

CHAPTER 12

NONTRAUMATIC UROLOGICAL CONDITIONS

INTRODUCTION

Urologists in Vietnam and Japan encountered numerous nontraumatic urological and associated medical conditions. For example, at the 483rd US Air Force Hospital, Cam Ranh Bay, Vietnam, the most frequent nontraumatic genitourinary disorders seen were renal calculi, venereal diseases, and epididymitis.¹ The authors' (JNW and JWW) experience in Japan in managing these and other nontraumatic urological and associated medical conditions is drawn primarily from our personal recollections of and reflections on these disorders. The exception is the section we present on testicular tumors, which is based on our review of case records and tabulated data.

FEVERS OF UNDETERMINED ORIGIN

During the 1960s and early 1970s, a fever of undetermined origin (FUO) was defined as a febrile illness without a specific cause that occurs within the first few days of admission in a hospitalized, evacuated patient.^{2(p78)} We saw a large number of patients with FUOs; they had been referred to us (in Japan) because of their urological problems, and it was often difficult to determine whether the fever was from a wound, urological condition, or another cause. In Vietnam, the most common causes of FUOs were tropical diseases—malaria, dengue, scrub typhus, chikungunya, leptospirosis, and Japanese B encephalitis—or undetermined causes (in 12%–55% in 5 FUO studies).² But the important thing to remember is that, then as now, urological patients with febrile events can and sometimes do have concomitant conditions.

In Japan, a significant number of patients with FUOs were found to have malaria (Figure 12-1), primarily that caused by the organism *Plasmodium falciparum*. More than 90% of the *falciparum* malarial infections that were acquired in Vietnam were resistant to chloroquine, whereas chloroquine–primaquine phosphate prophylaxis was highly effective in suppressing vivax malaria.³ Triple-drug therapy (quinine, pyrimethamine,

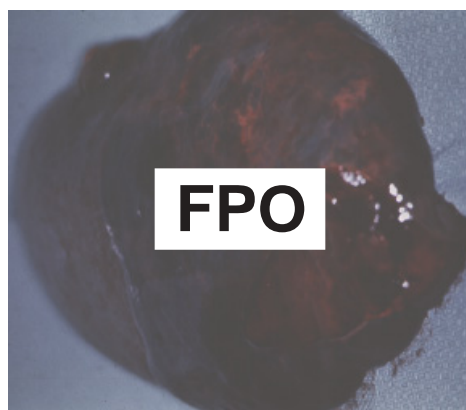


Fig. 12-1. This ruptured spleen is from a patient wounded in Vietnam who also had malaria.

and sulfonamide) cured 98% of the falciparum malaria drug-resistant infections. In addition to the development of chloroquine-resistant falciparum malaria, military personnel were seen who had developed vivax malaria either because they had refused to take their chloroquine–primaquine phosphate tablet, forgot to take the medicine, or skipped doses because of gastrointestinal side effects such as diarrhea.⁴

The diagnosis of malaria in the FUO patient often posed a serious diagnostic problem because of frequent (*a*) lack of the characteristic spiking fever and chills often seen early in the infection and (*b*) technical problems in reading the blood-stained smears (false positives in 14% and incorrect species identification in approximately 5% of cases).⁵ Today, the gold standard for the diagnosis of malaria remains with the findings on “thick” and “thin” peripheral blood smears. These are created with dilute Giemsa stain; smears are taken at 6- to 8-hour intervals and need not wait until the patient’s temperature rises. The prophylaxis and treatment of malaria are variable—with time, place, and nationality; therefore, the preferred drug regimen will vary from situation to situation [—DEL, ed].

