Journal of Medical Science & Technology

Review article Open Access

Sarcoidosis of The Epididymis

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Abstract

Sarcoidosis of the epididymis (SOE) is reported as the most common form of sarcoidosis affecting the male reproductive organs in the literature. Various internet data bases were searched to obtain information on publications related to SOE. Salient documentations related to SOE would be summarized as follows: SOE could be asymptomatic or present with a unilateral or bilateral, painless or painful hemi-scrotal mass which may or may not be associated with infertility. Features of a multi – systemic disease may also be present. SOE may be considered as a diagnosis of exclusion after ruling out malignancies, tuberculosis and other differential diagnoses. Increased susceptibility is seen in the black populace. There is no definitive diagnostic biomarker at present but angiotensin – converting enzyme, C-reactive protein and γ – globulin may be elevated. Treatment options include watchful waiting, medical or surgical therapy. SOE is as common as sarcoidosis of the testis and often co – exists with it.

Keywords: Sarcoidosis of testis, Boeck's disease, Schaumann bodies, asteroid bodies, watchful waiting, medical therapy, surgical therapy.

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Received: December 20, 2016 Accepted: March 1, 2017. Published: April 20, 2017.

Introduction

Sarcoidosis is a granulomatous disease of unknown aetiology that can involve multiple systems. 1 The most common affectation is pulmonary, seen in up to 84% of cases. [1,2] Sarcoidosis was first described by Jonathan Hutchinson in 1897, but it is also known as Boeck's disease after Caesar Boeck, who further described the histology, clinical features and multi - systemic nature of the disease. [3,4]

It involves the genitourinary organs in 0.2% of cases, and has a predilection for blacks. [5] Jorgen Schauman [6] reviewed four autopsies in 1936, one of which had sarcoidosis of the epididymis (SOE). That was the first description of such an entity in the English literature. He listed the epididymis as one of the "less common localizations" of sarcoidosis, among others like the prostate, hypophysis, intestines and trachea. [7] Prior to this, in 1919, J van Husen of Germany had actually reported a case of SOE in a 17 year old white male who also had cutaneous and ocular sarcoidosis. [8]

Literature review

OVERVIEW

Epidemiology: SOE is the most common form of genitourinary sarcoidosis occurring in 67 - 73% of male reproductive tract involvement, and accounting for 73% of 60 known cases of histologically confirmed disease. [9,10,11] The others involved were the testis (47%), spermatic cord (8%), tunica albuginea (5%) and prostate (3%). [11] SOE accounts for less than one percent of all cases of sarcoidosis and is bilateral in less than 1% of cases. [12, 13]

It is more common in men of African descent between the ages of 20 and 40 years. In a review of 23 cases of epididymal sarcoidosis, 17 (74%) were stated to be black. 8 It was previously more often than not, a post mortem diagnosis, in up to 51% of cases, but this has changed with increasing awareness [14]. Although it has been stated that almost all cases

of SOE co-exist with sarcoidosis of the testis, another author believes that SOE affects the testis by contiguity [15, 16]. Winter [17] however, documented that concomitant involvement of both the testis and epididymis is rare.

Aetiology: A genetic predisposition to developing sarcoidosis is raised by the predominantly Negroid affectation [7] and some patients with a positive family history. [14,18] Germans and Negroids with sarcoidosis have been found to have chromosomal mutation similarities involving chromosomes 6 and 5 respectively. [19] The actual aetiology has remained unknown. [20]

Anatomy: The epididymides lie posterior to the testes and are connected to the testes at the superior pole via 15 – 20 efferent ductules that fuse to a single convoluted tubule in the head of the epididymis (globus major). This convoluted tubule moves along the body to the tail of the epididymis (globus minor) from whence it leaves the epididymis as the vas deferens. [21]

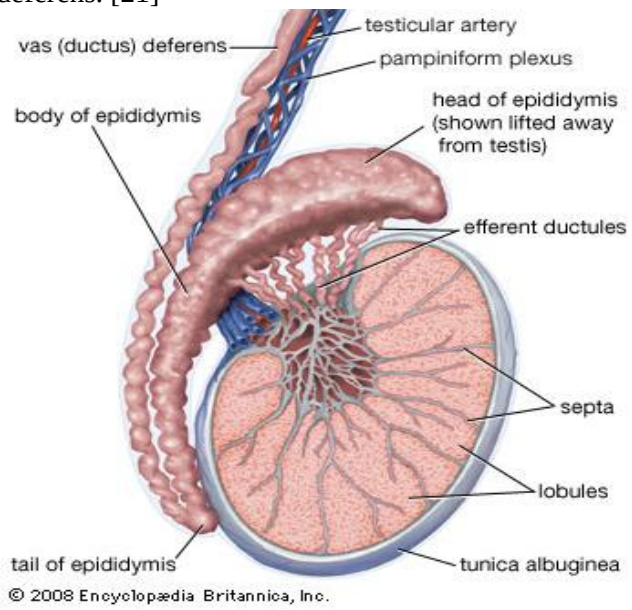

Figure 1: The anatomy of the epididymis. [epididyme. 2016. *Encyclopædia Britannica Online*. Retrieved 08 May, 2016, from http://www.britannica.com/science/epididyme] ("By courtesy of Encyclopaedia Britannica, Inc., copyright 2008; used with permission.")

Clinical presentation

SOE is usually unilateral and painless but could be bilateral. [8,10] It could present as a scrotal mass or less commonly, with a painful scrotal swelling due to acute epididymorchitis, [22,23] recurrent epididymorchitis [24] or as a remittent swelling of the epididymis. [2, 23] Gartman [22] reported that of 310 patients who presented with epididymitis, one had SOE.

SOE could also present with primary or secondary infertility due to obstructive azoospermia from extrinsic ductular compression by the granulomata within the globus major and/or body of the epididymis, or from Leydig cell damage. [2,8,10,25] The most common presentation however, is asymptomatic [26] and recognised incidentally during the course of radiologic investigations. [27,28]

Features of hypercalcaemia like abdominal pain, may be present. [29] The patient may also have constitutional symptoms like fever, lethargy, weight loss, lymphadenopathy or features of multi – systemic involvement. [14]

It may present as a de novo presentation of sarcoidosis but has also been reported to occur while treatment is being received for sarcoidosis involving other systems. [8] McGowan [30] reported the case of a scrotal mass that developed in a patient with sarcoidosis of the nasal septum and digits, who was already on corticosteroids.

Histology: A histological confirmation is important to clinch the diagnosis as multiple disease conditions could produce granulomata. Some of the early reports of suspected SOE lacked a histological confirmation of the diagnosis. [31–33]

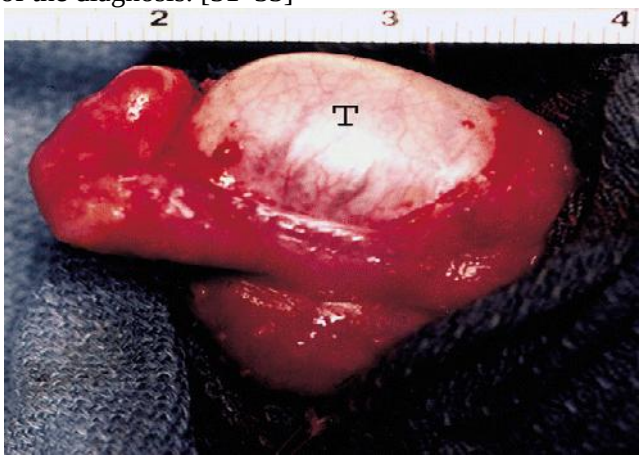

Figure 2: Sarcoidosis involving the head of the epididymis. (Fig 20b Woodward PJ. Extra – testicular masses. Radiologic – Pathologic correlations. 2003; 23 (1):215 – 240. With kind permission of the Radiological Society of North America)[35] T – Testis; E – Epididymal head with sarcoidotic nodule.

