



Sarcoidosis of the prostate gland

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Abstract

Sarcoidosis of the prostate gland (SOP) is rare and so far only 15 cases of SOP have been reported in men aged between 25 years and 78 years. SOP may be diagnosed following trans-rectal ultra-sound guided biopsy of the prostate during investigation for raised serum prostate-specific antigen (PSA) to exclude prostate cancer. SOP may present with pain in the penis, absence or reduction in the volume of ejaculate and histological examination of prostate biopsy specimen would then show features of SOP. SOP may also be diagnosed following histological examination of specimens obtained from trans-urethral resection of prostate or open prostatectomy undertaken for bladder outlet obstruction presumed to be due to benign prostatic hyperplasia or radical prostatectomy for carcinoma of prostate. SOP may co-exist with carcinoma of the prostate gland. There may or may not be a history of treatment for current or previous systemic sarcoidosis. Kveim test tends to be positive and serum angiotensin converting enzyme levels tend to be elevated. Histology examination of the prostate tends to show non caseating granulomas, Langhan's giant cells and may show conchoidal bodies. Immunohistochemistry of the prostate lesion tends to exhibit positive staining for angiotensin converting enzyme. Stains for tuberculosis and fungi would be negative. SOP tends to resolve spontaneously or with steroid treatment. New cases of SOP should be reported in other that the biological behaviour of the disease is well understood.

Key Words: Sarcoidosis of prostate, prostate-specific antigen, non-caseating granuloma, Kveim test, Serum angiotensin converting enzyme, asteroid bodies, Schaumann bodies

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Introduction

Sarcoidosis is an uncommon disease entity which tends to cause small patches of granulomas to develop in the organs of the body. Systemic sarcoidosis can affect a variety of organs and the symptoms of sarcoidosis would depend upon the particular organs involved by the disease. Sarcoidosis of the prostate has been reported sporadically over the years in the literature and to the knowledge of the

author about 15 cases of sarcoidosis of the prostate gland (SOP) have been reported in the literature. In view of the rarity of SOP majority of practitioners would be unfamiliar with the manifestations and biological behaviour of the disease. The ensuing literature review related to sarcoidosis with a focus on sarcoidosis of the prostate gland (SOP) is divided into two parts: (A) overview and (B) miscellaneous narrations and discussions from some reported cases.

Method

Various Internet data bases were searched including: Google, Google scholar, Educus, and PUB Med. Search words that were used included: sarcoidosis of the prostate, prostate sarcoidosis, sarcoid of the prostate.

Literature Review

(Section A) Overview

Definition

Sarcoidosis is an inflammatory condition which tends to affect multiple organs within the body, but on majority of occasions it tends to affect

the lungs and lymph glands. Granulomas tend to form in certain organs of the body and they may alter the normal architectural structure and also has the possibility of altering the way the affected organ functions.

) Sarcoidosis has also been defined as a disorder which causes tiny nodules called granulomas of inflamed tissue to develop in the organs of the body. These nodules have the ability to coalesce together to form larger nodules which tend to interfere with normal body functions for example breathing. Sarcoidosis almost invariably tends to involve the lungs; however, sarcoidosis can also affect other organs / tissues including the skin, eyes, nose, muscles, heart, liver, spleen, bowel, kidney, testes, nerves, lymph nodes, joints, and brain. Granulomas in the lungs have the ability to cause narrowing of the airways and inflammation and fibrosis of lung tissue. [1]

) Though sarcoidosis tends to affect multiple organs at times sarcoidosis may present as a single organ disease; however, in a number of cases of single organ manifestations of sarcoidosis a history of previous treatment for sarcoidosis may be obtained.

Epidemiology

La Rochelle and Coogan [2] stated the following:

o Sarcoidosis is an idiopathic multi-organ granulomatous disease which can affect virtually any organ of the body; nevertheless, sarcoidosis does not often involve organs of the genitourinary tract.

o Sarcoidosis has a peak incidence in the early stage of adulthood between the ages of 20 years and 40 years and with regard to race, sarcoidosis tends to exhibit predilection for the African-Americans in comparison with other racial groups

Sarcoidosis of the prostate gland is rare and since Dr Ernest Besnier first described sarcoidosis [3] less than 20 cases of sarcoidosis of the prostate gland have been reported in the literature, in view of this information related to sarcoidosis of the prostate gland is limited. However, sarcoidosis of the prostate gland has been reported in men whose ages have ranged between 25 years and 78 years (see table 1 from references 4 to 14).

