

# A CLINICOPATHOLOGIC STUDY OF TUBERCULOUS EPIDIDYMO-ORCHITIS IN THAILAND

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**Abstract.** Tuberculous epididymo-orchitis is an uncommon disease caused by *Mycobacterium tuberculosis* of the testis and epididymis. We reviewed 25 cases of tuberculous epididymo-orchitis, diagnosed at the Faculty of Medicine Ramathibodi Hospital, Mahidol University between July 2000 and June 2010. The mean age at diagnosis was 54.5 years (range: 30 to 91 years). Cultures from testicular and epididymal tissues were positive for *Mycobacterium tuberculosis* in 6 cases. The clinical presentations of tuberculous epididymo-orchitis included scrotal mass (80%), scrotal pain (44%), micturition syndrome (8%), urethral discharge (4%), and scrotal fistula (4%). One third of the patients had pulmonary tuberculosis. Four patients (16%) had underlying human immunodeficiency virus infection. Tuberculous epididymo-orchitis should be considered in the patients who present with a scrotal mass. The preoperative differentiation of tuberculous epididymo-orchitis from non-tuberculous epididymo-orchitis and testicular tumor is difficult. In patients who have epididymal and testicular lesions, surgical excision provides the diagnosis. Exact histopathologic categorization is important to select appropriate medical therapy.

**Keywords:** tuberculous epididymo-orchitis, *Mycobacterium tuberculosis*, caseous granuloma, clinicopathologic finding

## INTRODUCTION

Tuberculosis is an endemic disease in many developing tropical countries (Raviglione and O'Brien, 2008). Typically histopathology shows caseous granulomatous inflammation. Genitourinary tuberculosis is one of the most common manifestations of extrapulmonary tuber-

culosis and represents 15% of all extrapulmonary tuberculosis cases (Raviglione and O'Brien, 2008). Despite the prevalence of tuberculosis in Thailand, there have been few reports describing the clinical features of genitourinary tuberculosis (Muttarak *et al*, 2005; Tanthanuch *et al*, 2010). Tuberculous epididymo-orchitis (TBEO) is defined as a spectrum of conditions caused by *Mycobacterium tuberculosis* of the testis and epididymis. TBEO is difficult to diagnose; usually diagnosed after epididymo-orchidectomy. The preoperative differential diagnoses of TBEO includes epididymo-testicular tumors

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and bacterial epididymo-orchitis, among patients who present with a painless or painful scrotal mass, respectively. The objectives of the present study were to determine the clinicopathologic findings of TBEO.

## MATERIALS AND METHODS

We carried out a retrospective study of TBEO cases diagnosed by surgical specimens obtained from the Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, over a period of 10 years, between July 2000 and June 2010. The criteria for the diagnosis of TBEO were 1) the presence of acid-fast bacilli in an epididymo-orchidectomy specimen, 2) a positive mycobacterial study or 3) the histopathologic changes of caseous granuloma with clinical response to antituberculous treatment. Mycobacterial organisms were identified using special stains: a Ziehl-Neelsen stain or a modified Fite's stain. Information was obtained from urology medical records, including age, clinical manifestations, duration of symptoms, associated diseases, preoperative evaluation, results of culture, and treatment outcomes. The data were analyzed using the program SPSS, version 16 (SPSS, Chicaco, IL). This study was approved by the committee on human research at Faculty of Medicine Ramathibodi Hospital, Mahidol University (ID10-53-46).

## RESULTS

During the study period, 31 patients were diagnosed with granulomatous epididymo-orchitis by orchidectomy; 25 patients had complete clinicopathologic findings consistent with TBEO, affecting

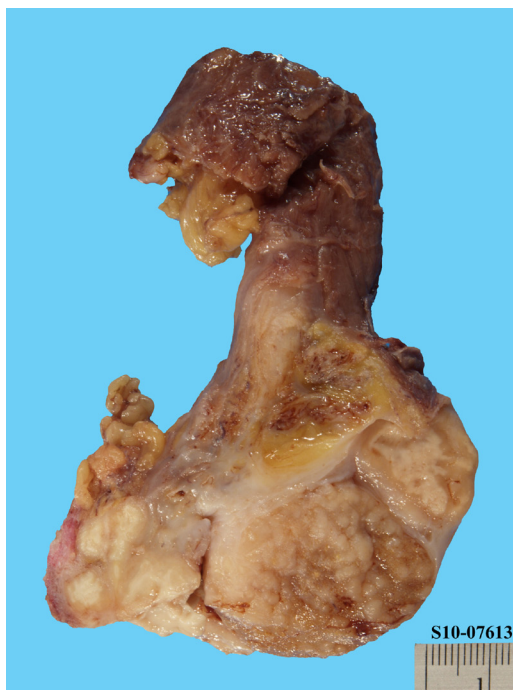


Fig 1—The cut surface showing caseous necrosis containing yellow-white, cheesy debris involving the epididymis and testis.

