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A Case of Metastatic Collecting Duct Carcinoma Whose Massive Skull Bone Metastasis was Prominently Reossified by Gemcitabine Plus Cisplatin Chemotherapy Combined with Zoledronic Acid

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ABSTRACT

The present case underwent right laparoscopic radical nephrectomy for collecting duct carcinoma (CDC). Recurrence occurred in the lung and the bone (skull and lumber vertebra) in 2011. Gemcitabine plus cisplatin (GC) chemotherapy and monthly zoledronic acid (ZA) was then started. The massive skull bone metastases were prominently reossified after several courses of the therapy. The patient received 16 courses of GC chemotherapy and monthly ZA, and pulmonary metastases and reossified skull bone metastases were stable for 23 months. Although we cannot verify the adoptive effect of ZA on the reossification, this combination may be effective for CDC bone metastases.

Introduction

Patients with metastatic collecting duct carcinoma (mCDC) have reportedly very poor prognosis.[1] Gemcitabine plus cisplatin (GC) chemotherapy is now recommended for the first-line treatment for mCDC in National Comprehensive Cancer Network (NCCN) guideline. Also, several case reports showed efficacy of targeted therapy for mCDC.[2] However, the treatment strategy for mCDC still needs to be improved to prolong patients' survival.

We here report a case of mCDC with bone and pulmonary metastases for in whom GC chemotherapy combined with monthly zoledronic acid (ZA) was effective.

Case presentation

A 70-year-old man presented with asymptomatic gross hematuria. A tumor in the right kidney was detected by imaging studies (Fig. 1A and B). The preoperative diagnosis was T1b renal cell carcinoma, and laparoscopic radical nephrectomy was performed in 2009. In operation adhesion around the tumor was severe and lymph node swelling at renal hilum was observed. After the removal of the right kidney a limited lymph node resection was performed. The pathological diagnosis was collecting duct carcinoma (CDC) (Fig. 1C and D) with severe lymphovascular invasion. Tumor cells were immunohistochemically positive for cytokeratin 7, high molecular weight cytokeratin (clone 34βE12) and α-methylacyl CoA-racemace (clone P504S), and negative for cytokeratin 20, epithelial membrane antigen, CD10, and WT1. The pathological tumor stage was T3a (invasion to perinephric fat tissue) and there was no pathological lymph node metastasis. In September 2011, a computed tomography (CT) showed multiple pulmonary nodules and pleural effusion (Fig. 2A). A diagnosis of pulmonary metastases and pleural dissemination of CDC was made because cytology of the pleural effusion showed malignant cells, and there were no primary malignancies detected in other organs by imaging studies, including positron emission tomography. Broad metastasis in the skull (Fig. 2C) and vertebral metastasis (L2) was also found by bone scintigraphy and CT scanning. GC chemotherapy (started with full dosages) and ZA (3 or 4 mg, every 4 weeks) was started in December 2011. After the start of the treatment, the patient's dyspnea gradually improved. After four courses of GC chemotherapy, his pulmonary metastases were stable and pleural effusion markedly decreased (Fig. 2B). In addition, osteolytic changes in the skull were noticeably reossified (Fig. 2D and E). The patient

