

PSYCHOSOCIAL CONSEQUENCES OF GESTATIONAL TROPHOBLASTIC DISEASE

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Gestational trophoblastic disease (GTD) comprises a spectrum of interrelated diseases including partial and complete molar pregnancy and choriocarcinoma with varying propensity for invasion and metastasis [1—4]. Despite the presence of widespread metastases, persistent gestational trophoblastic neoplasia (GTN) is highly curable with chemotherapy [2—6]. However, psychological shock is anticipated and understandable when the woman and her partner discover that their pregnancy is considered potentially cancerous and life threatening. It is within this context that we address short and long-term issues central to psychological, social, sexual, and overall quality of life adaptation.

Although a cure is generally anticipated, inherent psychosocial stressors exist for the patient and her partner. These stressors include loss of a pregnancy, a potentially life threatening diagnosis, surgical treatment and/or chemotherapy, and delay of future pregnancy. This diagnosis consequently poses a challenge to the woman and her partner since both are required to rapidly shift their sense of hopefulness and joy related to the pregnancy to a necessary challenge to manage a potentially life threatening condition.

This unique set of circumstances has led to investigation of the psychosocial impact of GTD. This chapter outlines several issues considered germane to a comprehensive understanding of the psychosocial implications of a GTD diagnosis. First, a brief discussion of interpretations of childbearing is reviewed to provide a foundation to understand the distress which may occur if a pregnancy is threatened and abruptly halted, as is the case with GTD. This discussion is then supported by data relevant to reproductive concerns after GTD. Second, psychosocial issues of GTD are presented, illustrating the sense of threat and anxiety often associated with this diagnosis. Third, perspectives on potential relationship issues and sexual dysfunction are reviewed. Finally, recommendations for future directions in an integrated clinical care and research approach are provided.

23.1 ASPECTS OF FEMALE IDENTITY, CHILDBEARING AND REPRODUCTIVE CONCERNS

All cultures have considered the ability to conceive and bear children as important to women. Historically, reproductive capacity for women has usually been closely tied to concepts of 'femininity' and gender identity. It has been stated that once having been pregnant, there is no return to a pre-pregnant psychology [7]. Consequently, when considering a diagnosis of GTD and its inherent abnormality, the initial psychological concomitants of GTD could be compared to high-risk pregnancies, where either maternal or fetal factors will adversely affect the outcome of pregnancy. For example, it has been noted that since the concept of motherhood carries so many social expectations and feelings, a woman's

self-esteem may be affected by the knowledge that her pregnancy is 'imperfect' [8]. The concept of 'imperfection' can be extended with GTD to feeling 'flawed', or lacking in femininity or attractiveness.

Considering the specific reproductive nature of this disease, and the age of onset, it could be hypothesized that fertility concerns related to this disease may negatively affect both short and long term perceptions of self. Therefore, in order to more formally assess reproductive concerns resulting from illness, we developed an 18-item self-report instrument, the Reproductive Concerns Scale (RCS), which was designed to measure sense of reproductive well-being as an aspect of quality of life. The psychometric properties of this scale on a sample of long-term GTD survivors ($n = 110$) appear strong, with respectable internal consistency (Cronbach's alpha = .93), and divergent and convergent validity evident through association with standardized scales. For example, greater reproductive concerns, as evidenced by higher scores on the RCS, were significantly more likely to be associated with poorer emotional and physical health, less social support, and less spiritual well-being. In addition, higher RCS scores were associated with younger age, which is also a robust association in predicting overall QoL [9]. These associations aid in defining potential QoL changes as a result of having had GTD.

Descriptive information derived from the RCS suggests that although women enjoy a good quality of life many years after GTD has been successfully treated, reproductive concerns may persist. In our cross-sectional study of 110 women who had been diagnosed with GTD 5-10 years earlier, results in general indicated that psychoemotional sequelae surrounding fertility may persist [10]. For example, 40% of participants felt that they had no control over their reproductive future, 35% indicated that they were not content with the number of children they had, 17% felt angry that their ability to have children had been compromised, and 31% reported mourning the loss of a pregnancy. Reproductive concerns should be recognized as one of the most significant factors associated with the GTD experience. However, it is possible that this issue may be only briefly acknowledged during the acute illness phase. It is noteworthy that the long-term significance to the GTD survivor is evident. These reproductive concerns and the impact of overall quality of life was very similar when assessed in a larger cohort of GTD, cervical cancer, and lymphoma (Hodgkin and non Hodgkin) survivors. For all three survivor groups the reproductive concerns primarily related to premature loss of fertility. Though the numbers were small, those women who wanted to conceive after surviving, but could not had significantly more reproductive concerns than those who did conceive. Likewise, those women who had children prior to their diagnosis were more distressed about their subsequent infertility than those who never had had children, thus suggesting that the inability to complete a family maybe as distressing as the inability to start a family [11].

