

Hepatocellular Carcinoma with Metastasis to the Pharynx: Report of a Case

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Hepatocellular carcinoma (HCC) is rarely metastasized to the pharyngeal region. We report the case of a 59-year-old man admitted to our hospital with a complaint of hematemesis. An endoscopic examination revealed a tumor located in the left piriform sinus. Histological examination showed metastasis from HCC. Subsequent abdominal examinations demonstrated mild liver cirrhosis due to chronic HCV infection and primary nodules in the lateral segment of the liver. The pharyngeal tumor was completely removed by endoscopic polypectomy after radical hepatectomy for HCC. The patient died of recurrence of HCC 8 months after the first admission. With the presentation of this case, we review the literature reported so far.

Key words : Hepatocellular carcinoma, pharynx, metastatic tumor

INTRODUCTION

Although autopsies of patients dying of hepatocellular carcinoma (HCC) have revealed the evidence of metastases in 50-75% of cases [1], the frequency of the extrahepatic metastases in clinical presentation is relatively low compared to that of other primary carcinomas. Usually metastasis from HCC occurs, in descending order of frequency, to the lung (41.4-51.6%), lymph nodes (26.7-37.9%), peritoneum (4.0-10.9%), gallbladder (4.3-11.6%), adrenal glands (5.8-10.9%) and bone (4.8-8.8%) [2]. Metastasis to the pharyngeal region is extremely rare. We recently experienced a case of HCC with metastasis to the hypopharynx, which was the first manifestation of the disease. There have been only nine previous cases reported in the literature. We review these cases, and discuss their diagnosis, metastatic pathways, and prognosis.

CASE REPORT

A 59-year-old man was admitted to Tokai University Hospital with a complaint of he-

matemesis in September 1997. On physical examination, his abdomen was soft and flat, and the liver was not palpable. Laboratory tests on admission revealed decreased red blood cell count ($325 \times 10^4/\text{mm}^3$) and hemoglobin (9.9 g/dl) level, and normal platelet count ($21 \times 10^4/\text{mm}^3$). His serum aspartate aminotransferase (AST; 208 U/l), alanine aminotransferase (ALT; 205 U/l) and alkaline phosphatase (ALP; 365 U/l) levels were elevated and albumin (3.5 g/dl) level was decreased. Other liver parameters, total bilirubin (T.B; 0.4 mg/dl) level and prothrombin time (11.8 sec), were within the normal limits. The serum alpha-fetoprotein (AFP; 23.5 ng/ml) level was slightly elevated. Hepatitis B surface antigen was negative and hepatitis C antibody was positive. Plain chest x-rays showed no remarkable changes. An endoscopic examination revealed a 6 × 15 mm pediculated gray-white mass in the left piriform sinus, and it was slightly umbilicated (Fig. 1a). A biopsied specimen of the tumor revealed metastatic HCC. Neck computed tomography (CT) demonstrated an enhanced mass in the hypopharynx, with-

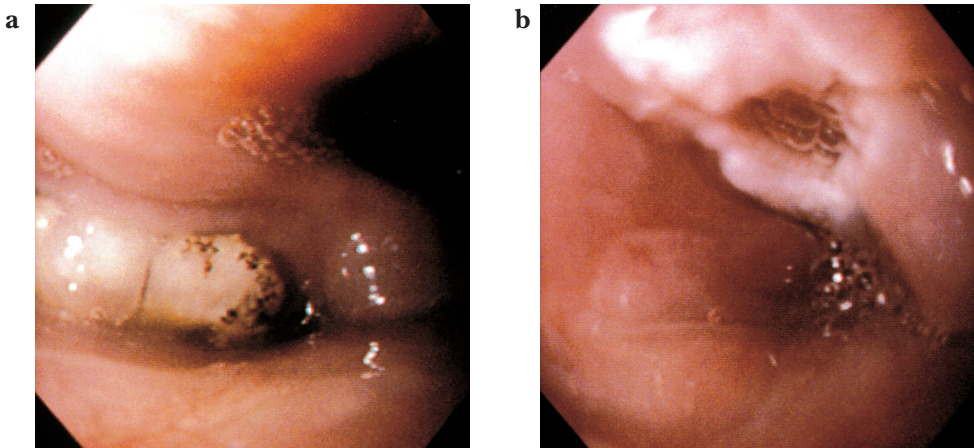


Fig. 1 a: Gastrointestinal endoscopy showed a pediculated gray-white tumor in the left piriform sinus of hypopharynx. b: The tumor was easily removed by endoscopic polypectomy.

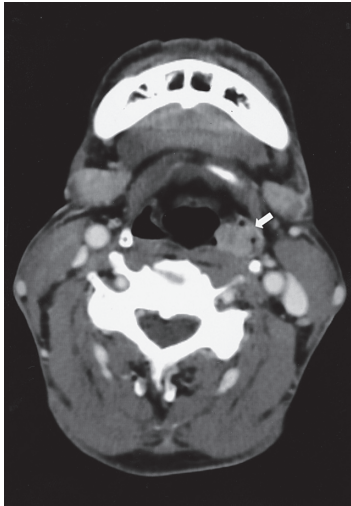


Fig. 2 Neck CT scan showed an enhanced mass in the hypopharynx (arrows).

