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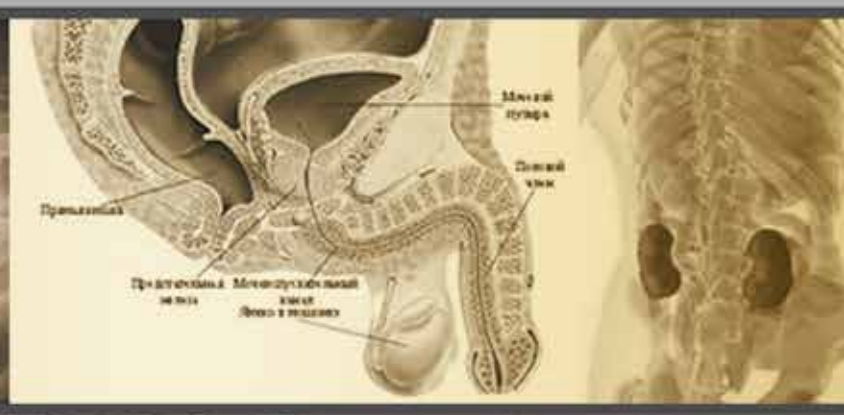

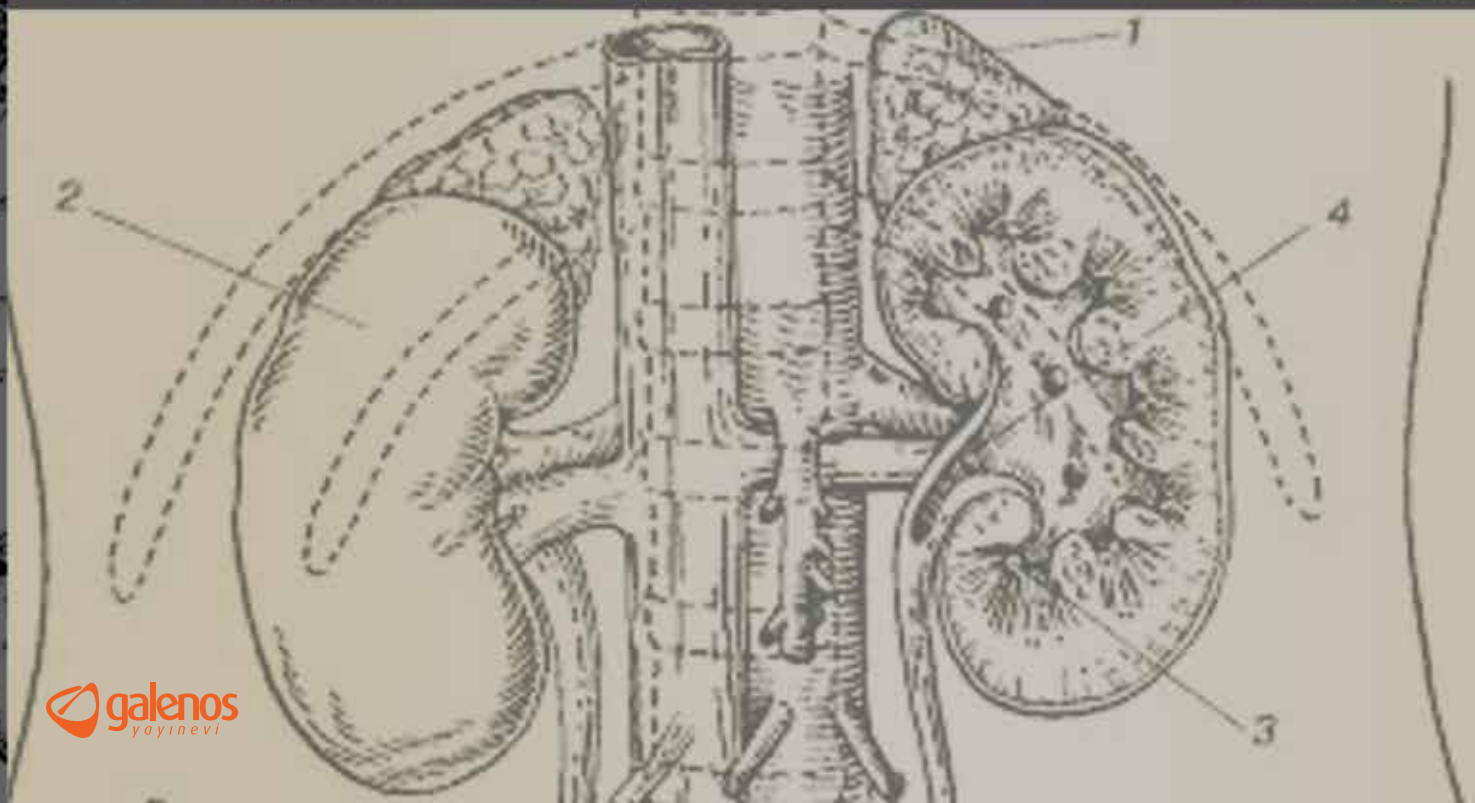

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REVIEW
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Urethral Stricture is an Unpleasant Complication after Prostate Surgery: A Critical Review of Current Literature

Prostat Cerrahisi Sonrası Can Sıkıcı Komplikasyon Üretral Darlık, Güncel Literatürün Kritik Analizi

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ABSTRACT

Urethral stricture is narrowing of the urethra due to inflammation that results in scarring. Prostatectomies for benign and malign prostatic diseases are common surgical procedures among men mainly after their fifties. Urethral stricture or bladder neck contraction following transurethral resection of the prostate (TURP) is seen in up to 19% of men in different series. Urethral stricture after laser prostatectomy is less frequently reported than TURP, which is about 3.6%. Open prostatectomy for benign prostatic hyperplasia is the oldest technique, nonetheless, it is a reasonable alternative for patients with larger prostates. Urethral stricture is reported in 1.9-4.8% of patients after open prostatectomy. Radical prostatectomy (RP) is the most common surgical procedure done worldwide for the treatment of localized prostate cancer. Contracture of the bladder neck at the level of the anastomosis is a well-recognized complication after RP occurring in 0.4-32% of patients. Strictures are mainly treated with endoscopic procedures. Rarely, urethroplasty with buccal mucosa grafts is needed for more complicated cases.

Keywords: Urethral stricture, prostate surgery, transurethral resection, open prostatectomy, radical prostatectomy

ÖZ

Üretral striktür enflamasyona bağlı olarak skarlaşma sonrası üretradaki daralmadır. Elli yaş üzeri erkeklerde benign ve malign hastalıklara bağlı olarak yapılan prostatektomiler oldukça yaygın olarak uygulanmaktadır. Prostatın transüretral rezeksiyonu sonrası farklı serilerde %19'a kadar çıkan oranlarda üretral darlık ve mesane boynu kontraksiyonu görülmektedir. Lazer prostatektomi sonrası üretral darlık prostatın transüretral rezeksiyonuna oranla daha az olarak görülmektedir, yaklaşık olarak %3,6 oranındadır. Açık prostatektomi en eski yöntem olmasına rağmen büyük prostat boyutlu hastalarda oldukça mantıklı bir alternatiftir. Açık prostatektomi sonrası yaklaşık olarak %1,9-4,8 oranında darlık bildirilmiştir. Radikal prostatektomi (RP) lokalize prostat kanseri tedavisinde bütün dünyada en yaygın olarak uygulanan yöntemdir. RP sonrası anastomoz seviyesinde mesane boynu kontraksiyonu olması iyi bilinen bir komplikasyondur ve yaklaşık olarak hastaların %0,4-32'sinde görülmektedir. Darlık büyük oranda endoskopik yöntemlerle tedavi edilmektedir, nadiren komplike olgularda bukkal mukoza greftli üretroplasti gerekebilmektedir.

Anahtar Kelimeler: Üretral darlık, prostat cerrahisi, transüretral rezeksiyon, açık prostatektomi, radikal prostatektomi

Introduction

Prostatectomy is one of the main causes of surgery in aging male population. Besides traditional techniques, novel minimally invasive approaches may also end up with certain complications following prostate surgery. Transurethral procedures may cause iatrogenic urethral trauma. Factors that may influence the development of iatrogenic endoscopic urethral strictures include "electrical dispersion" generated by unipolar current and the "diameter of the instruments" used. Those complications not only bother quality of life of the patients but also may cause various adjunctive procedures with an economical impact.

Urethral stricture is the abnormal narrowing of any segment of the urethra surrounded by corpus spongiosum. It specifically means varying degrees of spongiofibrosis that refers to scarring of the corpus spongiosum (1). Any inflammation of the urethra can result in scarring that can lead to a stricture or a narrowing of the urethra. Besides prostate surgery, trauma, infections, tumors or any other cause of scarring may trigger urethral stricture (2). A recent meta-analysis including 732 patients showed that idiopathic and iatrogenic etiologies were by far the most common, accounting for 33% and 33% of all cases, respectively. Inflammatory and post-traumatic etiologies were found in only 15% and 19% of patients, respectively (3).

Here, we tried to review the incidence and the basic risk factors that cause urethral stricture following prostate surgery.

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Stricture after Transurethral Prostate Resection

Lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) are considerably common in aging male population. Despite the development of novel minimally invasive methods, monopolar transurethral resection of the prostate (TURP) remains the gold standard surgical treatment for LUTS related to BPH (4). Annual re-operation rate after TURP is about 1-2%. A review analyzing 29 randomized controlled trials showed that re-TURP rate was 2.6% in a mean follow-up of 16 months. Bladder neck contracture and urethral stricture rates were 4.7% and 3.8%, respectively (5).

Geavlete et al. (6) evaluated long-term complications of monopolar TURP, bipolar TURP and photoselective vaporization of the prostate (PVP) in a prospective, randomized trial. Each study arm had 170 cases. They found that urethral stricture rates were similar in each arm (5.3%, 6.5%, 4.7%, respectively p=0.768). However, the rate of bladder neck stricture was significantly lower in PVP than in mTURP and bTURP groups (0.6%, 4.1% and 3.5%, respectively p=0.047). Autorino et al. (7) compared four years results of bTURP vs. mTURP and and found that urethral stricture rates were 3% vs. 6%, respectively (p=0.6). Sinanoglu et al. (8) compared the long-term outcomes of 85 monopolar TURP (mTURP) and 80 bipolar TUR (bTURP) patients and showed that the stricture rates were, 4.8% vs. 11.2%, respectively (p=0.171). Stucki et al. (9) prospectively randomized 137 BPH patients to mTURP (n=67) or bTURP (n=70) arms. There were no significant differences in urethral strictures, however, bladder neck stricture occurred significantly more often in the bipolar group (8.5% vs. 0%, p=0.02). Komura et al. (10) evaluated the impact of the bipolar TUR system on postoperative urethral stricture rates in a mean follow-up of 36 months. They have detected a significant difference in postoperative urethral stricture rates (6.6% in mTURP vs. 19.0% in bTURP p=0.022). After stratifying patients according to prostate volume, for the patients with a prostate volume of ≤70 ml, there was no significant difference between the two arms (3.8% in mTURP vs. 3.8% in bTUR p=0.547). However, for the patients with larger prostates (>70 ml) significantly higher urethral stricture rates were noted compared to mTURP patients (20% vs. 2.2%, respectively p=0.012). Tang et al. (11) performed a pooled analysis of late complications in more than ten studies. They have showed that bTURP occasionally caused a higher incidence of urethral strictures (4% vs. 3.9%, respectively p=0.95) and bladder neck contractures (2.7% vs. 4%, respectively p=0.08) that did not reach a significance.

Basic predisposing factors associated with stricture formation in patients undergoing TURP are increased prostate volume, presence of prostate cancer and the surgeon's experience (12). Mismatch between the size of the instrument and the diameter of the urethral meatus results as meatal strictures, whereas bulbar strictures occur due to insufficient insulation by the lubricant. In order to prevent strictures, lubricant gel must be reapplied when the resection time is getting longer (13,14).

Patients with comorbidities, such as hypertension (HTN), coronary artery disease (CAD) and diabetes mellitus (DM) are also candidates for urethral stricture (8). In patients with comorbidity, bTURP causes higher stricture rates than mTURP (p=0.000) (8,15).

