Tuberculous epididymitis and fertility in North Jordan

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ABSTRACT

Objectives: To describe the clinical characteristics of tuberculous epididymitis and its effect on male subfertility in a general hospital in the north of Jordan.

Methods: A retrospective case study of the hospital records of patients with genitourinary tuberculosis managed at Princess Basma Teaching Hospital in Irbid, North Jordan during the period of 1994-2001.

Results: Of the 16 patients with genitourinary tuberculosis, 9 were found to have tuberculous epididymitis. The mean age was 41.2 years. The main presentation was an insidious onset of painful scrotal swelling, mostly on the left side. Mean duration of symptoms was 10.6 weeks. Most patients had no history of previous tuberculosis and no *Mycobacterium Tuberculosis* in their urine. Six months of anti-tuberculous chemotherapy was effective, combined with surgery for scrotal abscesses. Although all patients recovered, the results on fertility are considerable.

Conclusion: Isolated tuberculous epididymitis is the most common form of genitourinary tuberculosis. A 6-month course of anti-tuberculous chemotherapy is effective in combination with surgery for large scrotal abscesses. The fertility outcome is of concern. Sperm retrieval and cryopreservation have to be considered for potential intra-cytoplasmic sperm injection.

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Although the prevalence of tuberculosis (TB) has fallen dramatically in developed countries,[1] its worldwide prevalence is still high and has remained almost unchanged over the last century. Its incidence is increasing in the developing countries, where more than 95% of the patients live.[2] Nearly 20% of patients with TB develop extra-pulmonary manifestations.[2] In males, epididymitis is often the first manifestation of genitourinary tuberculosis (GUTB). In approximately 28% of patients with GUTB, involvement is solely genital.[3] In patients with known TB, approximately 7% will manifest epididymal involvement.[4] Tuberculous epididymitis is not unusual, but epididymo-orchitis occurs rarely.[5] Tuberculous epididymitis should be considered in the differential diagnosis of scrotal swelling even without history of previous TB.[1] Although the effect of female genital TB on fertility has been extensively addressed in the medical literature, its male counterpart has not! This study reviews the fertility history and management of tuberculous epididymitis.

Methods. A retrospective study was conducted on all patients with GUTB managed at Princess Basma Teaching Hospital in Irbid, North Jordan during the period January 1994 to December 2001. Data were collected from the hospital's medical records. The obtained data included: age, site of infection, duration of symptoms at presentation, history of pulmonary TB, mode of presentation, methods of diagnosis, treatment modality, and reproductive history. All patients had bacteriological

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or histological, or both, confirmation of the diagnosis of tuberculous epididymitis. All patients underwent routine urine analysis, and culture, urine staining and culture for acid-fast bacilli (AFB), complete blood count, erythrocyte sedimentation rate (ESR), serum electrolytes and kidney function tests, ultrasound of kidneys, bladder, prostate and scrotum and intravenous urogram (IVU). Only one patient had cystoscopy. All patients were contacted in November 2003 to inquire about their post treatment reproductive outcome.

Results. During the study period (1994-2001), 16 patients with GUTB were managed at Princess Basma Teaching Hospital. Nine patients had tuberculous epididymitis, giving an incidence of 56.3%, with mean age of 41.2 years (range 26-60 years). The mean duration of their symptoms at presentation was 10.6 weeks (range 4-16 weeks). The clinical presentation is shown in **Table 1**. Other genitourinary organs were involved only in one patient (11.1%), where in addition to the right epididymis, the right kidney and bladder were also involved. Eight patients (88.8%) had ESR above 40mm/1 hour. In 2 patients (22.2%) *Escherichia Coli* was isolated from urine culture and appropriate antibiotics were given for 4 weeks. The epididymitis did not resolve despite that the urine cultures did not show any growth subsequently. Sterile pyuria was found in 3 patients (33.3%). Four patients (44.4%) showed no evidence of TB infection in their urine. Bacteriological investigations revealed AFB in 5 cases, and histological studies of infected tissue discovered tuberculosis in 4 cases. Ultrasound examination of kidneys, bladder and prostate was normal in all patients except one, who showed dilatation of calyces of the right kidney. Scrotal ultrasound examination showed enlarged heterogeneous epididymis in 6 patients, and in the remaining 3 patients it showed testicular abscess. Secondary hydrocele was found in 2 patients (22.2%). An IVU showed abnormality in one patient (dilated and irregular calyces). One patient underwent cystoscopy, which showed congestion around the right ureteric orifice and small ulcer, for which cold cup biopsy from its edge was performed. Histological examination showed tuberculotic epithelioid cell granulomas. In 3 patients, orchidectomy was performed as a treatment of large scrotal abscess. The histology showed TB of the epididymis in all of them with testicular involvement only in one. Short-term combined anti-TB chemotherapy was used in all patients. This consisted of 4 drugs (Rifampicin 300 mg/day orally, Isoniazid 600 mg/day orally, Streptomycin 1000 mg/day intramuscularly, and 20 mg/kg/day orally of Pyrazinamide) for 2 months, and 2 drugs (Rifampicin 300 mg/day orally, and Isoniazid 600 mg /day orally) for another 4 months. Three patients completed this course of