patients aged 30-91 years with a mean age of  $54.52 \pm 16.3$  years. The average age of diagnosis of TBEO among HIV infected patients was younger than among immunocompetent patients ( $38.75 \pm 9.22$  years *vs*  $57.52 \pm 15.71$  years,  $p = 0.031$ ). Patients presented with a variety of symptoms, including a scrotal mass (80%), scrotal pain (44%), micturition syndrome (8%), urethral discharge (4%) and a scrotal fistula (4%). The duration of symptoms ranged from three days to six years; 12% of the cases were shorter than one month and 16% were longer than one year. The left testis was more commonly involved than the right testis with a ratio of 15:9. The size of the lesion ranged from 1.5 to 10.5 cm with a mean size of 5.45 cm (Fig 1). Pulmonary tuberculosis, found

Table 1  
Co-morbid diseases among 25 patients with tuberculous epididymo-orchitis<sup>a</sup>.

Underlying diseases	Tuberculous epididymo-orchitis <sup>a</sup> (n = 25)	
	No. of patients	Percent
Pulmonary tuberculosis	8	32
Systemic hypertension	5	20
HIV infection	4	16
Diabetes mellitus	3	12
Gout	2	8
Prostatic adenocarcinoma	2	8
Syphilis	1	4
Myocardial infarction	1	4
Stroke	1	4
Urolithiasis	1	4

<sup>a</sup>The patients may have had one or more underlying diseases.

in 8 patients (32%), was the most common underlying disease, diagnosed with chest radiography and sputum examination. Co-morbid disease was found in 9 cases (36%) with systemic hypertension (5 cases, 20%), diabetic mellitus (3 cases, 12%) being the most common (Table 1). The ultrasonography (US) conducted in 4 patients, showed nonspecific chronic epididymo-orchitis and an epididymal mass in 3 and 1 patient, respectively (Figs 2-5). One patient had undergone a computed tomography (CT) scan (Fig 6).

Human immunodeficiency virus (HIV) infection was present in 4 cases (16%). Mean age of otherwise asymptomatic HIV infected patients was 38.75 years. One symptomatic HIV case had a history of syphilis and gonococcal infection. Three HIV infected patients were otherwise asymptomatic. Two patients had a history of prostatic adenocarcinoma, and underwent orchidectomy for hormonal therapy. Epididymo-testicular tissues staining for acid-fast bacteria were positive in 6 cases (24%). Tissue-cultures

were positive for *Mycobacterium tuberculosis* in 6 cases.

All reported cases of TBEO received both surgery and medical treatment. Twenty-five patients received standard antituberculous drugs. The majority of the patients did not complain of any side effects from their antituberculous treatment. One patient developed a drug eruption due to pyrazinamide. One HIV infected patient developed drug resistance to streptomycin and clinical drug resistance to standard antituberculous treatment. Treatment success occurred in 24 patients (96%).

## DISCUSSION

Genitourinary tuberculosis is a chronic infectious disease found predominantly in developing tropical countries (Gokce *et al*, 2002; Kulchavenya and Khomyakov, 2006; Zarrabi and Heyns, 2009; Hsu *et al*, 2010). TBEO is an uncommon disease and affects patients ranging in age from the third decade to the eighth decade

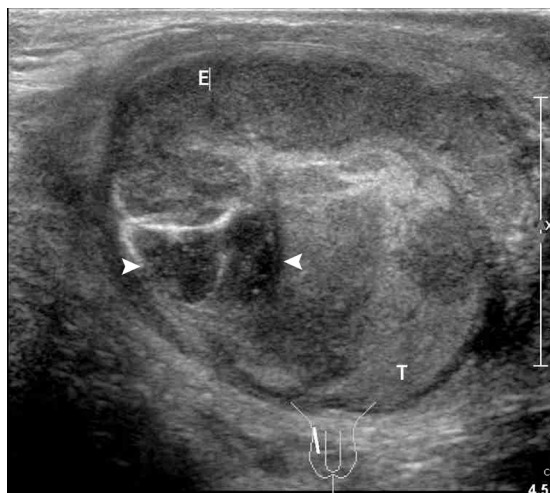


Fig 2—US of the epididymis and the testis. Diffusely enlarged heterogeneously hypoechoic epididymis (E) along with a diffusely enlarged ipsilateral testis (T), containing multiple small hypoechoic nodules. A cystic lesion (arrowheads) represents the testicular abscess.

