Original Article

Unusual metastasis of hepatocellular carcinoma

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ABSTRACT

Hepatocellular carcinoma is the most common primary tumor of the liver and is estimated to cause more than a quarter of a million deaths each year throughout the world. Extrahepatic metastasis of HCC occurs in about 30-50% of patients, and it depends on HCC stages.

Materials and methods: We carried out a retrospective study including 16 patients, 10 men and 6 women with a mean age of 58.5 years ranging from 37 years to 75 years. 13 patients had cirrhosis due to hepatitis C virus, 1 patient had cirrhosis due to viral B infection and 2 patients had HCC within a non-cirrhotic liver. All patients had one or more HCC, ranging in size from 2 to 10 cm. The AFP was normal in 11 cases and elevated in 4 cases (> 200 ng / ml). We collected 4 cases of adrenal metastases, 3 costovertebral metastases, 2 gastric metastases, 2 brain metastases, 1 cranial metastasis, 1 clavicular metastasis, 1 ovarian metastasis, 1 nasopharyngeal metastasis, and a case of metastasis in the path of percutaneous biopsy of HCC. In 4 cases the diagnosis of HCC and metastasis was synchronous while in 12 cases median time from diagnosis of hepatocellular carcinoma and extrahepatic HCC was 15.5 months. Therapeutic abstention was decided in 14 patients for the advanced stage of the disease. Cutaneous metastasis was resected surgically and HCC occurring in healthy liver was treated by lumpectomy and upper pole gastrectomy in gastric metastasis. The average survival was estimated at 14 months with a decline of 17.3 months, 6 cases were lost to follow and 6 deaths occurred in our series.

Conclusion: The incidence of unusual and extrahepatic metastasis of HCC diagnosed during clinical course was not frequent. The diagnostic procedures for extrahepatic metastases have not been standardized, however considering the substantial advances in treatment of HCC, the detection of extrahepatic HCC is crucial for patients to receive appropriate therapy, which ultimately determines patient survival.

Key words: Cystic Fibrosis, pancreatic function, pancreas insufficiency, Fecal elastase-1

INTRODUCTION

Hepatocellular carcinoma is the most common primary tumor of the liver and is estimated to cause more than a quarter of a million deaths each year throughout the world. Extrahepatic metastasis of HCC occurs in about 30-50% of patients, and it depends on HCC stages. The most frequent site is lung, followed by lymph node, bone, and adrenal gland. Extrahepatic metastases to unusually sites from HCC have been reported in a few case reports. We report cases of patients with unusual extrahepatic metastatic sites from HCC.

MATERIALS AND METHODS

We carried out a retrospective study of 16 patients with unusual extrahepatic metastasis of hepatocellular carcinoma out of 1047 cases of HCC treated at the hepatogastroenterology department "Medicine C" of the IBN SINA University Hospital during the past 22 years. The diagnosis was suspected based on clinical signs and imaging data, and confirmed by histology when the biopsy of the metastasis was possible, were excluded from this study, patients with lung metastasis, lymph node and portal thrombosis.
RESULT

Our study included 16 patients, 10 men and 6 women with a mean age of 58.5 years ranging from 37 years to 75 years. 13 patients had cirrhosis due to hepatitis C virus, 1 patient had a cirrhosis due to viral B infection and 2 patients had HCC within anonciritic liver. All patients had one or more HCC, ranging in size from 2 to 10 cm. The AFP was normal in 11 cases and elevated in 4 cases (> 200 ng / ml). We collected 4 cases of adrenal metastases, 3 costovertebral metastases, 2 gastric metastases, 2 brain metastases, 1 cranial metastasis, 1 clavicular metastasis, 1 ovarian metastasis, 1 nasopharyngeal metastasal, and a case of metastasis in the path of percutaneous biopsy of HCC. In 4 cases the diagnosis of HCC and metastasis was synchronous while in 12 cases median time from diagnosis of hepatocellular carcinoma and extrahepatic HCC was 15.5 months. Therapeutic abstention was decided in 14 patients for the advanced stage of the disease. cutaneous metastasis was resected surgically and HCC occurring in healthy liver was treated by lumpectomy and upper pole gastrectomy in gastric metastasis. The average survival was estimated at 14 months with a decline of 17.3 months, 6 cases were lost to follow and 6 deaths occurred in our series.