Table 1 - Clinical presentation of 9 patients with tuberculous epididymitis (TB).

Clinical presentation	N of patients
Site	
Left	5
Right	3
Bilateral	1
Symptoms	
Painful swelling	4
Scrotal abscess	3
Painless swelling	1
Draining scrotal sinus	1
History of previous TB	
Negative	7
Positive	2

Table 2 - Details of patients with history of tuberculous epididymitis.

Patient number	Age	Unilateral or bilateral	N of children before TB	N of children after TB	Serum volume	Sperm count	Sperm normal morphology	Sperm motility	Notes
1	60	Unilateral	1	0	2	0	0	0	
2	34	Unilateral	0	2	3	2	45	40	
3	26	Unilateral	0	0	1.5	0	0	0	Single testis and unilateral orchidectomy
4	28	Bilateral	0	0	1	0	0	0	Right orchidectomy
5	33	Bilateral	0	0	2	0	0	0	
6	52	Bilateral	0	0	2	0	0	0	
7	59	Unilateral	7	0	1.5	0	0	0	
8	31	Unilateral	1	0	2.5	27	30	32	
9	48	Unilateral	3	0	1	0	0	0	

treatment after orchidectomy. At present; after a mean follow up of 44.3 months (range 9-93 months); all patients had complete resolution and remained asymptomatic with no evidence of recurrence. Of the 9 patients with tuberculous epididymitis, 7 were interested in starting or extending the size of their families. Seminal fluid analysis confirmed azoospermia in 7 patients. Two patients had normal sperm count with a slightly decreased percentage of motility and increased percentage of morphological abnormality. Only one patient managed to reproduce successfully (**Table 2**). In the case of one patient (patient 3 in **Table 2**), azoospermia was due to the surgical excision of his single testis due to large abscess formation.

Discussion. In Jordan the incidence of TB (pulmonary and extra-pulmonary) has declined from 10.4/100,000 in 1994 to 6.4/100,000 in 2001.[6] This reflects the success of the Jordanian anti-TB program, which is supported by the World Health Organization. Genitourinary TB was reported to be the most common extra-pulmonary manifestation.[2] In Jordan, tuberculous lymphadenitis and TB of the gastrointestinal tract were reported to be the first and second most frequent forms of extra-pulmonary TB, while GUTB was the third most common form,[6] with renal TB being more frequent than that of the male reproductive organs.[7] Tuberculous epididymitis occurs most commonly between the ages of 20 and 50 years, during the time of greatest sexual activity.[8] This is comparable with the ages of patients in this study (mean age 41.2 years). It has been reported that approximately 7% of patients with known TB will manifest epididymal involvement[4] and 30-50% of patients with tuberculous epididymitis will have no history of pulmonary TB.[9] In this study; this percentage was higher at 78.8%. This is probably due to the higher incidence of TB in developing countries. It has also been reported that the incidence of tuberculous epididymitis when GUTB is present is approximately 70%.[5] In this study the epididymis was involved in 56.3%. Though tuberculous epididymitis is not uncommon, tuberculous orchitis is rarely experienced.[5] Only one patient in this study was reported to have tuberculous orchitis.