One patient had massive wounds of the bladder, abdominal wall, and external genitalia; his hospital course was complicated with cerebral malaria, an uncommon complication of falciparum malaria that usually manifests with headache, disorientation, hyperreflexia, restless agitation, and coma.⁵

Another soldier with urological problems who also had an FUO was found to have scrub typhus, a disease caused by miteborne rickettsia. Scrub typhus is classically manifested by the triad of rash, eschar, and positive therapeutic response to tetracycline. Fever and severe retroorbital headache are the most common complaints, and the most important feature on physical examination is the eschar (Figure 12-2), which typically resembles a cigarette burn.²

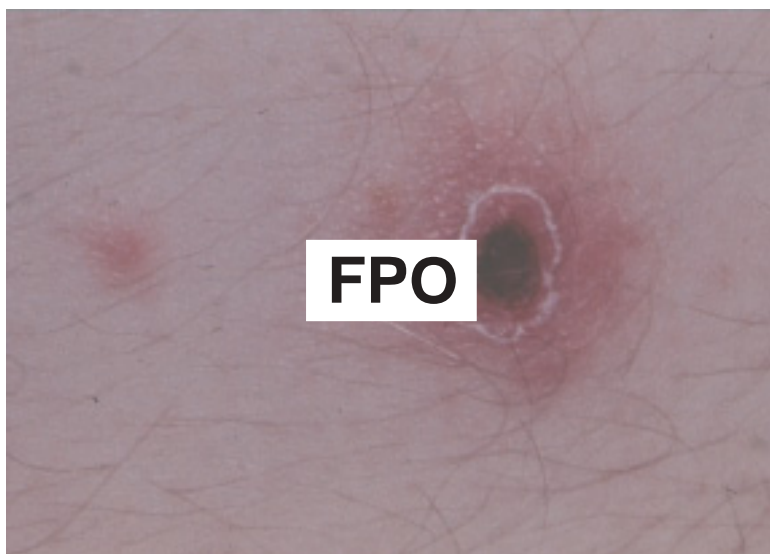


Fig. 12-2. The classic eschar seen in scrub typhus.

DRUG USE AND ADDICTION

Heroin was cheap and easy to procure in Vietnam and a fair number of hospitalized soldiers had used this drug in some form and to some extent. Patients in the medical evacuation system who developed insomnia were prime suspects for early withdrawal symptoms: restlessness, muscle cramps and pain, insomnia, diarrhea, nausea, and goose bumps. The withdrawal symptoms in these patients were managed by a program of Thorazine (chlorpromazine; SmithKline Beecham Pharmaceuticals, Philadelphia, Pa) and Demerol (meperidine hydrochloride; Sanofi Winthrop Pharmaceuticals, New York, NY), altering the proportion of each medication, until only Thorazine was administered. Withdrawal symptoms peaked at 24 to 48 hours and generally completely abated within a week. This approach was highly effective in managing short-term drug users.

At times, the withdrawal symptoms interfered with the evaluation and management of injuries and medical conditions, but overall this was not a major issue. Marijuana cigarette smoking was not uncommon, but it did not interfere with either patient care and management or ward discipline.

URINARY LITHIASIS

Upper urinary tract calculi were a common cause of nontraumatic urological admissions to hospitals in Vietnam.¹ Patients who required open surgery were either operated on in Vietnam, often convalescing in Japan, or evacuated for definitive management in Japan. Endoscopic manipulation of ureteral calculi in Vietnam was limited by the lack of stone baskets and appropriate ureteral catheters. Various mixtures of calcium oxalate and calcium phosphate composed the predominant stone composition in these patients, which was in accordance with the incidence in the general population.⁶

More than the usual number of uric acid stones occurred in patients with upper urinary tract calculi. This was attributed to the high environmental temperatures; profuse sweating; dehydration; and highly concentrated acidic urine, which holds much less uric acid in solution.⁷

All patients evacuated with active stone disease had basic screening metabolic blood chemistries done in Japan (serum calcium, phosphorous, uric acid, electrolytes, and blood urea nitrogen and serum creatinine) and appropriate radiographic definition of the stone or stones (a flat plate of the abdomen is performed to include the anatomical sites of the kidney, ureter, and bladder [KUB]; and an intravenous pyelography or retrograde urography or both). One patient with an elevated serum calcium and a palpable parathyroid neck mass had removal of a large parathyroid adenoma prior to basket extraction of a ureteral calculus.

HYDRONEPHROSIS

A few patients were evacuated to Japan with hydronephrosis, generally from congenital ureteropelvic junction obstruction detected in evaluation of flank pain

or tenderness, hematuria, or urinary tract infection. The noncareer 2-year soldiers were considered for military separation for preexisting medical condition. Others had renal exploration and some form of repair (pyeloureteroplasty).

