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Psychosomatic Aspects of Gynecologic Oncology: Present Status and Future Directions

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Summary

Among women genital malignancies are second in frequency only to breast cancer. Primary disease sites include the endometrium, cervix, ovary, and vulva. With early diagnosis and aggressive therapy, two-thirds of these women will survive for at least 5 years. This encouraging prognosis is in contrast to the distress that may be experienced by women during diagnosis, treatment, and recovery periods. A brief review of major avenues of current research and clinical work is provided, including: psychological responses to gynecologic cancer symptomatology; affective distress; sexual problems; and treatment-related distress. Areas for future investigation are highlighted, including difficulties occurring with disease recurrence; disruption of close relationships; and problems of the elderly woman with cancer.

Introduction

Within the domain of behavioral medicine, there has been increased attention to the psychological responses of individuals with chronic illnesses [e.g., 1,2]. There have been many foci of study, ranging from examination of psychological factors which may function as risk factors for disease onset [3] to the psychological outcomes of the chronic disease state [4]. The earliest substantive and systematic contributions to the study of the psychological responses of cancer patients was made by Aurther Sutherland and his colleagues in the early 1950s [e.g., 5,6]. Since that time, and particularly within the last 5 years, the field has rapidly expanded and study of the psychological responses of women with cancer occupies a central position [7].

An oft cited early study of gynecologic cancer patients was that by Schmale and Iker [8] examining the correlation of personality type and cancer diagnosis. In the intervening years, research with gynecologic cancer patients has examined such concerns as the interpretation of gynecologic cancer symptomatology [9,10], distress accompanying diagnosis, recurrence, or declining health [11,12], and anxiety surrounding difficult medical treatments [13], among others. The majority of research has, however, focused on sexual difficulties following treatment. From 30 to 90% of all patients experience significant disruption, and surveys indicate that such problems contribute a major source of distress to the woman attempting to cope with her disease and its treatment [14,15].

The present article has two major objectives. The first is to provide a brief overview of the major sites of gynecologic disease and the typical treatment regimens. Familiarity with such

information is critical to understanding the psychological responses of the gynecologic cancer patient. The second objective is to summarize 4 major avenues of research and clinical work with gynecologic cancer patients, including symptom interpretation, affective distress, sexual difficulties, and treatment-related anxiety. Current status of research in these areas will be summarized and new directions will be proposed.

Gynecologic cancer and treatment

There are 4 major sites for gynecologic cancer origin, the endometrium, ovary, cervix, and vulva. In combination, gynecologic sites represent the second most common locus for malignant disease among women, only preceded by breast cancer. If identified and treated when the disease is localized, 5-year survival rates for gynecologic sites are high and range from 70 to 80% [16]. Survival rates drop by roughly 50% if there is regional spread at the time of diagnosis (e.g., disease from the cervix extending to the pelvic sidewall), and would drop by an additional 50% with distant spread outside the pelvis (e.g., endometrial cancer with lung metastases).

Endometrial cancer

Endometrial cancer is the most common malignant tumor of the female genital tract. It accounts for approximately 8% of the new cancer cases annually and 49% of all new gynecologic malignancies [17]. This cancer occurs mainly in peri- and postmenopausal women where the most common symptom is abnormal vaginal bleeding. In a premenopausal patient, menorrhagia or intermenstrual bleeding may be the presenting complaint. Several histologic types of endometrial carcinoma exist. About 80% of endometrial malignancies are adenocarcinomas. Ten to 15% are adenosquamous carcinomas containing malignant squamous elements. Rarely, clear cell, squamous cell, or papillary serous carcinomas occur in the endometrium. The remainder of uterine corpus malignancies are sarcomas.

The primary treatment of early endometrial cancer is surgical. Patients at high risk for local recurrence are candidates for pelvic radiation, given in an attempt to prevent recurrent disease at the vaginal vault and pelvic sidewalls. External beam and brachy-therapy are used in various combinations pre- and postoperatively. Although early data regarding responsiveness of endometrial adenocarcinomas to hormone therapy were encouraging, recent in vitro and clinical studies are less optimistic, indicating a response rate in the 11% range [40]. Those cancers likely to respond to progesterone therapy are those that contain both estrogen and progesterone receptors, and those that are well differentiated and recur late.

