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Long survival metastatic ovarian neoplasm under bevacizumab maintenance strategy

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Summary

The prognosis of metastatic invasive epithelial ovarian tumor is poor, with a five-year survival rate under 20%. The author reports the case of a 71-year-old woman, diagnosed at the age of 65 years, with a serous papillary ovarian carcinoma with diffuse peritoneal carcinomatosis. She received four courses of neoadjuvant carboplatin plus paclitaxel chemotherapy, then underwent debulking surgery, followed by three courses of chemotherapy. Seventeen months later, diffuse metastases appeared. The patient received six cycles of carboplatin plus paclitaxel chemotherapy and obtained complete response. Ten months later, carboplatin plus gemcitabine plus bevacizumab were administered for a new relapse, followed by bevacizumab maintenance. After 28 months of bevacizumab treatment, the anti-VEGF therapy was stopped, because of proteinuria and renal failure. The patient is under hormonal therapy and has stable disease.

Key words: Ovarian carcinoma; Metastasis; Bevacizumab; Maintenance; Anti-VEGF; Proteinuria; Toxicity.

Introduction

Epithelial ovarian carcinoma is the most common cause of death among women with gynecologic malignancies. Approximately 75% of women have Stage III or IV disease at diagnosis.

Bevacizumab is a biologically and clinically active antineoplastic agent in the management of epithelial ovarian cancer. It has demonstrated in randomized phase III studies improvement in progression-free survival.

Herein the author describes a patient with a metastatic ovarian carcinoma that benefited from bevacizumab in maintenance for more than two years.

Case Report

A 65-year-old Caucasian woman with a thrombo-embolic past, familial cancer history, and positivity for BRCA2 mutation, presented with abdominal pain and discharge in September 2009. She underwent coelioscopy and histology showed advanced stage high-grade serous papillary ovarian carcinoma with diffuse carcinomatosis. She was treated with neoadjuvant four courses of carboplatin-paclitaxel regimen, followed by non-optimal interval cytoreductive surgery, and additional chemotherapy with three courses of carboplatin-paclitaxel.

Complete histology found a serous ovarian carcinoma with extensive carcinomatosis in both ovaries, fallopian tubes, uterus, appendix, and peritoneum. The tumor was positive for hormonal receptors (estrogen receptors 80%; progesterone receptors 10%). There were no metastatic nodes out of the 31 removed.

At the time of her first recurrence, 17 months later, she presented with liver metastasis, mediastinal lymphadenopathy, and peritoneal nodularity. Antigen cancer Ca-125 was at 74 U/ml (normal range < 35 U/ml). She was re-treated with carboplatin-paclitaxel regimen with a complete response.

Her disease recurred ten months later with splenic metastasis, carcinomatosis, and mediastinal lymphadenopathy. The patient began treatment with carboplatin-gemcitabine-bevacizumab, with a good partial response, followed by bevacizumab in maintenance, in association with exemestane. Imaging showed only a left iliac fossa nodule. Ca-125 was at 6 U/ml. After 28 months of bevacizumab plus exemestane, Ca-125 was at 7.79 U/ml and tomography scan was stable. However, the patient developed proteinuria at 2.30 g/day and renal failure. Bevacizumab was stopped. She is undergoing hormonal therapy alone.

Discussion

Several studies have assessed the activity of bevacizumab when added to chemotherapy in ovarian cancer [1-3]. Results from phase III randomized clinical trials suggested that adding antiangiogenetic agent bevacizumab to chemotherapy increased the time to disease progression.

Two phase III trials: OCEANS [3] and AURELIA [4], were conducted and led to the approval of bevacizumab by the European authorities for treating the first recurrence of platinum-sensitive or platinum-resistant ovarian cancer. OCEANS [3] and ICON 7 [5] studies showed a nearly four-months improvement in progression-free survival.

In November 2014, the FDA approved bevacizumab in combination with chemotherapy for the treatment of

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women with recurrent ovarian carcinoma; based on upon an improvement in progression-free survival. This explains why the present patient did not receive bevacizumab at her first recurrence in 2012. Nevertheless, it is well known that the administration of bevacizumab is frequently associated with adverse events. Importantly, there has been concern about toxicity, especially bowel perforation [6], renal dysfunction, proteinuria, and hypertension [7] associated with the use of bevacizumab. Practitioners should be aware of these side-effects and have to check blood pressure and proteinuria before each infusion, as recommended.

The place of hormonal therapy in the management of patients with ovarian cancer remains unsettled. Most trials of hormonal treatment in ovarian cancer have been retrospective, involved only limited numbers of patients, and lacking important patient-related data and information pertaining to tumor characteristics. A literature review shows that response to hormonal therapy even in a preterminal setting, is modest, with about 8% objective response but almost no side effects [8]. The place of hormonal therapy in the management of patients with epithelial ovarian cancer needs more thorough evaluation in well-designed randomized trials. The present patient received exemestane instead of tamoxifen, because of her thrombo-embolic past.

Conclusion

Bevacizumab is a very effective antineoplastic agent in the treatment of ovarian carcinoma. It allows prolonged progression-free survival. However, adverse events are frequent and practitioners have to be aware of their management.

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