BLADDER DISORDERS

Bladder infections were common and occurred primarily in patients who had wounds or other conditions requiring urethral and/or suprapubic catheter drainage, often for prolonged periods. The incidence of urinary tract infections in patients with indwelling urethral catheters is directly related to the duration of the catheterization—regardless of catheter care technique and type collecting system.⁸ However, it has been shown that the use of closed urinary drainage systems does significantly delay the incidence of associated infections from about 90% in 4 days to 30% to 40%.⁹ Late in 1968, the closed urinary drainage systems were introduced for use in some of the hospitals in Vietnam and Japan.

Although most patients with indwelling catheters tolerated their bacteriuria well, there were several incidences of secondary Gram-negative bacteremia, especially following urethral instrumentation by catheter change or urethral dilation for stricture disease. Vesicorenal reflux was not uncommon in patients with indwelling catheters and infected urine. Two of these patients required nephroureterectomy to manage their recurrent, acute, antibiotic-resistant pyelonephritis and Gram-negative sepsis.

Although the bacterium *Escherichia coli* was the predominant pathogen, 1 or more other organisms were frequently encountered: *Enterococcus* spp, *Pseudomonas aeruginosa*, *Klebsiella* spp, *Enterobacter* spp, *Proteus mirabilis*, and occasionally *Candida* spp. Many patients had polymicrobial bacteriuria, and the development of antibiotic-resistant bacteria was common because wide-spectrum antibiotics were generally liberally used in patients with traumatic injuries.

In patients with prolonged indwelling urethral or suprapubic catheters, no treatment technique will completely eliminate catheter-induced infections. The infecting strains of bacteria frequently change, and subclinical polymicrobial infections are common.⁹ Ideally, asymptomatic bladder bacteriuria should not be treated with antibiotics. Organism-specific antimicrobial therapy should be reserved for episodes of acute clinical pyelonephritis or urosepsis,⁹ or initiated 8 hours before the catheter is removed. In general, most patients who were evacuated catheter-free to the continental United States (CONUS) had sterile urine.

A few patients had bladder dysfunction secondary to injuries of the spinal cord or central nervous system. Intermittent catheterization, the preferred technique of management of the bladder dysfunction, was not in general use at this time. Thus, most patients with neurogenic bladders were treated with indwelling Foley catheters. Some patients subsequently required suprapubic cystostomy for catheter intolerance or complications.

Several soldiers with nocturnal enuresis were evacuated to Japan for evaluation and administrative disposition. "Bed wetters," because of the lack of privacy in close barracks or tent sleeping facilities, were usually identified early

by their peers and were frequently exposed to significant psychological ridicule and abuse. Eventually, these unfortunate soldiers would seek medical help or surface in sick call and enter the medical evacuation system. Many of the more self-conscious, sensitive, motivated soldiers with enuresis were sleep-deprived from sitting and reading in the lighted latrines for several hours at night to avoid the peer humiliation and abuse from this malady. We detected only a few soldiers with enuresis who were both poorly motivated and personally gained from their “apparent enuresis.” These patients required a physical examination, urinalysis, hemo-gram and blood chemistries, and a urological workup to exclude organic cause for enuresis. One soldier (managed by JNW) had chronic renal failure, with a creatinine value of 5.5 and a blood urea nitrogen value of 60, and massive bilateral reflux nephropathy. Most patients with enuresis were recommended for evacuation to CONUS and medical discharge under the physical qualifications and standards for retention or discharge: incontinence of urine due to disease or defect not amenable to treatment and of such severity that precludes satisfactory performance of duty.¹⁰

PROSTATIC DISEASE

An occasional soldier was evacuated to Japan with refractory symptoms of chronic prostatitis. Many of these patients had been treated in Vietnam with multiple antibiotics. They were routinely afebrile and were evaluated for persistent pain in the perineum, suprapubic area, penis, and often in the low back, testis, and groin. Irritable and obstructive voiding symptoms were common. Findings of digital rectal examinations varied from normal to mild prostatic congestion, and the patients often had pelvic pain. Urine cultures were negative for pathogens in this group. Usual treatment consisted of nonsteroidal antiinflammatory drugs; antibiotics, primarily tetracycline; and Pyridium (phenazopyridine hydrochloride; Parke Davis, Morris Plains, NJ) or Urised (a combination of Methanamine, Methylene Blue, Phenyl Salicylate, benzoic acid, atropine sulfate, and hyoscyamine; PolyMedica Pharmaceuticals [USA], Inc, Woburn, Mass) for dysuria and suprapubic discomfort. In patients whose conditions were more refractory to this treatment, cystoscopy occasionally revealed a urethral stricture or restriction of the bladder neck with what appeared to be the end result of congenital apical prostatic urethral valves with a collar constriction of the bladder neck. A few patients with debilitating symptoms that were unresponsive to treatment were evacuated to CONUS.

