An Example of Ovarian Cancer as a ‘Chronic Disease Process’ – 11-Year Survival with Multiple Treatments for Recurrent and Progressive Disease

Maurie Markman Vinay Malviya

The University of Texas M.D. Anderson Cancer Center, Houston, Tex., and Division of Gynecologic Oncology, Providence Cancer Center, Detroit, Mich., USA

Key Words

Ovarian cancer · Chemotherapy for ovarian cancer · Long-term survival in ovarian cancer · Treatment of recurrent ovarian cancer

Abstract

The 11-year survival of a woman with recurrent progressive advanced epithelial ovarian cancer emphasizes the potential for the disease process to be quite ‘chronic’ in nature.

Introduction

A previously published commentary has noted that for many women with recurrent or persistent advanced ovarian or primary peritoneal cancer, it is not unreasonable to consider the disease to be a very serious, but chronic disease process [1]. The implications of this statement include the fact that while cure is unfortunately not an objectively valid goal of therapy in this setting, prolonged survival is possible [2, 3], and that treatment strategies should essentially be designed to focus equally on the quality of life as well as the length of survival. The 11-year survival of a patient under the care of one of the authors of this report (V.M.) who has received multiple treatments for recurrent and progressive disease emphasizes the meaning and complexity of this far from theoretical management paradigm.

Case Report

The patient was diagnosed with stage IIIC papillary serous adenocarcinoma of the peritoneum in September 1997. Following primary cytoreductive surgery, the patient developed a vesicovaginal fistula

which was managed conservatively. Her primary chemotherapy consisted of carboplatin and paclitaxel. Due to the extent of the initial disease process, the patient received several sequential ‘maintenance approaches’, including paclitaxel, altretamine, and tamoxifen (each delivered as single agent). A secondary cytoreductive surgical procedure was performed due to the presence of documented recurrent macroscopic disease.

Since the documentation of recurrence the patient has received the following sequential antineoplastic regimens over a multi-year period: (a) carboplatin plus gemcitabine (with carboplatin, and subsequently gemcitabine, being discontinued due to hypersensitivity reactions); (b) cisplatin plus paclitaxel; (c) single agent altretamine; (d) cisplatin plus docetaxel; (e) single agent anastrozole; (f) cisplatin plus paclitaxel; (g) single agent paclitaxel; (h) single agent altretamine; (i) raloxifene (most recent treatment, initiated in May 2008). In addition to the antineoplastic drug therapy, the patient has undergone two additional major surgical procedures in 2004 and 2006 to resect progressive macroscopic cancer.

At the time of this report (September 2008), the patient remains without cancer-related symptoms, with no radiographic evidence of the malignancy (normal whole-body PET scan), and with a normal serum CA-125 antigen level, 11 years after the initial diagnosis of advanced ovarian cancer and following treatment of multiple episodes of progressive disease.

Discussion

An increasing number of therapeutic options are available to women with epithelial ovarian cancer who experience recurrence or persistence of their disease following the delivery of the initial treatment program [4, 5].

Surgery can play a critically important role in this setting, both to potentially improve the opportunity for a more prolonged response to subsequently delivered cytotoxic chemotherapy following an extended treatment-free interval [6], and to palliate distressing symptoms associated with progression of platinum-resistant cancer. Judicious use of radiation, most frequently in the presence of resistant disease symptomatically localized to the pelvis, can be particularly effective in the short-term palliation of pain.

Chemotherapy delivered in the setting of recurrent or platinum-resistant cancer has been documented to extend survival [7–9], may improve cancer-related symptoms, and can meaningfully delay further disease progression. Unfortunately, the selection of specific therapies considered during the course of an extended illness must be quite empiric, based principally on physician judgment, knowledge of specific toxicities experienced by the individual patient, limited data from clinical trials (mostly phase 2 studies), and patient choice.

It is often difficult to know if observed prolonged survival, such as in the case presented here, is the result of the unique natural history of disease in a particular individual, or represents the favorable impact of the multiple therapies employed, or (most likely) a variable combination of these two factors [10]. Of note, the recently reported results of a randomized phase 3 trial have impressively demonstrated that even when delivered in the ‘third-line’ setting to patients with platinum-resistant ovarian cancer, biologically active anticancer therapy can significantly improve overall survival in this malignancy [7].

The patient described in this report received multiple therapeutic agents, including some quite ‘old drugs’ (e.g., altretamine) as well as newer hormonal (e.g., anastrozole) pharmaceuticals. Despite the striking differences in the number of years these various agents have been employed in the management of ovarian cancer, the fundamental goal for the delivery of each of these treatments is the same: to extend survival and at the same time optimize the quality of life of the individual patient [1].

As this case makes clear, management decisions need to be individualized based on specific signs (e.g., progressive large volume intra-abdominal disease), symptoms (e.g., pelvic pain), and circumstances (e.g., the distance a patient lives from the treatment center). Inclusion of the patient and her family in this complex deliberative process is essential. Finally, while it is reasonable to conclude that currently this particular case history likely represents the unique management challenges associated with a patient whose course is at ‘the end of the tail’ of the recurrent ovarian cancer survival curve, it is not inappropriate to speculate that extended survival of this magnitude will be far less of a novelty in the not-so-distant future [1].

References

- 1 Markman M: Why study third-, fourth-, fifth-, ...line chemotherapy of ovarian cancer? *Gynecol Oncol* 2001;83:449–450.
- 2 Markman M: Viewing ovarian cancer as a ‘chronic disease’: what exactly does this mean? *Gynecol Oncol* 2006;100:229–230.
- 3 Markman M, Webster K, Zanotti K, Peterson G, Kulp B, Belinson J: Survival following the documentation of platinum and taxane resistance in ovarian cancer: a single institution experience involving multiple phase 2 clinical trials. *Gynecol Oncol* 2004;93:699–701.
- 4 Markman M, Bookman MA: Second-line treatment of ovarian cancer. *Oncologist* 2000;5:26–35.
- 5 Markman M: Pharmaceutical management of ovarian cancer: current status. *Drugs* 2008;68:771–789.
- 6 Bristow RE, Lagasse LD, Karlan BY: Secondary surgical cytoreduction for advanced epithelial ovarian cancer. Patient selection and review of the literature. *Cancer* 1996;78:2049–2062.
- 7 Vergote I, Finkler N, del Campo J, Lohr A, Hunter J, Matei D, Spriggs D, Kavanagh J, Vermorken J, Brown GL, Kaye S: Single agent, canfosfamide versus pegylated liposomal doxorubicin or topotecan in 3rd-line treatment of platinum refractory or resistant ovarian cancer: Phase 3 study results (abstract). *J Clin Oncol* 2007;25(suppl):966s.
- 8 ICON and AGO Collaborators: Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. *Lancet* 2003;361:2099–2106.
- 9 Pfisterer J, Plante M, Vergote I, du Bois A, Hirte H, Lacave AJ, Wagner U, Stähle A, Stuart G, Kimmig R, Olbricht S, Le T, Emerich J, Kuhn W, Bentley J, Jackisch C, Lück HJ, Rochon J, Zimmermann AH, Eisenhauer E: Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol* 2006;24:4699–4707.
- 10 Markman M, Hakes T, Barakat R, Curtin J, Almadrones L, Hoskins W: Follow-up of Memorial Sloan-Kettering Cancer Center patients treated on National Cancer Institute Treatment Referral Center protocol 9103: paclitaxel in refractory ovarian cancer. *J Clin Oncol* 1996;14:796–799.