Successful Treatment of Hurthle Cell Thyroid Carcinoma with Lung and Liver Metastasis Using Docetaxel and Cisplatin

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Received November 23, 2011; accepted August 18, 2012

A 36-year-old man was found to have Hurthle cell carcinoma, as diagnosed with surgical pathology after a lobectomy of the thyroid. A post-operative magnetic resonance imaging scan revealed a small mass in the lower pole of the right thyroid and a computed tomography scan showed bilateral nodules in the lungs and the neck, and multi-focal disease in the liver. He was treated with a docetaxel and cisplatin chemotherapy regimen. After six cycles of the docetaxel and cisplatin regimen, we could hardly find the lesions in the lungs and the liver, and the patient presented a complete tumor response lasting 17 months and has not shown any tumor recurrence till now. The docetaxel and cisplatin regimen may be an effective chemotherapy regimen for multi-metastases of Hurthle cell cancer.

Key words: Hurthle cell carcinoma – metastasis – chemotherapy

INTRODUCTION

Papillary and follicular cell carcinomas are the most pathological types of thyroid carcinomas, which account for 90% of all types of thyroid cancer. Hurthle cell thyroid cancer, first described in 1894 by Hurthle (1), is a rare type, accounting for only ~3–7% of all thyroid carcinomas (2,3). The majority of the patients first presented with a solitary thyroid mass. This kind of tumor has a tendency to metastasize bones and the lungs that are the most common metastasized organs. Liver metastasis is very rare and we report a case of metastatic Hurthle cell carcinoma (HCC) with both liver and lung metastases. The mortality of Hurthle cell cancer is higher than that of other types, treatment of metastatic HCC is not well advanced and few institutions have extensive experience in it. Lobectomy or thyroidectomy, and radioactive iodine treatment are recommended by most surgeons and oncologists. There is no sufficient evidence for the efficacy of chemotherapy. We tried to administer chemotherapy to the patient, because he had extensive metastases and nearly no uptake radioactive iodine. Doctaxel (docetaxel) and cisplatin (DC) are widely used for many cancers, and they are recommended for head and neck cancer. There are clinical trials and case reports that have shown that paclitaxel and docetaxel can be successfully used for differentiated and anaplastic thyroid cancer, so we gave him chemotherapy with DC. The patient presented a complete tumor response lasting 17 months and has not shown any tumor recurrence till now, and the response suggested that DC chemotherapy regimen may be an effective treatment for metastatic HCC.

CASE REPORT

The patient was a 36-year-old man who initially presented with a 4-cm mass in the right lobe of the thyroid in October 2010. When referred to a hospital, he did not complain of cough, dysphagia or pain. A thorax computed tomography (CT) scan showed non-unusual disease in the lungs and the mediastinum. He underwent excision of the right thyroid
lobe, and the surgically excised pathology specimen was initially found to be follicular adenoma with a cystic lesion with negative margins. At the same time, the pathology specimen was examined by another superior hospital and was reported to be Hurthle cell with low differentiation (Fig. 1). The immunohistochemistry demonstrated TTF-1 (++) , CK8/18 (+), PCK (+), VIM (+), TG partly (+), Syn (-) and Cga (-), and there was no evidence of aggressive capsular or vascular invasion. The patient was Stage II in accordance with the TNM staging system of the UICC/AJCC, 7th edition (4). After the operation, an MRI scan revealed a small residual mass in the lower pole of the right thyroid, and a CT scan showed bilateral nodular disease in the lungs and the cervical lymph nodes and multi-focal disease in the liver (Figs 2A and 3A). He did not complain of pain, pressure, difficulty in swallowing or any respiratory symptoms. Tumor markers as well as thyroid function were normal, and the thyroglobulin (Tg) level was at the normal range before and after the treatment. The patient was a farmer non-smoker and a teetotaller and had no history of exposure to ionizing radiation, no history of thyroiditis or benign thyroid adenoma, no history of hypertension or heart disease and had no family history of thyroid cancer or any other malignant carcinomas. Neck, thorax and abdominal CT scans showed an irregular nodule in the right thyroid lobe, bilateral nodules in the lungs and multi-focal disease in the liver. A Na 99 mTc 04 scan was negative in the thyroid region, and 99 mTc-MDP scan of the whole-body bone showed no accumulation of abnormal radioactivity. He was treated with a DC chemotherapy regimen. The administration schedule was as follows: docetaxel (75 mg/m², day 1) was administered intravenously for 60 min followed by cisplatin (25 mg/m², days 1-3); the treatment was repeated every 21 days. After two cycles of DC regimen, response evaluation through thorax and abdominal CT scans showed partial response of metastasis in bilateral lungs but no obvious change in the liver (Figs 2B and 3B). Then, he received another two cycles of DC regimen with the same dose. After four cycles of chemotherapy, a recheck CT scan suggested that the lung and liver nodules had reduced (Figs 2C and 3C); thyroid and cervix MRI showed no abnormal signal in the thyroid but several small cervical lymph nodes. Tumor markers were all negative and his thyroglobulin levels remained under normal range. According to the effective response, the patient was advised to continue chemotherapy, and he requested to return to the hospital in his native town for chemotherapy with the same regimen. After six cycles of DC regimen, thorax and abdominal CT scans were done again for reevaluation, and the results were exciting, we could almost see the lesions in the lungs and the liver (Figs 2D and 3D). The patient had good tolerance without several adverse effects except for mild anorexia and vomit (limited to Grade 1). After that, the patient returned to the hospital for regular follow-up, he did not complain of being uncomfortable and Tg remained under standard level, and there were no hints of tumor recurrence from imaging examinations.