The macroscopic appearance of an epididymis afflicted with sarcoidosis has been described as grey tan. The epididymis is usually firm to hard in consistency, nodular and well – encapsulated. [18,34] SOE may involve a part of the

epididymis or may diffusely affect the entire organ. [2,18]

Microscopically, the lesions in sarcoidosis are non – caseating epitheloid – like granulomata. [36,37] These lesions are B cell-negative and should be differentiated from the B cell-positive granulomata of sarcoid-like lesions which can be produced in response to immune stimulation by a cancer, for example. [38] This is because the pathology of sarcoidosis involves an altered TH cellular immunity with increased humoral activity of immunoglobulins, [13]

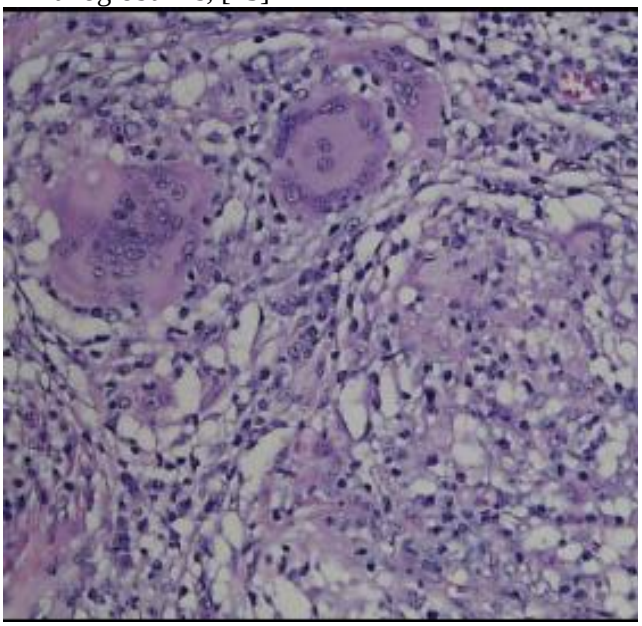

Figure 3: Non caseating granulomatous lesions in the wedge biopsy of the epididymis. [18] (Culled from Hey WD, Shienbaum AJ, Brown GA. Sarcoidosis Presenting as an Epididymal Mass. *J Am Osteopath Assoc*. 2009;109(11):609-610, with the kind permission of Wayne D Hey, DO.)

An increased amount of active fibroblasts and collagen deposits may be present [39] but the granulomata have variable surrounding fibroblasts which are proportional to the level of regression. With complete resolution, a fibrous scar would have replaced the granuloma. [40] In SOE, there may also be hyalinisation of the ducts and vascular fibrosis. [24]

Type B epithelioid type cells may be seen in SOE. [39] The granulomata are more often than not of the foreign body type containing inclusion bodies like Schaumann, asteroid or crystalline bodies. [14] It is uncommon for Schaumann and asteroid bodies to co – exist in the same lesion. [40] The asteroid bodies are also seen in many other granulomatous disorders like Tuberculosis (TB), leprosy, histoplasmosis, schistosomiasis and lipoidal granuloma. [40] They may occur along with fat vacuoles. [40] Schaumann bodies have also been described in regional ileitis and lymphogranuloma venereum. [40] There may also be lamellar bodies, intra – cytoplasmic vesicles, dense granules and intercalated finger – like processes. [39]

Various stains could differentiate the granulomatous lesions from those produced by tuberculosis or other acid – fast bacilli (AFB), fungi or spirochaetes. [11, 41] These could include Ziehl – Neelsen, Gomori silver-impregnation, mucicarmine, Periodic acid Schiff (PAS), carbol fuschin, Movat's pentachrome stain, haematoxylin - eosin, Warthin stains etc. [10,18,42,43] Lowenstein – Jensen culture medium may also be used for this purpose. [39] Historically, guinea pigs would be injected serially with an extract from the lesion and observed for granulomatous reactions that would suggest tuberculosis. [7,39] Fluorescence microscopy could also be used to rule out acid – fast bacilli. [39]

Investigations

Radiological investigations

Gray scale ultrasound scan of the scrotum may reveal a hyperaemic enlarged and/or heterogenous epididymis with hypoechoic lesions. [11] The lesions have also been described as homogenous and solid. [34] Less commonly, the lesion may be hyperechoic. [44] An increase in size and echogenicity may imply some degree of epididymitis. [29] Concomitant testicular masses may be seen. [10,11] There may be co-existing hydrocoeles noted on scrotal ultrasound scanning. [45,46] It is necessary to document the site and size of the lesion ab initio. This would serve as a baseline for the assessment of subsequent therapeutic response. [10] An ultrasound scan cannot differentiate between benign and malignant lesions of the epididymis unfortunately [11,47] but can differentiate between various benign epididymal and scrotal pathologies. [34]

A T2 – weighted magnetic resonance imaging (MRI) technique may be used in equivocal cases where it would appear as a heterogenous, hyper – intense lesion while a T1 – weighted image may show a lesion of medium intensity in the epididymis. [11] Similar findings would occur in inflammatory lesions making the investigation non – specific.

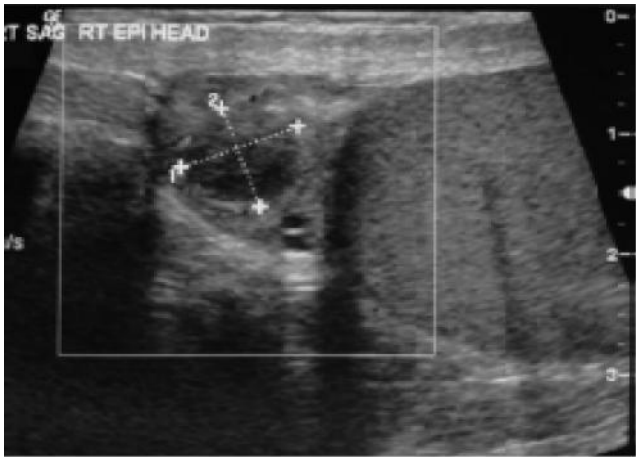

Figure 3: A hypo-echoic lesion in the epididymis. (From Smyth LG, Long RM, Lennon G. A case of epididymal sarcoidosis. With permission from the *Canadian Urological Association Journal*. 2011; 5(5): E90-E91. doi:10.5489/cuaj.10126) [48]

A chest X- ray may provide roentgenographic evidence of sarcoidosis. Scadding [36] graded this involvement from 0 – IV. 0 being normal, I showing bilateral hilar lymphadenopathy (BHL) alone, II showing BHL with pulmonary infiltrates (PI), III referring to PI without BHL and IV referring to PI with architectural distortion +/- bullae. [36] Pleural effusion may also be seen. [49] BHL with right paratracheal nodal enlargement (Garland or 1-2-3 sign) may be present. [50] A chest CT scan may be able to show thickening of interlobular septae or multiple intra – thoracic lymph nodes in addition. [49]