Recently, new studies showed that TURP inevitably leads to a degree of mechanical urethral stress, the extent of which may depend on the technique used, reflecting the surgeon's skills. Inappropriate axial/rotating movements of the resectoscope and relationship between instrument size and urethral meatus diameter, inadequate lubrication, or longer operating times may lead to urethral stress and stricture (16). Electrothermal trauma is also a specific procedural risk and both in M-TURP and B-TURP and electric current leakage can provoke stenosis (13,16,17,18). Gunes et al. (19) studied the effect of 24F versus 26F resectoscope size in meatal and bulbar stricture in 71 patients. In terms of meatal stricture, no difference was detected between the groups (5.7% vs. 4.9%, respectively, p=0.386). However, a significant difference was reported in terms of bulbar stricture formation (2.9% vs. 11.4%, respectively, p=0.018). In a recent large-scale study, the overall re-treatment rates including re-TURP, urethrotomy, and bladder neck incision were 5.8%, 12.3%, and 14.7% at 1, 5, and 8 years, respectively. The incidence of re-TURP was 2.9%, 5.8%, and 7.4% for the same follow-up periods, respectively (Table 1) (20).

Stricture after Laser Prostatectomy

PVP is a promising technique emerging as a feasible alternative to TURP over the last decades (21). Woo et al. (21) conducted a meta-analysis and reported the incidence of urethral stricture rates in 408 PVP and 353 TURP patients. Both groups had similar urethral stricture rates (3.6% vs. 6.5%, respectively) (Risk ratio (RR)=1.77, 95% confidence interval=0.94-3.33, p=0.08). Chung et al. (22) investigated complications related with PVP in 162 anticoagulated

Table 1. Urethral and bladder neck stricture rates in monopolar transurethral resection of the prostate and bipolar transurethral resection of the prostate patients

Authors	mTURP		bTURP		p	
	Urethral stricture	Bladder neck stricture	Urethral stricture	Bladder neck stricture	Urethral stricture	Bladder neck stricture
Sinanoglu et al. (8)	3/85 (4%)	-	8/80 (10%)	-	0.102	-
Stucki et al. (9)	1/67 (1.5%)	0/67 (0%)	1/70 (1.4%)	6/70 (8.5%)	1	0.02
Autorino et al. (7)	2/31 (6%)	1/32 (3%)	1/31 (3%)	1/32 (3%)	0.6	0.8
Geavlete et al. (6)	9/170 (5.1%)	7/170 (4.1%)	11/170 (6.3%)	6/170 (3.4%)	0.768	0.047
Komura et al. (10)	4/61 (6%)	-	12/63 (19%)	-	0.022	-
Tang et al. (11)	36/909 (3.9%)	37/852 (4%)	38/948 (4%)	25/899 (2.7%)	0.95	0.008
Mamoulakis et al. (16)	10/108 (9.3%)	2/108 (1.9%)	10/122 (8.2%)	8/122 (6.6%)	0.768	0.02

bTURP: Bipolar transurethral resection of the prostate, mTURP: Monopolar transurethral resection of the prostate

patients and no urethral stricture was reported. Batura et al. (23) studied the complications of PVP-120 W high performance system (GreenLight™ lithium triborate laser). According to study it has been showed that the rate of urethral strictures (4/117, 3.4%) was low and comparable with TURP in a mean follow-up of 20 months.

Holmium laser enucleation of the prostate (HoLEP) has emerged as an effective transurethral treatment option in patients with symptomatic BPH of any size (24). Krambeck et al. (25) reported results of 1065 holmium laser prostate enucleations. Urethral stricture was noted in 9 (0.9%), 11 (1.3%), 4 (1.3%) and 0 patients, and bladder neck contracture was found in 0, 7 (0.8%), 4 (1.3%) and 5 (6.0%) patients at short, intermediate, long-term and more than 5-years of follow-up, respectively. Elzayat and Elhilali (26) retrospectively analyzed urethral strictures in 225 patients with a median prostate volume of 126 grams. In a mean follow-up of 31 months, strictures occurred in 3 patients (1.3%), meatal stenosis in 1 patient and bladder neck contracture was noted in 1 patient (0.4%). Elmansy et al. (27) conducted a retrospective analysis of 949 patients treated with HoLEP. Bladder neck contracture and urethral strictures developed in 0.8% and 1.6% of patients, respectively, in 62 months of follow-up (27). HoLEP is now considered as new gold standard treatment for symptomatic BPH (Table 2, 3).

Stricture after Open Prostatectomy

At the beginning of the 20th century, open prostatectomy was accepted as the reference standard treatment option for BPH (28). Although open prostatectomy is the oldest technique, it is most frequently preferred option for patients with large prostates (>80 cc) (29). Open prostatectomy is not performed only in technologically underdeveloped areas of the world. Studies from several European countries, such as Sweden and France, have shown that this procedure is performed for 12-14% of prostatectomies (30,31).

Varkarakis et al. (32) reported long-term complications of open prostatectomy in 232 patients with prostates >75 grams. In a mean follow-up of 41.8 months, the rates of bladder neck contractions, urethral strictures and meatal stenosis were 3.3%, 0.6% and 1.3%, respectively. Another study from Turkey included 664 patients and it was shown that the rate of late complications, such as bladder neck stenosis and meatal stenosis occurred in 3.2% and 2.3% of patients, respectively (33). The Sicilian-Calabrian Society of Urology performed a retrospective study to assess the surgical management of BPH. Open prostatectomy accounted for 32% (1.804/31.558) of all surgical treatment alternatives (34). In that study, the most frequent late complications were urethral and/or bladder neck stenosis 87/1804 (4.8%) (34).

In underdeveloped countries, the selection of this approach is usually compulsory and dictated by the lack of transurethral instruments and endourological expertise (Table 4) (32).

Stricture after Radical Prostatectomy

Radical prostatectomy (RP) is the most common procedure worldwide to treat localized prostate cancer. Due to widespread use of prostate-specific antigen (PSA) testing, patients operated today are often younger and have organ-confined disease, justifying a more preservative surgery (35). Contracture of the bladder neck at the level of the anastomosis between the bladder and the membranous urethra is a well-recognized complication after RP, reportedly occurring in 0.4-32% of patients (36,37,38,39). The risk of vesicourethral anastomosis stricture (VUAS) has decreased by time with improved surgical techniques (35).

Wang et al. (40) evaluated the difference between the rates of vesicourethral anastomotic stenosis after open RP (n=707) and robot-assisted radical prostatectomy (RARP) (n=1038) and analyzed associated factors and the effect of stenosis on quality of life. The incidence of VUAS was higher in open RP than in RARP (7.5% vs. 2.1%, respectively, p<0.01). Open technique odds ratio (OR) (OR 3.0), PSA recurrence (OR 2.2), postoperative hematuria (OR 3.7), urinary leak (OR 6.0), and urinary retention (OR 3.5) were significant independent predictors of VUAS development (40). Sandhu et al. (41) studied predictors of symptomatic anastomotic strictures in 3.458 open RP (75%) and 1.134 laparoscopic RP (25%). The laparoscopic RP group included 97 robotic-assisted cases. Symptomatic anastomotic strictures developed in 198 patients (4.3%). On multivariate analysis, significant predictors included patient age (OR 1.03), body mass index (OR 1.04), Charlson score (OR 1.3), renal insufficiency (OR 4), individual surgeon experience (OR 0.08-9.7), and the presence of postoperative urinary leak (OR 2.3) or hematoma (OR 2.8). Borboroglu et al. (42) hypothesized that the presence of microvascular disease may lead to impaired healing and results in stricture. In their series including 467 patients treated with RP, vesicourethral stricture occurred in 11.1% of subjects. Recognized factors leading to microvascular disease, such as current cigarette smoking resulted in a significantly higher (26%) rate of VUAS (p<0.001). The VUAS rate was also increased in patients with CAD (26%, p<0.001), HTN (19%, p=0.015), and DM (21%, p=0.030). The mean surgery time was longer (271 vs. 249 minutes, p=0.025) and the estimated blood loss was greater (1639 vs. 1092 ml, p<0.001) in patients developing a VUAS.

Table 2. Comparison between photoselective vaporization of the prostate and transurethral resection of the prostate in terms of urethral and bladder neck stricture

Authors	PVP		TURP		p	
	Urethral stricture	Bladder neck stricture	Urethral stricture	Bladder neck stricture	Urethral stricture	Bladder neck stricture
Woo et al. (21)	15/408 (3.6%)	-	23/353 (6.5%)	-	0.08	-
Chung et al. (22)	0/162 (0%)	0/162 (0%)	-	-	-	-
Batura et al. (23)	4/117 (3.4%)	-	-	-	-	-

PVP: Photoselective vaporization of the prostate, TURP: Transurethral resection of the prostate

Table 3. Urethral-meatal stricture and bladder neck stricture after Holmium laser enucleation of the prostate

Authors	HoLEP	
	Urethral-meatal stricture	Bladder neck stricture
Elmansy et al. (27)	15/949 (1.6%)	7/949 (0.8%)
Elzayat and Elhilali (26)	4/225 (1.7%)	1/225 (0.4%)
Krambeck et al. (25)	24/1065 (0.02%)	16/1065 (0.01%)

HoLEP: Holmium laser enucleation of the prostate

Table 4. Urethral-meatal stricture and bladder neck stricture after open prostatectomy

Authors	Open prostatectomy	
	Urethral-meatal stricture	Bladder neck stricture
Varkarakis et al. (32)	3/232 (1.9%)	5/232 (3.3%)
Suer et al. (33)	15/664 (2.3%)	22/664 (3.2)
Serratta et al. (34)	87/1804 (4.8%)	

The majority of comparative studies report low and overlapping rates of anastomotic stricture in open RP (mean: 7.2%; range: 1.8-16%) and laparoscopic RP (mean: 3.0%; range: 0-6.4%). However, cumulative meta-analysis data reveals that strictures are significantly less common in laparoscopic RP (RR=2.92) (43,44,45,46,47).

Anastomotic tension, urinary extravasation, poor tissue handling and ischemia are the main proposed mechanisms for BNC after RP. Intraoperative and postoperative factors, such as excessive blood loss, type of bladder neck dissection, postoperative urinary leakage, adjuvant radiotherapy, previous TURP, current cigarette smoking, older age, obesity, surgeon experience, open vs. minimally invasive surgery, and acute postoperative retention treated with suprapubic tube placement also influence the VUAS rates (38,48,49,50,51,52).

Management of Urethral Stricture

Urethral Dilation

There are several methods for urethral dilation, such as dilation with a balloon, filiform and followers, urethral sounds or self-dilatation with catheters. Steenkamp et al. (53) showed that urethral dilatation and optical internal urethrotomy under local anaesthesia are equally successful as initial outpatient treatment. With regard to successful performance of the procedure itself, multiple, longer (>2 cm), post-traumatic, and previously untreated strictures are better managed with dilatation, whereas patients with complications or retention are better managed with internal urethrotomy.

Internal Urethrotomy

Direct vision internal urethrotomy (DVIU) is performed by using a cold-knife transurethral incision to release scar tissue, allowing the tissue to heal by secondarily at a larger caliber and thereby increasing the size of the urethral lumen. In different recent studies shows that overall long-term success rates are estimated to be just 20-30% (54,55). Recurrence is more likely influenced by length of stricture; the risk of recurrence at 12 months is 40% for strictures shorter than 2 cm, 50% for strictures between 2-4 cm, and 80% for strictures longer than 4 cm (56). Recurrence rates also vary according to stricture location; 58% of bulbar strictures will recur after urethrotomy, compared with 84% for penile strictures and 89% for membranous strictures (55).

According to recent studies, the efficacy of agents such as mitomycin C and triamcinolone injected into the scar tissue has been studied to decrease recurrence rates at the time of internal urethrotomy (57,58,59,60,61).

Laser urethrotomies are another method to manage the anterior urethral stricture with a reported success rate of 20-80% in different studies (62,63).

Urethroplasty

Several techniques have been used for urethroplasty, including excision and primary reanastomosis, onlay grafting and the use of flaps. Long-term success rates are much higher for urethroplasty (85-90%) than for urethrotomy (20-30%) (64).

In fact, urethroplasty is the most effective method for definitive correction of urethral strictures and this is generally considered to be the gold-standard treatment (61,65,66). Risk factors associated with failure include incomplete excision of scar tissue, anastomotic tension and the presence of lichen sclerosis (67).

The basic principle in treatment of urethral stricture is that internal urethrotomy promises an acceptable success rate only in short-term and first-time strictures. In a recurrent stricture, open reconstruction is technique of choice then repeated urethrotomies. It is very important that open reconstructive surgery should be carried out at experienced centers to achieve the best results (68).

Conclusion

Urethral stricture is an unpleasant complication after prostate surgery. In different studies, the incidence of urethral stricture, bladder neck contracture or VUAS has been reported to be less than 5% after endoscopic or open procedures. Urethral stricture management modalities can achieve a success rate of 20-90% in adequate experienced centers. Primary DVIU/dilation is indicated as the first-line therapy for short (<1-2 cm), single, bulbar urethral strictures. A second DVIU/dilation can be indicated for recurrent urethral strictures with favorable characteristics (<1-2 cm, single, bulbar stricture) with recurrence >3 months after previous treatment. A third DVIU/dilation is not recommended, except if necessitated by patient comorbidities or economic resources. Urethral reconstructions over repeat DVIU/dilation should be offered for urethral strictures that recur within 6 months or are refractory to a second DVIU/dilation. Surgeons should be aware of this unpleasant complication and be cautious to prevent it just before the prostate surgery.