DISCUSSION

Hurthle cell thyroid neoplasm, also known as oncocyctic or oxyphilic cell neoplasm, is considered a variant of follicular carcinoma (FC) of thyroid according to the World Health Organization. It is commonly referred to as FC, oxyphilic type. There are many factors that increase the risk of HCC, including iodine excess, previous history of thyroid disease and radiation exposure, and a germ-line mutation on chromosome 19p 13.2 has been documented in some patients with familial HCC (5). Clinically, female-to-male predominance ranges from 2:1 to 5:1 (6). The peak age of incidence is 50-60 years (3,6,7). About 20-30% of the cases had metastatic extension at the time of initial treatment (3,8).

Oncocytic cells in the thyroid are often called Hurthle cells, which were first described by Askanazy in 1898 (1). They are also called oxyphilic cells and eosinophilic cells. The Hurthle cell, which is a follicular-derived cell, has a ‘swollen’ cytoplasm because of substantial eosinophilic, abundant granular cytoplasm and accumulation of altered mitochondria (1). When Hurthle cells comprise >75% of an encapsulated nodule, the lesion is termed a Hurthle cell neoplasm (HCN). The proliferation of oncocytes gives rise to hyperplastic and neoplastic nodules.

Although HCC is classified as FC by the WHO, it has a different oncocyctic expression and worse prognosis, and now is considered a distinct pathologic type from FC (5,9). Compared with papillary and follicular thyroid carcinomas, HCC is characterized by higher rates of recurrence, metastasis and cancer-related mortality (5). A study reported that undifferentiated thyroid carcinomas has 100% mortality, and a median survival after diagnosis is 5.5 months, and Hurthle cell cancer has 75% mortality with a mean survival of 33 months (2). This patient with Hurthle cell cancer and low differentiation may have a worse prognosis.

HCNs of the thyroid are subdivided into benign Hurthle (Hurthle) cell adenomas (HCA) and malignant HCCs, and it is difficult to distinguish between them. A definitive way of diagnosing HCC is histopathological examination of the surgical specimen. Malignant disease is found to have vascular invasion, extrathyroidal tumor spread, and metastasizes to local lymph nodes or distant organs (10). There are also many clinical risk factors for predicting malignant HCC in the absence of a reliable preoperative diagnostic test, and for HCC progression and survival. The predictive factors for carcinoma are higher age, tumor diameter, thyroid volume, Tg concentration, higher tumor staging, sex and type of surgery (11,12).

