report the simultaneous occurrence of testicular sarcoidosis and testicular cancer; these have been reported to comprise any and all of the standard testicular tumor types.[74] Rayson *et al*.[75] reported that the sarcoidosis incidence among patients with testicular cancer was >6/10,000 or approximately 100 times the baseline incidence expected for young white males.

Aside from confusion between the two entities at the primary site, confusion may arise in distinguishing between metastatic testicular cancer from pulmonary and retroperitoneal manifestations of sarcoidosis. Wettlaufer and Modarelli[76] reported three cases in which patients with presumed localized testicular cancer developed suspicious thoracic pathology-all three were inflammatory lesions resulting from sarcoidosis. To further complicate the issue, a report by Trump *et al*.[77] documents the occurrence of sarcoid-like pulmonary lesions which appeared following cytotoxic and radiation therapy for testis cancer.

Sarcoidosis involving the epididymis may present as a discrete, palpable mass, which is either symptomatic or asymptomatic.[78] The lesions may extend to the tunica albuginea without directly involving the testicular parenchyma.[79] Ultrasound, CT scan, magnetic resonance imaging, and gallium scan have all been useful for diagnosis. Distinguishing these lesions from malignancy is extremely important. Another problem that epididymal sarcoidosis may be associated with is azoospermia, continuous or intermittent.[80] The primary treatment is with corticosteroids.[81] Several alternative therapies can be found in Ghazie and Bhatt.[82]

Finally, sarcoidosis may involve the paratesticular structures, independently of other scrotal contents and must be considered in the differential diagnosis.[83] The treatment of sarcoidosis, in its various manifestations, is by the long-term use of steroids. Treatment suppresses the inflammatory condition which may then return at short or long intervals following treatment cessation.

CONCLUSION

Extrapulmonary manifestations of sarcoidosis may affect up to 25–30% of patients with sarcoidosis. While GU involvement has traditionally been thought of as occurring rarely, many cases go undiagnosed. In fact, sarcoidosis may occur in any and all of the organs of the GU tract; its manifestations are protean, and it may mimic many other diseases, such as cancer. Urologists need to have knowledge and understanding of the various manifestations of GU sarcoidosis, which are outlined in this review. Direct involvement of the GU organs may cause direct or indirect clinical manifestations. In addition, being able to distinguish sarcoid involvement of the urinary tract from primary malignancies is critically important, to avoid unnecessary removal of the organ.

REFERENCES

1. Rybicki BA, Major M, Popovich J Jr., Maliarik MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: A 5-year study in a health maintenance organization. Am J Epidemiol 1997;145:234-41.
2. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007;357:2153-65.
3. Judson MA, Boan AD, Lackland DT. The clinical course of sarcoidosis: Presentation, diagnosis, and treatment in a large white and black cohort in the United States. Sarcoidosis Vasc Diffuse Lung Dis 2012;29:119-27.
4. Kodama K, Hasegawa T, Egawa M, Tomosugi N, Mukai A, Namiki M. Bilateral epididymal sarcoidosis presenting without radiographic evidence of intrathoracic lesion: Review of sarcoidosis involving the male reproductive tract. Int J Urol 2004;11:345-8.
5. Boeck C. Multiple benign sarcoid of skin. JAMA 1899;333:1620-1.
6. Rizzato G. Extrapulmonary presentation of sarcoidosis. Curr Opin Pulm Med 2001;7:295-7.
7. Mayock RL, Bertrand P, Morrison CE, Scott JH. Manifestations of sarcoidosis. Analysis of 145 patients, with a review of nine series selected from the literature. Am J Med 1963;35:67-89.
8. English JC 3rd, Patel PJ, Greer KE. Sarcoidosis. J Am Acad Dermatol 2001;44:725-43.
9. Brincker H, Wilbek E. The incidence of malignant tumours in patients with respiratory sarcoidosis. Br J Cancer 1974;29:247-51.
10. Sharma OP. Sarcoidosis and other autoimmune disorders. Curr Opin Pulm Med 2002;8:452-6.
11. Rajoriya N, Wotton CJ, Yeates DG, Travis SP, Goldacre MJ. Immune-mediated and chronic inflammatory disease in people with sarcoidosis: Disease associations in a large UK database. Postgrad Med J 2009;85:233-7.
12. Moller DR. Rare manifestations of sarcoidosis. Eur Respir J 2005;32:233-50.
13. Vesely DL, Maldonodo A, Levey GS. Partial hypopituitarism and possible hypothalamic involvement in sarcoidosis: Report of a case and review of the literature. Am J Med 1977;62:425-31.
14. Kuznitsky E, Bittoff A. Boecksches sarkoid mit beteiligung innerer organne. Munch Med Wochenschr 1915;62:1349-53.