Ethics

Peer-review: Internal peer-reviewed.

Authorship Contributions

Concept: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev, Design: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev, Data Collection or Processing: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev, Analysis or Interpretation: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev, Literature

Search: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev, Writing: Emrullah Söğütdelen, Hakan Bahadır Haberal, Bülent Akdoğan, Fuad Guliyev. Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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To Save or not to Save the Kidney: Relieving Unilateral Obstruction May Significantly Improve an Initially Low Split Renal Creatinine Clearance

Böbreği Kurtarmak ya da Kurtarmamak? Tek Taraflı Üreteral Obstrüksiyonun Tedavisi Erken Dönemdeki Düşük Kreatinin Klirensini Anlamlı Olarak Arttırabilir

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What's known on the subject? and What does the study add?

This is first study that evaluated the renal function change after relief of unilateral ureteral obstruction because of ureteral stones.

ABSTRACT

Objective

The aim of this study was to evaluate the change in acute/subacute unilateral renal function after the relief of complete unilateral ureteral obstruction by nephrostomy.

Materials and Methods

Thirty patients were prospectively enrolled in the study. All had ureteral stone, which were located in the upper ureter in 24 (80%) and in the middle ureter in 6 (20%) patients. As all patients had high-grade hydronephrosis, a percutaneous nephrostomy catheter was placed for the relief of obstruction. At the first week of urinary diversion, 24-hour creatinine clearance (CC) of both affected and normal kidneys were evaluated. In order to determine the difference, same evaluation was performed on the fourth week of nephrostomy placement.

Results

The mean age of the patients was 44.6 (36-54) years. The mean CC of the affected kidney was 38.8±4.9 ml/min in the first week of urinary diversion and increased to 42.5±5.4 ml/min at the end of the fourth week ($p<0.001$). All patients showed an improvement in CC levels ranging between 2.3% and 17.3% with a mean rate of 8.5±4.7%.

Conclusion

According to our results, kidney function may improve during the first month after the relief of obstruction. This improvement may be significant for borderline renal function to determine the curative treatment of an obstructed kidney

Keywords

Creatinine clearance, nephrostomy, obstructive uropathy

ÖZ

Amaç

Çalışmamızda akut/subakut tek taraflı komplet üreteral tıkanıklığa bağlı böbrek fonksiyonlarının nefrostomi ile tedavi sonrası değişimini göstermek amaçlanmıştır.

Gereç ve Yöntem

Otuz hasta prostpektif olarak çalışmaya dahil edilmiştir. Hepsinin üreter taşı olup 24'ünde (%80) üst üreter ve 6'sında (%20) orta üreter yerleşimliydi. Tüm hastaların ileri düzeyde hidronefrozu olduğu için perkütan nefrostomi takılması planlandı. Nefrostomi takıldıktan sonra 1. haftada etkilenen böbrek nefrostomiden ve diğer böbrek üretral kreatinin klirensi ölçümü ile değerlendirilmiştir. Değişikliği saptamak için de 1. ayda nefrostomi ve üretral kreatinin klirensleri hesaplanıp 1. haftadaki sonuçlar ile karşılaştırılmıştır.

Bulgular

Hastalarımızın ortalama yaşı 44,6'dır (36-54). Etkilenen böbreğin 1. haftadaki kreatinin klirensi 38,8±4,9 ml/dak iken 1. aydaki değer 42,5±5,4 ml/dk'ya yükselmiştir ($p<0,001$). Tüm hastaların kreatini klirens analizlerinde %2,3 ile %17,3 arasında artış saptanmıştır.

Sonuç

Çalışma sonuçlarımıza göre tek taraflı komplet üreteral tıkanıklığa bağlı bozulan böbrek fonksiyonu nefrostomi takılması sonrası 1. ayda 1. haftaya göre anlamlı olarak düzelmektedir. Bu düzelme böbrek fonksiyonları sınırda olan tek taraflı tıkanıklığı olan hastalarda asıl tedaviye veya nefrektomi yapmaya karar vermede etkili olacaktır.

Anahtar Kelimeler

Kreatinin klirens, nefrostomi, obstrüktif üropati

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Introduction

Intraluminal or extraluminal ureteral obstruction is the main cause of obstructive uropathy that may lead to cell death, tissue necrosis, progressive fibrosis and loss of renal parenchyma (1,2,3,4). Glomerular filtration rate (GFR) and renal blood flow (RBF) decrease with the unilateral ureteral obstruction (UUO) and progressively worsen until the obstruction is relieved. The response of the kidney to relief of UUO is species-specific and depends on age of the patient, duration and extent of obstruction, function of the contralateral kidney, and compliance of the ureter and renal pelvis (5). UUO demonstrates a triphasic pattern of RBF and ureteral pressure changes which is different from bilateral ureteral obstruction or UUO of a solitary kidney (6).

There are several studies demonstrating the effect of ureteral obstruction on renal function and the reversibility of some changes after the relief of obstruction (6). Indeed, most of the studies were on animal models and the human studies were generally retrospective studies (5,7,8). Several renal function variables, such as GFR, serum creatinine level, renal perfusion index, renal parenchyma thickness, resistive index, and scintigraphic methods were evaluated in those studies (5,7,8,9,10). Most of the human studies evaluated a heterogeneous group with different causes of ureteral obstruction, such as ureteral or pelvic stones, ureteric stricture, bladder cancer, ureteropelvic junction obstruction, etc. These diseases have different pathophysiological properties and this heterogeneity causes difficulty to reach a clear conclusion. In this study, we tried to prospectively evaluate the reversibility of renal function after relief of unilateral obstruction caused by ureteral stone in patients with a normally functioning contralateral kidney.

Material and Methods

With the permission of the local ethics committee, a total of 49 patients with UUO related to a ureteral stone were prospectively included in the study after obtaining informed consent. These were the patients who had undergone an unsuccessful attempt for ureteral stenting with double J and were referred to our hospital for percutaneous nephrostomy (PN). All patients had acute renal colic for a minimum of 5 and a maximum of 15 days before admission to our clinic. The initial evaluation included the history, clinical examination and biochemical analysis including serum creatinine level, urine analysis and culture. Radiological evaluation was performed by plain x-ray of the abdomen and urinary ultrasonography. Any patient who had a past history of renal stone, bilateral hydronephrosis, any chronic disease (diabetes, hypertension, etc.), abnormal creatinine level and hydronephrosis less than grade 3 in the affected kidney was excluded from the study that was 13 in number.

An intravenous pyelography (IVP) was performed in the remaining patients to determine the level of obstruction and evaluate the functional capability of the contralateral kidney. As all the patients were informed about the importance of early relief of obstruction, they were given the possibility of PN and a second chance for ureteral stenting. A total of 30 patients were included in the study for the evaluation of unilateral renal function (Figure 1).

At the end of the first day, the patients were discharged and recalled one week later to evaluate 24-hour creatinine clearance (CC) of the affected kidney with nephrostomy and urethral clearance separately. The patients were re-called 4 weeks later for the same evaluation. There was no significant change in the location of the stone seen on plain abdominal x-ray and urinary ultrasonography. There was no complication or complicated urinary tract infection during this follow-up period and all the patients underwent a definitive treatment with ureteroscopic lithotripsy or extracorporeal shock wave lithotripsy (ESWL) in a maximum of 6-week period after the insertion of PN.

SPSS version 16.0 was used for statistical analysis. Data in dependent groups were analyzed for normality with the Kolmogorov-Smirnov test. As our data was distributed normally, paired t-test was performed to evaluate the mean CC rates of patients at first and fourth week of PN and urethral CC.

Results

A total of 30 patients (19 male, 11 female) with a mean age of 44.6 (36-54) years were enrolled in the study. They all had a ureteral stone located in the upper ureter in 24 and at the middle ureter in 6 patients. The mean diameter of the ureteral stone (calculated as the longest diameter of the stone) was 10.2 mm (8-13 mm) on intravenous pyelography. There was no passage of radio-opaque material in the affected system with a grade 3 hydronephrosis in 9 and grade 4 hydronephrosis in 21 patients. All patients showed an improvement in CC levels ranging between 2.3% and 17.3% with a mean rate of 8.5±4.7% (Table 1).

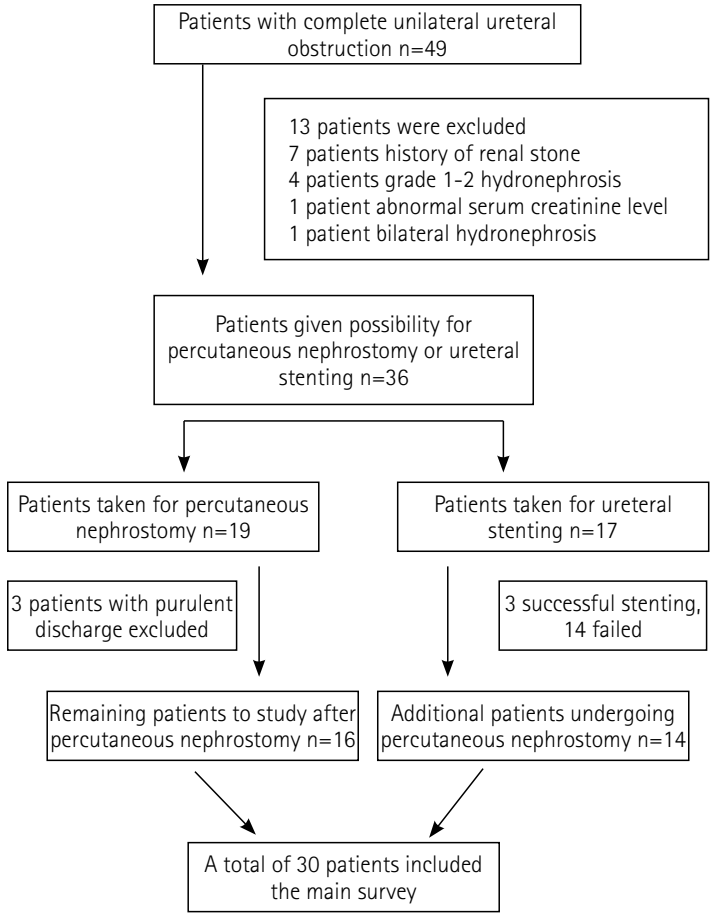

Figure 1. The diagram of study flow

There were 17 patients with CC of <40 ml/min (35.1±2.19) and 13 patients with >40 ml/min (43.6±2.74) in the first week evaluation (p<0.001). Among these groups, the mean percentage of CC improvement was 9.2±4.8% and 7.6±4.4%, respectively (p=0.339).

The mean value of separated renal function of the affected kidney was 45.94% and 48.32% in the first week and fourth week, respectively and the differences were statistically significant (p<0.001) (Table 2).

