

Histopathological Changes and Carcinoma In Situ in Postpubertal Cryptorchid Testis

POSTPUBERTAL KRIPTORŞİD TESTİSLERDEKİ HİSTOPATOLOJİK DEĞİŞİKLİKLER VE KARSİNOMA IN SİTU

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Summary

Cryptorchidism has long been known to be a risk factor for infertility and testicular cancer. Previous studies also indicated that the risk of carcinoma in situ (CIS) of the testis is greater in those men. There have been few publications concerning the morphological changes found in whole cryptorchid specimens after puberty. In our study, histological specimens of 42 men (20 to 27 years old), who presented with undescended testes were evaluated. All of the specimens revealed abnormal spermatogenesis and one of them carcinoma in situ (2.3%). This study confirms that postpubertal cryptorchid testes cannot contribute to fertility and may have significant malignant potential. Until the development of non invasive techniques, histological examination seems to be a valuable procedure for screening CIS of the testis in postpubertal cryptorchid patients.

Key Words: Cryptorchidism, Fertility, Carcinoma in situ

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Impairment of fertility rate has been found to be associated with cryptorchidism and a history of undescended testis is a well established risk factor for testicular cancer (1-3). The incidence of invasive testicular cancer is increased in men with a history of cryptorchidism (4). There have been few publications concerning the morphological changes found in whole cryptorchid specimens after puber-

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Özet

Kriptorşidizmin infertilite ve testis kanseri için bir risk faktörü oluşturduğu uzun zamandır bilinmektedir. Konuya ilişkin çalışmalar, bu kişilerdeki karsinoma in situ riskinin yüksekliğini de ortaya koymuştur. Literatürde kriptorşidli genç erişkinlerin tüm testisinin morfolojik incelenmesine dayalı çalışmalar azdır. Çalışmamızda inmemiş testis nedeniyle başvuran 20 ile 27 yaşları arasındaki 42 erkeğin testis histolojileri değerlendirildi. Tüm olgularda anormal spermatogenesis ve bir (%2.3) olguda karsinoma in situ (CIS) bulgusu saptandı. Bu çalışma histolojik olarak incelenen postpubertal kriptorşidik testislerin fertiliteye katkıda bulunmadığını ve malign potansiyel taşıyabileceğini doğrulamaktadır. Kriptorşid testislerin CIS açısından taranmasında noninvasif tetkikler gelişinceye kadar, histolojik değerlendirme halen geçerliliğini korumaktadır.

Anahtar Kelimeler: Kriptorşidizm, Fertilité,
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ty. The purpose of this study was to evaluate histopathological findings to predict the extent of spermatogenesis and carcinogenesis in cryptorchid patients who underwent orchidopexy or orchiectomy. We also reviewed prevalence and significance of carcinoma in situ (CIS) in those patients.

Patients and Methods

Forty-two military conscripts who presented to military hospital of Elazığ with postpubertal cryptorchidism (unilateral in 40, bilateral in 2) between January 1996 and August 1998 were retrospectively analysed. Patient ages ranged from 20 to 27 years (mean: 22). Four patients (%57) presented with pri-

mary infertility (unilateral in 3, bilateral in 1) in overall 7 married patients. Physical examination were completed in upright and supine position. The undescended testicles were palpable in 30 cases (75%). Clinical examination was negative for testicular tumors. Serum α -fetoprotein and B-human chorionic gonadotropin levels were analysed in 7 patients and found to be normal. All patients had a normal sexual phenotype and hormonal therapy were not applied before surgery.

All patients underwent surgical exploration of the undescended testis. Our treatment policy for these patients were to perform orchiectomy for unilateral hypoplastic testis and in cases which could not located to scrotum. Orchidopexy preferred for patients who refused orchiectomy and bilateral cases. Thirty patients (71%) underwent unilateral orchiectomy while 12 (29%) underwent open biopsy and dartos pouch orchiopexy. We evaluated the incidence of spermatogenesis and carcinogenesis in whole orchiectomy specimens removed and open biopsy specimens obtained from orchidopexy procedure in cryptorchid patients.

Whole testis and biopsy specimens were placed immediately in Bouin's medium and subsequently embedded in paraffin. Four mm. thickness of multiple sections were stained with hematoxylen and eosin, and examined by standard light microscope. The diagnosis of CIS were based on a criteria as described " clear cytoplasmic cells with large irregular nuclei, located on thick basal membrane " by Skakkeabek and associates (5,6).

Results

The location of testes and histological findings are listed in the Table 1. The exact location of the

cryptorchid testis determined intraoperatively was the superficial inguinal pouch in 27 (64.3%) cases, inguinal canal in 14 (33.3%), and abdominal in 1 (2.4%). Histology showed abnormal spermatogenesis in all orchiectomy and biopsy specimen, 12 had maturation arrest, and 24 had seminiferous tubular atrophy and / or Sertoli-cell-only syndrome with no spermatogenesis (Figure 1) and 8 Had a hypospermatogenesis. The only consistent histological feature between different specimens was the presence (spermatogenesis) or absence (no spermatogenesis) of germ cells within the tubules. There was apparently no relationship between the location and histological features of the testicular specimens. There was also no spermatogonia in the biopsy of 2 bilateral cryptorchidism case showing seminiferous tubular atrophy. These testes were located at the superficial inguinal pouch.

