Neuroendocrine tumor may occur at any site throughout the body and of ten metastasize to the liver, but it is extremely rare to originate in the liver. Compared with other primary and metastatic liver cancers, primary hepatic neuroendocrine tumor has been documented to have quite a favorable outcome. Therapeutic strategies include surgical debulking and systemic chemotherapy with or without transcatheter hepatic arterial embolization (TAE). Managements are based on whether the curative or palliative therapy is possible. Embolization is rarely used due to unsatisfactory results. Better prognosis is noted in the majority of patients treated with Tumor debulking by liver resection or combination of multiple treatment modalities. This is the first report on the success fully use of TAE for a patient of probable primary neuroendocrine tumor of liver, who had been followed for 18 months with out evidence of tumor recurrence.

CASE REPORT

This 64-year-old woman was a hepatitis B virus (HBV) carrier with years of history of liver by hypertension and diabetes mellitus. She be gan to suffer from fever, chills, nau sea and vomiting one month be fore admission. The initial clinical examination showed tenderness over epigastric area and right upper quadrant without hepatosplenomegaly. There was no hisory of ma jor surgery, cirrhosis, jaundice, hematemesis, bronchospasm, flush ing, diar rhea or body weight loss. No car diac mur mur and abnormal breathing sound were noted. The
chest X-ray and electrocardiogram were normal. The complete blood count revealed a white blood cell count of 5300/mm$^3$ with neutrophils 63%, a red cell count of 4.3 × 10$^6$/mm$^3$, and a platelet count of 134 × 10$^3$/mm$^3$. Routine serum biochemical test and tumor markers, such as alpha-fetoprotein (AFP), carcinoembryonic antigen-125, carcinoembryonic antigen-153, carcinoembryonic antigen-199 (CA-199) and squamous cell carcinoma (SCC), were within reference limits. Elevated serum level of carcinoembryonic antigen 23.77 ng/mL (normal range less than 3.8 ng/mL) was noticed. The hepatitis markers showed negative for hepatitis C virus antibody (anti-HCV IgG) and positive for hepatitis B surface antigen.

The initial abdominal ultrasound showed an isoechoic mass containing several small cystic areas in the central portion of the liver (S8). Except that another low-density hepatic nodule can also be noted at S3. (B) Pre-arterial embolization, common hepatic arteriography depicts a 4.3 × 4.7 cm hypervascular tumor with homogenous staining over right lobe. Neither arterioportal shunting nor tumor thrombus in the portal vein was seen. Another smaller hepatic tumor was noted in the left lobe.

Fig. 1. (A) Pre-arterial embolization contrast-enhanced CT scan of abdomen revealed a homogenous low-density mass (5.4 cm in size) with several small cystic areas in the central portion of that mass in the right lobe of liver (S8). Except that another low-density hepatic nodule can also be noted at S3. (B) Pre-arterial embolization, common hepatic arteriography depicts a 4.3 × 4.7 cm hypervascular tumor with homogenous staining over right lobe. Neither arterioportal shunting nor tumor thrombus in the portal vein was seen. Another smaller hepatic tumor was noted in the left lobe. (A) Pre-arterial embolization contrast-enhanced CT scan of abdomen revealed a homogenous low-density mass (5.4 cm in size) with several small cystic areas in the central portion of that mass in the right lobe of liver (S8). Except that another low-density hepatic nodule can also be noted at S3. (B) Pre-arterial embolization, common hepatic arteriography depicts a 4.3 × 4.7 cm hypervascular tumor with homogenous staining over right lobe. Neither arterioportal shunting nor tumor thrombus in the portal vein was seen. Another smaller hepatic tumor was noted in the left lobe.

Accordingly, she was presumed to be a case of primary neuroendocrine tumor of liver. The first course of TAE was done smoothly. On angiography, two hypervascular tumors with homogenous staining were noted in liver (Fig. 1B). The angiography right after TAE showed total occlusion of these tumors. Unforunately, gallbladder stones with acute cholecystitis occurred right after TAE. Then the laparatomy was done to remove the inflamed gallbladder. During operation, no other intra-abdominal focus of primary tumor was found by careful check-up over the pancreas and gastrointestinal tract. The follow-up abdominal CT scans done in 2, 5, 7 and 9 months after the first TAE (Fig. 3A, 5 months after the first TAE) showed regression of the right hepatic tumor and no obvious change in the size of small left hepatic tumor. After a stable period, she was admitted again ten months after the initial diagnosis due to recurrence of tu-
The follow-up angiography was performed but no residual tumor was found (Fig. 3B). The patient kept regular follow-up and was in stable condition even 18 months after the initial diagnosis and free of further recurrence.