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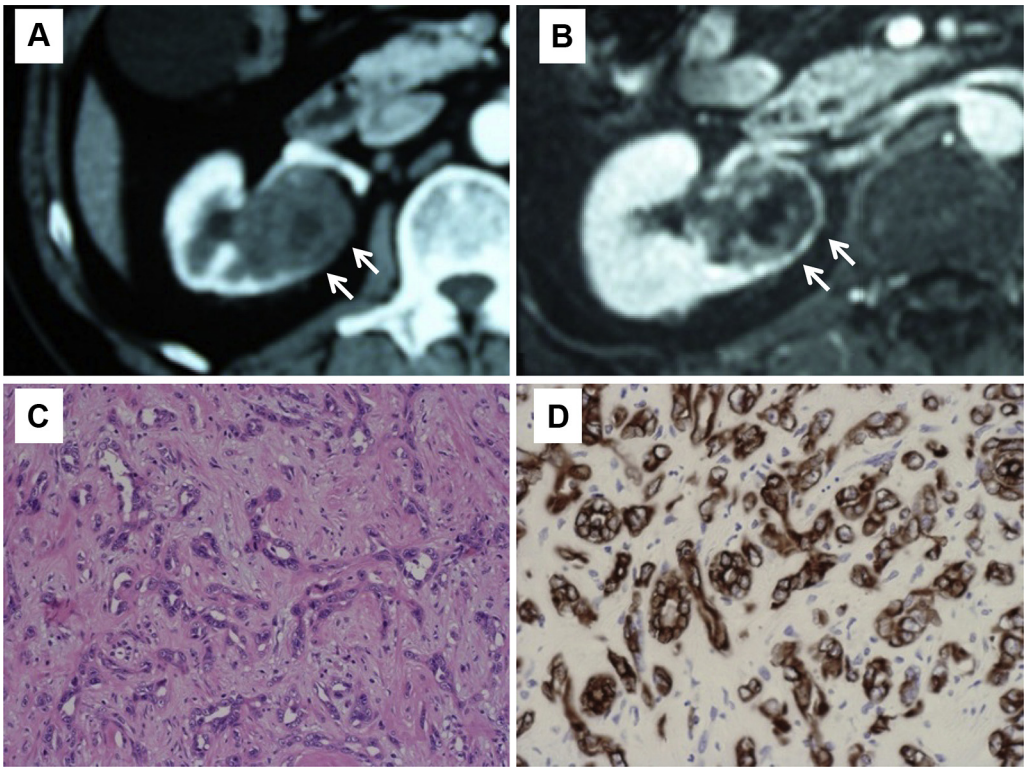

Fig. 1. A: Computed tomography (CT) image. CT showed poorly enhanced tumor (5 cm) in the upper side of the right kidney. B: MRI image. The renal tumor appeared to be covered by thin renal parenchyma. C: Hematoxylin-Eosin staining. The tumor was diagnosed as collecting duct carcinoma. Tumor cells invaded to the perinephric fat tissue at the renal hilus, and severe lymphovascular invasion were seen. D: Representative immunostaining (for cytokeratin 7). Tumor cells were strongly positive for cytokeratin 7.

received 16 courses of GC therapy combined with monthly ZA. Intermittent drug holidays were sometimes inserted considering patient's general condition. During the treatment, pulmonary metastases and reossified skull bone were stable (Fig. 2F). The main side effects were grade 3 neutropenia and grade 3 anemia. After 16 courses of GC chemotherapy, the performance status of the patient worsened considerably due to a subdural hematoma that occurred during fall accident, and subsequent febrile neutropenia caused by a fungal infection at the central venous catheter. The pulmonary metastases worsened as a result of the deterioration of his general condition. The patient died of carcinomatous lymphangitis of the lung 28 months after the metastasis presentation.

Discussion

Metastatic CDCs (mCDCs) have very poor prognosis in the majority of cases. Cytokine therapy is not effective; however, GC therapy appeared to be one of the treatment options because of the pathological similarity between CDC and urothelial carcinoma. Oudard reported that the median progression-free survival (PFS) and overall survival (OS) of patients with mCDC who received gemcitabine plus cisplatin or carboplatin chemotherapy were 7.1 and 10.5 months, respectively.[3] Although in the present case dose of cisplatin was reduced after several course of GC therapy because of mild renal dysfunction, response continued for about 2 years. Because appetite loss and fatigue due to the chemotherapy was prominent, intermittent drug holidays were inserted for a concern about the deterioration of his general condition. Insertion of drug holiday to improve general condition might be one of reasons for durable disease control.

Recently, molecular targeted therapy has been reported to be effective for some cases of mCDC.[2] Procopio et al showed possible efficacy of targeted therapies for mCDC treatment.[2] We should further evaluate the rule of molecular targeted therapy as the treatment of mCDC in future.

Pecuchet et al reported that five patients with mCDC who received bevacizumab maintenance therapy after six courses of gemcitabine plus CDDP or carboplatin showed complete response in one patient, partial response in three, and stable disease in one.[4] In that report, the median PFS was 15.1 months and OS was 27.8 months. Their study suggested the possible efficacy of the combination between chemotherapy and maintenance targeted therapy.

In the present case, bone metastases in the skull were prominently reossified by the combination of GC therapy with monthly ZA. Kijima et al also reported that bone metastasis of renal cell carcinoma was reossified by radiotherapy combined by ZA.[5] Their case report suggested that ZA might have effect on reossification of osteolytic metastatic lesions in combination with treatments for bone metastasis, such as radiotherapy. Although we cannot verify the adoptive effect of zoledronic acid on the reossification, this combination may be an effective treatment for bone metastases of CDC.