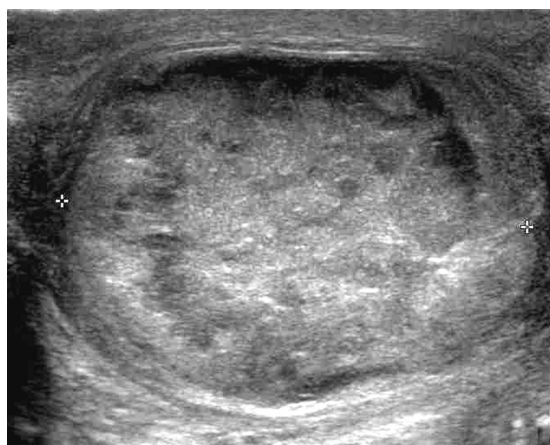


Fig 3—The testis of this patient is diffusely enlarged with heterogeneous echogenicity.

(Gómez García *et al*, 2010). The mean age of diagnosis is between the fifth and sixth decade. The common clinical manifestations of patients with TBEO include a scrotal mass, scrotal pain, a urinary tract infection, urethral discharge and nonspe-

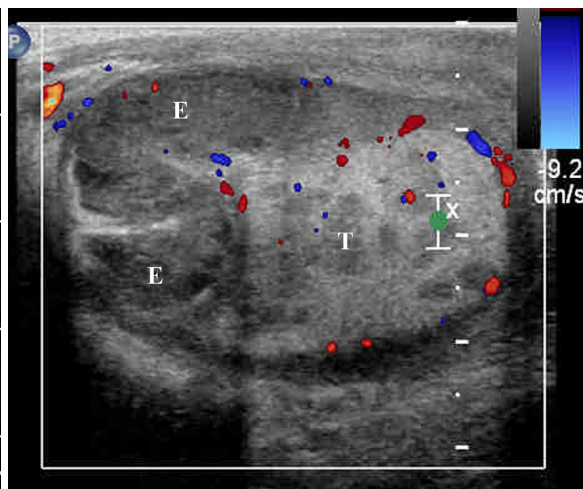


Fig 4—Increased vascular flow of the epididymis (E) and the testis (T) is shown on color Doppler ultrasound.

cific constitutional symptoms (Heaton *et al*, 1989; Madeb *et al*, 2005; Biswas *et al*, 2006; Gómez García *et al*, 2010). The duration of these symptoms varied greatly from days to years. Epididymotesticular induration associated with beading of the vas deferens was typically found on physical examination. Painful purulent fistulization and/or a scrotal abscess are common findings with TBEO (Gómez García *et al*, 2010).

High-resolution ultrasonography is currently the imaging modality of choice for evaluation of the scrotum and its contents (Muttarak *et al*, 2001; Muttarak and Peh, 2006). The spreading pattern of tuberculosis is essential for imaging interpretation. The abnormality usually begins at the epididymis, and then extends to the testis. This history is an important feature distinguishing infection from tumor. Because the pathogenesis of orchitis is usually caused by an infectious organism in the epididymis, a concur-