Aetiology

It has been stated that a number of postulates exist regarding the cause of sarcoidosis including: [13]

-) Environmental exposure
-) A genetically inherited predisposition to develop sarcoidosis
-) Viral infection
-) Over-activity of the immune system
-) A combination of the aforementioned factors.

Presentation

Sarcoidosis of the prostate could be a sporadic sarcoidosis or it may be part of systemic sarcoidosis and the presentation may be variable.

Generally sarcoidosis may present with respiratory, skin, and ocular involvement but on the whole any organ can be involved inclusive of joints, kidney, liver, gastrointestinal tract, heart, nervous system and the genitourinary system and the presentation of sarcoidosis would depend upon the organs involved.

o It has been stated that sarcoidosis (pulmonary sarcoidosis) tends to be found incidentally, based upon chest radiograph image findings, however, other non-specific symptoms including cough, fatigue, or dyspnoea on exertion and that within the United States of America, the typical triad of hilar lymph node enlargement, polyarthralgias, and erythema nodosum is encountered in approximately 10% of patients with sarcoidosis. [2] [14]

o It has been stated that it is uncommon for urologists to encounter sarcoidosis in their practice; nevertheless, sarcoidosis in urological practice may be encountered in association with hypercalciuria, which is found in 60% of cases of sarcoidosis, or its complications including nephrolithiasis, nephrocalcinosis or renal dysfunction. [2] [14]

o It has also been stated that the involvement of the genitourinary tract by sarcoidosis as well as sarcoidosis lymph node enlargement can simulate severe infections or metastatic malignant lesions involving the genito-urinary tract. [2] [14]

o It has been stated that sarcoidosis of the prostate tends to be asymptomatic, and that sarcoidosis of the prostate gland has been reported as autopsy findings, prostate biopsy finding, or histological examination of specimen of prostate in the evaluation to exclude cancer of the prostate. [14]

o A case of sarcoidosis of the prostate was established in the investigation of a man who presented with reduction in the volume of his ejaculate as well as pain in his penis [7]

o A patient with a past history of treatment for pulmonary sarcoidosis was referred to be seen by the urologist because of raised serum PSA and examination of his prostate biopsy specimen showed

sarcoidosis of the prostate and absence of prostatic cancer. It has been explained that raised levels of serum PSA could likely occur in sarcoidosis as a sequel of inflammatory disturbances within the ductal system of the prostate gland. [14]

○ A patient who has sarcoidosis of the prostate and associated benign prostatic hyperplasia or carcinoma of the prostate may or may not present with lower urinary tract symptoms. There is no specific presenting symptom that is diagnostic of sarcoidosis of the prostate and even a history of systemic sarcoidosis would not be indicative of sarcoidosis of the prostate because diagnosis of sarcoidosis of the prostate tends to be a diagnosis of exclusion of other common prostate pathologies.

On the whole the presentations of sarcoidosis of the prostate gland could be summarized as follows:

) Asymptomatic presentations in which sarcoidosis of the prostate is incidentally found on (a) histological examination of prostate specimens obtained after trans-urethral of prostate or open prostatectomy specimens when the operations were undertaken with a pre-operative provisional diagnosis of benign prostatic hypertrophy/hyperplasia

) Raised Serum Prostate Specific Antigen levels: Sarcoidosis of the prostate may be encountered incidentally when a patient undergoes prostate biopsy for raised levels of PSA to exclude prostate cancer.

) Investigation for a nodule or mass within the prostate gland to exclude prostate cancer

) Radical prostatectomy specimen for prostate cancer or open prostatectomy for presumed benign prostatic hypertrophy

) Lower urinary tract symptoms of urinary frequency, / urgency/poor flow

) Reduction in volume of ejaculate

) Penoscrotal pain

Clinical Examination findings

) There is no specific clinical examination finding which could be considered to be diagnostic of sarcoidosis of prostate. However, in cases of sarcoidosis of the prostate gland associated with systemic sarcoidosis there would be clinical signs of lesions related to the organs involved.