One case of melioidosis of the prostate was reported in a soldier who was evacuated to the 249th General Hospital in Japan for an enlarged, indurated, fixed prostate that was thought to be a prostatic carcinoma.¹¹ On endoscopic investigation, however, more than 3 oz purulent material was drained transurethrally from the right side of the prostate. The purulent material cultured positive for *Pseudomonas pseudomallei* [known now as *Burkholderia pseudomallei*—DEL, ed] and was sensitive to tetracycline. The patient was successfully treated with a 30-day course of tetracycline. The *Pseudomonas* organism is ubiquitous in the rice paddies and

damp soil in southeast Asia, is often associated with open wounds and burns, and may cause acute lethal fulminating infections. The Vietnam experience with infections from this organism has been extensively reviewed.¹²

One 22-year-old soldier was evacuated to Japan for obstructing voiding symptoms and an enlarged, firm prostate. On evaluation in Japan, the markedly enlarged, smooth, rock-hard prostate was detected. Subsequent intravenous pyelogram revealed a large mass defect at the base of the bladder from the enlarged prostate with "J-ing" of the terminal ureters and bilateral hydroureteronephrosis. Needle biopsy of the prostate revealed a rhabdomyosarcoma. This patient was evacuated to CONUS for further treatment.

URETHRAL CONDITIONS

Urethral problems were common: infection, inflammation, and stricture disease. Acute gonococcal urethritis (GU) was treated in Vietnam most often with a single intramuscular injection of 4.8 million units of aqueous penicillin, plus Probenecid, 1.0 g immediately, and 0.5 g at 6 and 12 h later. Tetracycline was also widely used and effective with appropriate patient compliance.¹³ Occasionally, a patient who was evacuated to Japan for other medical problems was found to have GU; the disease was diagnosed by urethral swab and culture of a urethral discharge. Current preferred recommended treatment for uncomplicated GU is ceftriaxone sodium 125 mg intramuscularly (1 dose only), plus azithromycin 1 g orally (1 dose only), or doxycycline hyclate 100 mg orally twice a day for 7 days.¹⁴

What was then called postgonorrheal nongonococcal urethritis (NGU) was common and frequently responded to Tetracycline. Since the Vietnam War, multiple studies have demonstrated that post-NGU develops in men who contact GU and chlamydial infections simultaneously and were treated with penicillin, to which *Chlamydia trachomatis* is not sensitive.¹⁴ *C trachomatis* can be recovered from the urethra in 25% to 60% of heterosexual men with NGU.¹⁵ The diagnosis of the presence of the *C trachomatis* organism was made by culturing (when available) endourethral material swabbed from 2 to 4 mm inside the urethra. Immunofluorescent antibody staining is then employed. [Today, chlamydial infections are usually diagnosed by swab and an antigen detection kit based on enzyme-linked immunosorbent assay (ELISA).—DEL, ed]

In Vietnam and Japan, there were no techniques to identify *C trachomatis*. In 20% to 30% of men with acute urethritis, the cause cannot be determined; however, infection with *Trichomonas vaginalis* should be excluded. The current recommendation for therapy for *Chlamydia*-positive and -negative NGU is azithromycin 1 g orally once daily or doxycycline 100 mg orally twice daily for 7 days. Currently, the Centers for Disease Control and Prevention recommended treatment of choice for all patients with NGU is either single-dose azithromycin or doxycycline for 7 days. In the absence of culture, *C trachomatis* should be assumed to be the cause of NGU. Men with *C trachomatis* respond best to this therapy.¹⁴

We consulted on a few soldiers with nonurological causes for evacuation. These soldiers had dysuria; obstructed voiding; and a variable, mucopurulent, nongonococcal, possibly noninfectious, urethral discharge found to be secondary to the presence of a foreign body called an intraurethral "swizzle stick." These foreign bodies, either plastic or wood, were commonly used for stirring alcoholic beverages and were apparently inserted for sexual stimulation and penile rigidity by a prostitute in conditions of soldier intoxication. Swizzle sticks were usually detected by palpation of the penile urethra and were occasionally noted on X-ray of the pelvis done for other injuries.