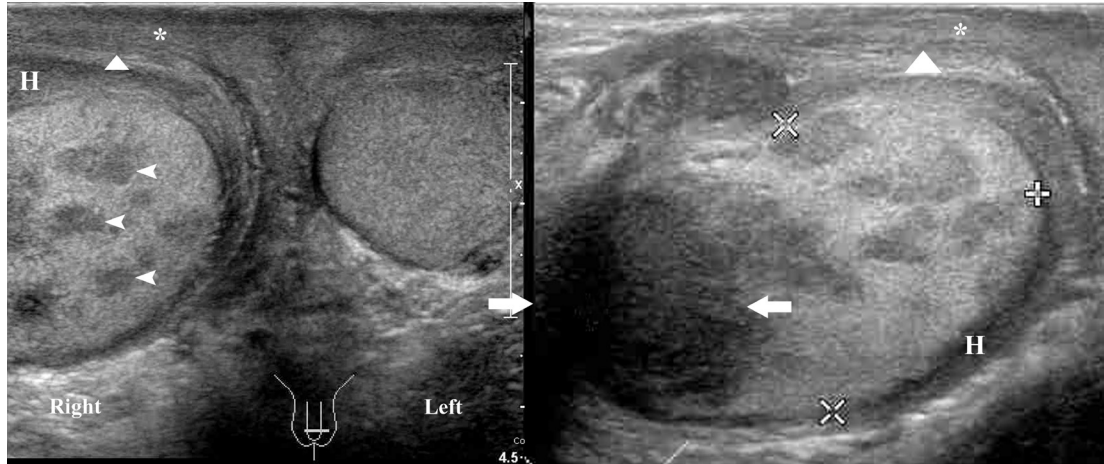


Fig 5—Tuberculous orchitis compared with the unaffected testis (5A). The right testis is diffusely enlarged. Multiple small hypoechoic nodules are noted (arrowheads). In contrast, the left testis has a normal size and echotexture. Associated findings suggestive of an inflammatory process include thickening of the scrotal wall (asterisk) and thickening of the tunica albuginea (triangle). A small hydrocele (H) is also present. The cystic component (arrows) in Fig 5B represents a scrotal abscess.

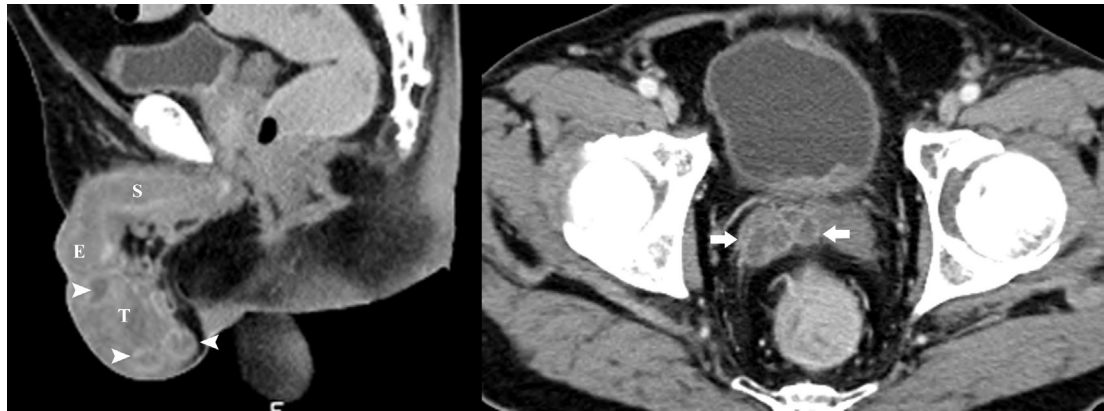


Fig 6—Contrasted enhanced CT scan of the sagittal view (6A) showing a diffusely enlarged right testis (T) and epididymis (E), extending to the spermatic cord (S). Multiple rim-enhancing lesions are also observed (arrowheads). On the coronal view (6B), there were diffusely enlarged bilateral seminal vesicles with rim enhancing lesions (arrow).

rently enlarged epididymal and testicular lesion is suggestive of an infectious process rather than a neoplasm. Primary tumor of the testis usually involves some part of epididymis only in the latter stages of disease. A heterogeneous hypoechoic

enlarged epididymis tends to be tuberculous epididymitis, unlike non-tuberculous epididymo-orchitis, which tends to be homogenous (Chung *et al*, 1997). A tuberculous epididymal abscess is usually larger and has less blood flow than a pyogenic

abscess (Yang *et al*, 2001). If the infection involves the ipsilateral testis, there may be four sonographic patterns present: 1) a diffusely enlarged, heterogeneously hypoechoic testis (Fig 2, 3); 2) a diffusely enlarged homogeneously hypoechoic testis; 3) a nodular enlarged, heterogeneously hypoechoic testis; 4) a miliary pattern of multiple small hypoechoic nodules in an enlarged testis. Doppler ultrasound has value to determine vascular flow. Epididymo-orchitis usually results in increased vascular perfusion (Fig 4). The presence of vascular flow can exclude testicular ischemia, which is associated with testicular torsion. Other ultrasonographic findings include thickened scrotal skin and tunica albuginea, hydrocele and scrotal abscess (Fig 5). Scrotal calcification and sinus tract formation are a diagnostic clue for TBEO (Chung *et al*, 1997). Sonography, as a non-invasive technique, plays an important role in the diagnosis of TBEO. It can help to avoid an unnecessary orchidectomy. Ultrasonography was performed in only 4 cases in our series. Further studies of cases utilizing ultrasonography may be necessary in order to determine its role in the diagnosis of TBEO among Thai patients.

