Successful response to docetaxel treatment in recurrent ovarian granulosa cell tumor: a case report

T. Shavit, I. Bruchim, Z. Ben-Harim, A. Fishman

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Meir Medical Center, Kfar Saba Israel, affiliated with the Sackler School of Medicine, Tel Aviv University, Tel Aviv (Israel)

Summary

Background: Ovarian granulosa cell tumor (GCT) is primarily treated surgically. Treatment for advanced or recurrent disease includes primary or adjuvant chemotherapy. Data about the efficacy of treatment with paclitaxel are limited, without data about the role of docetaxel in treating recurrent GCT. *Case:* A 68-year-old patient with Stage IA ovarian GCT diagnosed ten years earlier, presented with a third episode of recurrent disease. Following the first event of recurrent disease, she underwent a second laparotomy followed by BEP chemotherapy. Because of new liver masses, she was treated with paclitaxel, with complete response. Following diagnosis of new liver lesions, third-line chemotherapy with docetaxel was initiated, resulting in stable disease and a PFI of 24 months. *Conclusion:* Docetaxel might be a good alternative for treating recurrent GCT.

Key words: Granulosa cell tumor; Docetaxel.

Introduction

Granulosa cell tumor (GCT) represents 5% of all ovarian cancers and accounts for 70% of the ovarian sex cord-stromal tumors, with an incidence of 0.4 to 1.7 per 100,000. Adult GCT may occur at any age, but usually presents during the perimenopausal or early postmenopausal period. Most patients with GCT present with Stage I disease (78-91%), have a good prognosis, and require no further postoperative adjuvant treatment. However, they require long-term follow-up, owing to the potential for recurrent disease, with a median time-to-relapse of approximately four to six years [1]. Treatment of advanced or recurrent GCT consists of surgical debulking, followed by platinum-based chemotherapy, with the BEP (bleomycin, etoposide, cisplatin) regimen producing the best response rates [2, 3]. During the last several years, the limited data available indicated the possible activity of taxanes in GCT, as a single agent or in combination with other drugs [4-6].

Docetaxel is a semi-synthetic taxane agent that acts by disrupting the essential cellular microtubular network; thus, it interferes with the mitotic and interphase cellular functions. Several studies demonstrated that the use of docetaxel instead of paclitaxel in the standard platinum-based regimen used for treating epithelial ovarian cancer might result in less neuropathy and equivalent efficacy [7, 8]. Although docetaxel has exhibited significant activity in epithelial ovarian cancer, to the best of our knowledge, only one study, including three patients with recurrent GCT treated with docetaxel have been reported. We herein report a patient with recurrent ovarian GCT with a marked response to docetaxel treatment.

Case Report

A 68-year-old patient with ovarian GCT, diagnosed ten years earlier, presented to our department with a new episode of recurrent disease. At the time of her initial examination (1996), she was diagnosed with Stage IA following TAH-BSO and surgical staging. Six years later, she was diagnosed with the first relapse, manifested by intraperitoneal lesions. Consequently, she underwent secondary cytoreduction followed by BEP administration, with a complete response. During the following four years, she experienced two more episodes of recurrent disease including the current one that preceded our report. The second-line chemotherapy chosen for the second episode of recurrent disease consisted of weekly paclitaxel. This regimen achieved clinical complete response after nine cycles. However, it was discontinued after a total of 15 cycles, when the patient complained of neurotoxicity-related symptoms. After a progression-free-interval of four months, a computed tomography (CT) scan revealed new liver lesions (the largest was 2 cm). Based on the excellent results that were achieved with the previous taxane treatment, we chose docetaxel as the third-line chemotherapy. Docetaxel (25 mg/m^2), given on days 1, 8, and 15, in a 28-day cycle, was started in February 2006. The patient completed 14 cycles of docetaxel, after which the disease was stable, without any evidence of new metastatic lesions on physical examinations and repeated CT scans (every 3 to 5 months). She tolerated the treatment well, with only two episodes of significant side-effects (CTCAE v3.0): grade 2-3 diarrhea managed by supportive care and grade 2-3 stomatitis, which resolved spontaneously.

Discussion

Because GCT is a rare malignancy, clinical trials aimed at determining which treatment regimens have the highest efficacy in advanced or recurrent disease are limited; therefore, optimal chemotherapy for this disease has not been defined. In the last decade, the BEP combination was reported as the preferred regimen for recurrent ovarian GCT, with 33% complete response and 50% partial response rates [9]. Other regimens with reported

Revised manuscript accepted for publication September 26, 2011

anti-tumor activity include cisplatin, vinblastine plus bleomycin (PVB or VBP), cyclophosphamide, doxorubicin plus cisplatin (CAP), carboplatin plus etoposide, and doxorubicin alone. Several *in vitro* studies demonstrated the effect of paclitaxel on ovarian granulosa cells. These studies showed that paclitaxel causes a significant but reversible inhibition of granulosa cell steroidogenesis. We believe that docetaxel, which has the same inhibitory effect, might be as effective as paclitaxel for treating GCT.