Discussion

The only way of preventing obstructive uropathy is to relieve the obstruction (8,9,10,11). Better et al. (12) evaluated the change in CC in a patient with an obstructed kidney for a duration of 3 months after relief of obstruction. The CC of the affected kidney increased from 2.6 ml/min to 10.2 ml/min at the first week after relief of obstruction and remained unchanged thereafter. Shi et al. (13) have reported the ability of a kidney to return to normal GFR 4 weeks after relief of 3-day complete UUO. However, longer obstruction might cause irreversible defects and only a partial recovery of renal function would be seen after relief of obstruction (14). In a recent experimental study, Soliman et al. (15) have reported nearly 12% increase in CC rate in dogs 32 weeks after relief of a 4-week obstruction. In another experimental study, Cochrane et al. (16) have reported that the volume density of interstitium in the renal cortex of mice with UUO for 2 and 4 weeks recovered 13% after relief of obstruction. These were all experimental animal studies. It is well-documented that the response of kidneys to UUO is species-specific and animal models may not adequately reflect the exact mechanism (6). For this reason, we tried to design a human

Table 1. The creatinine clearance rates of patients in the 1st and 4th week after relief of obstruction and the percentages of change

	Creatinine clearance in the first week (ml/min)	Creatinine clearance in the fourth week (ml/min)	The difference between the groups (ml/min)	The percentage difference between the groups (%)
Patient 1	47.8	54.1	6.3	11.6
Patient 2	32.1	33.7	1.6	4.7
Patient 3	49.3	55.7	6.4	11.5
Patient 4	43.6	48.7	5.1	10.5
Patient 5	38.5	42.5	4.0	9.4
Patient 6	33.5	39.2	5.7	14.5
Patient 7	44.7	45.8	1.1	2.4
Patient 8	38.4	40.7	2.3	5.7
Patient 9	36.7	38.1	1.4	3.7
Patient 10	32.7	39.5	6.8	17.2
Patient 11	40.7	41.6	0.9	2.2
Patient 12	36.5	39.7	3.2	8.1
Patient 13	41.6	45.7	4.1	9.0
Patient 14	36	38.5	2.5	6.5
Patient 15	45.8	52.1	6.3	12.1
Patient 16	34.1	35.7	1.6	4.5
Patient 17	44.3	50.7	6.4	12.6
Patient 18	41.6	46.7	5.1	10.9
Patient 19	35.5	40.5	5.0	12.3
Patient 20	31.5	37.2	5.7	15.3
Patient 21	42.7	43.8	1.1	2.5
Patient 22	36.4	38.7	2.3	5.9
Patient 23	36.9	38.3	1.4	3.7
Patient 24	32.5	39.3	6.8	17.3
Patient 25	40.2	41.1	0.9	2.2
Patient 26	36.5	39.7	3.2	8.1
Patient 27	41.4	45.5	4.1	9.0
Patient 28	36.2	38.7	2.5	6.5
Patient 29	33.3	39	5.7	14.6
Patient 30	44.2	45.3	1.1	2.4
Mean	38.8±4.9	42.5±5.4	3.6	8.5
		p<0.001		

Table 2. The urethral creatinine clearance and the separated function of the affected kidney rates (ratio of affected kidney creatinine clearance to total creatinine clearance) in the 1st and 4th week after relief of obstruction

	Urethral creatinine clearance in the first week (ml/min)	Urethral creatinine clearance in the fourth week (ml/min)	Separated renal function of the affected kidney in the first week (%)	Separated renal function of the affected kidney in the fourth week (%)
Patient 1	48.3	47.8	49.80	53.09
Patient 2	39.4	41.2	44.89	44.99
Patient 3	52.6	52.9	48.38	51.28
Patient 4	49.1	48.6	47.03	50.05
Patient 5	45.3	46.1	45.90	52.03
Patient 6	43.7	44.5	43.39	46.83
Patient 7	48.2	47.6	48.11	49.03
Patient 8	42.6	42.9	47.40	48.62
Patient 9	43.5	44.1	45.81	46.81
Patient 10	45.1	44.4	42.03	47.07
Patient 11	43.2	42.5	48.51	49.46
Patient 12	43.6	44.1	45.56	47.37
Patient 13	47.3	47.6	46.79	48.98
Patient 14	41.3	41.8	46.57	47.94
Patient 15	54.2	53.5	45.80	49.33
Patient 16	41.3	41.6	45.22	46.18
Patient 17	52.4	52.7	45.81	49.03
Patient 18	48.2	48.9	46.32	48.84
Patient 19	45.6	45.1	43.77	47.31
Patient 20	41.3	42.5	43.26	46.67
Patient 21	45.6	45.1	48.35	49.26
Patient 22	43.2	44.3	45.82	46.62
Patient 23	42.3	41.6	46.59	47.93
Patient 24	45.6	44.1	41.61	47.12
Patient 25	43.1	42.5	48.25	49.12
Patient 26	43.1	43.8	45.85	47.54
Patient 27	52.3	51.1	44.18	47.10
Patient 28	41.1	40.4	46.83	48.92
Patient 29	43.6	44.1	43.30	46.93
Patient 30	49.2	48.4	47.32	48.34
Mean	45.51±3.8	45.52±3.6	45.94±1.99	48.32±1.75
		p=0.909		p<0.001

study evaluating the response of kidneys to the relief of UUO. To our knowledge, this is the first study evaluating relief of acute/subacute UUO in such number of cases (30 patients) with prospective design.

Gillenwater has concluded that the best method for determining the absolute degree of injury and recoverability was to relieve the obstruction with PN and monitoring the renal function by CC (17). Hussain et al. (18) have also investigated the most reliable method for determining the future recovery of renal function after relief of obstruction and concluded that PN with CC had 97.8% accuracy for this evaluation. In the present study, the mean rate of increase in CC in this period was 8.5%. Although this improvement rate varied, all patients showed somehow an increase in the CC rate of their affected kidney. Our results are compatible with the literature. Khalaf et al. (9) have investigated the recoverability of renal function in 91 patients after relief of chronic unilateral obstruction. They have used GFR for the evaluation of renal function and found an improvement in 63.7% of patients whereas 32% of patients had further deterioration after relief of obstruction. Different from our study, the authors have evaluated a heterogeneous group of patients with ureteric stricture, renal and ureteral stones, and ureteropelvic junction obstruction. Beside this, it has been pointed out that 25 of 91 (27.5%) patients in the study group had a GFR of <10 ml/min/1.73 in whom the recovery of renal functions was rarely expected. In another study, Shokeir et al. (19) have evaluated recovery of renal functions in 32 patients with complete obstruction with a non-functioning or absent contralateral kidney. They used serum creatinine level for determining the recovery

and reported a significant decrease in creatinine levels after relief of obstruction. This was also observed in our study.

Patient age is one of the factors that was found to be related with recovery rate (20). The conclusion on the importance of patients' age for the recovery of UUO comes from the studies of the treatment of ureteropelvic junction obstruction, a congenital chronic disease. Mikkelsen et al. (21) have reported that 30 years was the limit of age to expect a significant improvement in renal functions after the treatment of ureteropelvic junction obstruction. According to our knowledge, there is no age-specific evaluation for the relief of complete obstruction related to ureteral stones. In our study, we were not able to find any significant difference in terms of recovery of renal function between patients who were <45 years and >45 years of age. Although the difference in recovery rates between these groups was not significant, we observed a higher rate of recovery in patients who were younger. Similar finding were observed between the groups who had CC rates of <40 ml/min and >40 ml/min. Patients who had a CC rate of <40 ml/min had higher percentage of clearance improvement, but it was not statistically significant. For that reason, large number of patients may be needed to make an exact evaluation of the importance of age and CC.

One of the limitations of our study was the chronicity of ureteral obstruction. We were not able to determine the exact time of obstruction, but the CC of affected kidneys was over 35 ml/min in all patients. Although we cannot make a clear conclusion, this may give an idea that the obstruction was acute or subacute in most of our patients. The second limitation was about the severity of obstruction. We could not show that the obstruction in our patients was totally complete obstruction but the radiological evaluation brought out the idea that the obstruction was severe that we could not visualize contrast in the distal ureteral segment of obstruction. In our study, since all the subjects, who were taken PN for obstruction, had other chronic severe diseases (cancer, hypertension, infection, chronic obstruction etc.), we could not make up a control group. Therefore we compared the separate renal functions with two subsequent measurements. Another limitation of our study was that we did not evaluate the immediate renal function of patients at the time of relief of obstruction and we were not able to document possible recovery after the 4th week of the obstruction. The early evaluation of CC just after relief of obstruction may cause bias due to rapid physiological changes caused by relief of obstruction. In order to avoid this possible bias, we found it more acceptable to evaluate the renal functions at the first week of relief of obstruction. All patients had curative treatment after 4 weeks, for this reason, we were not able to evaluate the CC rates of the affected kidneys after 4 weeks of follow-up. In the literature, there are some studies reporting that a 4-week follow-up might be sufficient to evaluate the recovery of renal functions. Deng et al. (22) evaluated improvement of renal function in patients with ureteropelvic junction obstruction after insertion of nephrostomy and reported that paranchymal thickness increases in 4 weeks and tubular function returns to nearly normal levels in this period. In another study, Shokeir et al. (20) evaluated renal resistive index and reported that at the first week of relief of obstruction, the mean resistive index significantly decreased and stabilized till to the 4th week. According to these studies, we believe that a 4-week follow-up was enough to document recovery of renal functions after relief of obstruction.

Conclusion

Renal function of an obstructed kidney is the main determinant of the possible treatment opportunities. In order to decide the best treatment modality, evaluation of renal functions becomes very important. Although Khalaf et al. (9) have reported that renal damage was irreversible in patients with a GFR less than 10 mL/min/1.73 m^2, there are plenty of patients with intermediate functions that may lead to unnecessary indications for nephrectomy. Similar to the limited number of human studies, we found a significant increase in functional status of an obstructed kidney after relief of obstruction. According to our results, kidney function may improve by one month after relief of obstruction, thus, it may be reasonable to wait for determining the curative treatment of an obstructed kidney.

Ethics

Ethics Committee Approval: The study were approved by the Marmara University of Local Ethics Committee, Informed Consent: Consent form was filled out by all participants. Peer-review: Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Cenk Murat Yazıcı, İlker Tinay, Tufan Tarcan, Concept: Cenk Murat Yazıcı, Tufan Tarcan, Design: Cenk Murat Yazıcı, Tufan Tarcan, Data Collection or Processing: Cenk Murat Yazıcı, İlker Tinay, Analysis or Interpretation: Cenk Murat Yazıcı, Tufan Tarcan, Literature Search: Hasan Hüseyin Tavukçu, Writing: Hasan Hüseyin Tavukçu, Cenk Murat Yazıcı. Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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Influence of the Presence of Muscularis Propria on Recurrence and the Quality of Transurethral Resection in Low-Grade, Stage pTa Bladder Tumors

Düşük Dereceli Evre pTa Mesane Tümörlerinde Müskülaris Propria Durumunun Transüretral Rezeksiyon Kalitesi ve Rekürrens Üzerine Etkisi

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What's known on the subject? and What does the study add?

It was pointed out that muscularis propria presence in the pathology specimens of low-grade stage pTa tumours is an indicator of a high quality transurethral resection.

ABSTRACT

Objective

Transurethral resection (TUR) of the bladder and intravesical chemotherapy is the standard treatment option for non-muscle-invasive bladder tumors. Inadequate tumor resection results in early recurrence and staging inaccuracies, which all will change the course of the disease. High-quality TUR treatment is therefore an important factor in the treatment of non-muscle-invasive bladder tumors. In this study, we investigated the significance of detecting the presence of muscularis propria (MP) in pathology specimens of low-grade, stage pTa tumors in patients who were treated with TUR due to primary bladder tumors, with regard to recurrence, time to recurrence and progression.

Materials and Methods

Initially, 841 patients who were treated with TUR due to primary bladder tumors were enrolled in the study. A total of 597 patients were excluded from the study because they failed to meet the study criteria. Group 1 consisted of patients with MP detected in the pathology specimens; whereas group 2 consisted of patients whose TUR specimens did not include MP. The patients were evaluated with regard to gender, tumor number, presence or absence of MP, and recurrence status.

Results

MP was observed in only 14 (15.2%) of 92 patients with recurrence, but not in the remaining 78 (84.8%) (p=0.004). Progression occurred in 4

ÖZ

Amaç

Yeni kasa invaze olmayan mesane tümörlerinin standart tedavisi mesanenin transüretral rezeksiyonu (TURM) ve intravezikal kemoterapidir. Yetersiz tümör rezeksiyonu, erken nüks ve düşük evreleme gibi hastalığın seyrini değiştirecek durumları ortaya çıkarmaktadır. Bu nedenle kasa invaze olmayan mesane tümörlerinin tedavisinde kaliteli TURM önemli bir faktördür.

Gereç ve Yöntem

Primer mesane tümörü nedeniyle TURM olmuş 841 hasta çalışmaya alındı. Toplam 597 hasta bu kriterlerimize uymadığı için çalışmadan çıkarıldı. Grup 1'de patoloji spesmeninde müskülaris propria (MP) görülen hastalar bulunurken; grup 2, TURM örneğinde MP görülmeyen hastalardan oluşmuştur. Hastalar; cinsiyet, tümör sayısı, patoloji spesmenindeki tümör hacmi, MP durumu, nüks durumu, nüks zamanı ve progresyon açısından değerlendirildi.

Bulgular

Nüks eden 92 hastanın sadece 14'ünde (%15,2) MP bulunurken geriye kalan 78 (%84,8) hasta da MP görülmemiştir (p=0,004). Grup 1'de progrese olan hasta 4 (%14,2), grup 2'de 28 (%29) hasta olarak ortaya çıkmıştır (p=0,159). Tek değişkenli analizde, tümör multiplitesi (p=0,003) ve MP yokluğu (p=0,004) rekürrens üzerine etkili bulunmuştur. Çok değişkenli analizde yine bu iki parametre nüks üzerine etkili bulunmuştur (p=0,004).

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ABSTRACT

(14.2%) patients of group 1 and 28 (29%) patients of group 2 (p=0.159). In univariate analysis, tumor multiplicity (p=0.003) and the absence of MP (p=0.004) were found to have effects on recurrence. In multivariate analysis, these two parameters were also found to be have effects on recurrence (p=0.004).