Gallium – 67 scintigraphy may show hot spots indicating organ involvement in equivocal cases. [11] The Panda (increased uptake by the lacrimal and salivary glands) or lambda (increased uptake by the hilar and right paratracheal lymph nodes) signs may be visible on gallium scintigraphy. [51]

18F – Fluorodeoxyglucose positron emission tomographic (18F – FDG PET) scans can be used to make a diagnosis of SOE.[52] Unfortunately, the PET scans cannot differentiate malignant lesions from benign ones. [53]

Technetium – 99 scans may be used to investigate SOE, with increased uptake in affected areas. [54]

Histological investigations: Histological diagnosis may be obtained from associated peripheral tissue like the skin nodules or accessible lymph nodes, or from endoscopic procedures like a mediastinoscopy or bronchoscopy. [39] The epididymis may be explored and a biopsy taken, [55] or excised in toto (as an epididymectomy, [56] orchidectomy or radical orchidectomy / epididymectomy [57] specimen) and subjected to a histological diagnosis. The biopsy may be an excisional, incisional or frozen section biopsy. [58] Autopsy evaluations may reveal SOE. [7] Some authours believe that no biopsy is necessary when there is a clinical suspicion of SOE [15]

Other differentials of granulomatous lesions like tuberculosis, fungi, syphilis etc. may be ruled out using appropriate stains. [8]

Microbiological investigations: A seminal fluid analysis (SFA) would reveal any abnormalities if present. [10] These may include oligo- or azoo- or oligoasthenoteratozoospermia. [10,55] Rudin [59] recommends a semen analysis in all males prior to scrotal exploration for genital sarcoidosis.

Biochemical investigations

Angiotensin converting enzyme (ACE) levels may be elevated in sarcoidosis. [10] This is non – specific. Some cases of epididymal sarcoidosis have been reported to have normal ACE levels. [11]

Due to the high level of suspicion and the need to exclude a testicular malignancy, especially where there is a unilateral scrotal mass, tumour markers need to be assayed for. These are α – fetoprotein (AFP), β – hCG (BHCG) and lactate dehydrogenase (LDH). [11]

Serum calcium and urinary calcium assays may show normal values [24] or elevated values [14] in SOE. This may be due to an altered vitamin D metabolism due to increased α –hydroxylase activity in granulomata, with consequent increased calcium absorption from the intestines and bone resorption. [60] Concomitant parathyroid gland involvement may also be implicated in hypercalcaemia in patients with SOE. [14]

Immunological tests: Immunoglubulins may be normal with increased serum globulin levels. Elevated γ – globulin has been described in SOE. [39,54] Serum complement, [39] C – reactive protein [29] or Interleukin – 2 may also be raised. [28] Children especially have been shown to have hyperglobulinaemia. [61]

A tuberculin test may be done which should be non – reactive. However, some cases have been shown to have positive readings. [14]

Haematological investigations: The erythrocyte sedimentation rate (ESR) may be elevated in patients with SOE. [14,54] Eosinophilia may occur. [24] Eosinophilia is actually a common finding in children with sarcoidosis in general and is seen in up to 52%.

[62] Information on the prevalence of eosinophilia in adults was however not found.

Differential Diagnoses

Tuberculosis of the epididymis is a more common possibility when a patient presents with a supposedly benign epididymal mass. [7] The lesions may be suspected to be and treated as tuberculosis, in environments with a low index of suspicion for sarcoidosis. [13] Further compounding the problem is the fact that the epididymis is the most common site of genital tuberculosis. [63] Unfortunately, both sarcoidosis and TB could present with constitutional symptoms like fever, night sweats and weight loss. Longcope and Freiman14 tried to differentiate fever in acute sarcoidosis as being low grade, variable and irregular while that of tuberculosis is more high grade. The presence of cavitary lesions on a chest X ray is not sine qua non of TB, as some cases of sarcoidosis have been reported to cause cavitatory lesions. [64] Tuberculosis may be ruled out with a negative tuberculin test and by negative stains and cultures for acid fast bacilli (AFB). [8] There is usually anergy to the purified protein derivative (PPD) in patients with sarcoidosis but there have been noted cases of sarcoidosis which have positive responses. [14,40,61] Fluorescence microscopy may also be used to rule out AFB. [39]

SOE could be mistaken for an epididymal tumour, most of which are benign. A carcinoma of the epididymis usually progresses fast, is painful and metastasizes rapidly to the lungs. [8] A testicular tumour would also be a differential, especially of the unilateral scrotal mass. [8] This can be ruled out with the aid of serum assays for AFP, BHCG and LDH, which are otherwise within normal limits in SOE. An abdominopelvic CT scan may also show enlarged retroperitoneal lymph nodes in testicular malignancies, however, many cases of SOE have retroperitoneal nodal involvement as well. [10]

A spermatic granuloma or epididymal cyst may also be considered differentials. [23] With a spermatic granuloma, there may have been a preceding history of trauma. A biopsy of the lesion would show spermatozoa. [8]

Other lesions that bear a resemblance to epididymal sarcoidosis in the mode of presentation with a painless or painful scrotal mass include varicoceles, filariasis, syphilis, lymphogranuloma venereum, blastomycosis, coccidioidomycosis, actinomycosis, histoplasmosis, schistosomiasis, and Wegener's granulomatosis. [24,34,65,66] These may be differentiated using ultrasonography and various stains and/or cultures. [8]

Treatment

The management could be classified into three categories including: watchful waiting, medical and surgical therapy

Watchful waiting

Sarcoidosis usually regresses spontaneously within 2 to 3 years. [10,11] There are case reports of SOE that spontaneously resolved [17,67] or that remained stable [48,68] without any therapy. In the case report by Singer, [32] the epididymal lesion regressed while the patient was only using eye topical steroids. It has been documented that a solid extra – testicular mass is more likely to be benign. [69] Watchful waiting can be done when

- a diagnosis of sarcoidosis is confirmed without a doubt
- it is a solitary epididymal lesion [15] without testicular involvement. (In this case, not even a biopsy is recommended by some)
- Indications for intervention may include
- Pain, especially recurrent troublesome epididymitis – related pain [70]
- Impaired function of a vital organ or hypercalcaemia. [11] (This author recommends CS)
- Subfertility, Infertility or abnormal seminal parameters
- Hypogonadism

Medical therapy

Many historic treatments have been documented, which may include the use of arsenic, radium, Finsen light, nitrogen mustard or even calciferol. [14] These are no longer in use. Corticosteroids are the most widely accepted form of medical therapy to date. Given the side effects of steroids it is debatable whether or not ot commence CS in all cases. [11] Hackney [71] reported life – altering side effects of Cushing's syndrome, diabetes, weight gain that affected compliance in a patient with testicular sarcoidosis. Immunusuppression has been reported that increased the risk of opportunistic infections like Tuberculosis. [72] A case for the use of CS is shown in the 2 ½ year old child with bilateral SOE whose mother is said to have discontinued the medication when the lesions resolved, with consequent recurrence. [54] Recommencement of the CS led to resolution of SOE. [54] Associated hydrocoeles may resolve with corticosteroids. [45]