The incidence of TBEO has increased recently, due to a rising incidence of immunocompromised patients with HIV infection (Jacob *et al*, 2008). These patients have a mean age of diagnosis younger than immunocompetent patients. There should be high index of suspicion for TBEO among young men, especially in areas where HIV and tuberculosis are prevalent.

An important finding was the strong association between TBEO and pulmonary tuberculosis; 32% of TBEO patients had pulmonary tuberculosis in our study. Our findings differ from those of Gómez García *et al* (2010), but two thirds of TBEO

cases had normal chest radiography.

The effected epididymis and testis are typically moderately enlarged and indurated with a thickened tunica. Cut surfaces showed variably extensive destruction of the seminiferous tubules with fibrosis. Numerous granulomas were observed between the epididymal and testicular sections. An inflammatory process was detected in the interstitium and seminiferous tubules causing destruction of germ cells and Sertoli cells. Secondary hypogonadism and infertile commonly occur (Veenema and Lattimer, 1957). The granulomas contain a central necrotic area and a border zone with Langhans-type giant cells, epithelioid cells, lymphocytes and plasma cells. Caseous granulomata without detectable acid-fast bacilli were a common pathologic feature. In our study, 24% of patients with a caseous granuloma had acid fast bacilli. The acid-fast bacilli, demonstrated with a Ziehl-Neelsen stain, are characteristically seen in giant cells and at the margin of the caseous area. It is difficult to differential a granuloma from tuberculosis unless *M. tuberculosis* is found in the sputum, in a hemoculture, epididymo-testicular specimen culture or with polymerase chain reaction (PCR) identification of *M. tuberculosis*. Some tuberculous granulomas are indistinguishable morphologically from granulomas caused by other organisms, including atypical mycobacterial infections, melioidosis, syphilis and brucellosis (Navarro-Martinez *et al*, 2001; Jacob *et al*, 2008), therefore tissue-culture is required for definite identification. This is an important distinction because the choice of antibiotics is guided in part by the species identified. Genomic amplifications, including polymerase chain reaction (PCR) for *M. tuberculosis*, should be considered when the clinical finding is

suspicious for tuberculosis despite negative microbiologic and histopathologic investigations (Gómez García *et al*, 2010). However, PCR is much more expensive than the conventional method and requires a stringent laboratory technique to minimize false negative and false positive results. Because culture yields far better results, fresh surgical material should be obtained for microbiologic testing whenever tuberculosis is suspected.

Histopathology and culture of specimens remain the gold standard for diagnosis and may reveal unexpected findings of clinical importance. The histopathology of caseous granuloma is an important factor used to determine treatment with TBEO. The combination of clinical, radiological, histopathological and microbiological findings all play an important part in the diagnosis of TBEO. Early detection with high-resolution ultrasonography is important in the preoperative diagnosis of TBEO. Fine needle aspiration is done to obtain cytology and bacterial culture (Wolf and McAninch, 1991; Sah *et al*, 2006). These methods help to avoid an unnecessary orchidectomy.

The patients received standard antituberculous treatment in the form of isoniazid, rifampicin, pyrazinamide and ethambutol for 2 months followed by isoniazid and rifampicin for a further 4 to 7 months. The regimen and duration of treatment for TBEO was the same as for pulmonary tuberculosis. Treatment may need to be adjusted based on individual clinical response. Recurrence is uncommon in the case of complete antibiotic treatment following epididymo-orchidectomy. Subsequent antimycobacterial treatment is based on the results of drug sensitivity tests.

In conclusion, TBEO commonly

presents as a scrotal mass. It is important for urologists to recognize the varied presentations of TBEO and to be familiar with its resemblance to malignancy. It poses a particular diagnostic problem in tuberculosis endemic areas, such as South-east Asia. Recent imaging technology has not improved the overall accuracy of the diagnosis of TBEO. Histopathology and culture remain the gold standard for the diagnosis of TBEO. The clinical outcome of TBEO depends on prompt diagnosis and effective treatment. The present study offers a unique opportunity to assess the clinicopathological features of TBEO over a ten-year period at Ramathibodi Hospital.

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