A high percentage of evacuated patients had indwelling urethral catheters; secondary urethritis and bacteriuria were commonplace. A program for techniques for scrupulous daily catheter care was standard and enforced on all the urological wards in Japan, but such a program was difficult to implement in managing other services.¹⁶ Additionally, the catheters used were made primarily of latex, which resulted in significantly greater urethral irritation and inflammation versus the currently available nonallergenic silicone- or Teflon-coated catheters (Teflon: polytetrafluoroethylene; Du Pont Polymers, Wilmington, Del). Episodes of catheter-induced chronic and acute urethritis, cystitis, pyelonephritis, and Gram-negative bacteremia (urosepsis) were not rare.

Several cases of catheter-induced periurethral abscess developed, which required immediate incision and drainage of the abscess, removal of the urethral catheter, and placement of a suprapubic cystostomy. Abscesses resulted from catheter-induced pressure necrosis and erosion of the penoscrotal urethra, with subsequent bacterial invasion of the adjacent tissues.

Acquired postcatheterization urethral strictures were common; most of them occurred in the distal bulbar and penile urethra and distal penile shaft. Urethral dilation occasionally resulted in systemic Gram-negative bacteremic episodes. Therefore, preinstrumentation antibacterial prophylaxis was employed prior to urethral instrumentation.

EPIDIDYMITIS

Acute epididymitis was 1 of the most common causes of nontraumatic urological hospital admissions in Vietnam.¹ In the military, the most common cause of epididymitis in noninstrumented heterosexual young men is due to sexually transmitted organisms that cause urethritis: *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.¹⁴ The bacterial etiology of acute epididymitis is generally determined both by a Gram-stained urethral smear and a midstream urine culture. Laboratory examination of the smear that is negative for *N gonorrhoeae* and positive only for white blood cells indicates NGU (66% from *C trachomatis*). The cause of acute epididymitis in most of these patients will be *C trachomatis* and *N gonorrhoeae*; coliform bacteria are uncommon in this group. Most patients with acute epididymitis in Vietnam responded to bed rest, ice to the scrotum, and antibiotics as indicated.¹ A few patients whose conditions were refractory to this treatment were evacuated to Japan. They generally responded to prolonged treatment with tetracycline and bed rest.

A second nonvenereal cause of acute epididymitis, 1 that is secondary to catheter-induced coliform bacterial urethritis, was frequently experienced. Patients with this condition had all the signs and symptoms of acute bacterial epididymitis: severe local pain, systemic flulike reaction, and tenderness and swelling that started in the globus minor and spread to the body and head of the epididymis and at times the testicle. These patients were treated with wide spectrum antibiotics, bed rest, scrotal elevation, initially ice to the scrotum, and nonsteroidal antiinflammatory drugs. Several patients with progressive refractory disease had scrotal exploration; lysis of constricting funiculitis, epididymectomy, and/or orchiectomy for abscess or infarction was done. Scrotal–testis ultrasound was not available to assess testis involvement and viability. Some patients (who had associated acute swelling, erythema, and edema of the scrotal skin and tunicae with constrictive funiculitis and with secondary testicular ischemia) had testicular salvage following lysis of the spermatic cord tunicae.

CONDITIONS OF THE PENIS

Balanoposthitis, an inflammation of the foreskin and glans penis, was common in uncircumcised soldiers and was a major cause of morbidity and loss of duty days in Vietnam. The uncircumcised penis was especially vulnerable to the hot humid tropical conditions of Vietnam, especially when associated with poor personal hygiene and exacerbated by the inability to shower for days—especially under combat battle situations. This inflammation may subside with improved hygiene; retraction of the foreskin; and topical antibiotics, steroid creams, and antifungal ointment in any combination. However, continued inflammation may result in progressive contraction and fixation of the foreskin and result in acquired phimosis. Some patients developed a profuse purulent discharge under the unretractable prepuce and required evaluation for GU and NGU. Circumcision was often required for cure, either in Vietnam or in Japan.