Although the majority of recurrences will appear within 5 years following completion of treatment, up to one-third may occur later. Long-term follow-up therefore becomes critical in determining cure rates. When recurrent disease is limited to the pelvis, radiation is generally the treatment of choice if it was not used as part of the primary therapy. Recurrences within previously radiated sites or metastases to distant sites are initially treated with high dose progesterone, with long-term control rates in a small but significant percentage. If disease is not responsive to hormone manipulation or if it progresses after initial control, chemotherapy may be offered. Unfortunately there is a paucity of effective agents providing long-term control of endometrial carcinoma.

Cervical cancer

Once the most common gynecologic malignancy, carcinoma of the cervix has evidenced a world-wide decline in incidence. At present it accounts for approximately 3% of all new malignancies in women and 19% of all gynecologic cancers [17]. This is largely due to the existence of the preinvasive phase of the disease, cervical intra-epithelial neoplasia (CIN),

which can be detected by Papanicolaou smear and eradicated prior to the development of invasive disease. The most common presenting symptoms of cervical cancer are vaginal bleeding and a watery bloody discharge. Often the bleeding occurs post-coitally and is a significant disrupter to sexual activity prior to diagnosis (see Discussion below). Pain may also be reported though this occurs later in the course of the disease. Squamous carcinomas account for 80–85% of all cervical malignancies. About 10–15% are adenocarcinomas or mixed adenosquamous carcinomas. Sarcomas account for the remaining 2–3% of cervical malignancies.

Early stage disease may be treated either by radical hysterectomy and bilateral pelvic lymphadenectomy or radiation therapy. For patients requiring radiotherapy, both external and intracavitary treatments are required. Recurrent cervical disease is difficult to treat. Most cervical carcinomas are relatively resistant to chemotherapy. In addition, previous radiation decreases the vascularity of the pelvic tissues so that optimal tissue levels of the drug are not reached in local recurrences. Pelvic exenteration is reserved for patients who have a central recurrence. This surgery is radical and disfiguring, with removal of the uterus, tubes, ovaries, vagina, and the bladder and/or the rectum. The patient must learn to manage one — if not two — abdominal stomas, and vaginal reconstruction is necessary if cortical function is to be retained. Because of the drastic nature of the operation, it is not done for palliation, only for cure.

Ovarian cancer

While it only accounts for 4% of all cancers in women, ovarian cancer has the fourth highest death rate [17]. Unfortunately, most women who develop ovarian cancer are relatively asymptomatic prior to disease dissemination [41]. A patient may complain of non-specific abdominal or pelvic symptoms or irregular menses if pre-menopausal. Other symptoms such as urinary frequency or constipation (from a mass compressing the bladder or rectum) may occur. With advanced disease present in 70% of patients, abdominal pain, swelling, or vague gastrointestinal disturbances are usually present at diagnosis.

Treatment of ovarian carcinoma is difficult for the patient and physician alike. With the majority of patients presenting with disease that is beyond surgical resection alone, adjuvant chemotherapy or radiation is necessary following at least total abdominal hysterectomy and bilateral salpingo-oophorectomy. For most patients, the primary operation attempts to remove as much of the gross tumor as possible. Currently, the chemotherapeutic approach is a *cis*-platinum based multiple drug regimen.

Vulvar cancer

Vulvar carcinoma is the fourth most common genital malignancy, accounting for 5% of all gynecologic cancers. Epidemiologic data indicate that the median age for carcinoma in situ and early invasive disease is 48 years, whereas the median age for women with frankly invasive disease is 65 years. Patients generally present with a lump, although long-standing itching is common. A history of condyloma acuminata may be present. The role of human papilloma virus subtypes in the development of both preinvasive and invasive neoplasia is now beginning to be elucidated. Delay in the diagnosis of this disease is alarmingly common among patients and physicians alike. Squamous cell carcinoma accounts for 90% of vulvar cancers, and the remaining types include malignant melanoma, Bartholin's gland carcinoma, basal cell carcinoma, and vulvar sarcoma.

For non-invasive carcinoma, treatment alternatives exist. The original treatment advocated by Knight [18] was wide local excision of the lesion, but many gynecologists have preferred to remove the entire vulva (i.e., total vulvectomy) arguing that the disease is preinvasive and

frequently multicentric. This procedure incurs considerable emotional cost, and these and other complications have led physicians to consider other approaches, providing comparable recurrence rates. Surgical alternatives have included wide local excision of the lesion or a 'skinning' procedure in which the vulvar skin is removed and replaced by a split thickness skin graft from a donor site on the thigh [19]. The primary non-surgical approaches have included the topical use of chemotherapy or laser vaporization. Although the cosmetic and sexual results are believed to be better with these latter procedures, confirming data are not available and patient tolerance of the treatments is reportedly low due to their intense and protracted (usually greater than 2 weeks) painful nature [20,21].

