Treatment of esophageal cancer with multiple liver metastases: a case experience of sustained complete response

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Abstract
Esophageal squamous cell cancer with distant metastases has a poor prognosis. The metastatic sites usually involve the liver, bones, and lungs. Treatment of metastatic disease is essentially palliative and based on chemoradiotherapy. A 57-year-old man with a solitary metastatic mass of 82 × 58 mm in the left liver was treated on 19 October 2012. Irinotecan and cisplatin combination chemotherapy and nimotuzumab targeted therapy were administered. The liver metastatic mass was treated by stereotactic Gamma Knife radiosurgery. Complete remission of the primary disease and hepatic lesion was achieved, and no local or distant recurrence was found during the 7-year follow-up. Because extrahepatic lesions were ruled out and the local disease was completely locoregionally controlled, the use of stereotactic Gamma Knife radiosurgery to remove the hepatic lesion was justified and produced a reasonable outcome.

Keywords
Metastases, complete response, prognosis, esophageal squamous cell cancer, stereotactic radiosurgery, liver mass

Introduction
Esophageal squamous cell cancer (EPC) is a tumor with a poor prognosis, and the median survival time is only about 6 months. Treatments including radiotherapy, targeted therapy, and chemotherapy have made only limited progress in

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improving the generally disappointing outcomes in recent years. Targeted therapy is a useful treatment approach in breast cancer, lung cancer, and gastric cancer, but targeted therapy in esophageal cancer is still poorly defined. We herein report a case of EPC with large liver metastases that was successfully treated with radiotherapy, chemotherapy, and targeted therapy.

Case report
A 57-year-old man presented with a left liver mass of 82 × 58 mm that had been detected by B-mode ultrasonography. He had a history of untreated esophageal cancer and exhibited no progressive dysphagia, pain behind the sternum, melena, or bloody stool. Gastroscopy revealed irregular mucosal processes leading into the lumen, producing surface irregularity, erosion, and congestion about 35 cm from the teeth in the medial and lower esophagus (Figure 1). Histopathological examination revealed EPC (Figure 2(a)). Immunohistochemistry examination showed positive expression of epidermal growth factor receptor (EGFR) (Figure 2(b)). Abdominal computed tomography showed thickening of the medial and lower esophageal wall, many metastatic lymph nodes in the cardia, and several hepatic masses (Figure 3(a), (c)). Abdominal B-ultrasound showed that the liver size was within the normal range and that its capsule was smooth. The distribution of ultrasonic light spots was uniform. The left liver contained an 82-×-58-mm mass and the right liver contained an 87-×-75-mm mass; both had well-defined boundaries and slight hyperechogenicity. According to the American Joint Committee on Cancer Staging, the EPC was stage IV (T3N1M1). Irinotecan and cisplatin chemotherapy was administered, and nimotuzumab targeted therapy was given every 3 weeks for 3 cycles. The diameter of the hepatic lesions significantly decreased along with a remarkable reduction of the EPC by the end of the chemotherapy and targeted therapy sessions.

Figure 1. Gastroscopy showed esophageal squamous cell cancer about 35 cm from the teeth in the medial and lower esophagus.

Figure 2. (a) Histopathological examination revealed esophageal squamous cell cancer (hematoxylin and eosin, ×100). (b) Immunohistochemistry showed positive expression of epidermal growth factor receptor. (c) Negative control (negative expression of epidermal growth factor receptor).
The concurrent liver metastases were treated by stereotactic Gamma Knife radiosurgery (Figure 3(d)). No evidence of other organ metastasis was found during the 7-year follow-up.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Shaoxing University, Shaoxing People’s Hospital. The patient and his relative provided consent for publication of this report.

**Discussion**

The liver is one of the main sites of metastasis from EPC. Autopsy data show that considerable numbers of patients with EPC die of liver metastasis. The standard palliative treatment for metastatic EPC is combined chemotherapy. In the present case, neoadjuvant treatment was given with a targeted drug (cetuximab) and combined chemotherapy (paclitaxel and cisplatin), and partial remission was achieved as shown by the decrease in the diameter of the EPC and hepatic lesions.

In some studies, the response rate to irinotecan and cisplatin combination chemotherapy for EPC with metastasis was about 30%, with median progression-free survival of 4.5 months and overall survival of 8.8 months. Lee et al. assessed the efficacy irinotecan and cisplatin in 32 patients with metastatic EPC. The results showed that 31.3% of patients achieved a partial response, with median progression-free survival of 4.4 months and overall survival of
There is increasing evidence that combination chemotherapy with irinotecan and cisplatin may be well tolerated and can be an effective treatment option for patients with EPC.

EGFR is a member of the ErbB receptor tyrosine kinase family and is overexpressed in many types of tumors, including colorectal cancer, lung cancer, breast cancer, and nasopharyngeal cancer. EGFR expression is associated with a poor prognosis. Nimotuzumab is a humanized anti-EGFR monoclonal antibody. In recent years, nimotuzumab has been used to treat head and neck squamous cell carcinoma and nasopharyngeal carcinoma. In some studies, nimotuzumab downregulated the expression of EGFR in esophageal squamous cell carcinoma and correlated downstream genes to inhibit the growth of EGFR-positive cells and increase cell sensitivity to chemotherapy or radiotherapy. In the present case, nimotuzumab in combination with irinotecan and cisplatin was well tolerated in the treatment for EPC with liver metastases.

In conclusion, a patient with EPC with liver metastasis at the time of diagnosis underwent treatment with nimotuzumab in combination with irinotecan and cisplatin. Because extrahepatic lesions were ruled out and the local disease was completely locoregionally controlled, stereotactic Gamma Knife radiosurgery to remove the hepatic lesions was justified and produced a reasonable outcome.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

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Authors’ contributions
Jiangfang Wang obtained the patients’ medical history, searched and reviewed the literature, drafted the manuscript, and edited the final version. Chaoyang Xu obtained the patient’s follow-up information, carried out the histopathological studies, and edited the final version of the manuscript.

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