) Digital rectal examination of the prostate may reveal features of a benign prostate, but in some cases of sarcoidosis of the prostate associated with carcinoma of the prostate gland there may be a palpable nodule in the prostate or the area of the prostate gland involved with the carcinoma may feel hard but these findings would not be diagnostic of sarcoidosis of the prostate.

Investigations

Urinalysis microscopy and urine culture

) Urinalysis, urine microscopy and culture are routine examinations that tend to be undertaken to confirm there is not urinary tract infection and if there is urinary tract infection the sensitivity pattern of the organism to antibiotics is determined in order to appropriately treat the infection.

) Prostate biopsy is undertaken when there is no evidence of urinary tract infection but in cases of urinary tract infection the infection would be treated before proceeding to trans-rectal ultrasound scan of prostate and biopsy.

Haematological investigation

) Full blood count and coagulation screen tend to be undertaken as part of the general assessment of a patient with sarcoidosis of the prostate but the results would not be diagnostic of sarcoidosis. Considering the fact that tuberculosis of the prostate gland could be a differential diagnosis of sarcoidosis of the prostate gland if there is evidence of lymphocytosis other tests including urine microscopy and culture to exclude acid and alcohol fast bacilli (tuberculosis culture) would be undertaken as part of the general screening of the patient.

Biochemistry investigations

) Serum urea and electrolytes, liver function tests and serum glucose are routine tests that tend to be undertaken as part of the general assessment of the patient but these are not diagnostic of sarcoidosis of the prostate gland.

) Serum angiotensin converting enzyme levels may be elevated in a number of cases of systemic sarcoidosis and sarcoidosis of the prostate gland but the results of raised serum ACE levels though suggestive of the possibility of sarcoidosis would not be diagnostic of sarcoidosis of prostate they would rather be supportive of a diagnosis of sarcoidosis of the prostate gland based upon the histopathology findings of the prostatic specimen.

Kveim-Siltzbach test

) The Kveim-Siltzbach (KS) skin test has been in use globally for about 75 years. The test is a safe, simple, and specific outpatient technique which is used to confirm the diagnosis of sarcoidosis and to provide evidence of the state of activity of the disease. It has been stated that the test is helpful in the delineation of sarcoidosis as a cause of erythema nodosum, uveitis, liver granulomas, hypercalciuria, and meningitis. [15] The positive KS skin test would be suggestive of sarcoidosis; however, it is only a proven histopathological examination features of specimens of the prostate gland that would be

confirmatory of a diagnosis of sarcoidosis of the prostate gland.

Radiological Investigations

) Trans-rectal ultra-sound scan of the prostate gland

○ Trans-rectal ultrasound scan of prostate biopsies tend to be the usual way of assessing the prostate gland and obtaining specimens of the prostate gland for histological examination in the investigation of patients who have raised serum levels of prostate-specific antigen (PSA) and abnormal digital examination findings of the prostate gland. Based upon the histological findings a diagnosis of sarcoidosis of the prostate gland can be made and if there is another lesion of the prostate gland this can also be found. Trans-rectal ultrasound scan of the prostate gland can be used to measure the size of the prostate gland and to identify the echotexture of the prostate gland as well as differentiate between iso-echoic, hyper-echoic, and hypo-echoic areas of the prostate gland. The seminal vesicles and ejaculatory ducts can be assessed by the ultrasound scan. When a diagnosis of sarcoidosis of prostate gland is established via trans-rectal ultrasound guided biopsy of the prostate, subsequent trans-rectal ultrasound scan of the prostate can be undertaken after the patient has been on treatment with steroids to see if the size of the prostate gland had decreased as well as whether or not there has been reduction in size or resolution of abnormal areas in the prostate gland.

) Computed tomography (CT) Scan of abdomen, pelvis and thorax

○ CT scan of thorax, abdomen and pelvis when undertaken would show whether or not there are pulmonary or mediastinal lesions, intra-abdominal lesions, retroperitoneal lesions or pelvic lesions as part of systemic sarcoidosis and if there are lesions anywhere in the thorax, abdomen and pelvis these can be biopsied as part of the general investigation of the patient to establish the diagnosis of systemic sarcoidosis in addition to sarcoidosis of the prostate gland. CT scan of thorax, abdomen and pelvis can be undertaken as part of the follow-up of a patient who has been diagnosed with systemic sarcoidosis to assess for progress or resolution of the sarcoidosis.