The standard treatment for invasive disease includes radical vulvectomy (which includes removal of the clitoris and all labial tissue), and bilateral groin lymph node removal, with or without pelvic lymph node removal. If lymph nodes contain no tumor, this treatment is highly curative [42]. Radiation therapy is seldom used as primary treatment because of the severe irritation that results from radiation in an area of terminal circulation that is chronically moist. Chemotherapy is not presently used.

Psychological responses to gynecologic symptomatology

Local and national cancer societies have sought to reduce the time between an individual's first awareness of a cancer sign or symptom and medical consultation. Unfortunately, few gains have been made with studies documenting the problem of delay not only among cancer patients, but those with other chronic illnesses (e.g., cardiac disease) as well. As noted above, women eventually diagnosed with gynecologic cancer may present with a variety of symptoms, with the most common being bleeding irregularities. We have recently examined the relationship between symptom interpretation and delay in a sample of gynecologic cancer patients [10]. This was done in the context of psychophysiological comparison theory [22], a theory which posits how individuals evaluate their bodily signs and symptoms in order to achieve or maintain an understandable bodily condition. We found, among other things, that appraisal delay (i.e., the time elapsing between the moment the individual first noticed signs or symptoms to the time she concluded she was ill) accounted for over 70% of the total delay in seeking treatment. Further, over the course of the appraisal interval, the number of cancer explanations increased, whereas the number of normal-life explanations decreased.

The study by Cochran, Hacker and Berek in this issue provides an analysis of the relationship between symptom interpretation and delay in seeking medical treatment in a sample of endometrial cancer patients. This research and our own [10] has found that a common *mis*interpretation of the irregular bleeding by women is that of a benign process, menopause.

Affective distress

The diagnosis of cancer is traumatic. The concept of 'existential plight' has been offered to describe an individual's immediate reaction and the emotional turmoil that occurs in the next few months. Our data indicate that a unique emotional pattern occurs with the diagnosis of gynecologic cancer [11]. The emotions include a high level of depression and emotional confusion. Anxiety and fatigue, while also problematic, are at levels comparable to that reported by gynecology patients receiving treatment (e.g., hysterectomy) for benign conditions. Finally, it appears that the diagnosis of gynecologic cancer does not generate angry emotional distress, as some investigators have hypothesized [e.g., 8].

Depression is currently recognized as a major psychiatric complication of neo-plastic disease. The most important of the etiologic factors for depression may be those associated with the disease itself, in that the most apathetic, hopeless, or depressed pressed patients are also often in pain or more severely ill. A recent report by Evans et al. [23] studied the incidence of clinical

depression in a newly diagnosed gynecologic sample. They reported that 23% of their sample had major depression according to DSM-III criteria. The report by McCartney, Cahill and Wada in this issue examines the pattern of referral for psychiatric services on a gynecology oncology service. This investigation highlights the low base rate of referral in the context of the high base rate of affective disturbance among cancer patients.

Sexual functioning morbidity

Concern with the sexual problems of cancer patients in general [24–26] and women with gynecologic cancer in particular [27] has been voiced, with sexual functioning morbidity targeted as an important endpoint in psychological research with cancer patients. We have estimated that 30–90% of all gynecologic patients experience substantial sexual difficulties, with variability in the estimates due primarily to site of disease and magnitude of treatment.

Until recently, the sexually disruptive effects of the early signs and symptoms of gynecologic cancer had not been noted. We studied 41 women recently diagnosed with early stage cervical or endometrial cancer and a matched group of healthy women in no distress [9]. Data were obtained on the range and frequency of sexual behavior, level of sexual responsiveness, and the presence of sexual dysfunction. Prior to the onset of cancer signs and symptoms, the gynecologic cancer patients reported similar patterns of sexual activity and responsiveness as the healthy sample. With the appearance of disease indicants (i.e., fatigue, postcoital bleeding, vaginal discharge, pain), the women who subsequently received a cancer diagnosis reported significant sexual dysfunction. Since 75% of the women with cancer experienced a substantial change in sexual functioning, it is likely that such obvious and disruptive sexual problems influenced the women to negatively interpret their gynecologic disease signs/symptoms and seek medical consultation.