Several patients were evacuated to Japan for treatment of penile condyloma acuminata (a warty growth), a condition that had been refractive to topical podophyllin (0.5% to 1%) solution in Vietnam. The lesions were on the glans, penile shaft, and prepuce. This condition is caused by several subtypes of human papillomavirus and is transmitted by sexual contact.¹⁷ Intraurethral condylomata were limited to the most distal urethra and treated with electrofulguration. Condylomata responded to a variety of treatments: topical podophyllin, electrofulguration, circumcision, and local excision. Currently, these lesions are optimally treated with carbon dioxide laser¹⁸ or neodymium:yttrium aluminum garnet (ND:YAG) laser.¹⁹

One of us (JWW) saw a soldier with Buschke-Löwenstein tumor of the penis (giant penile condyloma) (Figure 12-3). This tumor differs from condyloma acuminata in that condyloma, regardless of size, remains superficial and never invades adjacent tissue, whereas the Buschke-Löwenstein tumor displaces, invades, and destroys adjacent structures by compression, often producing urethral erosion and fistulization. Associated bleeding, discharge, and odor are commonly seen in this tumor.¹⁷ The patient was evacuated to CONUS for probable partial penectomy.



Fig. 12-3. A 19-year-old soldier with Buschke-Löwenstein tumor of the penis (giant penile condyloma).

Another soldier had a superficial invasive squamous carcinoma of the penis that was treated with partial penectomy in Japan. Initially, he had had circumcision in Vietnam, but the tumor, which had invaded the superficial penile tissues, was incompletely resected.

TESTICULAR TUMORS

Although testicular cancers are uncommon, they are the most common cancer in males between the ages of 15 and 35. There are no early specific symptoms of testis tumor. A delay in diagnosis from the onset of the first symptom is common and is due to patient and physician ignorance about tumor frequency, signs, and symptoms.²⁰ Delay accounts for the high incidence of metastatic disease on diagnosis: 25% of patients with pure seminoma, and 66% of nonseminomatous

germ cell tumors.²⁰ Painless enlargement, heaviness, or a firm mass are the most common primary symptoms, and pains or a dull ache may be the only complaint. In most instances, careful bimanual scrotal testicular examination will reveal an intratesticular mass; acute epididymitis and hydrocele are the most common mistaken diagnoses.²⁰ Scrotal ultrasound, if available, should be used to separate extratesticular masses.

During the Vietnam War, the mortality for all stages of testicular cancer was greater than 50%; by 1997, the reported cure rate approximated 95%.²¹ This dramatic improvement in survival is due to several factors:

- marked advances in staging techniques (development of computed tomography scanning and accurate, sensitive, serologic tumor markers such as serum alpha fetoprotein and human chorionic gonadotropin);
- refinements and advances in surgical techniques;
- development of highly effective, platinum-based, multidrug chemotherapy; and
- integrated multidisciplinary treatment.

Appropriate management of the patient with testicular tumor is dictated by the primary histology and the clinical–pathologic staging. Germ cell tumors (GCTs) of the testis are composed of 5 basic cell types: seminoma, embryonal carcinoma, yolk sac tumor, teratoma, and choriocarcinoma.²² More than 50% of GCTs contain more than 1 cell type, and these are known as mixed GCTs.²³

Since the early 1970s, the most commonly used clinical–pathologic staging system for testicular cancer has been the I, II, III system^{20,24}:

- Stage I: tumor confined to the testis;
- Stage IIa–IIc: minimal, moderate, or bulky retroperitoneal metastasis;
- Stage III: widespread metastasis.