Gerstenhaber [8] recommends that where other sites exist that could be biopsied to make a diagnosis,

these should be used. In the two cases he reported the peripheral lymph nodes (inguinal and scalene) were used. He recommends that if however, the epididymal lesion develops while being treated for sarcoidosis it is mandatory to biopsy the mass to rule out tuberculosis or malignancy. [8] McWilliams [15] recommends that in isolated epididymal involvement, there is no need for a biopsy but if the testicle is also involved, histologic confirmation of sarcoidosis must be obtained, and more importantly, malignancy must be excluded. [15]

There is a good response to treatment with CS with regression of the lesions commonly [23] however, there have also been reports of worsened fibrosis in epididymal sarcoidosis [10] or enlargement of the lesion, despite CS, in which case epididymectomy or orchidectomy is recommended. [15]

A dose of 20 to 40 mg/day of Prednisolone is recommended. [19] Doses as high as 60 mg/ day may be given and tapered down gradually to 10 mg/day. In children 15 mg/ day on alternate days is recommended [62] or 1 mg/kg/day. [61]

Pulsed corticosteroid use may be helpful in obstructive azoospermia as this may caise regression of the granulomas that have blocked the ductules. [2,10]

Symptoms of hypercalcaemia may resolve with corticosteroids. [29]

Antimalarials may be effective in treating SOE. Chloroquine may be used. Ba [13] reported regression of the lesions with the use of CQ at 300 mg/ day. The patient was followed up for 4 years with good response. Hydrochloroquine is recommended in those with hypercalcaemia skin and/or neurological involvement. [19]

Antibiotics of the tetracycline family, especially minocycline have been shown to have some benefit in the medical therapy for sarcoidosis. [63] Immunosuppressants like Azathioprine, low dose Methotrexate, cyclophosphamide and cyclosporine may also be used. [63,73]

The duration for which the corticosteroids should be used should be individually determined, however, ATS/ ERS/ WASOG recommends that the need for continued therapy should be evaluated after 1 – 3 months of use. [1] Before discontinuing the steroids entirely, the dose should be tapered down. [74]

Surgical therapy

This may be organ – preserving, or complete excision. The approach to the scrotum should be via an inguinal incision. [28] Scrotal exploration affords the ability to adequately delineate the extent of involvement. This is still necessary as some reports have demonstrated the limitations of investigative modalities. For example, Obinata [75] reported a left epididymal tail involvement on USS but scrotal exploration also showed a contralateral involvement of the appendix testis, which was then subjected to nodulectomy.

La Rochelle [53] and colleagues proposed that if an African American patient presents with a bilateral scrotal mass and has negative testicular tumour markers, the lesion may be treated less aggressively as a pseudo – tumour and is amenable to organ – sparing surgery.

Options for organ – preservation include nodule excision [13] or removal of the affected part alone as a partial epididymectomy. [44] Togashi describes a case of a 13 year old with a unilateral scrotal mass that was confined to the epididymis major. A reluctance to do a complete epididymectomy may have been due to the patient's age. A partial epididymectomy was done.

Excision of the epididymis may be necessary to stop pain when incessant. [23,24] This excision may be simple or radical. [18,57]

An argument against surgery is that multiple cases still resort to corticosteroids after the excised specimen reveals a diagnosis of SOE. [56,76] It is still recommended however, that a high suspicion for a malignancy be maintained in the investigation and treatment of intrascrotal masses. [11]

Description of epididymectomy

The original epididymectomy was described by Bardenhauer in 1897 via an inguinal route, [77] which is preferred for scrotal exploration in SOE. This could be done under local anaesthaesia, but spinal or general anaesthaesia may also be used. A skin crease groin incision is used and deepened to the external oblique aponeurosis. [78] The external inguinal ring is visualised and the scrotal contents delivered into the wound. The affected epididymal structure may be excised paying attention to haemostasis. If the entire gland is to be excised, dissection should be as close to the epididymis as possible to avoid damaging testicular vessels on the medial aspect. A radical procedure involves removal of the vas as high as the external ring. [79]

Methods

Various search engines (PubMed, Google, Google Scholar, Deepdyve. ScienceDirect, Wiley Online library, Researchgate, Academia.edu) were

used to search for case reports and reviews on SOE. Key words were "sarcoidosis", "testis" and "epididymis"
Statistical analysis was with Statistical Package for the Social Sciences (SPSS) version 20.

Results

A total of 113 reports of sarcoidosis involving the testis or epididymis were retrieved. Seventy (61.9%) of these had SOE (40 had SOE alone without testicular involvement). Information for three pertaining the site involved could not be obtained. The median age was 30 years, ranging from 2.5 to 72 years. (The mean age was 32.6 ± 12.5 years). The median duration of symptoms was three months, with a range between one week and 11 years. The median follow – up duration was 6 months, ranging between 6 months and 10 years.

Regional Notes

Reports from Africa are sparse, however, some were found. It is important to note that many reports had blacks without a trace made of genealogy. A report from Senegal was found with unilateral left epididymal sarcoidosis [13] and another from Egypt. [25]

Many reports were found on the Asian front, especially from Japan. [80] Two of the reviewed case reports were from Turkey [58,81] and one from Iran. [82] (See Figures 5 and 6)

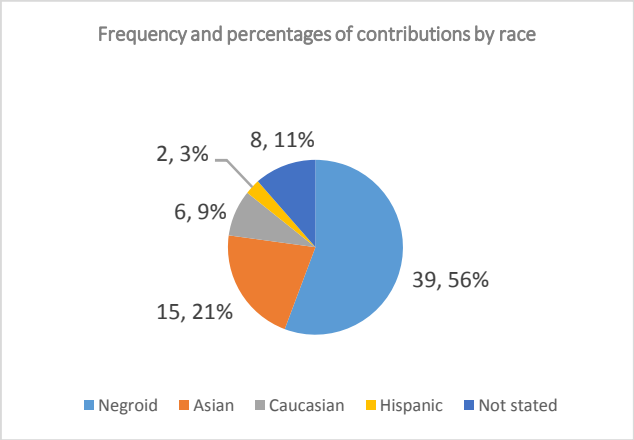

Figure 4: Distribution of SOE among various races

Thirty nine cases presented with scrotal swellings (55.7%), 12 (17.1%) presented with other symptoms like respiratory symptoms, submental, parotid or tonsillar swellings or ocular symptoms; 7 (10%) had constitutional symptoms and a scrotal swelling while 2 (2.9%) had constitutional symptoms like fever, weight loss, lethargy and lymphadenopathy. Ten (14.3%) had no information retrievable.