23.2 PSYCHOSOCIAL ADAPTATION AND QUALITY OF LIFE AFTER GESTATIONAL TROPHOBLASTIC DISEASE

Several retrospective studies have described psychosocial variables

which appear altered as a result of the GTD diagnosis and treatment [11-14]. It is likely that results of these studies are dependent on the cultural perspective regarding such concepts as society's view of women, childbearing, and the type and amount of medical information preferentially communicated to women with an illness. Chinese researchers have considered the important cultural perspective of their community in defining a woman's role and meaning within that society [12]. They recognized that when a woman is unable to bear children she may label herself inadequate, particularly since the capability of a couple to have children is very much regarded as the responsibility of the woman.

To better understand these assumptions, as well as the psychosocial aspects of GTD, they consecutively selected 105 Chinese residents of Hong Kong to study their emotional responses to GTD and its effects on family life. GTD was categorized as either molar pregnancy ($n = 53$), or persistent gestational trophoblastic disease ($n = 53$). The majority of patients (71%) thought the disease occurred by chance, while 25% considered themselves responsible for the disease. Fear of future pregnancy, congenital abnormality and/or infertility persisted, despite reassurance from physicians. In addition, 34% of the molar pregnancy patients reported an emotional impact of the loss of the pregnancy.

Issues of self-worth were again addressed with a U.S. GTD survivor cohort who had achieved complete remission [13]. Although patients were assured that full recovery was anticipated, they acknowledged experiencing shifts in self-esteem, marital relationships, and attitudes toward future pregnancies. Similar to the Chinese population, those treated with chemotherapy expressed feelings of defectiveness, sadness and loss. Further, 76 women from the New England Trophoblastic Disease Center who had been diagnosed with GTD were retrospectively assessed to determine their current mood status, marital satisfaction, sexual functioning, response to illness, and report of the most stressful event occurring within the past year [14]. Data were analyzed according to disease type to include partial mole, complete mole and non-metastatic persistent GTD or metastatic disease.

Although the Chinese study found only moderate differences retrospectively between molar versus persistent disease patients, we observed that the metastatic disease group in the U.S. study displayed significantly greater mood disturbance, actually elevated into the clinically significant range of distress [14]. Patients with metastatic disease also had significantly greater levels of distress in response to the illness. Specifically, the women with metastatic disease were more likely to state that more than one year from diagnosis was needed before life seemed back to normal, and were more likely to desire emotional support from a mental health care professional after completing the study questionnaires. Other subcategories of women were identified through this study as potentially at higher risk for distress. For example, women with active disease reported significantly greater levels of distress in response to the illness than those in gonadotropin remission. They also appeared more likely to suffer negative feelings toward self which they attributed to the disease.

These studies provided a strong foundation for further investigation into long-term survivorship. As previously noted, we utilized a cross-sectional descriptive design to describe the quality of life and long-term

psychosocial sequelae of women diagnosed with GTN 5-10 years earlier [10]. Survivors were enrolled through the New England Trophoblastic Disease Center ($n = 48$), and the United Kingdom (Weston Park Hospital, Sheffield; Charing Cross Hospital, London) ($n = 63$). Results from this study indicated that although this disease-free sample enjoyed an overall good QoL, 51% of respondents expressed that they would likely participate in a counseling program today to discuss psychosocial issues raised by having had GTN, and 74% stated that they would have attended a support group program during the initial treatment if it had been offered.

A sizeable proportion of women stated that during or shortly following treatment, the most significant challenges included treatment side effects (22%), functional QoL problems (20%), emotional problems (19%), and fertility concerns (11%). At the time of diagnosis, women stated that they desired more support (32%), and more medical information/communication (29%). Interestingly, although half of the participants could not identify a challenge related to having had GTD, approximately 15% continued to identify reproductive/fertility issues, emotional issues, and fear of recurrence as troublesome features of survivorship. In addition, 10% of the sample continued to desire emotional support related to the disease, and 21% suggested that they would benefit from ongoing medical information. When asked what they believe health care professionals should know about GTD and survivorship, the largest proportion of responses focused on emotional/psychological concerns (15%), and enhancing education and communication between health care professionals and their patients (13%). This information suggests that while survivorship challenges may decrease over time, patients continue to desire medical information and attention to remaining concerns.