Conclusion

In this study, it was pointed out that MP presence in the pathology specimens of low-grade stage pTa tumors is an indicator of a high quality TUR and, a well-done TUR is important for the prevention of recurrence.

Keywords

Bladder tumor, recurrence, tumor volume, muscularis propria

ÖZ

Sonuç

Bu çalışmada düşük dereceli evre pTa tümörlerin patoloji örneklerinde MP varlığının kaliteli bir TURM'nin göstergesi olduğu ve nüksleri önlemede iyi yapılmış TURM'nin önemine dikkat çekilmiştir.

Anahtar Kelimeler

Mesane tümörü, rekürrens, tümör hacmi, müskülaris propria

Introduction

The risk of bladder cancer increases particularly with age in industrial societies. In approximately 75% of patients, the bladder tumors are confined to the mucosa [stage pTa, carcinoma in situ (CIS)] or submucosa (pT1) at the time of diagnosis (1). Bladder tumor ranks 7th among all malignancies in men, whereas 17th in women (2). Worldwide the incidence is 9 in hundred thousand in men and 2 in hundred thousand in women (2,3).

The established standard treatment for non-muscle-invasive bladder tumors is transurethral resection (TUR) of the bladder and intravesical chemotherapy. The primary objectives of TUR are; (i) to remove all visible tumors, (ii) to ensure an accurate pathological tumor staging and grading and (iii) to determine the clinically significant prognostic factors (4,5). However, these objectives may not always be achieved due to; (i) bad cystoscopic image, (ii) a large tumor, (iii) multiple tumors, (iv) difficult localization, and (v) bleeding and perforation (6). As a result, consequences may occur that change the course of the disease, such as inadequate resection of the tumor, early recurrence and staging inaccuracies.

Residual tumor after TUR can be seen as high as 64% (7), and the recurrence rate at the first cystoscopy as 70% (8). Although these figures vary between clinics, this variance was attributed to the quality of TUR and the importance of high quality TUR was underlined in the study by The European Organisation for Research and Treatment of Cancer (EORTC) (9). The recurrence after first cystoscopy is rather attributed to the quality of previous TUR and overlooked tumor cells rather than tumor biology (6,9,10). Mariappan et al. (11) have shown in their study that the presence of MP in TUR specimens was a marker indicating the quality of TUR and experience of the surgeon. High-quality TUR is therefore an important factor in the treatment of non-muscle-invasive bladder tumors. In this study, we investigated the significance of detecting the presence of MP in pathology specimens of low-grade, stage pTa tumors in patients treated with TUR due to primary bladder tumors, with regard to recurrence, time to recurrence and progression.

Materials and Methods

A total of 841 patients, who underwent TUR treatment for primary bladder tumors in our clinic between January 2000 and December 2013, were enrolled in the study. Prior to TUR operation, urinary cytology was carried out as a standard procedure in our clinic, and afterwards, the tumors in the bladder were mapped with 30-degree and 70-degree optical angles and the detected tumors were completely resected with bipolar or monopolar TUR resection. Smaller tumors were resected en bloc and resection of larger tumors were performed in fractions. Then, the tumor base and tumor side were sampled separately and sent to pathology in separate containers. If there was no bleeding or any sign of perforation and a complete tumor removal was deemed, then a single dose of Epirbucin was given intravesically within the first 6 hours. When the pathological investigation revealed stage pT1, high-grade tumor or incomplete resection was suspected, then repeat TUR (reTUR) was planned within 2-6 weeks Then, risk stratification of patients was performed and intravesical mitomycin C or Bacillus Calmette Guarin (BCG) treatment was planned. Exclusion criteria of this study were: patients with pathologic stage pT1, pT2 and CIS, suspected of incomplete TUR, those who missed post-operative a single dose of intracavitary chemotherapy, and failed to show up at regular cystoscopy follow-up. Although we normally plan intravesical mitomycin C or BCG treatment according to risk stratification in routine application, some patients cannot receive this treatment due to social reasons or because they cannot obtain these drugs. In order to exclude the effects of intracavitary treatment on recurrences, patients, who had received intravesical chemotherapy before the first cystoscopy, were also excluded from the study. Based on the aforementioned criteria, a total of 597 patients were excluded from the study. We have included 244 patients who met the inclusion criteria of the study e.g., having low-grade pTa as the result of first TUR, post-operative single dose intravesical chemotherapy and complete TUR. The patients were divided into two groups: Group 1 included patients whose pathology specimens revealed MP; whereas group 2 consisted of patients without MP in TUR specimens. The patients were evaluated with respect to gender, the number of tumors, tumor volume in pathological specimens, MP status, recurrence status, time to recurrence, and progression. Unlike other studies, instead of tumor size, tumor volume in pathological specimens was used in this study. Univariate and multivariate logistic regression analysis and t-test were used to show the relationship between the variables. All statistical analyses were performed using SPSS version 13.0 (Chicago, IL, USA). A p value of 0.05 was considered statistically significant.

Results

Out of 244 patients, 220 (90.1%) were male, 24 (9.9%) were female, and the average age was 60 (24-82) years. MP was observed in 52 (21.3%) patients (group 1) while not in 192 (78.7%) patients (group 2). Recurrence occurred in 28 (53.8%) of 52 group 1 patients, and 156 (81.2%) of 192 group 2 patients (p=0.004). Median time to recurrence was 34.4 months in group 1 and 41.1 months in group 2 (p=0.218). Out of 184 patients having recurrence, only 28 (15.2%) displayed MP, while the remaining 156 (84.8%) did not (p=0.004). Progression was detected in 8 (14.2%) patients of group 1 and 56 (29%) patients of group 2 (p=0.159). Time to progression was 29.7 and 41.7 months in groups 1 and 2, respectively (p=0.488). No difference was observed in terms of tumor multiplicity between the two groups (p=0.479); the mean tumor volume was found to be 2.8 cc in group 1, and 1.6 cc in group 2 (p=0.001). The mean follow-up period was 110.3 months in group 1, and 116.2 months in group 2 (p=0.135). The tumor was found to be solitary in 28 patients of group 1 and in 24 patients of group 2 (p=0.472) (Table 1).

In univariate analysis, tumor multiplicity (p=0.003) and MP absence (p=0.004) were found to be influential on recurrence. In multivariate analysis, again these two parameters were found to have an effect on recurrence (p=0.004) (Table 2). Considering the factors influencing progression, only tumor volume was observed to be significant according to univariate analysis (p=0.005) (Table 3). In the subgroup analysis of patients with solitary tumor (n=116) upon univariate analysis, MP (p=0.003) and tumor volume (p=0.003) were found to have an effect on recurrence. When these figures were used in multivariate analysis, again MP (p=0.002) and tumor volume (p=0.019) were found have an effect (Table 4).

Discussion

An accurate histopathological evaluation and resection of the apparent tumor are intended by TUR in bladder tumors (4,5). Smaller tumors are removed by en bloc resection, for larger tumors, however, resection is recommended in fractions (3). It should be noted that TUR is an oncologic surgery and the principles of major operations should be taken into consideration for TUR as well. High-quality TUR has been first suggested in studies conducted by the EORTC, and its impact on the accurate staging and subsequent recurrence has been highlighted (9). Considering particularly the fact that about 75% of patients have non-muscle-invasive bladder tumor which can be completely cured by a quality TUR; the importance of the procedure is manifested (6). The EORTC has related the best indicator of the TUR quality with early recurrence rates and reported the factors affecting early recurrence as overlooked tumor during TUR and inadequate tumor resection (9).

Mariappan et al. (6) have demonstrated that (i) multiplicity, (ii) stage and (iii) MP presence of the tumor are the factors influencing recurrence in the first cystoscopy after TUR. In their study, Herr and Donat (12) have highlighted the importance of MP presence for the quality of TUR. Another similar study has stated that MP presence in the specimen submitted to pathology is an indicator of TUR quality (6,11). In a study by Mariappan et al. (6), tumor was shown to occur in the first cystoscopy in 69.6% of patients with non-MP pathology and in 39.1% of patients with MP pathology and these results were

Table 1. Demographic data and distribution of patients in both groups

	Group 1 (MP+) (n=52)	Group 2 (MP-) (n=192)	Total/mean	p value
Male (n)	48	180	228	0.808
Female (n)	4	12	16	0.794
Age (year)	61.8	54.3	56	0.003*
Recurrence (+) (n)	28	156	184	0.004*
Time to recurrence (month)	34.4	41.1	40.4	0.218
Progression (+) (n)	8	56	64	0.159
Time to progression (month)	29.7	41.7	40.2	0.488
Solitary tumour (n)	28	88	116	0.472
Multiple tumours (n)	24	104	128	0.479
Tumour volume (cc)	2.8	1.6	1.8	0.001*
Follow-up period (month)	110.3	116.2	113.6	0.135

MP: Muscularis propria

Table 2. Factors influencing recurrence

	Recurrence (+) (n=184)	Recurrence (-) (n=60)	p value (univariate)	p value (multivariate)
Gender M/F (n)	180/4	48/12	0.978	
Multiple tumour (n)	76	52	0.003*	0.003
Tumour volume (cc)	1.8	1.7	0.687	
MP absence (n)	156	36	0.004*	0.004
Age (year)	56.2	54.9	0.06	

M: Male, F: Female, MP: Muscularis propria

found to be statistically significant. In this study, recurrence was shown to occur in the first cystoscopy in 84.7% of patients with non-MP pathology and in 60% of patients with MP pathology and, these results were found to be statistically significant.

The rate of absence of MP ranged between 30% and 50% in published series (13,14). High residual tumor rate and tumor upstaging rates of 40-51% were observed in non-MP stage pT1 patients (14,15,16,17). The absence of MP has been shown to be associated with increased risk of early recurrence, even in low-grade pTa tumors (6). Jesuraj et al. (18) has demonstrated MP presence in 45.8% of TUR applications of inexperienced surgeons and 67.3% of experienced surgeons and argued that the presence of MP is an indicator of surgeon's experience and the quality of TUR. In addition, Mariappan et al. (6) showed that higher rates of MP was detected in TUR applications performed by experienced surgeons and, an inexperienced surgeon was recognized as an independent risk factor for early recurrence. In this study, MP presence was reported to be the most powerful factor for early recurrence. The high rate of MP even in TUR performed by experienced surgeons proves the importance of TUR quality. In our study, upstaging was not assessed because our series were stage pTa patients. We do not perform re-TUR in these patients.

Treatment plan for bladder tumor patients is formed according to TUR pathology and depth of invasion. For this reason, the guidelines, while recommending high quality TUR, describe TUR quality as the presence of MP in pathology specimen (13). All the studies have shown that lower pathological staging and residual tumor are not rare and, thus, a well-done TUR is significant for local recurrence and therapy management of the patient (19). All the relevant studies emphasize the impact of quality of TUR on the patient's recurrence and progression. One of these studies is the one by Badalato et al. (19) with 114 patients having high-grade T1. In this study, the first TUR pathological specimens in high-grade stage pT1 patients, who have undergone radical cystectomy, were examined and in 78% of the patients whose pathology showed no MP were identified as low-staging and, eventually, the presence of MP in TUR specimens was emphasized as predicting low staging.

In the present study, recurrence, time to recurrence, progression, and time to progression were evaluated according to MP presence in pathological specimens of the patients who were treated with TUR due to a newly diagnosed bladder tumor and whose pathology results revealed low-grade stage pTa. Patients who had a history of a previous TUR, high-grade tumor and intravesical therapy were excluded from the study in order to establish a homogeneous group of patients and to avoid the effect of intravesical treatment on recurrence. In univariate and multivariate analyses, in accordance with the literature, the presence of tumor multiplicity and MP presence were determined as the factors predicting recurrence (6,11,12,15,20,21). Recurrence has been shown to be statistically significantly more frequent in patients with non-MP (Table 2). Considering the subgroup analysis in patients with a solitary tumor by excluding patients with multiple tumors, the absence of MP was determined to be a predictive factor for recurrence. The effect of MP absence on time to recurrence, progression and time to progression was not statistically significant. We believe that studies with larger series are required for the significance of these values. Evaluation of the MP status in patients with solitary and multiple tumors, however, displayed no statistically significant difference in terms of the presence of MP between these two groups.

When we evaluated our results in the light of the literature, the presence of MP in TUR was found to affect the quality of TUR and probability of following recurrences positively.

Although lamina propria is not invaded by pTa tumors, the effect of MP presence on recurrence should be attributed to the fact that MP presence is an indicator of the quality of TUR and, in turn, the effect of high quality TUR on recurrence. In our study, instead of tumor size in cystoscopy, the volume of the pathological specimen was considered as the tumor burden. We believe that tumor size does not provide an accurate prediction cystoscopically. Large-scale studies are needed to evaluate our prediction.