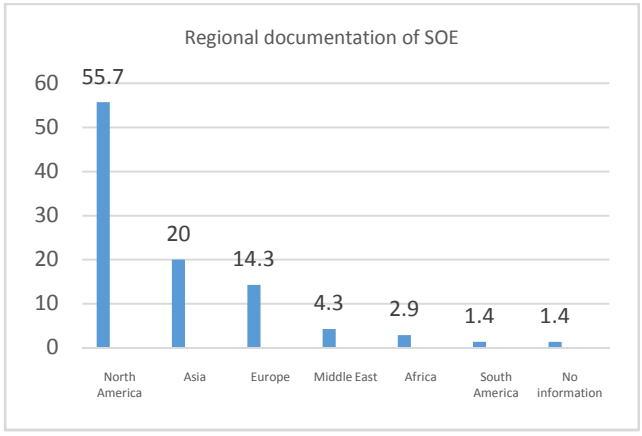

Figure 5: Percentage distribution of SOE reports among various regions

Lesions were associated with pain in 14 (20%) of cases and were painless in 31 (44.3%) of cases. No information on pain was found in 25 (35.7%) of cases. Contralateral involvement of SOE was seen with one contralateral appendix testicular involvement and one contralateral testicular involvement. (Refer to Table 1)

Bilaterality of SOE	Frequency	Percent	Valid Percent	Cumulative Percent
Yes	29	41.4	53.7	53.7
No	23	32.9	42.6	96.3
contralateral	2	2.9	3.7	100.0
Sub - total	54	77.1	100.0	-
No information	16	22.9	-	-
Total	70	100.0	-	-

Table 1: Laterality of SOE

Four patients were documented to have either primary or secondary infertility. Two of these had SOE without SOT. One such person had azoospermia. Three others had abnormal SFA results: severe oligospermia (1), oligospermia (1), oligoasthenoteratozoospermia (1). Four (5.7%) had hypercalcaemia, 13 (18.6%) had elevated levels of ACE. None had an elevated AFP or BHCG. One, being treated for pulmonary sarcoidosis, had an elevated LDH reading a year before the scrotal mass developed.

There was spontaneous resolution in 2 (2.9%) of cases, progression in one (1.4%), persistence of the lesions in 2 (2.9%), and stable lesions in 6 (8.6%) cases. One defaulted while 25 (35.7%) had no retrievable or available information on the outcome. The bulk of the patients, (25 [35.7%]), with documented outcomes had regression

of the lesions with the treatment offered. The rest died from complications of multi – systemic involvement.

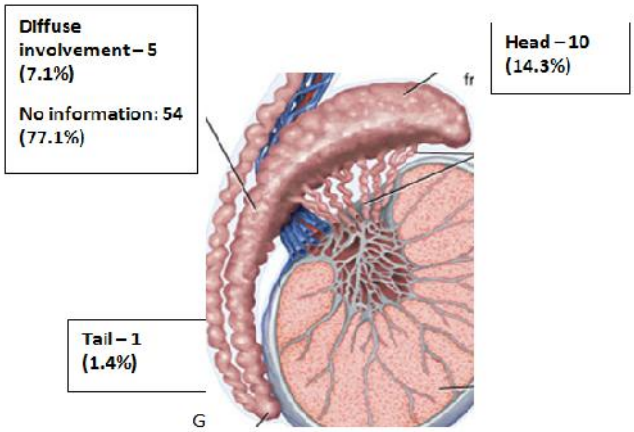

Figure 6: Anatomical involvement of the epididymis by sarcoid lesions. Adapted from The anatomy of the epididymis. [epididyme. 2016. Encyclopædia Britannica Online. Retrieved 08 May, 2016, from http://www.britannica.com/science/epididyme] By courtesy of Encyclopaedia Britannica, Inc., copyright 2008; used with permission.

Site	Frequency	Percentage
Chest	47	67.1
Testis	30	42.6
Skin	16	22.9
Eye	16	22.9
Liver	14	20
Spleen	10	14.3
Prostate	4	5.7
Kidney	3	4,3
Bone	3	4.3
Brain	3	4.3
Chest wall	2	2.9
Penis	2	2,9
Spermatic cord	2	2.9
Spine	1	1.4
Appendix testis	1	1.4

Table 2: Multi – systemic involvement in SOE

Treatment modality	Frequency	Percent	Valid Percent	Cumulative Percent
Watchful waiting	5	7.1	9.8	9.8
Corticosteroids	18	25.7	35.3	45.1
Chloroquine	1	1.4	2.0	47.1
Supportive care	3	4.3	5.9	52.9
Partial excision	7	10.0	13.7	66.7
Epididymectomy	10	14.3	19.6	86.3
Radical orchidectomy	1	1.4	2.0	88.3
Radical epididymectomy	1	1.4	2.0	90.3
Epididymectomy	5	7.1	9.8	100.0
+ steroids				
Sub – Total	**51**	**72.9**	**100.0**	
No information	19	27.1		
Total	70	100.0		

Table 3: Summary of treatments offered to patients with SOE

Chest pathology	Frequency	Percent
SG 0	7	10
SG I	15	21.4
SG II	14	20
SG III	3	4.3
Cavitation	1	1.4
Pleural effusion	1	1.4
No information	31	44.3

Table 4: Nature of lung pathology as described in Chest X – rays. SG: Scadding grade

Miscellaneous narrations from reported cases

A post-mortem diagnosis?

Rao and Sabenegh [10] reported a case of a 42 year old African American man who presented with a painless right hemiscrotal swelling and infertility. Initial examination revealed an epididymal mass which later involved the testis. He had BHI and paratracheal lesions. These regressed with the use of inhaled and oral CS. He declined surgical intervention for the scrotal lesions, which progressed and became more firm.

Gerstenhaber reviewed 23 cases of epididymal sarcoidosis, two of which he reported in a 17 and 27 year old males. Both had constitutional symptoms of weight loss and generalised lymphadenopathy. A description of what is now known as the "Panda" and "lambda" signs on Gallium scans was obtained in the former patient. The diagnoses were confirmed from the peripheral nodes biopsied. No statement was made of the treatment given or of spontaneous resolution. Six of the cases were reviewed were post – mortem diagnoses, lending to the prior belief that genital sarcoidosis is more often than not, diagnosed following autopsies.

Testicular and epididymal involvement was noted as autopsy findings in a 72 year old Japanese with multi – systemic involvement, who died from pulmonary arterial hypertension – related complications.[83]

Non-treatment or watchful waiting

Kodama [11] reported a case of a 46 year old African American man who presented with a week's

duration of painless bilateral scrotal masses which were nodular on examination. He had no constitutional symptoms. Ultrasonography showed hypoechoic lesions in the epididymides without testicular involvement. This was firther investigated with MRI, findngs of which suggested sarcoidosis. A chest X – ray was normal so a Gallium scan was done which found hot spots in the skin and the anterior chest wall. A biopsy of one of the skin nodules was consisitent with sarcoidosis negative for acid – fast bacilli. No further treatment was rendered.

Smyth [48] reported a 25 year old Causcasian with a painless right epididymal swelling of a month's duration which gradually grew in size to involve the testis. USS showed hypoechoic lesions in the epididymis as shown in Figure 1 above. He also had pulmonary involvement and hilar lymphadenopathy. Tumour markers were negative while ACE was elevated. The diagnosis was confirmed via a frozen section biopsy taken from the tesis and epididimis using an inguinal approach. No treatment was offered to the patient, with good outcome.

Surgical intervention, approach and options

Treatment by excision of a part of the affected epididymis alone in a 30 year old black male who was otherwise asymptomatic, was reported by Hey and colleagues. [18] Total epididymectomies have also been reported [34] as well as a radical epididymectomy. [57]

The rationale for treatment of sarcoid lesions may fall under scrutiny after reading the report by Maganty [84] in which the patient had a right epididymectomy and a nodular excision of the right testicular nodule following presentation with a painful scrotum. The patient's asymptomatic pulmonary lesions regressed without steroids. Thus, the questions arise as to whether the testicular or epididymal lesions may have resolved without any treatment. It may be argued here that the pain was an indication for surgery. Another question arises as to whether the stimulus for the regression of the pulmonary lesions was due to a reduction of burden of disease by the epididymectomy and excision biopsy undergone, as may happen with metastatic lesions of renal cell carcinomata following a cytoreductive nephrectomy primary tumour. [85]

Rehman [86] reported a case of a 29 year old man who presented with right testicular pain, dyspnoea and constitutional symptoms of weight loss and fever. An incidental finding of bilateral testicular masses and a left epididymal mass was made on ultrasonography. His chest CT showed lung cavitations and BHI. Tuberculosis and HIV were ruled out. The markers for testicular tumours were negative. The initial suspicion of TB or a metastatic testicular tumour was deemed unlikely, especially with the bilaterality of the lesions. A frozen section biopsy via an inguinal incision confirmed a diagnosis of sarcoidosis.