HCC is a rare type of malignant carcinoma (carcinoma), and few institutions have enough experience in it. Therapeutic administrations for metastatic Hurthle cell cancer are limited. Surgery is the primary mode of treatment, and whether patients with HCC should be treated by total...
thyroidectomy or less extensive thyroidectomy is controversial. Most Hurthle cell cancers almost do not uptake radioactive iodine, and some probably do because of the uptake in the follicular component. The clinical role of radioactive iodine treatment is largely limited to post-surgical ablation. But many patients have actually received the treatment for metastatic disease, recurrent lesions or small residuals after surgery, and have had a satisfactory effect (8,12), and it has been reported that although radioactive iodine treatment has no survival benefit, it shows better outcomes for adjuvant ablation therapy (13). Hormone withdrawal and recombinant human TSH stimulation have been used with variable success rates. Somatostatin receptor scintigraphy may image HCC, especially when Tg is >10 ng/ml. Therefore, a somatostatin analog has the potential for the treatment of HCC (14). Radiofrequency and cryoablation have gained clinical interest recently (15). These procedures, which have been used to treat difficult metastases in liver, lung, renal and prostate cancers, may alleviate pain and reduce tumor bulk, even if survival data are not readily available.

Figure 1. Pathological specimen, Hurthle cells are large cells with large hyperchromatic nuclei, and nuclear division can also be seen (hematoxylin–eosin, original magnification ×400).

Figure 2. Pathological specimen: (A) before chemotherapy; (B) after two cycles of docetaxel and cisplatin chemotherapy; (C) after four cycles of chemotherapy and (D) after six cycles of chemotherapy. The arrows show the metastasized nodulars in the lungs.
Chemotherapy is not validated to be effective (13). I have not heard of any clinical trials that administered docetaxel + cisplatin for Hurthle cell cancer. But there are trials for DC in head and neck cancer (16,17). DC are widely used for differentiated thyroid cancer, and there are clinical trials and case reports to show that paclitaxel and docetaxel are effective in anaplastic thyroid cancer, which is one of the most aggressive malignant carcinomas and resistant to chemotherapy. Ain et al. (18) reported that in a phase II study, 10 of 19 patients with anaplastic thyroid cancer responded to paclitaxel, including 1 complete response and 9 partial responses. Kawada et al. (19) showed that in seven anaplastic thyroid cancer patients who were given docetaxel treatment, one achieved complete response and two maintained a stable response, and the response rate was 14%. A retrospective analysis in Australia (20) showed that radiation combined with docetaxel was effective for anaplastic thyroid cancer, four of the six patients presented complete tumor response and two of them partial response. This patient had Hurthle cell cancer with multiple metastases after surgery, and systematic chemotherapy may be a proper treatment for him. From the above experience paclitaxel and docetaxel have been shown to be effective in treating differentiated and anaplastic thyroid cancer. So we gave the patient this regimen though there is not experience in Hurthle cell cancer.

It is crucial to understand the natural course, genetics and biology of these aggressive and rare tumors and develop efficacious therapies. The management of high-risk thyroid cancers can be enhanced by the use of novel multi-modality imaging and therapeutic techniques. Our patient had several adverse prognostic indicators, including sex, the Hurthle cell histology, low differentiation and distant metastatic disease involving the lung and liver occurring shortly after the surgery. Metastases to liver are unusual. We got two reported cases of liver metastasis (metastasis) (7,21): one of the patients, who showed solitary liver metastasis, was treated with hepatic lobectomy and got good clinical conditions, and the other received chemotherapy, surgical resection and external irradiation and achieved a complete locoregional control, but ultimately died of liver metastasis 5 years after the treatment. For our patient, we preferred chemotherapy because the metastatic disease was extensive and was not accessible to surgical resection or radiation. The patient achieved nearly complete remission of lung metastasis and primary tumor and >50% remission of metastases in the liver after four cycles of DC regimen chemotherapy. Then he received another two cycles and had complete remission of lung and liver metastases after six cycles. He excitingly achieved complete response lasting 17 months and is still alive. The DC chemotherapy regimen may be a promising treatment for HCC with extensive metastasis, but many clinical trials are needed to verify its efficacy.

**Conflict of interest statement**

None declared.

**References**