CIS was identified diffusely throughout the seminiferous tubules in 1 specimen (2.3%) which was removed (Figure 2). The patient was 24 years old and the testis (7.2 ml) located upper part of the inguinal canal. Histological evidence suggesting prior torsion (seminiferous tubular atrophy with focal haemorrhagic necrotic area) were demonstrated in 2 specimens. Other common histological findings included thickening and hyalinisation of the basement membrane of the seminiferous tubules in 27 and 5 cases, respectively and Leydig cell hyperplasia in 21.

Discussion

It is now widely accepted that testicular maldevelopment is due to intrinsic abnormality of the testis and the most reliable relative risk calculations indicated a 4-10 fold increase in invasive germ cell cancer in cryptorchid cases (7,8). Moreover, approximately

Table 1. Location and histological features of cryptorchid testis

Histology	No. (%)	Location (No.)
No spermatogenesis	24 (55)	
Atrophy	15 (34)	Superficial inguinal pouch (10), inguinal canal (5)
Sertoli-cell-only	9 (21)	Superficial inguinal pouch (6), inguinal canal (2), abdominal (1)
Spermatogenesis	20 (45)	
Maturation arrest	12 (27)	Superficial inguinal pouch (9), inguinal canal (4)
Hypospermatogenesis	8 (18)	Superficial inguinal pouch (4) inguinal canal (3)
Total	44 (100)	

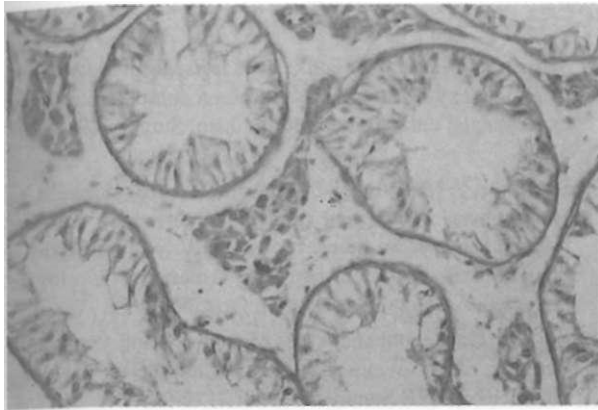


Figure 1. The testis slide containing sertoli-cell-only with no spermatogenesis. (HE x 200)

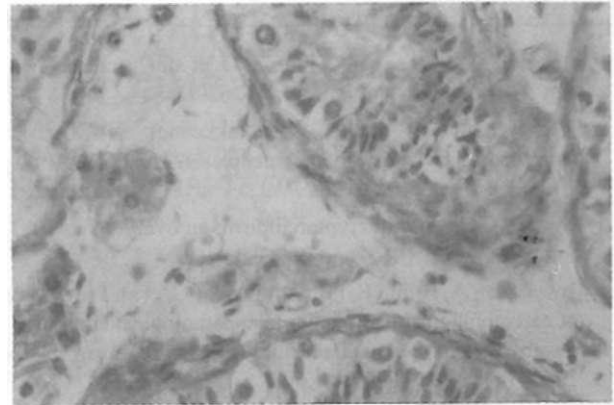


Figure 2. CIS of the testis. Clear cytoplasmic cells with large irregular nuclei, located on thick basal membrane. (HE x 400)

10% of patients presenting with testicular tumors have a history of cryptorchidism (9). Giwercman and associates recommended that all men with a history of cryptorchidism should be offered a biopsy of the affected testis when they reach adulthood (4).

Skakkeback introduced the term of CIS according to abnormal germ cells found in 2 cryptorchid infertile men (5). True prevalence of carcinoma in situ in men with a history of cryptorchidism has been established approximately 2 to 3% (10). This is in correlation with our study. We found CIS in 1 (2.3%) patient which was in orchiectomy group.

Testicular maldescent retards the production of spermatozoa and causes atrophy. The review of current literature revealed that undescended testis have also a detrimental effect on contralateral side testis appearing normal and may cause future infertility (11,12). Morphological alterations have been demonstrated in cryptorchid testes even in the first month of life (13). There have been few publications concerning the morphological changes found in whole cryptorchid testes after puberty (14,15). Study regarding the analysis of cryptorchid testes in postpubertal male patients showed that the majority could not contribute to spermatogenesis (16). Small testis, the abdominal testis and the testis with most histologic changes would appear to be at the greatest risk for defects in spermatogenesis (17). Our study has confirmed that spermatogenesis was impaired in all cryptorchid gonads. Complete sper-

matogenesis in none of the tubules was found in cryptorchid testes.

The principles of treatment in infantile cryptorchidism and the standards of orchidopexy has been definitely showed (18). Most physicians are likely to recommend treatment of the undescended testis when detected if the child is older than six months (18,19). But, there are inadequate data indicating whether treatment before puberty decrease the risk of infertility. On the other hand, all palpable testes should either removed or placed in a position to allow palpation and patients with palpable undescended testes less than 32 years of age (8,17).

Although recent aspects concerning orchidopexy time in favor of early infancy, cryptorchidism is still being diagnosed in military conscripts in our country because of patients shyness or insufficient health insurance. Our analysis of cryptorchid testes in military conscripts confirmed that none of them can contribute to fertility and may have a malignant potential.

In conclusion, postpubertal cryptorchidism is not only associated with an increased prevalence of CIS but also showed abnormal spermatogenesis. Until the development of non invasive techniques, histological examination still is a valuable procedure for screening CIS of the testis in postpubertal cryptorchid patients. Our study also indicated the importance of early diagnosis and treatment of cryptorchidism in infancy.

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