Family history, genetics and prediction of site of involvement

A positive family history was reported in two case reports. [14,18] Another reported the patient to be on treatment for an autoimmune disorder, specifically psoriasis, which also has a genetic predisposition. [10] The ACCESS (A Case Control study Etiologic Study of Sarcoidosis) study was unable to find an aetiology for sarcoidosis but identified a five – fold risk of increased susceptibility if a sibling has or had the disease.[20]

Contralaterality of lesions involving a testis and epididymis was reported by Seaworth [65] and of the epididymis and appendix testis by Obinata. [75] Whether or not a factor determines such a presentation pattern is not known at this time.

Infertility

Epididymal involvement, even without testicular sarcoidosis, could result in infertility. Hassan [25] described a case of a 29 year old man with primary infertility who was found to have bilateral diffuse epididymal sarcoidosis. He was azoospermic. Semen parameters did not improve with steroid therapy necessitating intracystoplasmic sperm injection. It could be argued however, that there was a confounder in this case as the patient had bilateral medium – sized varicoceles. There was no documentation of a varicocelectomy in the course of evaluation of this patient.

Differential diagnoses

Misdiagnoses of SOE have occurred. The most common suspicions include testicular malignancy and TB. [87] Joel reported that despite a bronchoscopy and biopsy that was negative for TB and showed NCG, the patient was still commenced on a 6 – month course of anti-tuberculosis drugs to which he did not respond. Despite having negative testicular tumour markers, he was still subjected to a

left orchidectomy via an inguinal route. [87] The orchidectomy specimen showed NCG. It was thereafter that corticosteroids were commenced. The patient was deemed stable by the 2 – year follow – up.

Conflict of interest: None

S.No	Reference	Year of patient reported	Age	Race	Presentation	Investigations	Treatment	Outcome	Comment
1	Kodama et al[11]	2004	46	African – American	Painless bilateral scrotal masses	Normal CXR USS – bilateral hypoechoic lesiosn T1 – MRI: Medium intense lesions T2 – MRI: high intensity lesions Ga – 67: skin and anterior chest wall hot spots	Wedge biopsy	Good	No constitutional symptoms
2	Rao [10]	2009	42	African American	Painless right hemiscrotal mass Infertility Cough and low grade fever Autoimmune disorder (prosriasis)	Grade II chest involvement Right testicular and epididymal involvement	Inhaled and systemic CS	Regression of pulmonary and hilar lesions Progression of scrotal mass	Declined surgery
3	Smyth [48]	2011	25	Caucasian	Painless right epididymal mass which eventually involved the testis	CT - Mediastinal and bilateral hilar involvement with bilateral lower lung zonal involvement USS – E + T ivolvement FSB via inguinal approach	None	Good outcome	-
4	Ishii [83]	2011	72	Mongoloid	Severe dyspnoea	No features of TB Subnormal ACE Centrilobular pulmonary nodules on CT	Supportive care	Died	Post – humous diagnosis
5	Gerstenha	1977	17	Negroid	Painless bit	CXR – Grade	None stated	Not stated	

	ber [8]				tender left epididymal mass Weight loss Generalised LN	II = mediastinal nodes Gallium scan – Panda sign ACE elevated Teesticular tumor and tuberculosis excluded			
6	Gerstenhaber [8]	1977	27	Negroid	Painless left epididymal mass Weight loss Generalised LN	CXR – Grade II + paratracheal nodes Fungi, mycobacteria excluded.	None stated	Not stated	
7	Hey [18]	2009	30	Negroid	Painless right epididymal mass	USS – hypoechoic epididymal lesion Chest CT – BHI	Excision biopsy	No recurrence	Family history
8	Astudillo [88]	2004	28	Negroid	Bilateral epididymal and testicular masses Recent onset uveitis Pre-existing skin nodules	USS- diffuse heterogenous epididymal involvement and hypo-echoic testicular lesions Ga [67]- Uptake in both testes, epididymides, lungs	CS	Complete resolution	
9	Svetec [2]	1998	34		Arthralgia Generalised LN Bilateral pinful epididymal masses Secondary infertility	USS – lt caput nodule with diffuse bilateral epidiymal involvement Azoospermia and oligospermia at different itmes	Partial epididymetomy Pu;lsed CS use fir oulmonary lesion	Intermittent improvement in semen analysis parameters and epididymalgia Non-response to CS subsequently	
10	Burke [89]	1990	27	Negroid	Knoen sarcoidosis of eye Right scrotal mass	USS – multiple hypoiechoic epididymal and testicular nodules	Nodulectomy		
11	Vahid[90]	2006	29	Negroid	3 year painful scrotal swelling Bilateral	USS – right epididymal lesion Chest CT,	CS	Resolution	

					inguinal LN Incidental right epididymal non tender swelling	Brain MRI – normal HIV, TB, fungi and spirochaetes ruled out			
12	Forte [34]	1988	20	Negroid	Painless rt epididymal swelling	USS – homogenous hypoechoic mass CXR – BHI + BP + paratracheal LN	Epididymectomy		
13	Rehman [86]	2005	29		Painful rith testicle with constitutional symptoms Dyspnoea Incidetal finding of bilateral testicular and left epididymal involvement	USS – Hypoechoic lesions CXR- PI Chest CT- BHI +cavitations FSB - NCG			Asymptomatic epididymal lesion
14	Corse [5]	1994	29	Negroid	Bilateral hemiscrotal swelling Cough, dyspnoea Subcutaneous nodules LN	USS – Lt globus major and Bilateral testicular hypoechoic lesions CXR – Grade II Chest CT Biopsies of skin nodule, peripheral LN and lt testicular lesion – NCG	CS	Persistence of only the left testicular lesion which was removed by an excision biosy after 8 months of CS	
15	Maganty[84]	2008	28	Negroid	Tender right testicular and epididymal swellings	USS – hypoechoic T/E lesions CXR – Grade I	Right epididymectomy + excision of right testicular lesion	Regression of pulmpnary lesion	Wouldth e T/E lesions have resolved spontaneously? Was it a debulk that prompted resolution?
16	Frates [91]	1997	27	Negroid	Bilateral epididymal swelling with peripheral LN	USS – Diffuse hypoechoic T/E lesions LN biopsy – sarcoidosis	Systemic therapy, likely CS	Regression	