The results from this descriptive work enabled us to generate predictors of quality of life among this cohort of long term survivors of gestational trophoblastic disease. [15]. Using multivariate analysis 6 variables were noted to have significant influence on long term quality of life; cancer-specific distress, social support, spiritual well-being, reproductive concerns, gynecologic pain, and sexual functioning. These 6 variables accounted for 77% of the variance in overall QoL scores. Cancer-specific distress was associated with a worse spiritual well being, more attempts of coping with the disease, more gynecologic pain, sexual dysfunction, and reproductive concerns. Spiritual well being and social supports were a buffer against illness related stress. Interestingly, older patients had a greater spiritual well being.

Another group published their data evaluating the impact of molar pregnancy on the psychological symptomatology, sexual function, and quality of life of survivors [16]. Using validated questionnaires (Hospital Anxiety and Depression Scale (HADS), Satisfaction with Life Scale (SWLS), and Sexual History Form – 12) these authors noted a larger percentage of the survivors had high overall HADS scores, particularly on the anxiety scale, and was independent of the use of chemotherapy. SWLS and sexual dysfunction were similar to community, unaffected controls. Unlike the previous work by Wenzel [11] having a child at the time of diagnosis or subsequently after a molar pregnancy was protective and associated with better psychologic function and QoL. Sexual dysfunction was not associated with age, time since the diagnosis,

chemotherapy use to treat the molar pregnancy, or children. As others have shown, successful coping with these stressors was influenced by a strong support network including partners, family, and Molar Pregnancy Support Groups.

In a more recent study, similar themes regarding psychological morbidity and sexual functioning were observed. Importantly this study highlights the potential long term impact of this diagnosis on QoL. Despite having completed treatment and follow up, the psychological impact of GTD can linger. In a cross sectional analysis of 176 women at a mean time from diagnosis of 4.7 years, 22% and 26% of participants were noted to have elevated levels of depression and anxiety respectively. Approximately 20-50% of women were bothered by some GTD-specific traumatic stress expressed as intrusive thoughts or attempts to avoid GTD-related stimuli. These thoughts and actions were more common among women who did not receive chemotherapy highlighting that psychosocial morbidity is not always related to objective severity of disease. Approximately 50% of patients reported sexual dysfunction and half of these women directly attributed their GTD diagnosis to the sexual problem. Objective measures of sexual functioning were not associated with time from diagnosis, use of chemotherapy, or type of GTD. Socially disadvantaged women (less educated, unmarried, unemployed, and poorer) and those who failed to conceive subsequent to their GTD diagnosis experienced poorer psychosocial outcomes and represent a target group for greater support/intervention [17].

23.3 DISEASE IMPACT AND RELATIONSHIP ISSUES

Although there is burgeoning discussion on the psychosocial impact of malignancies on women, there has been a conspicuous absence of information related to the effects of the disease on partners of the affected woman. This has left us historically with only one window in which to assess the impact of diagnosis and treatment over time. Yet, given the interplay of issues of a disease occurring as a reproductive anomaly, it seems clear that at least some psychosocial or sexual aspects of the disease may impact on the partner.

Some research has suggested that the GTD diagnosis did not appear to affect overall marital satisfaction [12,18]. In fact, females and males rated their marriages overall as highly satisfactory regardless of the type of GTD or its treatment. However, differences in perception related to sexual functioning were observed. Generally, women were significantly more likely to report a sexual desire problem, and attribute desire difficulties to ill health, stress or, not uncommonly, the diagnosis of GTD. Interestingly, although men and women were equally likely to attribute sexual dysfunction to the disease during the active phase of treatment, women were significantly more likely to continue to pursue this attribution as a prolonged, hidden stressor of sexual disturbance, even after disease remission.

GTD may affect the quality of the woman's sexual functioning, with a proportion of women suffering long-term consequences which they attribute to the disease. The primary dysfunction was described as a loss of sexual desire. In the absence of prospective data, however, one might validly question whether the desire problem possibly pre-dated the

GTD, particularly given the frequency of sexual desire problems in the general non-clinical population of women [19]. In addition to a desire problem, Cagayan noted approximately 40% of women treated for GTN also experienced dyspareunia (42%) and had lubrication issues (45%) both of which can contribute to sexual dysfunction and may be directly related to treatment rather than the disease itself [20].