) Magnetic Resonance Imaging (MRI) Scan of thorax, abdomen and pelvis

○ MRI scan of thorax abdomen and pelvis can be undertaken in cases of systemic-sarcoidosis associated with sarcoidosis of the prostate as part of the investigation of the patient and any lesions found can be biopsied for pathology examinations to

establish the diagnosis of sarcoidosis. Subsequent MRI scans of thorax, abdomen and pelvis can be undertaken in the follow-up of the patient to ascertain whether the sarcoidosis lesion or lesions are progressing or resolving.

) Special bacteriological stains for AFB and fungi

○ Special bacteriological stains for acid fast bacilli (AFB) and fungi tend to be undertaken to exclude tuberculosis and fungal infection of the prostate, in order to confirm the diagnosis of sarcoidosis of the prostate gland.

Pathology investigations

) Macroscopic features

○ There have been no distinct macroscopic characteristic features described that would be specifically diagnostic of sarcoidosis of the prostate gland.

) Microscopic features

Some of the microscopic features of sarcoidosis of the prostate gland have been summarized by Maurice and Zhu as follows: [14]

○ Evidence of noncaseating epithelioid granulomas in the prostate specimen tend to be the hallmark diagnostic feature of sarcoidosis (see figure 1 for example). Maurice and Zhu [14] explained that there is the belief that sarcoidosis granulomas tend to develop at sites of inflammation which emanate pursuant to exposure to an inciting agent which is not yet known.

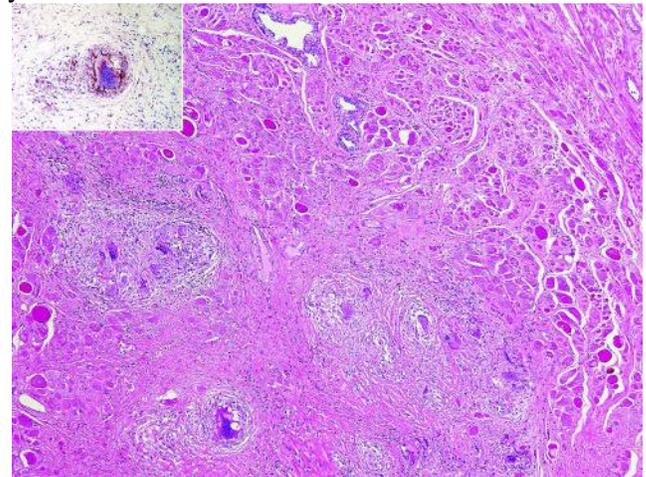


Figure 1: Non-caseating epithelioid, granuloma in anterior fibromuscular stroma (H&E, x 40) Inset, angiotensin-converting enzyme (ACE) positive in epithelioid histiocytes (anti-ACE, x 160) Reproduced from: [12] Furusato B, Koff S, McLeod D G, Sesterhenn I A. Sarcoidosis of the prostate. J. Clin. Pathol 2007 Mar; 60(3): 325 – 326. DOI: 10.1136/jcp.2006.039222 copyright © 2007 The BMJ Publishing Group and the Association of Clinical Pathologists which states that articles published in in these Journals are in the public

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- Sarcoid granulomas characteristically tend to be composed of an organized collection of epithelioid histiocytes, multi-nucleated Langhans-type giant cells and encompassing lymphocytes which usually tend not to be associated with necrosis. It should be pointed out that the aforementioned cytological features in the absence of granulomas would perhaps point towards a diagnosis of chronic prostatitis.

- Some other non-specific cytoplasmic inclusions may be observed in sarcoidosis of the prostate and these would include: stellate asteroid bodies; laminated calcific Schaumann bodies; small oval, brown Hamazaki-Wesenberg bodies; as well as calcium oxalate crystals.

- Immunohistochemistry

- Maurice and Zhu [14] stated that immunohistochemistry study of the prostate-biopsy specimen could be utilized to localize angiotensin-converting enzyme to the epithelioid component of sarcoidosis granulomas; nevertheless, the aforementioned finding is not pathognomonic of sarcoidosis.

- Special stains for acid-fast bacillus and fungi

- Considering the fact that the differential diagnoses of sarcoidosis of the prostate gland include tuberculosis and fungal infections special stains for acid fast bacillus and fungi tend to be undertaken to confirm there is no fungal or tuberculous infection of the prostate gland.