17	Frates [91]	1997	30	Negroid	Bilateral epididymal swelling with peripheral LN	USS – Diffuse hypoechoic T/E lesions LN biopsy – sarcoidosis	Systemic therapy, likely CS	Unknown to authour	
18	Amenta [42]	1981	36	Negroid	Known uveal and pulmonary sarcoidosis On prednisone Bilateral testicular and epididymal swellings after a year of treratment	CXR – mediastinal nodes Fungi and AFB ruled out	Excision biopsy of left testicle and epididymis		
19	Seaworth [65]	1983	29	Negroid	2 year cough 1 year left testicular swelling Incidental finding of contralateral epididymal cystic transillumina blemass	CXR – Grade I Fungi, syphilis, AFB were ruled out. BHCG – negative FSB – Granulomatou s inflammation	Left orchidectomy + excision biopsy of epididymal mass		Contralat eral involvem ent
20	Rutchik [92]	2001	31	Negroid	Skin lesions Respiratory symptoms Bilateral testicular selling Incidental right epididymal involvement	CXR – in keeping with sarcoidosis CT abdomen – retroperitoneal LN Tumor markers – Negative	Radical Rt orchidectomy Biopsy of left testicular lesion CS	Regression of Lt testicular lesion	
21	Hassan [25]	2009	29	Caucasian	Primary infertility Bilateral inguinal LN	USS – bilateral disffuse epididymal lesions CXR – BHI Chest CT- BHI + mediastinal LN Testicular + epididymal biopsy – NCG + leydig hyperplasia Semen analysis – Azoospermia	CS	Remained azoospermic	
22	Longcope [14] *	1952	40	Negroid		Autopsy: Liver, kidney, dura, heart,			

						penis			
23	Longcope [14]	1952	34	Negroid	Known sarcoidosis Uveoparotid fever Haematuriia, polyuria Lt facial N. palsy Lt ptosis Skin lesions Cough, dyspnoea Died of uraemia	CXR – Grade II Ca, Phosphorus ↑ Autopsy: Kidney (cortical and medullary tubular calcification), testes, epididymis, spleen, uvula, parathyroid gland (hyperplasia), bone marrow			Family history (Two brothers)
24	Longcope [14]	1952	31	Negroid	Fever,Visual impairment, Seizures Polyuria, Wt loss, Atrophic testicles The prostate was not enlarged	LN biopsy – NCG Autopsy: Epididymis, testes, pituitary, lungs, tonsils, spleen, nasal mucosa, eye (optic chiasm, choroid, left fundus)			
25	Longcope [14] *	1952	29	Negroid		Epididymis, prostate, uvea No histologic confirmation			
26	Longcope [93] *	1941	29	Negroid	Pituitary, Epididymis	Histological confirmatiom			
27	Winter [17]	38	1995	Caucasian	Left sided scrotal swelling	USS – hypoechoic left testicular lesion CXR – PI Chest CT – BHI + MLN FSB – NCG Operative finding: Left epididymal and superior testicular pole involvement	Patient defaulted before commencement of definitive therapy		
28	Metcalfe [76]	1998	30	Negroid	Right painless epididymal swelling Cough, night sweats	USS – hypoechoic lesions in both E + T CXR – Grade I ACE ↑ Normal Ca	Right orchidectomy Corticosteroids Anti - TB		

						Tumour markers - Negative Rt orchidectomy specimen – NCG			
29	SultanAli [94]	2005	30	Negroid	Painful left hemiscrotal swelling Paraparesis Weight loss	USS – solid left epididymal mass. Apparently normal testis CXR – Normal CT – BHI + MLN + iliac LN; hepatosplenomegaly Spine MRI – T10 – 11 intradural extramedullary mass Tumour markers- Negative TB ruled out Intra-op finding – Left testicular and epididymal mass Orhidectomy Specimen - NCG	Left orchidectomy CS	Regression of lesions Restoration of limb power	
30	Woolf [95]	2010	50	Negroid	3 month history of cough, cervical LN Progressive wt loss A year later, left sided scrotal mass	USS – Hypoechoic left testicular lesions CXR – BHL LFT – cholestasis LN + liver biopsy – NCG Tumour markers - Negative Hypercalciuria Orchidectomy specimen – NCG in testis, epididymis and spermatic cord	Left orchidectomy CS	Regression	
31	Iwasaki [96]	2009	47	Asian	3 month history of Uveitis Scrotal	CT – BHI + MLN Ga scint – Bilateral	Epididymectomy + Testicular biopsy		

					swelling	scrotal hot spots BAL-lymphocytosis Op finding: Epididymal and testicular involvement			
32	Esnakula[97]	2013	33	Negroid	8 month history of chest pain, cough and weight loss Scrotal skin lesions Rt hemiscrotal mass involving the testis and eoididymis Right inguinal LN	CT – pleural effusion, BHI + PI BAL – CD4:CD8 reversal ACE ↑ Negative TM + LDH Rt lung biopsy – NCG	Right radicsl orchidectomy CS		
33	Zamora – Chavez [46]	2016	12	Hispanic	Pulmonary involvementErythema nodosum Symptomatic hypercalcaemia Left hemiscrotal swelling LN Eye involvement	USS – Diffuse rt epididymal and testicular lesions + hydrocele CD4:CD8 reversal LN – biopsy ACE ↑ Negative TM Hypercalcaemia	CS	Resolution of lesions	
34	Balaban[81]	2011	25	Mongoloid	Known pulmonary sarcoidosis Painful scrotal mass				
35	Handa [29]	2003	25	Mongoloid	Left hemiscrotal pain Uveitis LN Parotid Lungs Symptomatic hypercalcaemia	CXR – Grade II USS – Hyperechogenic epididymides (suggestive of epididymitis) + diffuse testicular involvement. T2 MRI – Bilateral epididymal and testicular lesions Ga scint – Hot spots in	CS	Resolution	Presented with epididymitis

						parotid, MLN, hilum, left hemiscrotum ACE↑ Hypercalcaemia Tumour markers - Negative LN biopsy/ Bronchoscopy – NCG BAL - CD4:CD8 reversal			
36	Paknejad [82]	2011	42	Mongoloid	A month's history of scrotal pain Cough, weight loss On steroids for sarcoidosis Infertile (Failed IVF)	Semen analysis – oligospermia → azoospermia USS – heterogenous epididymis + hypoechoic testicular lesions CXR – Grade 0 Chest CT – LN ACE ↑, LDH ↑ Ca - normal Negative TM, Fungi and AFB ruled out	CS	Boosted sperm count Assisted reproduction repeated	
37	Bonachera [98]	1984			Pulmonary involvement	Testicular + epididymal sarcoidosis			
38	Vasu [23]	2006	30	Negroid	5 month's history of right sided scrotal swelling LN Splenomegaly	USS – hypoechoic epididymal mass + multiple bilateral testicular lesions CXR – Grade II + MLN ACE ↑, Negative TM AFB and fungi ruled out LN FNAC – NCG	CSs	Resolution	
39	Esser [27]	2003	43		Known rt spermatic cord sarcoidosis	Spermatic cord tumour biopsy, Mediastinoscopy - NCG	Lt partial epididymectomy		