Additionally, GCTs had been traditionally classified into 2 broad histological categories—seminomas and nonseminomatous germ cell tumors (NSGCTs)—because of their different natural histories and response to different treatment modalities, allowing for variation in treatment strategies. Seminomas are highly radiosensitive, and until recently were treated, with high cure rates, with external beam radiation in all stages. Currently, radiation to nonbulky retroperitoneal lymphatic seminoma (stages IIa and IIb) is standard treatment, whereas stages IIc and III are treated with chemotherapy.²⁰ Today, NSGCTs are treated with various strategies utilizing retroperitoneal lymph node dissection for all stages of tumor, with and without multidrug, platinum-based chemotherapy.^{21,24}

In the late 1960s and early 1970s, effective chemotherapy was essentially nonexistent and tumor staging was inaccurate, nonspecific, and insensitive in defining tumor locus and burden. Some of the urologists in Vietnam had seen only an occasional testis tumor in their training, and only a few urologists had significant training and expertise in the performance of retroperitoneal lymphadenectomy. Furthermore, external beam radiotherapy for abdominal retroperitoneal metastasis was still routine in Europe and the United States, and in US military centers for all patients with testicular carcinoma. Then, testicular cancers were treated as a relative emergency with prompt inguinal orchiectomy and consideration for retroperitoneal lymphadenectomy for NSGCTs was standard of care.

We managed the treatment of 19 soldiers with testicular carcinoma who had been evacuated to Japan. The racial distribution included 16 white, 1 African-American, and 1 Hispanic. The ages ranged from 19 to 40 years; the median age was 24 years. Tumor occurred in the right testis in 13 and in the left in 6. Six had inguinal orchiectomy in Vietnam and 13 had orchiectomy in Japan. One patient who had exploratory surgery in Vietnam for an apparent torsion had reexploratory surgery in Japan, where his tumor was diagnosed and treated with an inguinal orchiectomy. Two orchiectomy specimens were lost in transit in evacuation to Japan, delaying the histological diagnosis for several weeks.

The primary histology revealed NSGCTs in 10 specimens and seminomas in 9 testicles. The NSGCTs included 1 adult teratoma, 4 with pure embryonal carcinoma, and 5 with various mixtures of embryonal carcinoma with teratoma and/or choriocarcinoma or seminoma. Of the 9 with only seminoma histology, 2 had significant mitosis and were classified as anaplastic seminomas. In staging the extent of the primary tumor, 4 specimens demonstrated cancer in the spermatic cord structures (Stage pT3),²³ and 1 revealed intratesticular vascular tumor invasion. All 4 soldiers with spermatic cord tumor (Stage pT3) were

found to have metastatic tumor to the retroperitoneum or lung (stages II or III).

In Japan, all patients had the following clinical staging evaluation: physical examination, serum metabolic analysis (SMA-12), 24-hour urinary collection for human chorionic gonadotropin, chest X-ray, and intravenous pyelogram. The limitations of these staging studies versus currently employed techniques have been noted; nevertheless, metastatic tumor to the retroperitoneum was detected in some by either a palpable abdominal mass or ureteral deviation and/or hydronephrosis on intravenous pyelogram. Chest X-ray was effective in defining pulmonary metastasis, and enlarged supraclavicular nodes were obvious.

Seven of the 9 patients with seminoma were thought to have no evidence of metastatic tumor on clinical staging (Stage I); however, 1 of the 7 had retroperitoneal lymph node dissection because of anaplastic seminoma and had large-volume (stages IIb–IIc) retroperitoneal metastasis. Two patients had palpable abdominal masses (Stage IIc).

Eight of the 10 NSGCTs had retroperitoneal lymph node dissection: 1 in the Republic of Vietnam for pathologic Stage I teratoma, and 7 in Japan. Of these 7, 2 had pathologic Stage I disease; 2, pathologic Stage IIa; 2, pathologic Stage IIb; and 1, pathologic Stage IIc, which was unresectable. Two patients had pulmonary metastasis (Stage III). A mild ileus was the only postoperative complication in the 9 patients having retroperitoneal lymph node dissection. All patients were evacuated to CONUS to major Army medical centers for further evaluation and treatment.