The spread of *Mycobacterium tuberculosis* to the epididymis is thought to occur via hematogenous seeding, retrograde canalicular descent of organisms via the vas deferens from the hematogenously infected prostate, and following intravesical Bacilli Calmette-Guérin (BCG) therapy for superficial bladder tumors.[1,10,11] We think that the hematogenous route of infection is the most common, as only one of our patients had renal involvement and none of them had signs or symptoms of prostatitis or history of intravesical BCG therapy.

The clinical features of tuberculous epididymitis in this study were variable but consistent with those described in other studies. These range from acute to chronic inflammation with some cases of painful enlargement of the epididymis and redness of the scrotum, or with a posterior scrotal sinus. Fever is infrequent as are other constitutional symptoms.[3] Several clinical clues may suggest the diagnosis of tuberculous epididymo-orchitis such as prostatic, seminal vesicle, or vas deferens abnormalities, hydrocele, sterile pyuria, evidence of TB elsewhere in the body, and posterior scrotal sinus.[5] Our study corroborates the recommendations that when GUTB is clinically suspected, 3-5 consecutive early morning urine samples (EMUs) should be cultured for AFB. Examination of scrotal discharge, and multiple urine cultures were effective in diagnosing tuberculous epididymo-orchitis in this study as in others.[5] Microscopy of EMUs with Zeehl-Neelson staining is usually unrewarding because there is much urine debris in the urine sample.[12] Cahill et al[12] suggested that the urine must be cultured on Lowenstein-Jensen slopes for up to 9 weeks and at least 6 EMUs should be requested, and more if TB is clinically or histologically suspected.[12] Microbiological cultures on seminal fluid was not carried out in this study as none of the patients had any symptoms suggestive of prostatitis, but perhaps this might have been of some value. Similarly, as none of the patients had a suspicion of tuberculous orchitis, fine needle aspiration cytology (FNAC) was omitted. It has been shown that FNAC of suspicious areas in the testicle provides useful material for cytological and microbiological examination.[3] Recently, molecular probes have been utilized for more rapid identification of the organisms in the urine.[13]

Although the ultrasound appearances of tuberculous epididymitis were non-specific in our patients, the investigation of scrotal swellings with high-resolution ultrasound using a 7.5 MHz or 10 MHz probe is a rapid and helpful non-invasive method of assessing scrotal contents, particularly in the presence of hydrocele.[8] Ultrasound readily detects the presence of testicular abnormality, but differentiation of infection from tumor is often not possible on ultrasound appearances alone.[8] It has been suggested that IVU is indicated in patients with epididymitis where there is a history or evidence of previous TB, or where patients have sterile pyuria or microscopic hematuria.[1]

Medical treatment of GUTB is the method of choice.[2] Although different anti-TB drugs have been introduced, the general therapy regimen of the past 20 years is still a combination of 3 or 4 drugs of the following: isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin and prothionamide. The

treatment duration has been reduced in these combination therapies from 2 years down to 9 or only 6 months.[2] We used a short term anti-TB chemotherapy (6-month regimen) in 2 steps: the first step was daily treatment with 4 drugs (streptomycin, rifampicin, isoniazid and pyrazinamide) over 2 months, followed by a 2-drug regimen (isoniazid and rifampicin) daily over the next 4 months. This regimen proved to be very effective. Although, orchidectomy may eventually be necessary in case of poor response to chemotherapy, for the removal of a large scrotal abscess or to rule out malignancy. Three of our patients had large testicular abscess and were treated by orchidectomy followed by chemotherapy. This was followed by good response to anti-TB chemotherapy. In agreement with other authors, we believe that orchidectomy should be avoided as a primary diagnostic measure.[3] The incidence of post tuberculous epididymitis azoospermia in this study is high. Most probably obstruction is the prime cause. Medical literature is scant on the spermatogenesis studies of testicular biopsies after tuberculous epididymitis. The plethora of reported successes with the technique of intra-cytoplasmic sperm injection (ICSI) utilized in assisted reproduction centers offers hope for this group of patients.[14]

In conclusion, we believe that a 6-months course of anti-TB chemotherapy is an effective therapy for tuberculous epididymitis. Surgery is indicated only in cases of large scrotal abscesses or chemotherapy failure. Intra-cytoplasmic sperm injection technology should be investigated as a potential method in assisting patients with azoospermia post tuberculous epididymitis.

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