					13 yrs later, developed a left epididymal swelling				
40	Horie [80]	2007	75	Mongooid (Japanese)	Prior history of TB Bilateral scrotal swelling LN Visual loss	Bronchial lavage – Negative for TB CXR – Grade I Chest CT – BHL + PI ACE ↑ Bronchoscopy + biopsy – NCG	CS		Suspicion f TB epididymitis entertained
41	Mikhail [39]	1972	41	Negroid	Dry eyes Stuffy nose Difficult speech Generalised sinusitis Bilateral parotid enlargement Bilateral epididymal swelling Skin lesions No LN	CXR – Grade II Multiple bone cysts Mediastinoscopy ECG – heart involvement Kveim test – Positive Globulin ↑ Complement ↑ IgG, IgM – normal Skin, lt epididymis, nasal mucisa, MLN biopsies - NCG	CS	Regression	
42	Schaumann [7]	1936	42		Cattle rearer No prior TB LN Swollen nose Skin lesions Dactylitits Tonsils Wt loss Abdominal pain Diabetes insipidus (cause of death) Atrophic testes	Autopsy: Heart, spleen, liver involvement No testicular involvement Bilateral epididymal sarcoidosis			
43	Hines [67]	1964	21	Negroid	Skin lesions Epididymal involvement	Histological confirmation			
44	Van Husen [99]	1919	17	Caucasian	Eye Skin Epididymis	Histological confirmation			
45	Ricker [40]	1949	25	Negroid	Blurring of	CXR –Grade			

					vision Died of heart failure	II LN biopsy – NCG Autopsy: Epididymis, prostate, kidney, lung, liver, spleen, pancreas, brain, meninges, retina, pituitary, thyroid, skeletal muscle			
46	Riley [100]	1950	47	Negroid		Autopsy: Epididymis, uvea, skin, heart, liver, spleen			
47	Singer [32] *	1959	31	Negroid	Erythema nodosum, Uvea	Histological confirmation			
48	Singer [32] *	1959							
49	Gartman [22]	1961			Epididymitis				
50	Cowdell [101] *	1954				No histological confirmation			
51	McGowan [30] *	1967	38	Negroid	Known sarcoidosis Nasal septum Fingers Scrotal mass	No histological confirmation			Already on CS for sarcoidosis before SOE manifested
52	Rudin [59] *	1974	29	Hispanic	Known sarcoidosis Epididymal involvement	Kveim test – positive Liver biopsy – NCG			
53	Engleman [33] *	1951	24	Negroid	Uvea Epididymis Testis	No histological confirmation			
54	Yamamoto [68]	1991	59	Mongoloid (Japanese)	4 month's history Bilateral painless scrotal swelling Parotd swelling	Biopsy – NCG	No treatment	Stable	
55	Weinberg [54]	1982	2.5		6 week history of fever Bilateral hemi – scrotal	CXR – Grade 0 Technetium [99] scan – Increased	Trimenthoprim – sulfamethoxazole (without improvement)	Resolution of epididymal lesions with CS	

					swelling Joint pains	uptake ESR ↑ ACE ↑ γ – globulin ↑ IVP, MCUG, AFB - Negative	CS Mother non – compliant leading to recurrence	Lesions recureed when CS was discontinued	
56	Winnacker [24]	1967	33	Negroid	11 year's history of recurrent epididymitis, with 2 – 3 week pain – free intervals Axillary LN	CXR – Grade I + PTLN LN biopsy – NCG Hepatomegaly Normal Ca ESR ↑ Eosinophilia PPD – Negative	Lt epididymectomy CS Rt epididymovasectomy		
57	Togashi [44]	1993	13	Mongoloid (Japanese)	Right hemiscrotal mass	CXR – Grade II + MLN USS – hyperechogenic mass confined to the head of the epididymis Lung biopsy – NCG	Partial epididymectomy		
58	Obinata [75]	2007	31	Mongoloid (Japanese)	Painless scrotal swelling Known pulmonary sarcoidosis On CS	CXR – Grade I + pleural effusion USS – Lt epididymal tail involvement ACE ↑ Op findings: lt epididymal, right testicular and appendix testicular involvement	Scrotal exploration Lt epididymectomy Nodulectomy of appendix testicular nodules	Stable	
59	Ba [13]	1995	41	Negroid	Nasal Limbs Skin lesions Chest wall nodules Lt epididymis	CXR – Grade I Skin biopsy – TB Epididymis node resction / Nasal mucosa biopsy - NCG	Anti – TB (No response) Chloroquine	Regresseion of lesions	Suspicion of TB
60	Ying – Sheng Shen [55]	2010	20	Mongoloid (Chinese)	2 week's history of scrotal mass	SFA – oligoasthenospermia CXR – Grade II Chest CT – As CXR + MLN USS – Bilateral epididymal lesions Mediastinosco	CS		

						py/epdididymis biopsy – NCG			
61	Suzuki [57]	1994	43	Mongoloid (Japanese)		USS – heterogenous lesion in the epididymal head CXR – Grade I ACE – normal	Left radical epididymectomy		
62	Takagi [56]	1986	29	Mongoloid (Japanese)	Right epididymal swelling Generalised LN	CXR – Grade II Nasal mucosal/transbronchial/LN biopsy/ epididymectomy specimen – NCG	Rt epididymectomy CS		
63	Aga [52]	2013	33			LN, liver, epididymis, muscles, subcutaneous tissue, bilateral uvea	Immunosuppressive therapy	Regression	
64	Ryan [16]	1993	27	Negroid	Scrotal nodules				
65	Ryan [16]	1993	34	Negroid	Known sarcoidosis 10 month's on CS Rt testicular mass	Epididymal involvement found on exploration			
66	Canguven [58]	2011	25	Caucasian	Known pulmonary sarcoidosis 1 year's history of right scrotal stiffness 6 month's history of left scrotal pain Skin lesions	Normal testosterone levels FSH - ↑ SFA – severe oligospermia T1 MRI – enhanced lesions FSB – NCG TM – Negative	High dose CS, tapered down	Sperm count increased Hormone profile normalised	
67	Shibata [102]	1997	52		Eye involvement	Left epididymal head BHL NCG ACE - normal	Epididymectomy		
68	Sasaki [28]	2009	33	Mongoloid (Japan)	Poor vision Right hemiscrotal swelling	Mass in epididymal head Epididymal biopsy – NCG Chest CT – MLN + clavicular LN	Topical eye steroids		

69	Aga [52]	2013			Bilateral epididymal involvement Skin lesions LN	18F FDG–PET scan - Liver, muscle involvement	Immunosuppressive therapy	Complete resolution	
70	Kraus [103]	1958	41		Scrotal mass Skin lesions	Epididymis Rt testis CXR – Grade I	Epididymectomy Orchidectomy		

* = Information retrieved from Gerstenhaber due to limited access to articles

Table 5: Summary of articles on SOE reviewed. IgA: Immunoglobulin A; IgM: Immunoglobulin M; NCG: Non-caseating granuloma; CXR: Chest X-ray; MLN: Mediastinal lymph node; PTLN: Paratracheal lymph node; BP: Bronchopulmonary; BHI: HI: Hilar infiltrate; BHL: Bilateral hilar lymph node; Lt: left; Rt: Right;E: Epididymis; T: testis; ACE: Angiotensin-converting enzyme; AFB: Acid-fast bacilli; TM: Tumour markers; CT: Computerised Tomographic Scan; BAL: Bronchoalveolar lavage; LDH: Lactate dehydrogenase; IVF: In vitro fertilisation; Ga-67 scint: Gallium scintigraphy; MRI: Magnetic resonance imaging; USS: ultrasound scan; HIV: human immunodeficiency; TB: Tuberculosis; FSB: Frozen sectionbiopsy; BHCG: B-human chorionic gonadotrophin; ESR: Erythrocyte sedimentation rate; FNAC: Fine-needle aspiration cytology; FDG-PET: Fluorodeoxyglucose positron emission topography; SFA: seminal fluid analysis.

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