15. Garland HG, Thomson JG. Ureo-parotid tuberculosis (febris ureoparotidea of Heerfordt). Q J Med 1933;2:157-77.
16. Bergner R, Hoffmann M, Waldherr R, Uppenkamp M. Frequency of kidney disease in chronic sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 2003;20:126-32.
17. Albright F, Reifenstein EC Jr. The Parathyroid glands and Metabolic Bone Disease: Selected Cases. Baltimore: The Williams and Wilkins Company; 1948.
18. Klatskin G, Gordon M. Renal complications of sarcoidosis and their relationship to hypercalcemia; with a report of two cases simulating hyperparathyroidism. Am J Med 1953;15:484-98.
19. Muther RS, McCarron DA, Bennett WM. Renal manifestations of sarcoidosis. Arch Intern Med 1981;141:643-5.
20. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med 1997;336:1224-34.
21. Marinides GN, Hajdu I, Gans RO. A unique association of renal carcinoma with sarcoid reaction in the kidney. Nephron 1994;67:477-80.
22. Lucci S, Rivolta R, Fazi M, Iorio L, Raschellà GF, Merlino G, *et al.* Sarcoidosis and clear cell carcinoma of the kidney: The sixth case? G Chir 2002;23:75-8.
23. Bottone AC, Labarbera M, Asadourian A, Barman A, Richie C. Renal sarcoidosis coexisting with hypernephroma. Urology 1993;41:157-9.
24. Kovacs J, Varga A, Bessenyei M, Gomba S. Renal cell cancer associated with sarcoid-like reaction. Pathol Oncol Res 2004;10:169-71.
25. Singer AJ. Sarcoidosis and renal cell carcinoma. Infect Urol 2002;15:4.
26. Fukutani K, Kawabe K, Moriyama N, Kitamura T, Murakami T. Carcinoma of the renal pelvis and bladder associated with sarcoidosis: A case report. Urol Int 1987;42:224-6.
27. La Rochelle JC, Coogan CL. Urological manifestations of sarcoidosis. J Urol 2012;187:18-24.
28. Rohatgi PK, Liao TE, Borts FT. Pseudotumor of left kidney due to sarcoidosis. Urology 1990;35:271-5.
29. Amouroux J, Michon J, Gurly R, Olivieri P, Michaud B, Roujeau J. Sarcoid pseudo tumor of the kidney. Arch Anat Pathol (Paris) 1967;15:301-3.
30. Miyazaki E, Tsuda T, Mochizuki A, Sugisaki K, Ando M, Matsumoto T, *et al.* Sarcoidosis presenting as bilateral hydronephrosis. Intern Med 1996;35:579-82.
31. Seidemann W. Hydronephrosis caused by enlarged retroperitoneal lymph nodes in sarcoidosis. Dtsch Med Wochenschr 1987;112:1583-5.
32. Hannedouche T, Grateau G, Noël LH, Godin M, Fillastre JP, Grünfeld JP, *et al.* Renal granulomatous sarcoidosis: Report of six cases. Nephrol Dial Transplant 1990;5:18-24.
33. Singer DR, Evans DJ. Renal impairment in sarcoidosis: Granulomatous nephritis as an isolated cause (two case reports and review of the literature). Clin Nephrol 1986;26:250-6.
34. Agrawal V, Crisi GM, D'Agati VD, Freda BJ. Renal sarcoidosis presenting as acute kidney injury with granulomatous interstitial nephritis and vasculitis. Am J Kidney Dis 2012;59:303-8.
35. Ahmed MM, Mubashir E, Dossabhoy NR. Isolated renal sarcoidosis: A rare presentation of a rare disease treated with infliximab. Clin Rheumatol 2007;26:1346-9.
36. Berliner AR, Haas M, Choi MJ. Sarcoidosis: The nephrologist's perspective. Am J Kidney Dis 2006;48:856-70.
37. Kalia V, Vishal K, Gill JS, Gill A. Ureteric sarcoidosis – A rare entity. Br J Radiol 2010;83:e247-8.
38. Mariano RT, Sussman SK. Sarcoidosis of the ureter. AJR Am J Roentgenol 1998;171:1431.
39. Hashimoto Y, Kudoh S, Yamamoto H, Hatakeyama S, Yoneyama T, Koie T, *et al.* Sarcoidosis of the ureter. Urology 2012;79:e81-2.
40. Tammela T, Kallioinen M, Kontturi M, Hellström P. Sarcoidosis of the bladder: A case report and literature review. J Urol 1989;141:608-9.
41. French AJ, Mason JT. Malakoplakia of urinary bladder and sarcoidosis. J Urol 1951;66:229-33.