Differential diagnosis

- Maurice and Zhu [14] stated that some of the causes of granulomatous inflammations of the prostate gland that occur include: Infection; surgical manipulation; intra-vesical instillations with Bacillus Calmette-Guerin (BCG), [also called BCG prostatitis]; systemic granulomatous diseases affecting the prostate gland and other uncommon diseases.

- Idiopathic granulomatous prostatitis constitutes the majority of cases of granulomatous prostatitis [14]. In idiopathic granulomatous prostatitis histological examination tends to show marked replacement of the parenchyma of the prostate gland by inflammatory cells and fibrosis.

- Tuberculosis prostatitis is another differential diagnosis and acid fast staining is useful in excluding tuberculous prostatitis [14]

- Fungal prostatitis is yet another differential diagnosis of sarcoidosis of the prostate gland and

silver staining is useful in excluding fungal prostatitis from sarcoidosis of the prostate [14]

With regard to differentiating sarcoidosis of the prostate gland from other granulomatous prostatitis, it has been stated that (a) post-operative granulomatous prostatitis tends to exhibit distinct circumscribed granulomas that are comprised of central fibrinoid necrosis as well as palisading histiocytes; (b) Post intra-vesical BCG instillation induced prostatitis tends to exhibit discrete, well-formed granulomas close to benign prostate gland tissues, with or without evidence of caseation and they also tend to be preferentially situated along the peri-urethral-zone and furthermore they tend to contain acid-fast bacilli. [14]

Morris et al. BJU [7] also stated that other causes of granulomatous prostatitis can mimic sarcoidosis of the prostate gland and these include:

- Trauma including trans-urethral resection of prostate gland

- Tuberculosis

- Fungal infections

- Non-specific granulomatous prostatitis

Treatment

Considering the fact that less than 20 cases of sarcoidosis of the prostate gland have been reported there is no consensus opinion on the best management option for sarcoidosis of the prostate gland. Options of management of sarcoidosis include: Conservative wait and see approach, medical therapy with steroids, and surgical treatment.

- Conservative treatment

- Considering the fact that various cases of sarcoidosis have been associated with spontaneous resolution it could be argued that patients who are diagnosed with sarcoidosis of the prostate gland should be given the option of the conservative wait and see approach to the management of the disease but if there is no resolution or improvement then they should be offered the other alternative forms of treatment. For instance if a patient is investigated for raised serum PSA levels and lower urinary tract symptoms and is found to have a benign enlarged prostate but the histological examination shows only sarcoidosis of the prostate and benign prostatic hyperplasia and the symptoms are significant the patient can be given an alpha blocker treatment to help improve the lower urinary tract symptoms provided urethral stenosis is excluded. If the symptoms improve then no further treatment may be required. In the same way patients who do not have lower urinary tract symptoms who are investigated for raised serum PSA who undergo trans-rectal ultra-

sound guided biopsies of prostate of which histological examination shows sarcoidosis of the prostate can be observed and followed up with serum PSA surveillance, symptomatic follow-up and subsequent trans-rectal ultra-sound scan looking for resolution of the lesion in the prostate. In such situations if the serum PSA level subsequently drops then medical treatment in the form of steroids would not be required.

Medical treatment

A number of cases of sarcoidosis tend to resolve with steroid treatment; hence patients who are diagnosed with sarcoidosis of the prostate gland can be offered the option of medical treatment and they can be offered steroids (prednisolone) and followed-up for resolution of the disease.

Surgical treatment

A number of cases of sarcoidosis generally have been treated by means of surgical excision of the lesions if they do not respond to medical treatment. In some cases if the lesions are excised totally before histological diagnosis of sarcoidosis is obtained then the patients can be observed or offered medical treatment with steroids as additional step to speed up resolution of other sarcoidosis lesions in cases of systemic sarcoidosis.

In the event a patient undergoing trans-urethral resection of prostate or open prostatectomy for lower urinary tract symptoms with a presumptive diagnosis of benign prostatic hypertrophy and histological examination of the specimen shows sarcoidosis, if the patient’s symptoms improve after the operation there would be two further options of wait and see (conservative approach) or further medical treatment with steroids in cases of associated systemic sarcoidosis if the patient wants it.