Conclusion

GC chemotherapy combined with monthly ZA appeared to be an effective treatment for CDC bone metastases. The metastasis in the skull prominently reossified and was controlled for 23 months by this therapy.

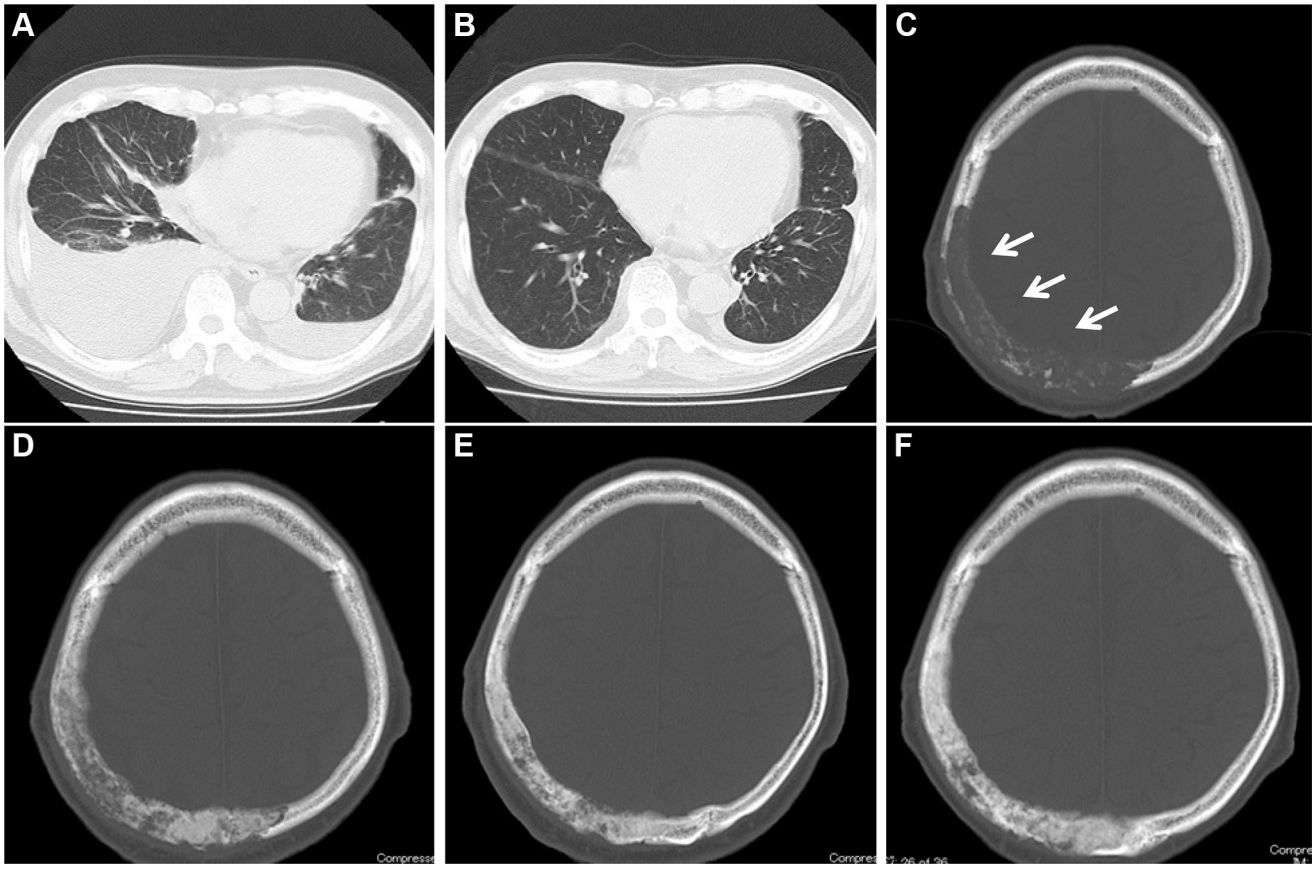

Fig. 2. A: Multiple lung metastasis (not seen in this picture) and pleural effusion were seen before systemic treatment. B: The pleural effusion markedly decreased after 4 courses of GC therapy. C: Broad metastasis in the skull before systemic therapy. D: The skull metastasis was markedly reossified after 4 courses of GC therapy. E: The skull metastasis after 7 courses of GC. F: The skull metastasis after 15 courses of GC.

Conflict of interest

None.

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