In our study, the number of patients in group 1, namely patients with MP in pathology specimens, was found to be quite low when compared with the literature (21%) (13,14). We attribute this result to the problems in the assistant training in our clinic. Nonetheless, we believe that TUR training should be held in the later years of the specialization period and in a controlled manner because this low rate may adversely affect our oncologic results.

Being a retrospective study besides the small number of patients in group 1 are the prominent limiting factors of our study. However, this is the first study which excluded the effects of intravesical chemotherapy on recurrence, which is a prominent feature.

Table 3. Factors influencing progression

	Progression (+) (n=64)	Progression (-) (n=180)	p value (univariate)
Gender M/F (n)	60/4	168/12	0.082
Multiple tumour (n)	32	96	0.092
Tumour volume (cc)	1.18	2	0.005*
MP absence (n)	56	136	0.159
Age (year)	59	54	0.576

M: Male, F: Female, MP: Muscularis propria

Table 4. Factors influencing recurrence in patients with solitary tumour

	Recurrence (+) (n=36)	Recurrence (-) (n=22)	p value (univariate)	p value (multivariate)
Gender M/F (n)	60/12	20/4	0.268	
Multiple tumour (n)	1	1.5	0.029*	0.571
Tumour volume (cc)	40	24	0.003*	0.019*
MP absence (n)	51.1	56.3	0.003*	0.002*

M: Male, F: Female, MP: Muscularis propria

Conclusion

In conclusion, according to our study, the presence of MP in the pathological results of low-grade stage pTa tumors is an indicator of a quality TUR, and in turn, a well done TUR is important in the prevention of recurrences. If our findings would be supported by new studies conducted by larger patient series, this will probably demonstrate the need for reTUR for non-MP stage pTa patients as well, as it is for stage pT1 bladder tumors.

Ethics

Ethics Committee Approval: Ethics committee approval was not obtained because this was a retrospective study, Informed consent: Written informed consent was not obtained from patients because this was a retrospective study, Peer-review: Internal peer-reviewed.

Authorship Contributions

Concept: Hakan Türk, Ferruh Zorlu, Design: Hakan Türk, Sıtkı Ün, Ferruh Zorlu, Data Collection or Processing: Hakan Türk, Sıtkı Ün, Analysis or Interpretation: Sıtkı Ün, Hüseyin Tarhan, Rauf Taner Divrik, Literature Research: Hakan Türk, Sıtkı Ün, Writing: Hakan Türk. Conflict of Interest: No conflict of interest was declared by the authors. Financial Disclosure: The authors declared that this study has received no financial support.

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The Effect of Pre-Procedure Anxiety on Pain Perception During First Session of Shock Wave Lithotripsy

İlk Seans Şok Dalga Litotripsi Öncesi Anksiyetenin İşlem Esnasında Ağrı Üzerine Etkisi

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What's known on the subject? and What does the study add?

It is known that shock wave lithotripsy is a painful procedure for some patients as much that they cannot complete. We evaluated the effect of patient's anxiety on pain during shock wave lithotripsy and found that it is effective.

ABSTRACT

Introduction

Although shock wave lithotripsy (SWL) is a common noninvasive procedure, it can be very painful and a serious source of anxiety which may affect pain perception. The aim of this study was to evaluate the association between patient's anxiety and SWL-related pain.

Materials and Methods

A total of 54 patients, who underwent the first session of SWL treatment between January and April 2014 due to a single renal pelvic stone with a diameter less than 20 mm, were included in the study. All patients were particularly informed about the procedure and, then, the validated Hospital Anxiety and Depression scale was administered in order to identify the anxiety level before the procedure. All relevant data, such as age, sex, stone size, body mass index (BMI), anxiety score, visual analog scale (VAS) score, skin-to-stone distance, and total energy were recorded.

Results

The mean age of the study population was 41.11±16.35 years. The mean stone size, anxiety level before procedure, VAS score during SWL, BMI, skin-to-stone distance and energy level were 10.69±4.75 mm (5-20 mm), 5.2±3.87; 6.5±2.46; 25.77±4.16; 7.23±2.10 cm; 56.53±16.74 joule, respectively. Anxiety prior to procedure, energy level and the number of total shock wave had a significant effect on VAS score ($p<0.05$). Sex, stone size, BMI and skin-to-stone distance did not significantly affect the VAS scores ($p>0.05$).

Conclusion

According to our results, reducing patient anxiety, if any, can provide some additional pain control during SWL procedure and can improve patient compliance.

Keywords

Shock wave lithotripsy, pain, anxiety

ÖZ

Amaç

Şok dalga litotripsi, üriner sistem taş hastalığı tedavisinde kullanılan invazif olmayan yöntemlerin başında gelmesine rağmen oluşturduğu ağrı ve anksiyete nedeni ile bazı hastalar tarafından tolere edilememektedir. Bu çalışmada şok dalga litotripsi öncesinde hastada oluşan anksiyetenin işlem esnasındaki ağrıya etkisi araştırıldı.

Gereç ve Yöntem

Çalışmaya Ocak 2014-Nisan 2014 tarihleri arasında 20 mm'den küçük tek böbrek pelvis taşı nedeni ile ilk defa şok dalga litotripsi tedavisi yapılan 54 hasta dahil edildi. İşlem öncesinde tüm hastalar şok dalga litotripsi hakkında detaylı olarak bilgilendirildikten sonra valide edilmiş Hastane Anksiyete Depresyon ölçeği doldurtularak anksiyete seviyeleri ölçüldü. İşlemden hemen sonra ise şok dalga litotripsi süresince hissettikleri ağrı vizüel ağrı skalası doldurtularak değerlendirildi. Ayrıca yaş, cinsiyet, taş boyutu, vücut kitle indeksi (VKİ), deri-taş mesafesi, uygulanan toplam enerji miktarı da kayıt altına alınarak tüm bu değişkenlerin ağrı ile ilişkisi araştırıldı.

Bulgular

Kırk beş (83,3%) erkek 9 (16,7%) kadın toplam 54 hastanın ortalama yaşı 41,11±16,35 idi. Ortalama taş boyutu, işlem öncesi anksiyete seviyesi, işlem esnasındaki ağrı skoru, VKİ, deri-taş mesafesi, şok dalga litotripsi için uygulanan toplam enerji seviyesi sıra ile 10,69±4,75 mm, 5,2±3,87; 6,5±2,46; 25,77±4,16; 7,23±2,10 cm; 56,53±16,74 jul idi. İşlem öncesi anksiyete seviyesi, toplam uygulanan enerji ve şok dalga sayısı ağrı skorları üzerine istatistiksel olarak anlamlı derecede etkili bulundu ($p<0,05$). Yaş, cinsiyet, taş boyutu, VKİ, deri-taş mesafesinin ise ağrı skorlarına etkisi istatistiksel anlamlı seviyede bulunmadı ($p>0,05$).

Sonuç

Elde ettiğimiz sonuçlara göre işlem öncesi anksiyete şok dalga litotripsi esnasında ağrıyı etkileyen faktörlerden birisidir ve anksiyeteye yönelik alınacak önlemler ağrı kontrolüne, dolayısı ile hasta uyumuna katkı sağlayabilir.

Anahtar Kelimeler

Şok dalga litotripsi, ağrı, anksiyete

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Introduction

In the last decade, open surgery was almost completely replaced by shock wave lithotripsy (SWL) and endourologic techniques, such as ureterorenoscopy and percutaneous nephrolithotomy in the treatment of urinary stone disease (1). SWL offers important advantages for the treatment of renal and ureteral stones. In particular, it is noninvasive, is readily performed on an out-patient basis and can be very effective in treating solitary uncomplicated stones (2). However, despite the advantages of SWL, pain resulting from shock wave treatment is still commonly bothersome to the patients. This may be one of the reasons for some patients to hesitate in preferring SWL treatment (3). At the same time, it is known that SWL procedure can cause significant anxiety influencing the success of the SWL treatment by decreasing patient compliance (4). Several clinical factors, such as sex, body mass index (BMI), delivery of shock wave energy for stone fragmentation and stone location, have been determined as predictive factors for SWL-related pain (5,6). However, little clinical data are available regarding patient pre-procedure anxiety that may affect the pain perception during SWL. The aim of this study was to evaluate the association between patient anxiety and SWL-related pain.

Materials and Methods

After receiving local ethics committee approval and patient informed consent, a total of 54 patients, who underwent the first session of SWL treatment between January and April 2014 due to a single renal stone measuring less than 20 mm in diameter and located in the renal pelvis, were included in the study. All diagnoses and radiologic calculations were performed with non-contrast computed tomography and intravenous pyelography. There was not any bone superposition to stones. Treatment decision for SWL was made according to stone size, patient preference and anatomical convenience, such as suitable infundibulopelvic angle, suitable skin-to-stone distance less than 10 cm with no obstruction in the urinary system. Patients who had contraindications for SWL treatment, such as active urinary tract infection and bleeding disorders were excluded from the study. Single urologist elaborated the procedure and then the patient filled the anxiety section of the validated Hospital Anxiety and Depression scale (A/0-21) (7,8) while waiting for the procedure in order to identify anxiety level just before the procedure in the waiting room at the SWL section. Intramuscular injection of 75 mg diclofenac sodium was performed for pain relief thirty minutes before SWL. All patients were treated with Lithoskop© SWL device (Siemens AG, Munich, Germany), with a maximum of 70 joule energy at 90 shocks per minute frequency up to 3000 shock waves. Immediately after the procedure, while patients were on the table, the degree of pain due to SWL was evaluated by using a 10-point visual analogue scale (VAS/0-10). All relevant data, such as age, sex, stone size, BMI, anxiety score, VAS score, were analysed by dividing the patients into three groups as low (0-3), intermediate (4-6) and high (8 and above), and total energy level of the lithotripter, skin-to-stone distance, and the number of the total shock wave were recorded. We performed statistical analysis in order to evaluate the effect of anxiety on pain perception during SWL by using all these data.

The statistical data were analyzed by using the Statistical Package for Social Sciences (SPSS™, Chicago, IL, USA) version 16.0 for Windows. All values were expressed as mean ± standard deviation. The differences between means were analyzed by using the Mann-Whitney U test, Pearson correlation coefficient, chi-square test. Multivariate analysis was done at 95% confidence interval. A p value of less than 0.05 was considered statistically significant.

Results

The mean age of the patients [45 men (83.3%) and 9 women (16.7%)] was 41.11±16.35 years. The mean stone size was 10.69±4.75 mm (5-20 mm). The mean anxiety level before the procedure was 5.2±3.87 and the mean VAS score during SWL was 6.5±2.46. The mean BMI was 25.77±4.16, skin-to-stone distance - 7.23±2.10 cm, energy level - 56.53±16.74 joule, and the mean shock wave number was 2713.48±457.34 (Table 1). There was no difference in anxiety levels and VAS scores between male and female patients (Table 2). We found statistically significant difference between anxiety prior to procedure and VAS score (Table 3). The patients who had more anxiety felt more pain during the procedure. The other correlations on VAS score were the energy level (r=0.644, p=0.002) and the total number of shock waves (r=0.605, p=0.005). Any negative effect of stone size on VAS scores could not be pointed (r=0.018, p=0.896). BMI and skin-to-stone distance also did not affect VAS scores significantly (r=0.203, p=0.505 and r=0.147, p=0.632, respectively) (Table 4). The variables (pre-procedure anxiety, energy level and number of session) were analysed by using multivariate analysis to determine any independent factor affecting VAS score, but the result could not reach statistically significant level (p=0.238).