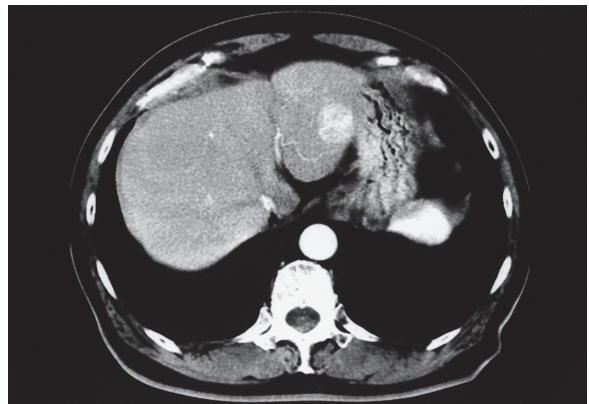


Fig. 3 Enhanced abdominal CT scan revealed well defined masses in the lateral segment of the liver.

out invasion to the ambient organs (Fig. 2). Subsequent abdominal CT scan revealed well defined masses in the lateral segment of the liver (Fig. 3), and arteriograms confirmed the presence of these lesions. Furthermore, abdominal x-ray and CT scan showed the bone metastasis of HCC to the 4th lumbar vertebrae. On October 1997, lateral segmentectomy was performed successfully. Four days later, the metastatic tumor, which was motile and had no adhesion to the surrounding tissue, was easily removed by endoscopic polypectomy (Fig. 1b). Macroscopically intact squamous mucosa was overlying the nodule. Microscopic examination showed a

diffuse infiltrate of atypical polygonal cells which contain hyperchromatic nuclei in the eosinophilic cytoplasm. The tumor cells were arranged in trabecular structures with irregular lobulation. These features were consistent with metastatic HCC with moderate differentiation (Fig. 4a, b, c). The resected margin was free from carcinoma. The patient received a course of adjuvant radiotherapy consisting of 60 Gy to the resected site in the hypopharynx over 5 weeks. One month later, the serum AFP level decreased to 3.6 ng/ml. He remained free from any symptom for 5 months postoperatively, until he developed jaundice. Abdominal ultrasonog-

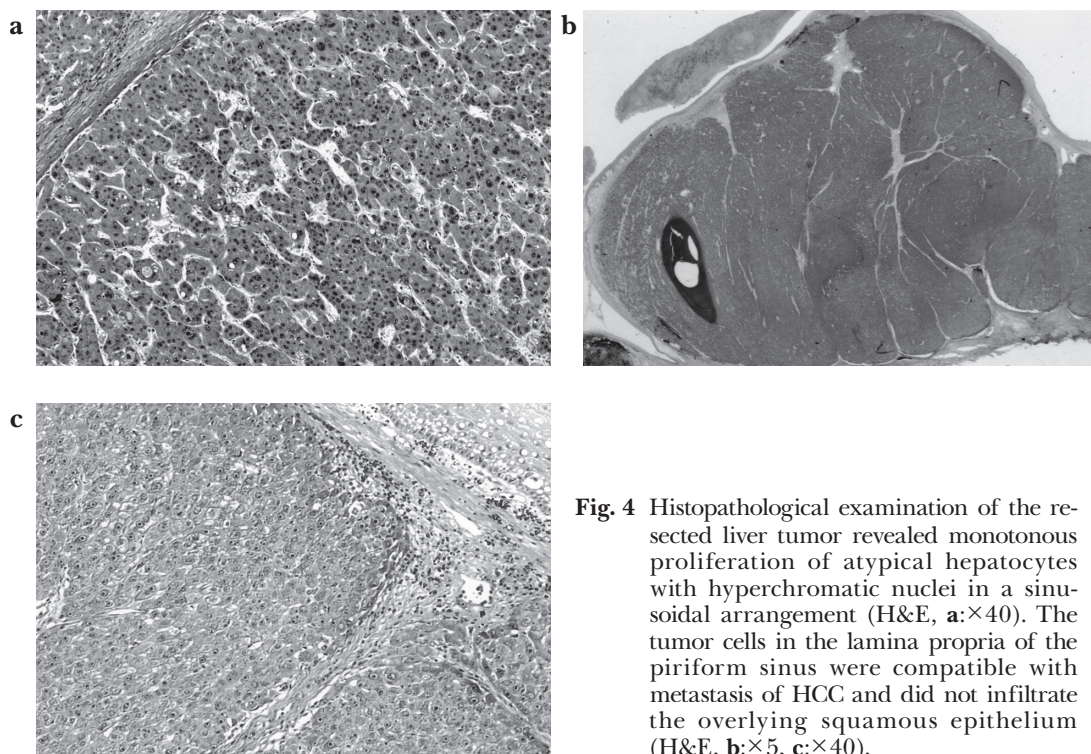


Fig. 4 Histopathological examination of the resected liver tumor revealed monotonous proliferation of atypical hepatocytes with hyperchromatic nuclei in a sinusoidal arrangement (H&E, **a**: $\times 40$). The tumor cells in the lamina propria of the piriform sinus were compatible with metastasis of HCC and did not infiltrate the overlying squamous epithelium (H&E, **b**: $\times 5$, **c**: $\times 40$).

raphy detected multiple recurrent nodules in the liver. AFP level was again elevated to 21.5 ng/ml. After his 2nd admission in March 1998, recurrent hepatic tumors grew rapidly, and the patient's condition deteriorated day by day. He died of liver failure 8 months after his first presentation. Autopsy was not performed.