An additional point addressing relationship issues bears mention. It appears that regardless of disease type, if GTD has been diagnosed within a year, both patient and partner are likely to label this diagnosis as the most stressful event occurring in both of their lives. Although the impact of the disease on the patient has been assumed, this piece of data highlights the significant impact the disease has on her partner as well, and underscores the importance of including the partner clinically, as medical information and recommendations unfold.

Similar to the impact of molar pregnancy on the psychological symptomatology, sexual function, and quality of life of survivors, the impact of molar pregnancy on male partners has also been evaluated. Again using the HADS, SWLS, and sexual health form 12, researchers from Australia showed that 32.5% of male partners met case criteria for anxiety. This was double the expected community rates. Written comments from male partners, noted this anxiety was related to a sense of frustration consequent to experiencing loss of control over their fertility, inability to have another child, or fear for their partners well being. The prevalence of depression was 12.5%. This was consistent with the general community rates and lower than rates previously reported in women with molar pregnancy. Despite this, overall QoL and sexual functioning was on par with the community standards. In univariate and multivariate analysis, children were protective and were associated with better psychological functioning and QoL in male partners, while the need for chemotherapy and time from diagnosis did not impact outcomes. [21]

23.4 CONSIDERATIONS FOR FUTURE RESEARCH AND ENHANCED CLINICAL CARE

The cross-sectional data cited throughout this chapter clearly demonstrates that a minimum standard of care should involve education related to the disease, treatment and treatment side effects, reassurance related to a generally favorable prognosis, and reassurance that no deleterious effects will occur on subsequent pregnancies after cure from GTD has been attained. This minimum standard would help to enhance compliance, allay fears, and potentially reduce QoL and relational disruption. It is hoped, however, that practitioners would exceed minimum standards to address the salient psychological, social and sexual issues related to this disease. These salient issues should include attention to issues of self blame, guilt and fear, and acknowledgment of the potential social and sexual difficulties which may arise at key times in the disease trajectory. Throughout that trajectory, and into survivorship, specific reproductive concerns may require proactive attention. Within these discussions, it may also be worth noting that it is not unusual for people to have remaining concerns for an extended time, but that these concerns can often be remedied through counseling with knowledgeable practitioners. To that end, it would be important to

encourage the patient and partner to attend clinical meetings together with the physician and staff. This approach would help to enhance support within the relationship, and is likely to foster a more open discussion.

Many health care settings are currently forced to disseminate resources only to those in greatest need. In the realm of psychosocial care for women with GTD, this would necessitate identifying risk factors early during the diagnostic and treatment period, then allocating care proactively. The literature suggests that issues such as comorbid illness, including depression, and less social support, would increase risk for adjustment difficulties. For women with either active disease, a diagnosis within the past year, no children, or metastatic disease, proactive attention should be provided through an initial comprehensive psychosocial evaluation and follow-up contact with staff to provide education, reassurance and counseling as indicated. This approach should assist in decreasing the severity of emotional reactions, and provide the patient and her partner with the needed support to sustain them in this 'crisis' until remission is achieved. When indicated, this is likely to reduce the magnitude of mood disturbances experienced by women with metastatic disease, provide coping skills for dealing with the challenges of the disease and treatment, and enhance communication between the patient and her partner. Additionally, given the impact of this diagnosis on male partners it is reasonable to recommend including them in the ongoing emotional support.

The literature to date represents cross-sectional studies, which are valuable in providing descriptive data at one point in time. This data has armed us with sufficient information to ask both global and specific QoL research questions. To date, no known prospective, longitudinal trials have addressed psychological, social or sexual issues which accompany the disease trajectory. Only with prospective analyses can we can develop predictive models to identify those most likely to benefit from additional psychoeducational efforts. Consequently, the logical next step would involve prospective assessment of quality of life issues known to affect women with GTD. For example, in addition to general QoL domain assessment (e.g., emotional well-being, functional well-being), pertinent issues for the GTD patient would include her fear of future pregnancy, additional reproductive concerns, as well as indirect effects of the disease on the partnership (i.e. self-blame, guilt, sexual dysfunction). Although we are now poised to efficiently assess women with GTD from diagnosis through years of survivorship and can test optimal psychoeducational interventions and the benefits of this type of supportive intervention, it still has not occurred. Reasons for lack of a randomized psychoeducational trial are unclear, but might include a funding agency or reviewer bias that this disease is rare and of low public health relevance, or that the majority of women will survive to live and long and healthy life. Nevertheless, demonstrated efficacy could assist in establishing the evidence base necessary to recognize and launch psychosocial care in this relatively neglected area of women's health care.

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