Discussion

Advances in technology have changed the treatment strategies of urinary stone disease. In the recent era, minimal invasive techniques are getting more and more popular in all over the world (1). Definitely, SWL is the first choice among these approaches for suitable small kidney and proximal ureteral stones due to its low complication rate and non-invasive nature (9). Although it is known that SWL does not require general anesthesia, sometimes SWL is a painful procedure for many patients resulting in procedure withdrawal (3). Although there are many studies evaluating SWL-related pain and its relief, there are few studies focusing specifically on the patient anxiety and its effect on pain perception during the first SWL session. Thus, we performed this

Table 1. Patient's data

Sex	Female	9
	Male	45
Age		41.11±16.35
Stone size (mm)		10.69±4.75
BMI		25.77±4.16
Skin-stone distance (cm)		7.23±2.10
VAS score		6.5±2.46
Anxiety score		5.2±3.87
Energy (joule)		56.53±16.74
Total shock wave number		2713.48±457.34

BMI: Body mass index, VAS: Visual analogue scale

Table 2. Analysis of anxiety level and visual analogue scale score according to sex

Sex		Anxiety score	VAS score
Male (n=45)	Mean	5.29	6.44
	SD	4.01	2.52
Female (n=9)	Mean	4.78	6.78
	SD	3.23	2.22
p		0.90	0.87

No statistically difference was achieved (p>0.05), SD: Standard deviation, VAS: Visual analogue scale

Tablo 3. Analysis of pre-procedure anxiety level according to visual analogue scale groups

Mean VAS score	Mean pre-procedure anxiety level
Low (0-3) →2.33±1.5	3.89±5.58
Intermediate (4-7) →5.95±0.95	4.73±3.48
High (8 and above) →8.65±0.78	6.17±3.37
	p
Low ↔ intermediate	0.167
Intermediate ↔ high	0.118
Low ↔ high	0.022*

*Statistically significant, VAS: Visual analogue scale

Table 4. Correlation analysis results of possible factors that may influence visual analogue scale

Variables	VAS
Anxiety score	r=0.619 p=0.024*
Energy level	r=0.644 p=0.002*
Total shock wave number	r=0.605 p=0.005*
BMI	r=0.203 p=0.505
Skin to stone distance	r=0.147 p=0.632
Stone size	r=0.018 p=0.896

*p<0.05 was deemed statistically significant, VAS: Visual analogue scale, BMI: Body mass index

study in order to evaluate the effect of anxiety prior to first SWL session on pain perception. On the other hand, it can be easily hypothesized that patient anxiety may also contribute to procedural pain perception.

Contrary to previous studies, we were not able to demonstrate any statistically significant difference between men and women in terms of prior anxiety and VAS scores (5.29 vs. 4.78, p=0.90 and 6.44 vs. 6.78, p=0.87) (10,11). However, the number of female patients included in the study was very small and we concluded that it may not be enough to make a certain decision and a generalization.

The most important result of our study was the positive correlation between the patient's pre-procedural anxiety and pain perception. The increased anxiety level made the procedure more painful and this result was statistically significant alike with Vergnolles' results (12). Our results suggest that pretreatment evaluation of anxiety level may change the pain control protocol to be applied to the patients, e.g., additional anxiolytic treatment prior to the procedure can help better pain control.

In our study, increased level of shock wave energy and the total number of shock waves significantly increased the pain perception similar with that in the literature (13). It was an expected result since the main traumatic factor is energy applied to stone and tissues.

Similar to the results of a study by Vergnolles et al. (12), but contrary to that of Tailly et al. (14), no significant correlation was observed between stone size and pain perception. Tailly et al. (14) concluded that smaller renal stones were associated with a higher analgesic requirement, explained by a higher proportion of the energy absorbed by the surrounding renal parenchyma and not by the stone itself. We minimized the parenchymal trauma by frequently checking the focus if it was on the stone. This strategy may explain the difference between our results and that of Tailly et al. (14) BMI and skin-to-stone distance was relevant as expected. Their effect on VAS score was not statistically significant in our study contrary to the study by Bach et al. (15). The reason might be that there was no significant difference between the body weight of our patients. If this study compared slim and obese patients, the results might have been different.

One limitation of our study is that we did not evaluate the SWL time for each patient and its effect on VAS scores. Additionally, we did not evaluate the hardness of the stone which may also affect the procedure time. Although all patients had the same SWL protocol starting and increasing with similar energy level, the overall procedure time could have been different for each patient due to different stone fragmentation time and, also increased duration of procedure could affect pain perception.

Conclusion

Despite its noninvasive nature, SWL is a painful procedure and it may cause anxiety that increases pain perception and decreases patient compliance. According to our results, reducing patient anxiety, if any, can provide some additional pain control during SWL procedure and may increase the success of SWL.

Ethics

Ethics Committee Approval: The study were approved by the Gülhane Military Medical Academy, Haydarpaşa Training Hospital of Local Ethics Committee, Informed Consent: Consent form was filled out by all participants. Peer-review: Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Fırat Saraçoğlu, Concept: Ömer Yılmaz, Design: Hasan Soydan, Data Collection or Processing: Murat Zor, Analysis or Interpretation: Ferhat Ateş, Literature Search: Ercan Malkoç, Writing: Ömer Yılmaz, Temuçin Şenkul. Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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CASE REPORT
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Management of Neonatal Priapism: Report of Two Cases and Review of the Literature

Yenidoğan Priapizmine Yaklaşım: İki Olgu Bildirimi ve Literatür Derlemesi

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ABSTRACT

Priapism in a newborn is a rare entity with only 15 cases reported in the literature since 1879. The most commonly detected etiologic factor is polycythemia, but most of the cases are idiopathic. Conservative treatment seems to be sufficient and surgical approach is usually unnecessary. Here, we present a prolonged erection in two newborns which occurred at the first day of life and detumescence was achieved with conservative approach at the 6th and 7th day of life, respectively. We also reviewed the literature to investigate the most adequate evaluation and management criteria.

Keywords

Idiopathic, conservative, priapism, neonatal, management

ÖZ

Yenidoğan priapizmi nadir görülen bir hastalık olup 1879'dan şimdiye kadar literatürde 15 olgu bildirimi yapılmıştır. En sık rastlanan etiyolojik faktör polisitemi olsa da, çoğunlukla idiyopatiktir. Yenidoğan priapizmi genellikle iskemik olmayan tipte seyreder. Tedavide çoğu zaman cerrahi müdaheleye gerek kalmaz. Konservatif yaklaşım en iyi seçenek olarak görünmektedir. Bu olgu sunumunda konservatif izlem ile yaşamın 6. ve 7. günlerinde gerileyen iki yenidoğan priapizm olgusunu sunulmaktadır. Olgu sunumu ile beraber en uygun yaklaşım ve değerlendirme için yol göstermesi amacıyla literatür derlemesi de sunulmuştur.

Anahtar Kelimeler

İdyopatik, konservatif, priapizm, yenidoğan, yaklaşım

Introduction

Preservation of normal erectile function is the major goal in the management of priapism. Ischemic priapism is a urological emergency due to compartment syndrome after 4 hours of prolonged erection. However, ischemic priapism has not yet been reported in a neonate. Priapism in newborn is challenging situation for pediatric urologists because of the lack of experience due to paucity of cases, and well-established guidelines. Therefore, evaluation and management strategy remains unclear. Here, we present the latest two cases of newborn priapism and review of the literature.

Case Presentation

First case was the second child of a 31-year-old woman. The newborn was delivered by cesarean section at the 39th week of gestation with a birth weight of 2870 g. Appearance, Pulse, Grimace, Activity, Respiration (APGAR) test scores were 9/10 and 9/10 at 1 and 5 minutes, respectively. There was no evidence of blood group incompatibility and hematological pathology in the newborn. Blood count, biochemical analysis, and physical examination revealed no abnormality and, neurological examination was normal. Maternal hypothyroidism, for which she used levothyroxine, and a history of smoking during pregnancy was noted. Routine prenatal examinations were performed regularly. The patient was referred to the pediatric urology department at the second day of life with prolonged erection which was noticed at the first day of life by the parents. Physical examination showed rigid penis without cyanosis and tenderness (Figure 1). The testes were descended bilaterally and normal on physical examination. Projectile voiding was observed without restlessness and, defecation was normal. Penile Doppler ultrasound scan revealed normal arterial and venous flow and there was no evidence of ischemic priapism. Polycythemia and other hematological disorders were ruled out after pediatric hematology consultation. The patient underwent conservative follow-up. Spontaneous detumescence was achieved at the 6th day of life without any surgical intervention. His course was uneventful. No recurrence and abnormality was observed during 6 months of follow-up.

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The second case was the first child of a 28-year-old woman. The newborn was delivered vaginally at the 40th week of gestation with a birth weight of 3280 gr. APGAR scores were 9/10 and 10/10 at 1 and 5 minutes, respectively. Routine neonatal evaluation was normal. Maternal smoking history was denied. The patient was referred to the pediatric urology department at the first day of life with prolonged erection. Physical examination showed a rigid penis without cyanosis or tenderness (Figure 1). The testes were descended bilaterally and were found to be normal on physical examination. Hematological evaluation showed no pathology. Penile Doppler ultrasound imaging was not performed for this case. Finally, the detumescence was achieved on the 7th day of life without any surgical intervention. No recurrence and abnormality was observed during 3 months of follow-up.

Discussion

Priapism is rare in children, especially in neonates. Fifteen cases have been reported in the literature since 1879 (1,2,3,4,5,6,7,8,9,10).

Figure 1. Prolonged penile erection of the first case at the 4th days of life (A) and prolonged penile erection of the second case at the first day of life (B)

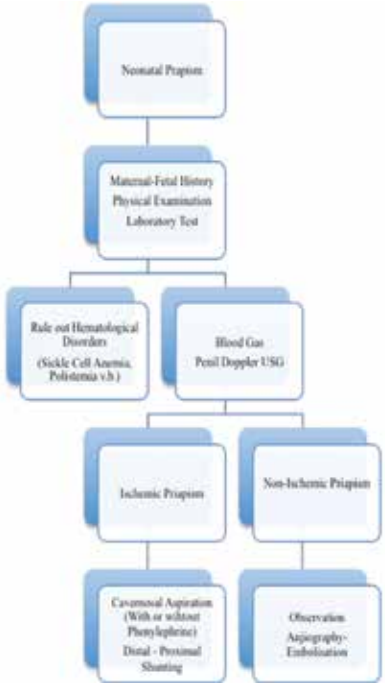

Figure 2. Algorithm of neonatal priapism management

Estimated incidence of idiopathic neonatal priapism is 15 per 100.000 live births based on a surveillance study performed between 1974 and 1988 (1). Current experience on neonatal priapism is based on mostly similar individual case reports. Thus, evaluation, treatment and follow-up are challenging in pediatric urology practice. We present two cases of neonatal priapism treated in our department. These cases represent our first experience on this rare disorder. Since a limited number of cases have been reported, no clinical guideline has been established for neoanatal priapism. We review the literature to propose a clinical approach for these cases (Table 1).

The most common cause for newborn pariapism is idiopathic (8,9). However, other etiologic factors should be excluded. The possible causes include blood dyscrasias, malignancy, trauma, neurological pathologies and drug-related side effects (11). Although, sickle cell anemia is common in children, it is negligible in neonates because of the predominance of fetal hemoglobin. Among them, polycythemia is the most known detected etiology (3,7). In the literature, there are 4 reported cases of neonatal priapism attributed to polycythemia and one to blood transfusion, where all other 10 cases were idiopathic (Table 1). Polycythemia was ruled out in our two cases and there was also no any other significant finding in evaluation. Therefore, we also defined our cases as idiopathic. We detected maternal hypothyroidism and a history of maternal smoking during pregnancy in our first case. Our management of neonatal priapism algorithm is shown in Figure 2.

Neonatal priapism was non-ischemic in all reported cases. Our two cases were also non-ischemic priapism. Increased blood flow may be the cause of priapism in cases with polycythemia. But non-ischemic course of priapism was seen in the reported 4 cases with polycythemia. We support the hypothesis of Meijer and Bakker (2) that neonatal priapism should be the form of non-ischemic priapism because this form presents with a painless erection and conservative management is possible. Therefore, Doppler ultrasound and cavernosal blood gas analysis can be reserved for cases suspicious for ischemic priapism.

Treatment of this pathology is not clear yet. Suggested management options include observation, intravenous ketamine admission, phlebotomy and exchange transfusion. Majority of cases were managed with observation, and spontaneous detumescence was achieved. However, intravenous ketamine admission in one case (3), phlebeotomy in one case and exchange transfusion in one case (4) have been reported. Intravenous ketamine admission and exchange transfusion resulted in immediate detumescence where it occurred four days after phlebotomy. In all other cases including ours, detumescence was achieved mostly in 5 to 6 days. Follow-up showed no abnormality, althought we don't have long term results. Therefore, observation should be the first approach in idiopathic neonatal priapism.