The following table summarizes all cases of unusual extrahepatic metastasis of hepatocellular carcinoma collected in our study:

Table 1 : all cases of unusual extrahepatic metastasis of hepatocellular carcinoma collected in our study

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<th>Cases</th>
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DISCUSSION

Hepatocellular carcinoma (HCC) is the most frequent primary tumor of the liver representing the 6th digestive cancer in Morocco with an incidence of 0.8/100000 habitants. It is a devastating tumor, with a mean survival of much less than 1 year if left untreated. It often occurs in the background of cirrhosis present in about 90% of patients and commonly caused by hepatitis B or C infection, or alcohol consumption. Also, HCC may complicate noncirrhotic NAFLD with mild or absent fibrosis. The treatment of HCC depends entirely on the tumor stage. Despite advances in treatment of hepatocellular carcinoma (HCC), prognosis with extrahepatic metastasis remains poor. Their presence is an indicator of the aggressiveness of the primary HCC as a whole rather than an independent prognostic determinant. Extra-hepatic metastases in HCC occur in the advanced stages in about 30–50% of
patients. Patients with an advanced tumor stage reserves are not candidates for curative surgical treatments and are left with only palliative therapy. The detection of extrahepatic metastatic disease, therefore, becomes crucial when planning potential therapy for patients with HCC and should be used to avoid unnecessary surgical intervention. Since extrapathic metastases of HCC are relatively rare at the time of initial diagnosis, diagnosis procedures for extrapathic metastases have not been standardized. Positivity for viral markers, larger tumor diameter, multiple tumor nodules, the presence of vascular invasion, and the elevated tumor markers were associated with the development of extrapathic metastasis. The tumor frequently metastasizes via the lymphatic system, intrapathic blood vessels or direct infiltration. The most common sites of extrapathic metastasis are the lungs, followed by abdominal lymph nodes and bones. The most frequent location for metastatic HCC in our study population was the adrenal gland (%) which appears to be the second most common organ of hematogenous metastasis from hepatocellular carcinoma in autopsy reports although paradoxically there is found to be a very scarce number of the adrenal metastasis in clinical practice. These adrenal metastases should be differentiated from adrenal adenomas statistically more common. The arterial phase enhancement in an adrenal mass should suggest metastatic disease. Head and neck or subcutaneous metastases from HCC are uncommon. In literature HCC muscle and cutaneous metastases are caused by diagnostic procedures or locoregional ablative treatments. Cutaneous or subcutaneous metastases that are not related to biopsy needle tracks are rare. We report in this study a case of cutaneous metastasis caused by diagnosis procedure. Risk of tumor seeding with liver biopsy is estimated of 2.29%, with PEI (percutaneous ethanol injection) and biopsy was 1.4% while 0.61% with radiofrequency ablation (RFA) without biopsy and 0.95% with RFA and biopsy. Skeletal metastasis of HCC occurs less frequently compared with other cancers. Metastatic spread to the bones occurs in 13 to 16% of HCC patients and has been described thoroughly. It is considered a rare primary form of presentation. They appear to be unique among various hematogenous metastasis of HCC because they can occur before clinical manifestations of liver disease and are usually symptomatic. The most frequent location in our study was the axial skeleton which is similar to that reported in the literature. Gastric metastases of HCC are quite rare and hepatocellular carcinoma with gastrointestinal involvement has been reported in 4-10% of cases and mostly via direct invasion, hematogenous metastasis being rather rare. Shuangshoti et al reported that the secondary intracranial hepatic carcinomas were 1.3%-2.9% among intracranial metastatic tumors. Salvati et al suggested that the cerebral localization of the disease can be explained by both the important vascularization of the tumor and the frequent hemocoagulative alterations caused by the cirrhosis. Other unusual metastatic sites from HCC (diaphragm, pancreas, gall bladder, colon, pleura, peritoneum, shoulder soft tissue, ovarian and nasopharyngeal in our study) were published indicating that HCC can metastasize in any locations and suggesting that metastatic HCC should be a consideration in patients with a history of HCC or risk factors for the disease and present with unexplained lesions or symptom.

CONCLUSION

The incidence of unusual and extrapathic metastasis of HCC diagnosed during clinical course was not frequent. The diagnostic procedures for extrapathic metastasis have not been standardized, however considering the substantial advances in treatment of HCC, the detection of extraintrahepatic HCC is crucial for patients to receive appropriate therapy, which ultimately determines patient survival.

Figure 1: CT: Right adrenal metastasis (Case 1)

Figure 2: Endoscopy gastric metastasis (Case 8)

Figure 3: Cerebral metastasis (Case 12)
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