Reference Year reported	Age years	Prostatic symptoms	Indication for biopsy or resection of prostate	PSA Results	Other organs involved by sarcoidosis	Presence or absence of carcinoma of prostate
Case 1 Schaumann [2] 1936	42 years	Not reported	Autopsy	Not available to author	Lungs	No prostate cancer
Case 2 Ricker & Clark [3] 1949	25 years	Not reported	Autopsy	Not available	Not reported	No prostate cancer
Case 3 Todd & Garnick. [4] 1980	78 years	No symptoms	Nodule in prostate	Not available to author	Skin	Yes associated prostate cancer
Case 4 Morris et al. [5] 1993	28 years	Yes et symptomatic	Penile pain & reduced volume of ejaculate / retrograde ejaculation	Not available to author	Skin & lungs	No prostate cancer
Case 5 Deliveliotis et al. [6] 2002	48 years	No symptoms	Carcinoma	Not available to author	Lungs	Yes associated prostate cancer
Case 6 Brown et al. [7] 2002	53 years	Not reported	Carcinoma	Not available to author	Not reported	Yes associated prostate cancer
Case 7 Brown et al. [7] 2002	72 years	Not reported	Carcinoma	Not available to author	Not reported	Yes associated prostate cancer
Case 8 Brown et al. [7] 2002	74 years	Not reported	Carcinoma	Not available to author	Lungs	Yes associated prostate cancer
Case 9 Brown et al. [7] 2002	69 years	Not reported	Carcinoma	Not available to author	Skin & Lungs	Yes associated prostate cancer
Case 10 Brown et al. [7]	49 years	Not reported	Carcinoma	Not available to author	Lungs	Yes associated prostate cancer

2002						
Case 11 Hardebeck [8] 1953	Age not available to author	Not reported	Not available to author	Not available to author	Not available to author	Not available to author
Case 12 Ros et al. [9] 1996	Age not available to author	No symptoms	Carcinoma	Not available	Not reported	Yes associated prostate cancer
Case 13 Furusato et al. [10] 2007	55 years	Not reported	Carcinoma	Raised serum PSA level	Yes but the site of sarcoidosis was not reported	Yes associated prostate cancer
Case 14 Mulpuru et al. [11] 2008	45 years	Yes symptomatic	Raised serum PSA level	Raised serum PSA 7.15 ng / ml (normal range 0 to 4 ng/ml).	Lungs, kidney & liver	No associated prostate cancer
Case 15 Maurice A J & Zhu H [12] 2013	65 years	Asymptomatic but had raised serum PSA	Raised serum PSA	7.2 ng/ml	Previous treatment 2 years earlier for pulmonary sarcoidosis	No associated prostate cancer

Outcome

) In view of the rarity of sarcoidosis the biological behaviour of the disease is not well known; nevertheless, the disease is generally considered to exhibit benign biological behaviour and tends to be self-limiting. [14]

) Some authors had stated that even though sarcoidosis of the prostate gland and carcinoma of the prostate gland may quite often co-exist, there is so far no information that supports a causative relationship of sarcoidosis of the prostate gland and carcinoma of the prostate gland. [13] [16] [17]

) It has been stated that sarcoidosis of the prostate gland can cause a rise in serum PSA levels as other forms of granulomatous prostatitis cause a rise in serum PSA levels; nevertheless, biopsy of the prostate gland is the only way a definite diagnosis can be established. Furthermore, it has been stated that knowledge of a pre-existing sarcoidosis should not exclude biopsy of the prostate gland with particular reference to the African American men which constitute a group of men that are known to have a higher risk for the development of sarcoidosis as well as prostate cancer. [14]

) Maurice and Zhu [14] recommended that irrespective of comorbidity of the patients with sarcoidosis, prostate biopsy should be undertaken in age and risk appropriate men with raised serum levels of PSA and / or abnormal rectal examination of prostate findings as has been recommended by the American Urological Association. [18]

) On the whole it would be said that majority of cases of sarcoidosis of the prostate would resolve

or improve with conservative and / medical treatment with steroids.