Here, we report on a patient with refractory GCT who experienced successful treatment with docetaxel, resulting in long-term, stable disease. Even though docetaxel was given as a third line, there was a significant response, with a relatively long progression-free-interval with only minor side-effects. In the last few years, only a few investigators have reported the role of paclitaxel in treating ovarian GCT, with only one report of docetaxel treatment for these patients. Tresukosol *et al*. reported the first case of a patient with recurrent ovarian GCT who had a dramatic response to paclitaxel treatment. In their case, partial response was noted after the second cycle of paclitaxel, and it was maintained for 12 months [5]. Powell *et al*. reported on recurrent juvenile GCT treated with six cycles of paclitaxel and bleomycin as salvage chemotherapy, which resulted in 44 months of disease-free survival [6]. Brown et al. evaluated the efficacy of taxanes in treating 37 patients with ovarian sex cord tumor (SCT). The total response rate in the 34 patients who were treated with paclitaxel as a single agent was 18%, and 60%, when combined with platinum. Unlike the good results with paclitaxel in this report, the three patients who were treated with docetaxel exhibited progressive disease [4]. In a later publication, Brown et al. compared the results of two chemotherapy regimens in patients with ovarian SCT (21 patients with BEP vs 44 patients with paclitaxel) [10]). There was no significant difference in response rate (82%) for newly diagnosed patients, with a median overall survival of 97.2 months and 52 months, respectively. Among patients treated for recurrent measurable disease, the response rate was higher in the BEP group but was not statistically significant, 71% and 37%, respectively. The median progression-free survival rate was similar in both groups (11.2 and 7.2 months, respectively). However, the toxicity profile was better with taxane regimens. They concluded that taxanes demonstrated activity against SCT of the ovary and might be less toxic than BEP [10].

Our patient experienced significant clinical and symptomatic improvement upon docetaxel treatment. To the best of our knowledge, this is the first case in the literature involving response to docetaxel in patients with recurrent GCT. Further experience with this drug is needed to establish its efficacy in this group of patients.

References

[1] Colombo N., Parma G., Zanagnolo V., Insinga A.: "Management of ovarian stromal tumors". *J. Clin. Oncol*., 2007, *25,* 2944.

[2] Gershenson D.M., Copeland L.J., Kavanagh J.J., Stringer C.A., Saul P.B., Wharton J.T.: "Treatment of metastatic stromal tumors of the ovary with cisplatin, doxorubicin, and cyclophosphamide". *Obstet. Gynecol.,* 1987, *70,* 765.

[3] Gershenson DM, Morris M, Burke TW., Levenback C., Matthews C.M., Wharton J.T.: "Treatment of poor-prognosis sex cord-stromal tumors of the ovary with the combination of bleomycin, etoposide, and cisplatin". *Obstet. Gynecol.,* 1996, *87,* 527.

[4] Brown J., Shavartsman H.S., Deavers M.T., Burke T.W., Munsell M.F., Gershenson D.M.: "The activity of taxanes in the treatment of sex cord-stromal ovarian tumors". *J. Clin. Oncol*., 2004, *22,* 3517.

[5] Tresukosol D., Kudelka A.P., Edwards C.L., Charnsangavej C., Narboni N., Kavanagh J.J.: "Recurrent ovarian granulose cell tumor: a case report of a dramatic response to Taxol". *J. Gynecol. Cancer,* 1995, *5,* 156.

[6] Powell J.L., Connor G.P., Henderson G.S.: "Management of recurrent juvenile granulosa cell tumor of the ovary". *Gynecol. Oncol.,* 2001, *81*, 113.

[7] Francis P., Schneider J., Hann L., Balmaceda C., Barakat R., Phillips M. *et al*.: "Phase II trial of docetaxel in patients with platinum-refractory advanced ovarian cancer". *J. Clin. Oncol.,* 1994, *12*, 2301.

[8] Vasey P.A., Jayson G.C., Gordon A., Gabra H., Coleman R., Atkinson R. *et al*.: "Phase III randomized trial of docetaxel-carboplatin versus paclitacel-carboplatin as first-line chemotherapy for ovarian carcinoma". *J. Nation Cancer Instit.,* 2004, *96,* 1682.

[9] Homesley H.D., Bundy B.N., Hurteau J.A., Roth L.M.: "Bleomycin, etoposide, and cisplatin combination chemotherapy of ovarian granulosa cell tumors and other stromal malignancies: a Gynecologic Oncology Group study". *Gynecol. Oncol.,* 1999, *72,* 131.

[10] Brown J., Shvartsman H.S., Deavers M., Ramondetta L.M., Burke T.W., Munsell M.F., Gershenson D.M.: "The activity of taxanes compared with bleomycin, etoposide, and cisplatin in the treatment of sex cord-stromal ovarian tumors". *Gynecol. Oncol.,* 2005, *97,* 489.

Address reprint requests to:
I. BRUCHIM, M.D.
Division of Gynecoogic Oncology
Meir Medical Center
Tschernihovsky 59
44281 Kfar Saba (Israel)
e-mail: ilan.bruchim@gmail.com.ca