42. Suzuki M, Ohya K, Nagamatsu H, Mizuo T. Sarcoidosis in a young woman with bladder carcinoma. J Urol 1998;160:123.
43. Carreiro M, Margarit-Coll N, Sailler L, Roussel C, Dahan S, Uro-Coste E, *et al.* Localized amyloidosis of the bladder and sarcoidosis: Analysis of a fortuitous association. Rev Med Interne 2002;23:668-9.
44. Knausz J, Lipták J, Andrásovszky Z, Baranyay F. Vesico-cutaneous fistula revealing abdominal wall malakoplakia accompanied by Boeck's sarcoidosis. Orv Hetil 2010;151:220-3.
45. Brownstein PK, Mannes H, Bogaev JH. Sarcoidosis and malakoplakia. Urology 1975;6:249-51.
46. Fukutani K, Kawabe K, Moriyama N, Kitamura T, Murakami T. Carcinoma of the renal pelvis and bladder associated with sarcoidosis: A case report. Urol Int 1987;42:224-6.
47. Redewill F. Malakoplakia of the urinary bladder and generalized sarcoidosis, striking similarity of their pathology, etiology, gross appearance and methods of treatment. J Urol 1943;49:401-7.
48. Chouaib A, Cabanis P, Billebaud T, El Machkour M. Spinal cord sarcoidosis: An unusual cause of neurogenic bladder dysfunction. J Neurol Res 2011;1:74-7.
49. Cuervo Pinna MA, Cuervo Pinna C, Macías Castillo S, Bureo Dacal JC, Espada Alonso MJ, Pimentel Leo J. Lung sarcoidosis following instillation of mitomycin C in the urinary bladder. An Med Interna 2001;18:641-3.
50. Carr LK, Honey RJ, Sugar L. Diagnosis and management of urethral sarcoidosis. J Urol 1995;153:1612-3.
51. Ho KL, Hayden MT. Sarcoidosis of urethra simulating carcinoma. Urology 1979;13:197-9.
52. Mulpuru SK, Gujja K, Pai VM, Chen CY, Levey RL. A rare and unusual cause of PSA (prostate-specific antigen) elevation: Sarcoidosis of the prostate. Am J Med Sci 2008;335:246-8.
53. Maurice MJ, Zhu H. Sarcoidosis of the prostate. J Urol 2013;190:711-2.
54. Morris SB, Gordon EM, Corbishley CM. Prostatic sarcoidosis. Review of genitourinary sarcoidosis. Br J Urol 1993;72:462-4.
55. Furusato B, Koff S, McLeod DG, Sesterhenn IA. Sarcoidosis of the prostate. J Clin Pathol 2007;60:325-6.
56. Brown CT, Christmas TJ. Prostatic carcinoma and sarcoidosis. BJU Int 2002;90:351-3.
57. Wei H, Friedman KA, Rudikoff D. Multiple indurated papules on penis and scrotum. J Cutan Med Surg 2000;4:202-4.
58. Rubinstein I, Baum GL, Hiss Y. Sarcoidosis of the penis: Report of a case. J Urol 1986;135:1016-7.
59. Whittaker M, Anderson CK, Clark PB. Sarcoidosis of the penis treated by radiotherapy. Br J Urol 1975;47:325-30.
60. Vitenson JH, Wilson JM. Sarcoid of the glans penis. J Urol 1972;108:284-9.
61. Carli G. Boeck-Schaumann sarcoid of the balanopreputial sulcus. Minerva Dermatol 1955;30:178-80.
62. Longcope WT. Sarcoidosis of Besnier-Boeck-Schaumann's disease. JAMA 1941;177:1321-7.
63. Whittaker M, Anderson CK, Clark PB. Sarcoidosis of the penis treated by radiotherapy. Br J Urol 1975;47:325-30.
64. Mahmood N, Afzal N, Joyce A. Sarcoidosis of the penis. Br J Urol 1997;80:155.
65. Niedner R, Wokalek H. Disorders of potency caused by sarcoidosis. Hautarzt 1985;36:563-5.
66. Vahid B, Weibel S, Nguyen C. Scrotal swelling and sarcoidosis. Am J Med 2006;119:e3-5.
67. McLaughlin SS, Linquist AM, Burnett JW. Cutaneous sarcoidosis of the scrotum: A rare manifestation of systemic disease. Acta Derm Venereol 2002;82:216-7.
68. Hausfeld KF. Primary sarcoidosis of the scrotum: Case report. J Urol 1961;86:269-72.
69. Ricker W, Clark M. Sarcoidosis; a clinicopathologic review of 300 cases, including 22 autopsies. Am J Clin Pathol 1949;19:725-49.
70. Schaumann J. Lymphogranulomatosis benigna in the light of prolonged clinical observations and autopsy findings. Br J Dermatol 1936;48:399-446.