(B). Miscellaneous narrations from some reported cases

The first case of sarcoidosis of the prostate gland was reported by in 1936 in a patient who had disseminated multi-system sarcoidosis. [4] In 1949, Ricker and Clark [5] undertook a review of the clinicopathological features of three hundred cases of sarcoidosis which included findings from twenty autopsies in which they found one case of sarcoidosis of the prostate gland. [5] Morris et al, [7] reported a man who had a known history of sarcoidosis who presented with pain in his penis as well as reduction in the volume of his ejaculate. He had prostate biopsy and histological examination of the specimen showed many granulomas. Todd and Garnick [6] reported a patient who had hypercalcemia, adenocarcinoma of the prostate gland, and sarcoidosis of the prostate gland. They stated that their case was the second reported case of sarcoidosis associated with adenocarcinoma of the prostate gland and their case would depict the intriguing association between systemic sarcoidosis and malignancy.

Morris et al. [7] in 1993 reported a 28-year-old man who had presented in 1986 with pain in his penis as well as reduction in the volume of his ejaculate. His mother did have a history of having had pulmonary as well as sarcoidosis of the skin. Five years prior to his presentation he had had a skin lesion and he had had X-ray of his chest at that time and the features of the skin lesion as well as the changes on his chest radiographs were adjudged to be

consistent with sarcoidosis. At that time five years earlier he had a Heaf test which was normal and because he was lost to follow-up he did not have a chance to have Kveim test. At the time of his presentation in 1986 he did undergo trans-rectal biopsy of the prostate gland and histological examination of the specimen had shown a tiny focus of central necrosis. Mycobacterium was not seen on microscopic examination of the specimen and tuberculosis stains and cultures for acid and alcohol fast bacilli were negative. His symptoms did not improve pursuant to a trial of anti-tuberculous therapy. He next underwent trans-urethral resection of his prostate gland and histological examination of the specimen did show non-specific inflammation. Two years after he had undergone trans-urethral resection of his prostate gland he presented with worsening pain in his right epididymis which on examination was found to be nodular. He had another Heaf test which was negative. He underwent right epididymectomy and histological examination of the specimen findings mimicked the findings of the original prostate biopsy specimens. Acid and alcohol fast stains of the specimen were negative. He had a skin lesion which was excised and histological examination of the specimen showed non caseating granulomas. His serum angiotensin converting enzyme level was slightly higher than the upper limit of the normal range and based upon the aforementioned findings, a diagnosis of sarcoidosis was made. He was next treated by means of daily prednisolone therapy which resulted in symptomatic relief. He remained asymptomatic for some time but subsequently developed peno-scrotal pain and again had another biopsy of the prostate gland. Histological examination of the prostate biopsies again showed granulomas. His symptoms improved spontaneously except for his retrograde ejaculation.

Furusato et al. [12] reported a 55-year-old African-American man whose serum prostate specific antigen (PSA) level was noted on routine screening to be 6.53 ng / ml. He had rectal examination which had revealed his prostate gland to be normal. He had trans-rectal ultrasound guided biopsy of the prostate gland and histological examination of the specimen revealed features which was adjudged to be consistent with adenocarcinoma of the prostate gland Gleason 5+3 = 8 and the tumour was then staged as T1c. He underwent radical prostatectomy in January 2003 and pathological examination of the specimen showed seven foci of Gleason 3 + 4 = 7 adenocarcinoma of the prostate gland in the largest tumour and the pathological stage of the tumour was adjudged to be T3a. Pathological examination of the

specimen also showed a group of non-caseating, epithelioid granulomata adjoining the anterior-fibromuscular stroma and also adjoining one of the tumours (see figure 1). The granuloma contained Langhans-type giant cells, and one of them contained a calcified conchoidal (Schaumann) body. Immunohistochemistry studies of the specimen showed that the epithelioid cells were positively stained for angiotensin-converting enzyme (see figure 1 inset). The distribution of the granulomas was reported not to be that of non-specific granulomatous prostatitis (unlike granulomatous prostatitis) where the granulomas tend to be centred, around the ducts and the glands. There was no evidence of necrosis which would indicate a granulomatous inflammation due to microorganisms. The typical appearance of post-transurethral resection of prostate granulomas was not observed. The histological appearance of the granulomas was adjudged to be diagnostic of sarcoidosis. In support of the diagnosis, there was a history of the patient having undergone treatment for sarcoidosis four years earlier. There was no report of the long-term follow-up outcome of the patient at the time of the report of the case.

