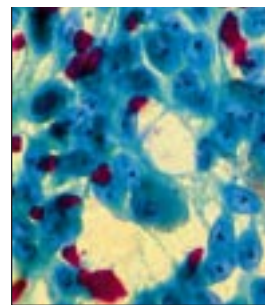


ERECTILE DYSFUNCTION IN THE CANCER PATIENT

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Introduction

Erectile dysfunction is defined as the inability to achieve and/or maintain an adequate erection satisfactory for penetration. It is an underdiagnosed problem and often attributed to a consequence of aging rather than a disease that can be treated. The estimated prevalence of erectile dysfunction in men 40 to 70 years of age is 52%, with higher rates in men older than 70 years.¹ Erectile dysfunction in the cancer patient is even more common due to the various surgical, medical, pharmacological, and psychological aspects involved in cancer care. When properly diagnosed, the treatment of erectile dysfunction can enhance the quality of life that is so important in a patient afflicted with cancer.

Physiology

In order to understand the causes and treatments of erectile dysfunction, the normal erection process must be appreciated. The main arterial supply to the penis is the cavernosal artery, a branch of the pudendal artery, that supplies the trabecular erectile tissue and the sinusoids in the corpora cavernosum. The venous drainage is to the pudendal vein and the periprostatic plexus.²

The innervation of the penis consists of two components: the autonomic (sympathetic and parasympathetic) and somatic (sensory and motor) nerves. While the sympathetic fibers (T11-L2) via the hypogastric plexus are responsible

for detumescence and ejaculation, the parasympathetic fibers (S2-4) via the pelvic plexus are responsible for tumescence. The somatic component is responsible for sensation of the penis and contraction of the bulbocavernosus and ischio-cavernosus muscles.² It is important to note that the parasympathetic and sympathetic nerves can be injured separately without any effect on the other. For instance, damage to the parasympathetic nerves during radical prostatectomy may result in erectile dysfunction but not anorgasmia, while damage to the sympathetic nerves during retroperitoneal lymph node dissection for testicular cancer may result in anejaculation but not erectile dysfunction.

Nitrous oxide is the principal mediator responsible for penile erection within the phallus. It is hypothesized that nitrous oxide induces the formation of cyclic guanosine monophosphate (cGMP) in the vascular system. Cyclic GMP is an important cellular messenger in the vascular system responsible for rigidity of the phallus. Endothelin and vasoactive intestinal polypeptide are other important mediators in erection.¹

The hormones responsible for the erection process are the androgens, mainly testosterone, arising from the testes and the adrenal glands through the pituitary-hypothalamic pathway.²

The psychologic aspect of erectile function cannot be ignored or underestimated. It functions through an elaborate neural

complex involving the cerebral cortex. Visual, auditory, olfactory, and sensory stimulation are all very important in achieving and maintaining an erection.

Pathogenesis

The causes of erectile dysfunction vary but always include at least one of the following mechanisms: vascular supply, nerve supply, hormonal milieu, and psychological component. Usually, the cause in an individual patient is multifactorial with the psychological component being evident as a secondary phenomenon, but any one of these mechanisms can account solely as the cause. Discussion in this article is limited to the causes most frequently seen in the cancer patient.

Surgery

Any surgery involving the pelvis can affect erectile dysfunction. The most common cancer surgeries causing erectile dysfunction are radical prostatectomy, radical cystectomy, and resections of the sigmoid colon or rectum. The cause of erectile dysfunction is usually neurogenic with injury to the branches of the pelvic plexus. Uncommonly, the cause may be vasculogenic with damage to the branches of the internal iliac artery. The injury to the nerves may be avoided in some cases with careful dissection during a radical prostatectomy by using the nerve-sparing technique with preservation of potency, especially

in younger men.³ It is important to note that orgasms can still be achieved even in impotent men following prostatectomy since the sympathetic fibers are not injured. However, semen production is absent since the majority of the semen is formed in the prostate and seminal vesicles that are all removed during surgery.

Another surgery that can affect sexual performance is the retroperitoneal lymph node dissection performed for testicular cancer. These men will not have any problems with erectile dysfunction, but they may lose the ability to ejaculate because of potential injury to the sympathetic chain. Using a modified surgical template and careful dissection, the sympathetic fibers can be spared and anejaculation may be avoided.⁴

Radiation

Radiation therapy can also cause erectile dysfunction by damaging the nerve supply and blood supply of the phallus. Any form of radiation to the pelvis, such as external beam or brachytherapy, may damage the branches of the pudendal nerves. Because the effect of radiation on tissue is gradual, the onset of erectile dysfunction may be gradual or delayed even for years following treatment.^{5,6}

Chemotherapy

Although chemotherapy is known to affect sperm produc-

tion, it also may affect the erection process. The vinca alkaloids, such as vincristine and vinblastine, are known to be neurotoxic. The erectile dysfunction associated with chemotherapy can also be secondary and can be a function of the patient's performance status and other related comorbidities or treatments, rather than the result of a direct toxic effect of the drug itself.