DISCUSSION

The metastasis to the pharyngeal region is extremely rare. Only 9 HCC cases with metastasis in the pharyngeal region have been reported [2-5]. Table 1 describes the 9 previously reported cases as well as the present case. The age range was from 33 to 71 years old, 61 being the average. All of these patients were men. Eight of ten patients had tonsillar metastasis in the pharynx or palatine. Our patient was the second described case of metastasis present in the lamina propria of the pharynx, and this metastasis appeared before the carcinoma had started clinically manifesting itself. In general, the symptoms caused by the pharyngeal metastatic lesion are unspecific, but depend on the size of the tumor and on secondary

alterations such as ulceration and infection [6]. In our case, it was thought that due to flexibility and vascularity of the tumor and lack of cervical adenopathies, just bleeding occurred without pharyngeal discomfort and swallowing difficulty.

Concerning the diagnosis, usually a gross and endoscopic examination does not provide any specific hallmark. Marker [7] *et al.* has reported that severe bleeding was a usual complication in patients with HCC in which a biopsy was carried out. However, the reviewed literature showed that in 8 of the 10 cases (80%), including ours, the metastatic tumors were diagnosed by biopsy without great loss of blood, and some authors emphasize the importance of the biopsy for immediate diagnosis and treatment [2].

The mechanism of metastasis to the pharyngeal region is controversial. A hematogenous route has been quoted to be characteristic for primary neoplasms of the abdomen [8]. HCC also likely causes hematogenous metastasis to other organs [9]. Tumor cells may circulate through the vena cava, beyond the pulmonary filters to the heart, finally being distributed to the pharyngeal region

Table 1 Previously reported cases of metastasis to the pharyngeal region from HCC.

No.	Patient data			Metastasis in the pharyngeal region				After diagnosis of the metastasis	
	First author	Age	Gender	Symptom	Location	Verification of diagnosis	Interval after diagnosis of HCC	Treatment	Outcome
1	Funai	33	M	Bleeding	Palatine tonsil	Biopsy	2m	Operation	Died 4m
2	Saeki	66	M	Neck mass	Palatine tonsil	Biopsy	1y6m	Chemo	Died 2m
3	Kato	58	M	Dysphagia	Pharynx	Biopsy	6y5m	Chemo	Died 4m
4	Ciriza	71	M	Bleeding	Pharyngeal tonsil	Polypectomy	3y	None	Died 8m
5	Llnes	71	M	?	Palatine tonsil	Polypectomy	-	None	Died 10m
6	Takesaki	65	M	Bleeding	Palatine tonsil	Biopsy	8m	None	Died 1m
7	Nakahara	69	M	Pharyngeal discomfort	Palatine tonsil	Biopsy	-	Operation	Alive
8	Sadanaga	54	M	Pharyngeal discomfort	Palatine tonsil	Biopsy	-	?	?
9	Ueda	65	M	Pharyngeal discomfort	Palatine tonsil	Biopsy	-	Polypectomy	Died 6m
10	our case	59	M	Bleeding	Hypopharynx	Biopsy	-	Polypectomy+RT	Died 8m

M, male; F, female; ?, unknown(not described); y, years; m, month; -, no interval; Chemo, chemotherapy; RT, radiotherapy

throughout the arterial systemic circulation. However, others reported that tumor cells in the majority of cases reach the head and neck by bypassing the lungs, possibly through the vertebral venous plexus of Baston [10]. In the present case, due to the cascading fashion of the defect from the pulmonary metastasis [11] and the evidence of vertebral involvement, we also speculate that the vertebral venous plexus may contribute to this metastasis.

The metastasis has been treated by surgery, radiotherapy, and chemotherapy. Our patient was the first case of the metastasis successfully treated by endoscopic procedure. Usually, metastases are a late event in the progression of HCC, and therefore prognosis after the assessment of these lesions is generally poor. Kanazawa and Sato [12] have previously reported that the mean survival rate after the appearance of oral metastases was 21 weeks, with a range between 2 weeks and 2 years. Similarly, in the cases with the pharyngeal metastasis, 8 patients (80%) died within one year after the first presentation of pharyngeal metastasis. Although the pharyngeal metastasis is rare, physicians should be aware of the clinical and prognostic implications and thus make efforts to palliate the patient's symptoms as far as possible.

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