Our retrospective assessment of the Vietnam–Japan experience with GCTs and knowledge of the current state of the art in the management of GCTs leads to several conclusions:

- Testicular carcinoma should be considered in the differential diagnosis of all palpable scrotal testicular abnormalities in young men (aged 20–40 y), especially in those with refractory epididymitis, hydroceles, and ill-defined testicular anatomy.
- Scrotal testicular ultrasound should be used to differentiate intratesticular from extratesticular masses and pathology.
- Diagnosis is made by inguinal exploration and orchiectomy for intratesticular masses. This may be best accomplished in well-equipped and -staffed medical treatment facilities where pathologic evaluation is available.
- Suspected testicular carcinoma is not a management emergency that justifies immediate surgical exploration in a poorly equipped forward medical treatment facility. Such patients should be promptly evacuated to major military medical centers in CONUS.
- There is absolutely no justification for retroperitoneal lymph node dissection in the combat zone medical facility. Treatment decisions for all GCTs should be made at major medical centers in CONUS.
- Testicular carcinoma is a urological disease; the diagnosis and management should be directed by the urologist.

AMINOGLYCOSIDE TOXICITY

Aminoglycosides are a group of bactericidal drugs that share chemical, antimicrobial, pharmacological, and toxic characteristics. Presently the group includes streptomycin, neomycin, kanamycin sulfate, amikacin sulfate, gentamicin, tobramycin, sisomicin sulfate, netilmicin sulfate, paromomycin sulfate, and spectinomycin hydrochloride. After parenteral injection, the drugs preferentially distribute themselves in tissues that have urinary levels 10 to 50 times higher than serum levels. Excretion is almost completely by glomerular filtration.²⁵

Early in the Vietnam War, streptomycin was frequently used in combination with penicillin in Japan. Later, kanamycin sulfate became available and was used for the more-severe Gram-negative infections in combination with other antibiotics such as Coly-Mycin (colystimethate sodium; Parke-Davis, Morris Plains, NJ). Neomycin was often used for irrigation of infected wounds and joints and, in patients with colostomies, as a cleansing enema for the removal of residual fecal material in the distal, defunctionalized colon and rectum.

All aminoglycosides can cause ototoxicity and nephrotoxicity. The ototoxicity is usually irreversible and cumulative. It usually causes damage to the cochlea and hearing loss, initially with loss of high-frequency tones. It can also cause vestibular damage, which manifests as vertigo and ataxia.²⁵ We encountered patients with progressive hearing loss attributed to kanamycin sulfate and neomycin. The hearing loss was often initially apparent in patients who progressively increased the audio on their portable radios, louder and louder in the hospital wards. Early in the Vietnam War, wounds and joints were primarily irrigated with neomycin. This antibiotic solution can be absorbed and result in toxicity.²⁵ Whether patients absorbed sufficient amounts of this irrigant to cause hearing impairment is not known but presumed. Subsequently, this practice was discontinued and replaced with Betadine (povidone-iodine; Purdue Frederick, Norwalk, Conn) when this product became available for wound and joint irrigation. Kanamycin sulfate and neomycin sulfate are more ototoxic (particularly for the auditory portion of the eighth cranial nerve) than gentamicin, tobramycin, or netilmicin sulfate.

Nephrotoxicity from proximal renal tubular damage (necrosis), resulting in nonoliguric acute renal failure manifested by rising serum creatinine levels, is more common than the ototoxicity seen from aminoglycosides. Most patients recover complete renal function.²⁶ Gentamicin has become the most commonly used aminoglycoside. A review of multiple studies indicates that the average incidence of gentamicin toxicity is approximately 15%. In order of decreasing frequency, the aminoglycosides most associated with inducing nephrotoxicity are gentamicin, tobramycin, amikacin sulfate, and netilmicin sulfate.²⁶ Current strategies use once-daily dosing of either gentamicin or tobramycin according to a normogram utilizing serum creatinine and drug levels. This has substantially decreased the incidence of drug toxicity and maximized the bactericidal effect.⁹

In Japan, acute renal failure secondary to aminoglycoside antibiotic toxicity was not uncommon. Patients with this iatrogenic problem generally had complete resolution of their acute renal failure. Serum assays for drug levels were not available then. Since the late 1960s and early 1970s, systemic use of the following aminoglycosides has been abandoned, primarily because of oto- and nephrotoxicity: streptomycin, neomycin, kanamycin sulfate, and paromomycin sulfate.²⁵ Today the aminoglycosides, mainly gentamicin and tobramycin, are primarily reserved for the treatment of severe Gram-negative infections. Aminoglycosides, when combined with trimethoprim-sulfamethoxazole or ampicillin, are the preferred drugs of choice for the treatment of urosepsis.⁹

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