71. Koyama T, Ueda H, Togashi K, Umeoka S, Kataoka M, Nagai S. Radiologic manifestations of sarcoidosis in various organs. Radiographics 2004;24:87-104.
72. Rao PK, Sabanegh ES. Genitourinary sarcoidosis. Rev Urol 2009;11:108-13.
73. Gross AJ, Heinzer H, Loy V, Dieckmann KP. Unusual differential diagnosis of testis tumor: Intrascrotal sarcoidosis. J Urol 1992;147:1112-4.
74. May M, Gunia S, Siegsmund M, Kaufmann O, Helke C, Hoschke B, *et al.* Coincidence of testicular germ cell tumor and sarcoidosis: A diagnostic challenge. Urologe A 2006;45:1176-80.
75. Rayson D, Burch PA, Richardson RL. Sarcoidosis and testicular cancer. Cancer 1998;83:33-8.
76. Wettlaufer JN, Modarelli RO. Thoracotomy in re-staging germinal testis tumors. J Urol 1979;122:845-8.
77. Trump DL, Ettinger DS, Feldman MJ, Dragon LH. 'Sarcoidosis' and sarcoid-like lesions. Their occurrence after cytotoxic and radiation therapy of testis cancer. Arch Intern Med 1981;141:37-8.
78. Naseem S, Lindley R, Mufti GR. Testicular sarcoid. Urol Int 2001;67:100-1.
79. Oliva E, Young RH. Paratesticular tumor-like lesions. Semin Diagn Pathol 2000;17:340-58.
80. Svetec DA, Waguespack RL, Sabanegh ES Jr. Intermittent azoospermia associated with epididymal sarcoidosis. Fertil Steril 1998;70:777-9.
81. Rees DA, Dodds AL, Rathbone N, Davies JS, Scanlon MF. Azoospermia in testicular sarcoidosis is an indication for corticosteroid therapy. Fertil Steril 2004;82:1672-4.
82. Ghazie H, Bhatt S. Testicular sarcoidosis: Sonographic findings. J Diagn Med Sonogr 2011;27:126-30.
83. Schaeffer J, Nussbaum M, Meyersfield S. Paratesticular mass as a presenting sign of sarcoidosis. Pediatrics 1980;66:462-3.

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