Mulpuru et al. [13] reported a 45-year-old African American man who had a routine laboratory blood test as part of an assessment for a job which showed abnormal renal function and liver function test results. He had lost 34 pounds over the preceding 2 years in the absence of loss of appetite. Over the preceding 3 months he had been having hesitancy and urinary frequency. He had had trans-bronchial biopsy 4 years earlier and histological examination findings of the specimen had confirmed pulmonary sarcoidosis for which he received oral prednisolone treatment for 3 to 4 months which had improved his symptoms and the treatment was stopped. His general and systematic examinations were normal and he had a rectal examination which revealed a normal feeling prostate. In view of the fact that he had impaired renal and liver function he had autoimmune workup and the test results were normal. He had other investigations which were reported as follows: Serum angiotensin converting enzyme (ACE) level was raised at 141 U/L (normal range, 8 – 52 U/L). He had biopsies of the kidney and liver and histological examination of the specimens showed sarcoidosis granulomas. He had a family history of carcinoma of the prostate. He had a serum PSA, of 7.15 ng / ml (normal range 0 to 4 ng/ml). His urinalysis was normal except for mild proteinuria of 1+. He had a skin test for latent tuberculosis which was normal. He had a chest radiograph which showed marked hilar lymph adenopathy that was bilateral associated with

prominent reticular pattern of lung markings that was adjudged to be consistent with stage II sarcoidosis. He underwent prostate biopsies and histological examination of the specimen showed non caseating epithelioid granulomas with multi-nucleated giant cells which did confirm the diagnosis of sarcoidosis of the prostate gland. Mycobacteria and fungi were not seen in the specimen on special staining. Immunohistochemistry studies of the specimen with CK908 (which is a marker for keratins) showed a tiny focus of atypical prostate glands which had a breach in the basal cell layer. Nevertheless, the pathologist felt that the focus was too tiny to be categorized as a carcinoma therefore it was decided to follow the progress of the serum PSA clinically upon the basis of the diagnosis of sarcoidosis of the prostate gland. His repeat serum PSA 3 months later was 6.7 ng/ml and he had remained under serum PSA surveillance at the time of publication of the paper. Mulpuru et al. [13] stated the following:

) Sarcoidosis of the prostate gland and carcinoma of the prostate gland are two separate disease entities that tend to be prevalent among African American population.

) Nevertheless, sarcoidosis of the prostate gland is an extremely rare clinical condition.

) The association of sarcoidosis with carcinoma of the prostate gland has been described in clinical case series publications.

) The use of serum prostate-specific antigen (PSA) test for the purpose of screening for carcinoma of the prostate gland may be associated with false-positive results in the African American population.

Whilst it is known that raised serum levels of prostate-specific antigen (PSA) could be related to urinary tract infection, carcinoma of the prostate gland, prostatitis and with ordinary benign enlargement of the prostate gland, this case report would indicate that sarcoidosis of the prostate gland though rare is one of the clinical conditions that may be associated with elevated serum levels of PSA.

Maurice and Zhu, [14] reported a 65-year-old African American man who was investigated for having a raised serum prostate specific antigen level of 7.2 ng/ml. He underwent trans-rectal ultrasound guided biopsy of his prostate gland and histological examination of the specimen showed non-caseating granulomas in the left lobe of the prostate without any evidence of malignancy of the prostate gland. Staining for acid-fast bacilli and fungi revealed negative results. It became apparent that the patient had undergone treatment two years earlier for pulmonary sarcoidosis. The patient did not have any

previous history of urinary tract infection, intra-vesical instillations of bacillus Calmette-Guérin (BCG) instillations, previous biopsy of prostate gland, or trans-urethral resection of prostate gland. Based upon the aforementioned findings a diagnosis of sarcoidosis of the prostate gland was made and this diagnosis was said to be consistent with his history of previous treatment for sarcoidosis. Maurice and Zhu [14] stated that their case was an example of systemic sarcoidosis which had involved the prostate gland. They also stated that in 2008 Mulpuru [13] had stated that 14 cases of sarcoidosis of the prostate gland had been reported.

Conclusions

Sarcoidosis of the prostate gland has been rarely reported in the literature. Whether the rarity of sarcoidosis of the prostate gland in the literature is truly due to the rarity of the disease or clinicians do not have a high index of suspicion for the existence of the disease cannot be ascertained. Clinicians should have a high index of suspicion of SOP and they should report cases of SOP they encounter in order to throw more light into the biological behaviour of the disease.

Conflict of Interest: None

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