DISCUSSION

Neuroendocrine tumors arise from Kulchitsky cells, react positively with antichromogranin A antibody and contain neurosecretory granules with positive argentophilic reactions. A recent publication clarifies all neoplasms that display neuroendocrine differentiation (including carcinoid tumor) as “neuroendocrine tumors”. Neuroendocrine tumor is common in the gastrointestinal tract, but is extremely rare in the liver. The possible histogenesis of hepatic neuroendocrine tumor is...
aberrant pancreatic tissue in liver, neuroectodermal or germ or multipotential primitive cells, and neuroendocrine-programmed ectoblast. The diagnosis of a neuroendocrine tumor of hepatic or germ origin may be very difficult, because the liver is a frequent site of metastasis from intestinal neuroendocrine tumors, which can be difficult to detect. In our patient, the hepatic or germ of the tumor was presumed by the absence of any alternative primary source for the tumor by careful history and clinical examinations (UGI endoscopy, small intestine, barium enema, colonoscopy, CXR, ECG, tumor marker, etc.), surgical exploration due to acute cholecystitis, and 18 months of follow-up. However, the possible existence of an extremely small primary neuroendocrine tumor of non-hepatic origin with hepatic metastasis cannot be completely ruled out. Therefore, these hepatic tumors nodules should be diagnosed as “probable primary hepatic neuroendocrine tumor.”

Our present case is a 64-year-old woman with history of chronic hepatitis B infection, and present with persistent abdominal distention. The patients with primary hepatic neuroendocrine tumor were reported to be aged 8 to 81 years, with most being older than 40 years. No apparent sex predilection was noted. Their usual presenting symptom at initial examination was a large liver mass without overt clinical manifestations. Additionally, the hepatic neuroendocrine tumor may be single or multiple and is often located in the right hepatic lobe. Early intrahepatic and regional lymph nodes metastases are common. However, distant metastases are uncommon. The abdominal CT scan of our patient demonstrated multiple hepatic tumor masses, some daughter nodules around a major tumor in the right lobe. No regional lymph node metastases was found in the imaging studies. In the present case, no evidence of synchronous tumor was observed as previously reported. Furthermore, hepatocellular carcinoma and cholangiocarcinoma with carcinoid feature were also excluded due to normal serum level of AFP, CA-199, special immunostaining on the biopsy specimens, and characteristic imaging presentation.

Patients with a static hepatic neuroendocrine tumor of ten present with varying degree of endocrine syndrome, and had survived less than 2 years in earlier reported. Several therapeutic strategies can improve quality of life and survival. Many investigators have reported hepatic arterial embolization as a simple and safe method to reduce tumor mass and relieve symptoms without serious complications. Further more, embolization can often be repeated for recurrence of symptoms. Although some authors suggested that hepatic arterial embolization may prolong life of patients with hepatic neuroendocrine tumor, more others agree that embolization therapy has no benefit on patient survival.

In comparison with patients with metastatic hepatic neuroendocrine tumor, the patients with primary neuroendocrine tumor of liver had more favorable prognosis. The longer life span of the patients with primary tumor came from more limited disease and better response to treatment. Recently, Rückert et al. have presented two cases of their own and collected 44 cases of primary hepatic neuroendocrine tumor reported in the literature until 1999. Their series found that most of the patients were treated with hepatectomy (Hx) (29/46), chemotherapy (C/T) (15/46), radiation (3/46), transcatheter arterial embolization (TAE) (2/46), TAE and Hx (1/46), TAE combined with Hx and C/T (1/46). The patient with the longest survival was a 25-year-old female treated with C/T, TAE and Hx, who had a follow-up period of more than 204 months. By contrast, the survival of two patients who received TAE was 4 and 3.7 months, respectively. The efficacy of TAE in primary hepatic neuroendocrine tumor was still controversial. No other follow-up treatment results of TAE in patients with primary neuroendocrine tumor of liver can be found in literature. We reported the first case of primary neuroendocrine tumor of liver that was successfully treated with TAE. It is suggested that in patients with unresectable hepatic neuroendocrine tumor, TAE is a good alternative choice of treatment.

REFERENCES

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