Of all gynecologic cancer patients, women with invasive cervical disease have received the greatest study. In the retrospective investigations, estimates of diminished or completely disrupted sexuality range from 6% to 19% for the radical hysterectomy patients and from 44% to 79% for the radiation therapy patients surveyed. In a well-controlled prospective investigation [14] the estimates for the two treatments were comparable, with about 30% of patients reporting disruption. Our controlled longitudinal research compared the sexual functioning of women diagnosed and treated for early stage cervical or endometrial cancer with that of women with benign gynecologic disease treated with hysterectomy and healthy women with no gynecologic disease [28]. Patients were initially assessed following diagnosis but prior to treatment, and on 3 occasions during the first year after treatment. Preliminary analyses indicate significant differences between groups and across time on the measures of sexual behavior (e.g., frequency of intercourse) and the excitement and resolution phases of the sexual response cycle. In contrast, there were no differences between groups on the indicants of sexual desire and the measures of orgasm only approached significance ($P = 0.14$). These are the first data to indicate that the sexual difficulties resulting from cancer diagnosis and the more radical gynecologic treatment result in a specific pattern of sexual difficulties for the gynecologic cancer patient.

Pelvic exenteration is considered for some women with recurrent cervical disease or with extensive but resectable disease at diagnosis. It is a disfiguring operation, involving removal of the uterus, tubes, ovaries, vagina, urinary bladder and/or the rectum. Clinical reports, not surprisingly, have commonly reported the cessation of sexual activity for most women (i.e., 80–90% of these surveyed) following surgery. We have found that while vaginal reconstruction may offer the possibility of maintaining sexual activity that can include intercourse, many sexual difficulties often remain [29].

Despite the mutilating nature of surgeries for vulva cancer, there has been minimal study of the sexual outcomes for such patients. Treatments for in situ disease include total (simple) vulvectomy, wide local excision of the lesion, skinning vulvectomy, laser, and chemotherapy. In a retrospective investigation comparing 35 patients with 35 age- and menopausal status-matched healthy women we found significant differences between the two samples in terms of sexual activity and responsiveness [30]. For the vulvectomy sample, disruption was also correlated with the magnitude of surgical intervention. The report by Tamburini, Filiberti, Ventrafridda and De Palo in this issue provides important data describing the nature of sexual and psychosocial functioning following radical vulvectomy for invasive disease. They replicate earlier studies [15] which estimated that 70–90% of these patients experience major sexual difficulties.

Cancer treatment distress

Certainly one source of distress for the woman with gynecologic cancer is anticipating, experiencing, and recovering from difficult cancer treatments. It is not surprising that a primary focus of the research and clinical efforts has been on patients' anxiety reactions — including their description, prediction, and methods for their reduction. As described earlier, treatment modalities include surgery, chemotherapy, and radiotherapy.

Surgery occupies a primary role in the treatment of gynecologic cancer. In comparison to normal healthy individuals undergoing surgery for benign conditions, cancer surgery patients report more feelings of experiencing a crisis and a strong sense of helplessness [31]. Further, these feelings dissipate quite slowly following treatment.

Perhaps more than other treatment modalities, chemotherapy also elicits significant patient distress. Ovarian cancer patients represent the largest group of gynecologic cancer patients receiving chemotherapy. While multiple side effects can occur for any particular drug regimen, nausea and vomiting have, perhaps, received the greatest attention for intervention. While posttreatment reactions are difficult, the occurrence of *anticipatory* reactions, patients reporting nausea and/or vomiting as they approach the time and/or circumstances of their chemotherapy, are particularly disturbing. Multivariate research has indicated that important predictors of anticipatory reactions are the magnitude of posttreatment vomiting in the earliest cycles, longer infusion times (e.g., 1 h), self-reported anxiety, and previous susceptibility to motion sickness [32,33].

Roughly 60% of gynecologic oncology patients will receive external and/or internal radiation therapy as either primary treatment or in combination with surgery or chemotherapy. It is only recently that radiotherapy has received substantial psychological study. We previously examined individual differences in the psychological reactions of 45 patients undergoing external treatment [34]. Evaluation included pre- and postradiation assessments of the subjects' state and trait anxiety, somatic complaints, and treatment side effects. Most interesting of the findings were the changes in state anxiety that were obtained from pre- to posttreatment: (a) patients with an initial high level of anxiety reported a significant reduction, although they remained the most anxious subgroup; (b) patients with a moderate level of pretreatment anxiety reported no change; and (c) patients with low levels of anxiety reported significant increases in state anxiety. Illustrative of other descriptive efforts is the report by Nail, King and Johnson in this issue which includes extensive data from gynecologic patients on emotional distress and treatment side effects during and following external radiotherapy. The final paper by Karlsson and Andersen provides a comprehensive review of the empirical data on patients' psychological responses to radiotherapy and overviews strategies for reducing patient distress.