Ethics

Informed Consent: Consent form was filled out by all participants.
Peer-review: Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Haydar Kamil Çam, Cem Akbal, Mehmet Özay Özgür, Çağrı Akın Şekerci, Concept: Cem Akbal, Çağrı Akın Şekerci, Design: Cem Akbal, Çağrı Akın Şekerci, Data Collection or Processing: Çağrı Akın Şekerci, Farhad Talibzade, Analysis or Interpretation: Çağrı

Table 1. Data of 17 cases [Rearranged with additional four cases from reference (2) and two cases from reference (5)]

Reference	Onset	Treatment	Duration of priapism (days)	Proposed etiology	Follow up
Humbert et al. (12)	Day 1	Observation	2	Polycythemia	Normal
	Day 4	Phlebotomy	5	Polycythemia	Normal
Larocque and Cosgrove (6)	Not reported	Observation	4	Polycythemia	Not reported
Amlie et al. (7)	Day 37	Observation	12	Blood transfusion	Normal
Leal et al. (8)	At birth	Observation	6	Idiopathic	Normal
Shapiro (9)	At birth	Observation	3	Idiopathic	Not reported
Merlob and Livne (1)	At birth	Observation	6	Idiopathic	Normal
	Day 1	Observation	5	Idiopathic	Normal
	Day 5	Observation	4	Idiopathic	Normal
	Day 1	Observation	5	Idiopathic	Normal
Stothers and Ritchie (10)	At birth	Intravenous ketamine	3	Idiopathic	Normal
Walker and Casale (3)	At birth	Exchange transfusion	4	Polycythemia	Normal
Meijer and Bakker (2)	Day 1	Observation	4	Idiopathic	Normal
Burgu et al. (4)	Day 1	Observation	3	Idiopathic	Normal
Aktoz et al. (5)	Day 1	Observation	4	Idiopathic	Normal
Marmara	Day 1	Observation	6	Idiopathic	Normal
Marmara	Day 1	Observation	7	Idiopathic	Normal

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CASE REPORT
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Isolated Renal Metastasis from Neuroendocrine Tumor: How Rare is Rare? A Case Report and Review of the Literature

Nöroendokrin Tümörün İzole Renal Metastazı: Seyrek Ne Kadar Seyrektir? Bir Olgu Sunumu ve Literatür Derlemesi

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ABSTRACT

Neuroendocrine tumors (NETs) are epithelial neoplasms arising from neuroendocrine cells that are widely distributed throughout the body. The kidney is a rare site for primary NETs and is even rarer as a metastatic site. We report an extremely rare case of a 58-year-old female with metastatic renal NET from a rectal primary without prior or concurrent liver metastasis. Diagnosis of NET of kidney can be challenging due to its rarity. Use of appropriate immunohistochemical markers and awareness of occurrence of these rare lesions in the kidney will enhance the diagnostic accuracy.

Keywords

Neuroendocrine tumors, metastatic neuroendocrine tumors, metastatic renal neuroendocrine tumor

ÖZ

Multil Nöroendokrin tümörler (NET) vücutta yüksek oranda yaygın olan nöroendokrin hücrelerden meydana gelen epitelyum neoplazmalardır. Böbrek primer NET'ler için nadir bir yerleşim yeridir ve metastaz yeri olarak bile nadirdir. Bu olgu sunumunda bir rektal primerden kaynaklanan metastatik renal NET olan ve geçmiş veya eş zamanlı karaciğer metastazı bulunmayan oldukça nadir 58 yaşında kadın bir olguyu sunduk. Böbrek NET'in tanısı seyrek görülmesinden dolayı oldukça zor olabilir. Uygun immüno-histo-kimyasalların kullanımı ve bu böbrekte seyrek lezyonların oluşabileceğinin farkında olunması tanının doğruluğunu arttıracaktır.

Anahtar Kelimeler

Nöroendokrin tümörler, metastatik nöroendokrin tümörler, metastatik renal nöroendokrin tümörler

Introduction

Neuroendocrine tumors (NETs) are epithelial tumors arising from neuroendocrine cells that are diffusely distributed throughout the body, most commonly in the gastrointestinal tract and the bronchopulmonary system. Primary renal NETs are rare due to the absence of neuroendocrine cells in the renal parenchyma. Metastatic renal NETs are even rarer with only 2 reported cases in the English literature (1,2). We present a very rare case of metastatic renal NET from a rectal primary. To our best knowledge, this is the first reported case of metastatic renal NET from the rectum without liver metastasis.

Case Presantation

Our patient is a 58-year-old female with a history of pT2N1M0 rectal NET (equivalent to grade 2 using current World health organization classification) in 2009 (Figure 1). She presented with rectal bleeding and she was found to have a rectal polyp. Subsequent biopsy revealed NET that was positive for chromogranin and synaptophysin, requiring an abdominoperineal resection. In 2013, the patient was found to have a solid mass in the lower pole of the left kidney, suspicious for neoplasm on computed tomography (CT) images of the abdomen and pelvis, without evidence of any other masses, especially in the liver. Biopsy of the renal mass showed a grade 2 NET. The patient was then referred to the urology clinic for left laparoscopic nephrectomy.

We received a left kidney weighing 240 grams and measuring 11.0x8.0x3.0 cm. The kidney was bivalved, revealing a lower pole, completely encapsulated firm white lesion, with a hemorrhagic cut surface (Figure 2), measuring 4.0x3.0x3.0 cm, reaching the renal capsule without invading the perinephric fat. Histological examination of the tumor revealed cords and nests of moderately pleomorphic cells with rare mitotic activity, eosinophilic granular cytoplasm and rounded nuclei with stippled chromatin. The nests were separated by scant stroma and multiple dilated blood vessels (Figure 3). The mass was fully encapsulated and surrounded by a compressed renal parenchyma. The tumor cells stained positive for chromogranin, synaptophysin and CD56 and showed up to 18% proliferation by Ki-67. The histological findings and the immunohistochemical staining results were compared to the primary rectal tumor and were

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considered similar except for a new CD56 positivity and a higher Ki-67 index indicating a more aggressive behavior. Based on the clinical and pathological findings, a metastatic NET of the kidney was diagnosed.

Discussion

The neuroendocrine cell system can be divided into cell types that form the glands (parathyroids, adrenal medulla, paraganglia) and others that are diffusely distributed, i.e., the disseminated/diffuse neuroendocrine system that populate the skin, thyroid, lung, thymus, pancreas, gastrointestinal tract, biliary tract and the urogenital tract (3).

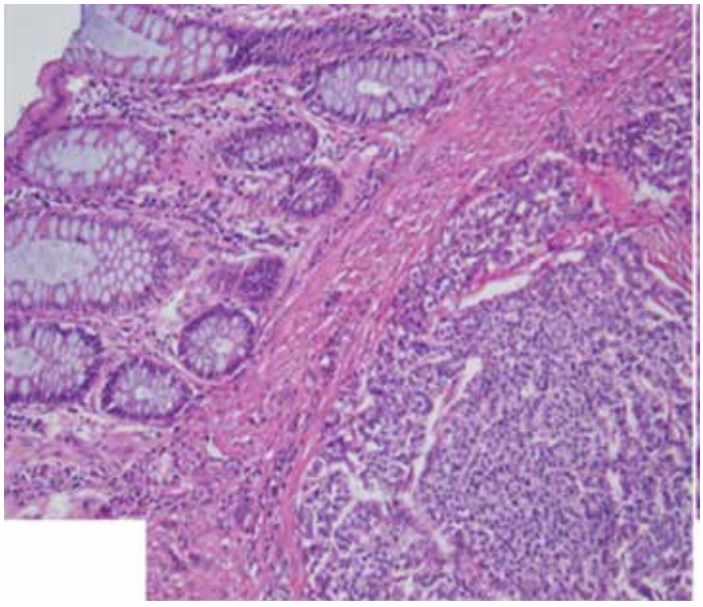

Figure 1. H&E (20x) of the rectum with submucosal neuroendocrine tumor. The tumor consists of cords and nests of moderately pleomorphic cells with rare mitotic activity, eosinophilic granular cytoplasm, and rounded nuclei with stippled chromatin supported by vascularized stroma

Figure 2. Full cross section of the renal tumor revealing areas of hemorrhage. The tumor is encapsulated and surrounded by a compressed renal parenchyma (arrows)

Epithelial NETs are derived from neuroendocrine cell compartments. Approximately 60% of carcinoid tumors arise from the intestine, and greater than 25% arise within the Kultschitzky cells in the respiratory epithelium of the bronchopulmonary system, reflecting the high density of neuroendocrine cells in these organs. NETs arising from other organs occur less frequently and in more obscure sites (4). The liver is considered the predominant site of metastatic spread from NETs, regardless of the primary site. Patients with liver metastases may present with symptoms of carcinoid syndrome (e.g. diarrhea, flushing and wheezing) or symptoms secondary to tumor burden. Neuroendocrine cells have been described in the urinary bladder, urethra, and the renal pelvis, but they are not found within normal renal parenchyma, thus, primary NETs in the kidney are rare and sometimes associated with congenital anomalies, such as horseshoe kidney (5,6) and polycystic kidney disease (7) or in the background of a teratoma (6). Primary NETs can occur in the kidney as a result of metaplastic change, neuroendocrine differentiation of totipotential primitive stem cells, or migration of bronchial or intestinal epithelium to the kidney during development. Metastatic renal NETs are even rarer. To our knowledge; there have been only 2 reported cases of metastatic renal NETs.

The first one by Tal et al. (1); the patient was a 64-year-old woman, status post upper lobectomy of the left lung to remove a bronchial carcinoid tumor. 2 years later, she was admitted for investigating a left neck mass. Abdominal ultrasonography revealed a 3.6x6.7 cm hyperechoic solid lesion in the right kidney, and multiple hypoechoic lesions occupying both liver lobes. Abdominal CT demonstrated an 8.0x5.0 cm solid heterogeneous lesion of the right kidney invading the renal pelvis and renal vein but not the inferior vena cava.

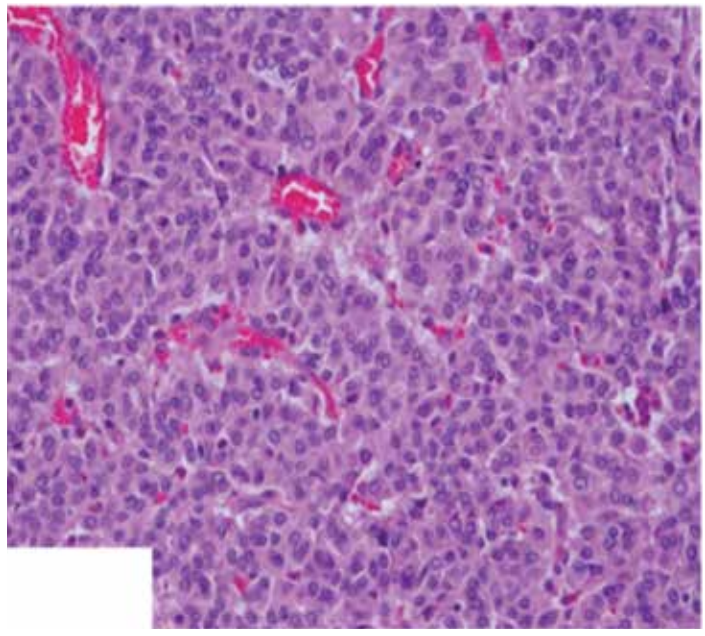

Figure 3. H&E (40x) of the renal tumor comprised of cords and nests of moderately pleomorphic cells with rare mitotic activity, reminiscent of the rectal neuroendocrine tumor

Right radical nephrectomy and excision of the hepatic lesion were performed. Microscopically and immunohistochemically, the liver and kidney tumors were consistent with metastatic carcinoid tumor.

The second case by Kato et al. (2); the patient was a 56-year-old man, status post rectal carcinoid resection and resection of liver metastases from the rectal carcinoid, twice. He presented 10 years after the initial presentation during a general check-up with a 3-cm relatively well-defined mass in the lower pole of the left kidney on ultrasonography, and the interior of the mass was low echoic, unclear of margin, and hypovascular. Contrast-enhanced abdominal CT demonstrated a poorly enhanced, well-defined mass at the above-mentioned site in both the arterial and venous phases. A left nephrectomy was performed and histological examination of the renal mass was consistent with those of hematoxylin and eosin staining of specimens of the rectum and liver. As such, a metastatic renal carcinoid was diagnosed.

Our case is unique as the patient presented with a renal mass after initial resection without local recurrence or metastasis to other sites (e.g. liver), in the interim period of 4 years. This clinical course can cause a great diagnostic challenge to the urologist and pathologist as an incidental primary renal neoplasm will be a more likely clinical consideration. Furthermore, metastatic tumors to the kidney are much less common as opposed to primary renal neoplasms.

Due to the rarity of metastatic renal NETs, especially without liver metastasis, a high index of suspicion and thorough proper comparative histologic examination of both the primary tumor and the metastasis will aid in arriving at a correct diagnosis.

Ethics

Informed Consent: Informed consent was obtained from the participant. Peer-review: Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Irma Lengu (urological surgery), Concept: Mohga Ali, Irma Lengu, Santhi Ganesan, Design: Mohga Ali, Data Collection or Processing: Mohga Ali, Analysis or Interpretation: Mohga Ali, Santhi Ganesan, Literature Search: Mohga Ali, Writing: Mohga Ali. Conflict of Interest: No conflict of interest was declared by the authors. Financial Disclosure: The authors declared that this study has received no financial support.

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