Complete remission of pulmonary metastases of Bellini duct carcinoma with cisplatin, gemcitabine and bevacizumab

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Summary

Background: Bellini carcinomas, rare tumors of kidney, are aggressive and have a poor prognosis. For these cancers, there is no standard treatment regimen and chemotherapy for urothelial cancer is usually used.

Case Report: In a 44-year-old man with hematuria, a tumor was diagnosed in the right kidney. After radical nephrectomy, pathologic analysis revealed Bellini carcinoma, staged pT3apN0, Fuhrman grade 3. Secondary pulmonary lesions occur one year later. Chemotherapy (gemcitabine, cisplatin and bevacizumab) was started and after 2 cycles of chemotherapy, Thoracic CT scans showed good response to treatment, with almost complete regression of the pulmonary lesions. After the third cycle of chemotherapy, maintenance treatment with bevacizumab continued. Fifteen months after diagnosing pulmonary metastases, hilar adenopathies progressed slightly and cisplatin-gemcitabine was started again leading to a partial response after five courses. Approximately 2 years after the diagnosis of lung metastases, the patient presented a second relapse, so carboplatin-gemcitabine was started, while bevacizumab was continued. 24 months after the diagnosis of lung metastases, the patient was still alive with controlled disease.

Conclusions: In view of our findings, a prospective multicenter trial with cisplatin, gemcitabine and bevacizumab in patients with metastatic collecting duct carcinoma is planned.

key words: Bellini carcinoma • Complete response • bevacizumab

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BACKGROUND

Collecting duct carcinomas of the kidney (Bellini duct) account for ~1% of all renal epithelial carcinomas, are aggressive and have a poor prognosis [1]. The 1-, 5- and 10-year disease-specific survival rates in patients with collecting duct carcinoma are 69%, 34% and 14%, respectively [2].

No standard treatment regimens exist for collecting duct carcinoma and neither immunotherapy nor chemotherapy are particularly effective. Chemotherapy for urothelial cancer is usually used, but the results are generally disappointing [2,3]. There are few reports of vascular endothelial growth factor-targeted therapy in patients with collecting duct carcinoma. We describe a patient with metastatic disease who received chemotherapy plus bevacizumab followed by bevacizumab maintenance therapy.

CASE REPORT

A 44-year-old man with no significant medical history presented with hematuria. A tumor was detected in the right kidney using ultrasound and confirmed by CT scan. The patient underwent right radical nephrectomy (July 2008). Pathologic analysis revealed renal collecting (Bellini) duct carcinoma: the 7 cm tumor was stage pT3apN0, Fuhrman grade 3. Immunohistochemistry showed a positive stain for Ulex Europaeus (typical of Bellini duct carcinomas) and cytokeratin-8, but a negative for thyroid transcription factor 1 (excluding metastasis of a lung carcinoma).

One year later (June 2009) PET-CT scans revealed several secondary pulmonary lesions ~1 cm diameter with bilateral hilar lymphadenopathies and evidence of locoregional relapse consisting of several nodular centimetric lung metastases and bilateral fluorodeoxyglucose (18F)-positive hilar adenopathies. Wedge excision showed adenocarcinoma expressing Ulex Europaeus. Thyroid transcription factor 1 and carcinoembryonic antigen were negative. The patient’s only symptom was chronic cough while his perforation status was normal.

Chemotherapy (gemcitabine, cisplatin and bevacizumab) was started following informed consent: cisplatin 70 mg/m² on day 1 and gemcitabine 1000 mg/m² on days 1, 8 and 15, every 4 weeks, plus bevacizumab 6.5 mg/kg every 3 weeks. During chemotherapy, grade 2 neutropenia and thromboembolism were observed.

After 2 cycles of chemotherapies, thoracic CT scans showed good response to treatment, with almost complete regression of the pulmonary lesions. However, scans revealed a pulmonary embolism of the segmental artery (lower-left lobe); the patient was asymptomatic and started treatment with a low-molecular-weight heparin. A third cycle of cisplatin-gemcitabine-bevacizumab was given, then chemotherapy was stopped and maintenance treatment with bevacizumab every 3 weeks continued. Maintenance therapy was well-tolerated. Eleven months after diagnosing pulmonary metastases, disease was clinically/radiologically stable without sign of tumor progression.

Fifteen months (September 2010) after diagnosing pulmonary metastases, hilar adenopathies progressed slightly and cisplatin-gemcitabine was started again leading to a partial response after five courses. Approximately 2 years after the diagnosis of lung metastases (May 2011), the patient was well and still receiving bevacizumab maintenance therapy, but presented a second relapse, so carboplatin-gemcitabine was started, while bevacizumab was continued.

As of June 2011, 35 months after the initial diagnosis and 24 months after the diagnosis of lung metastases, the patient was still alive with controlled disease.

DISCUSSION

Combination cisplatin and gemcitabine with low-dose bevacizumab followed by bevacizumab maintenance therapy produced a complete response lasting 12 months in a patient with metastatic collecting duct carcinoma. At relapse, the same regimen was restarted leading to partial remission. The disease is under control 24 months after the diagnosis of pulmonary metastases.

There appears to be only one published report describing the use of an anti-angiogenic agent in collecting duct carcinoma. Two patients were treated with radical nephrectomy and four courses of adjuvant chemotherapy with cisplatin-gemcitabine; multiple-site metastases and mediastinal lymphopathy were subsequently observed and survival time was 8 months [4]. At relapse, both patients were treated with second-line sunitinib. Multiple liver, lung, and bone metastases and mediastinal lymphopathy were observed after 2 cycles of therapy and both patients died eight weeks later. Their survival time was 8 months from initial diagnosis.

CONCLUSIONS

The concept of bevacizumab maintenance therapy is relatively new and data from prospective clinical trials in ovarian cancer are just emerging [5]. In view of our findings, a prospective multicenter trial with cisplatin, gemcitabine and bevacizumab in patients with metastatic collecting duct carcinoma is planned.

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