Summary and future directions

Despite the systematic notice given to the psychological aspects of cancer in the early 1950s, concern for the unique responses of the gynecologic cancer patients has occurred only recently. However, research is rapidly progressing beyond descriptive clinical reports to, in some cases, controlled prospective longitudinal investigations tracing the development of difficulties among gynecologic cancer patients. These important investigations will lay the empirical groundwork for the development of intervention programs targeted to the specific difficulties of the gynecologic cancer patient.

The 4 areas highlighted in this paper represent a subset of the issues which need to be addressed for the gynecologic cancer patient. Each is characterized by a different stage of research development. For the first, symptom interpretation, few reports have focused on the psychological process involved in women detecting early or recurrent signs/symptoms of gynecologic cancer. Since this disease can be treated effectively at the earliest stages, further research might have important survival benefits if diagnostic delay could be reduced.

It appears that there has been sufficient examination of the magnitude of affective problems among cancer patients [35]. Several other issues remain less clear. These include: (a) the substantive differences in affective symptomatology between distressed cancer patients and other relevant comparison groups (e.g., healthy psychiatric patients); (b) the training of health care professionals to recognize significant affective distress in their patients; and (c) developing and evaluating interventions, both psychological and pharmacologic, to treat affective distress; among others.

There has been rapid progress in determining the nature and magnitude of sexual dysfunction among gynecologic cancer patients. Sufficient descriptive study of cervix and endometrial patients has been completed so that the design and evaluation of intervention programs for prevention of sexual difficulties can begin. Further descriptive research is necessary, however, for other groups such as women with invasive or non-invasive vulva disease. Study of the latter group would be particularly important because information on sexual morbidity could be useful when choosing among treatments offering comparable cure rates. It is unknown whether or not current behavioral sex therapy techniques will be beneficial for women with gynecologic cancer since their sexual difficulties will have, at least in part, functional bases. Thus, research needs to discover the mechanisms producing sexual dysfunction in this population.

Much is known about cancer treatment anxiety. All treatment modalities have received extensive descriptive study. In addition, many interventions to reduce medical treatment distress have been evaluated [36,37]. Further research can examine individual differences in treatment efficacy, the timing of intervention delivery, and prevention models.

These 4 areas represent major areas of research with gynecologic cancer patients. Several others, however, remain for future efforts. We highlight three of particular importance for women with gynecologic cancer. The first is to address the needs of the woman with recurrent disease. Ovary cancer patients represent the most obvious subgroup since the vast majority are diagnosed with disseminated disease. Treatment history often includes surgery–chemotherapy–‘second-look’ surgery cycles. Also, since gynecologic disease tends to recur in the pelvis, a variety of pelvic symptoms — pain, bowel complications, fistulas — produce considerable discomfort and debilitation. Our research indicates that significantly greater emotional distress occurs at the time of a first recurrence over that experienced at the initial diagnosis [38]. Pain is also a significant contributor to distress for these women as it is often severe, constant, and difficult to treat.

A second area important for focus is the examination of women's close relationships following cancer [39]. As noted above, a significant number of women experience sexual difficulties following treatment. Among healthy women and women with cancer at other sites, sexual difficulties are a significant source of marital distress. For many young gynecologic cancer patients, usually those with cervical disease, child bearing capacity may be lost and thus present another source of marital distress. Finally, those women with children residing in the home often experience the difficulties of attempting to maintain their household, marital, and maternal tasks while recovering from difficult treatments. Thus, at times when a woman might have a greater need for social support and concern, relationships may undergo the greatest strain.

Finally, a significant portion of the remaining women with gynecologic cancer are elderly and unmarried, divorced, or widowed. There is continuing concern about the delay in seeking health care and the lower levels of compliance among the elderly with cancer. The additional circumstance of lesser social support among women without partners may add another source of stress. As women with families have unique difficulties coping with their illness, women without families have unique problems as well.

We have focused on a subset of the salient areas of psychosocial difficulty for the women with gynecologic cancer. Others will emerge with continued empirical study. Still, it is important to note that many women cope effectively with their disease and its consequences, aided by their own resources and the assistance of others. Thus, the goal of research in psychosomatic aspects of gynecologic oncology is to describe the problems for patients at risk for difficulty, design and evaluate psychological preventive interventions, and elaborate the etiologic mechanisms for such difficulties.

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