Psychogenic and Other Causes

Although psychogenic erectile dysfunction can be a primary phenomenon, it is usually secondary to other causes especially in the cancer patient. Anxiety, depression, chronic debilitating diseases, and cachexia can cause erectile dysfunction. Loss of self-esteem is common in the patient with cancer, especially after disfiguring treatment such as loss of limb or body part and use of prosthesis or external devices.

Many medicines used today can contribute to erectile dysfunction.⁷ Although the common medications include antihypertensives and antidepressants, other drugs have been implicated,⁸ including narcotics, alcohol, tobacco, marijuana, tranquilizers, and cimetidine.⁹

If we have reached the limits of modern medicine, the quality of life becomes as important as quantity of life. Understanding and treating the various causes of erectile dysfunction become integral parts of care in the cancer patient.

Treatment

The treatment of erectile dysfunction ranges from counseling to medical therapy to surgery. The choice of treatment must be individualized according to the needs and wishes of the patient and his partner. Patients may be reluctant to try one method for various reasons despite its potential effectiveness. In general, patients prefer the lesser invasive treatments, such as oral medication as first-line therapy, followed by gradually more invasive measures such as penile injections or prosthesis.

The first effective oral medication, Viagra (sildenafil; Pfizer Inc, New York, NY), has revolutionized the treatment of erectile dysfunction. Its mechanism of action is due to the inhibition of the phosphodiesterase isoenzyme affecting nitrous oxide and cGMP. The enzyme is also present in other tissues such as the heart and eyes.¹⁰ Viagra is relatively safe and effective; its few side effects include headache, flushing, dyspepsia and, rarely, a blue haze in vision.¹¹ Although several deaths have occurred as a result of its use, they have generally been as a consequence of the concomitant use of nitrates, a known contraindication. Because it is easy to use, it is usually recommended as first-line therapy in most patients. It must be taken at least one hour prior to sexual activity, and sexual stimulation is necessary for a quality erection. The recommended initial dose is 50 mg, but 25 mg may be adequate in the younger patient while 100 mg may be necessary in some men.

Several similar medications are currently being studied.

The intraurethral medication Muse (alprostadil; Vivus Inc, Mountain View, Calif) is inserted in the urethra prior to coitus. It is absorbed through the corpus spongiosum and into the corpus cavernosum initiating a vascular response causing tumescence.¹² The actual medication being absorbed rather than the technique of insertion can cause pain sufficient enough to prohibit further use. For a majority of patients, this method has become much less popular since the introduction of Viagra, and it is not as effective as intracavernous injection of alprostadil (prostaglandin E1).¹³

Vacuum erection devices have been used with varying degrees of efficacy but require some manual dexterity and may be painful to use. The penile engorgement that is created may be uncomfortable as well. These devices can be cumbersome to use and have obvious external appliances such as a ring, which can be left on for only a short period of time. Different versions are available through several manufacturers that vary in price and quality. However, like the intraurethral applications, the vacuum devices are less popular than Viagra.

Penile injection therapy with vasoactive agents revolutionized the diagnosis and treatment of erectile dysfunction in the 1980s in the same way that Viagra has done in the 1990s. Papaverine with or without phentolamine and prosta-

glandin (PGE-1) is the most common agent used presently for intracorporal injections.¹⁴ The patient must have manual dexterity for self-injection and be comfortable with needles. Diabetic patients may find this therapy acceptable due to their comfort level with using small needles. All patients must be warned of the possibility of priapism, which can result from overdosing or repeated injections. In general, patients who adhere to the dosage and the required titration lessen the risk of this serious but treatable complication.¹⁵ Other complications include scarring or plaque formation of the corpora from prolonged repeated injections and bleeding at the injection site. Despite the invasive nature of penile injection therapy, it remains an effective modality that usually has little morbidity. Patients who have undergone a radical prostatectomy may use this therapy without hindering the natural spontaneous return of erections.¹⁶

Penile prosthesis requires surgical intervention and should be considered a permanent procedure. Because removal of the device usually renders the patient completely flaccid, removal is reserved for strict indications such as infection or malfunction. Generally, penile prosthesis may be indicated in the cancer patient who has a good prognosis and a good performance status. Risk factors for complications include diabetes, peripheral vascular disease, concomitant infections, poor wound healing, a radiated pelvis or perineum, and an immunocompromised host. Cancer patients may

certainly have some of these risk factors. Complications include infection of the prosthesis and erosion. Several different types of prosthesis are available, eg, rigid, semirigid, and two- or three-piece inflatable prosthesis, depending on patient and surgeon preference.

Conclusions

Patients with cancer of any type who complain of erectile dysfunction need to be evaluated and treated. The treatment must be individualized depending on the specific causes of the erectile dysfunction as well as the patient's needs, the performance status, and prognosis. Improving a patient's quality of life, which includes sexual intimacy, is imperative in the patient with cancer.

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