Primary gastrointestinal stromal tumor of the liver treated with sequential therapy

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The tumor was microscopically composed of spindle cells and epithelioid cells, and immunohistochemistry results showed positive staining for CD117 and CD34 expression. A genetic analysis revealed a heterozygous point mutation and deletion in exon 11 of c-KIT. After an R0 resection, imatinib mesylate was administered for 1 year until its use was discontinued due to severe side effects. Two years after the original operation, the tumor recurred in the residual liver and was completely resected again. Imatinib mesylate was administered for 2 years until it was replaced by sunitinib malate because of disease progression. The patient has survived for 53 mo after undergoing a sequential therapy consisting of surgical excision, imatinib and sunitinib.

Key words: Gastrointestinal stromal tumor; Diagnosis and treatment; Tyrosine kinase inhibitor; Sequential therapy; Liver

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Core tip: The tumor was detected by computed tomography and diagnosed based on histopathological and genetic analyses. Metastases from gastrointestinal stromal tumors were excluded using computed tomography, ultrasound, esophagastroduodenoscopy and colonoscopy. The patient was treated with an extended sequential therapy consisting of surgery, imatinib mesylate, and sunitinib malate. The patient has survived for 53 mo after the start of therapy.

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INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common abdominal tumors of mesenchymal origin. GISTs primarily occur in the gastrointestinal tract and frequently contain a gain-of-function mutation of the KIT or PDGFRA genes[1]. Currently, diagnosis of GISTs is based on histopathological features, including the immunohistochemical staining of CD117, DOG-1, CD34, SMA, desmin and S-100. A minor subset of GISTs occur in other areas of the body, such as the mesentery, omentum, retroperitoneum, pancreas, uterus, gallbladder and liver[2-5], and are referred to as “extra-gastrointestinal stromal tumors”. Here, we report a case of primary GIST of the liver.

CASE REPORT

A 67-year-old female complained of fatigue for 6 mo without any abdominal symptoms. The patient had a history of hypertension, gastritis, and hysteromyoma. Additionally, she had undergone a cholecystectomy at the age of 55 years. The abdominal physical examination was unremarkable. The levels of tumor markers, such as carbohydrate antigen 199, carbohydrate antigen 125, carcinoembryonic antigen and α-fetoprotein (AFP), were all normal. Liver function tests were normal. An enhanced abdominal computed tomography (CT) scan showed a 7.4 cm × 6.2 cm solid-cystic mass in the right hepatic lobe. However, no other abdominal neoplasm was evident (Figure 1A). Esophagogastroduodenoscopy (EGD) and colonoscopy were performed before resection; however, no tumor was found.

The hepatic mass was excised in August 2009. No other masses were found during the operation. A postoperative abdomen ultrasound (US) revealed no other lesions in the liver. Pathologically, the margins of resection were negative, and the tumor was composed of spindle cells and epithelioid cells with high mitotic activity (8/50 HPF) (Figure 2A). Immunohistochemical staining for CD117, CD34, desmin, SMA, CK19, HMB45, and AFP revealed positive results for CD117 and CD34 (Figure 2B and C). A heterozygous mutation was detected in a hot spot region of c-KIT exon 11. Specifically, codon 550 was mutated (AAA → ATA), and codons 551-555 were deleted (CCC-ATG-TAT-GAA-GTA).

Imatinib mesylate was administered at 400 mg per day for 2 mo, beginning 1 mo after surgery. However, the patient experienced severe musculoskeletal pain from the medication, and the dosage was reduced to 200 mg per day for 1 year. In September 2011, a 6 cm × 5 cm lesion was detected in the residual right liver (venous phases in the axial plane). The tumor was completely resected again (Figure 1B). The results of immunohistochemical staining and genetic analysis of the specimen were consistent with the initial mass. Thus, recurrent hepatic neoplasia was diagnosed, and 200 mg of imatinib mesylate per day was administered beginning in October 2011.

In October 2013, a 6 cm × 5 cm mass was detected in the right iliac fossa using CT. An emission CT scan showed several bony metastases in the thoracic vertebrae, lumbar vertebrae and sacrum. Based on the disease progression while undergoing 2 years of imatinib mesylate therapy, the patient was switched to 37.5 mg of sunitinib malate per day.

DISCUSSION

GISTs are the most common gastrointestinal mesenchymal tumors and often occur due to a KIT or PDGFRA gene mutation. GISTs are similar to interstitial cells of Cajal (ICC) pacemaker cells in the gut musculature; thus, GISTs are considered to originate from ICCs[6]. Furthermore, some researchers have observed “ICC-like” interstitial cells in organs outside of the gastrointestinal tract[7]. Other studies have suggested that GISTs originate from a group of undifferentiated cells, such as stem cells or primitive ancestor cells, and then differentiate into ICCs[8]. It has been recently reported that ICCs, ICC-like cells and primitive ancestor cells are present in the gallbladder wall, myometrium, and pancreas, respectively[3,4,9]. Rusu et al[10] discovered the existence of portal interstitial cells of Cajal in the portal space, portal septa and periphery of the hepatic lobules based on immunohistochemical staining of...
A 67-year-old female complained of fatigue for 6 mo without any abdominal symptoms. Imaging examinations, including CT, US, EGD and colonoscopy, revealed that some lesions in the gastrointestinal tract. Primary hepatic gastrointestinal stromal tumors (GISTs) in the right hepatic lobe. The differential diagnosis included hepatic carcinoma, hepatic hemangiomata, hepatic cyst and metastases from gastrointestinal stromal tumors (GISTs).

**Clinical diagnosis**

Abdominal physical examination was unremarkable.

**Differential diagnosis**

The differential diagnosis included hepatic carcinoma, hepatic hemangiomata, hepatic cyst and metastases from gastrointestinal stromal tumors (GISTs).

**Laboratory diagnosis**

The results of routine blood tests, tumor markers and liver function tests were within normal limits.

**Imaging diagnosis**

An enhanced abdominal computed tomography (CT) scan showed a 7.4 cm × 6.2 cm solid-cystic mass in the right hepatic lobe.

**Pathological diagnosis**

Postoperative pathology revealed a mixed-type gastrointestinal stromal tumor that was CD117- and CD34-positive.

**Treatment**

The patient was treated with a sequential therapy consisting of surgical excision, imatinib mesylate, and sunitinib malate. The patient was treated with a sequential therapy consisting of surgical excision, imatinib mesylate, and sunitinib malate. Treatment was interrupted one year later due to severe side effects of imatinib mesylate. However, the dosage was reduced to 200 mg per day, and the treatment plan was interrupted one year later due to severe side effects of imatinib mesylate.

**Related reports**

Genetic analysis revealed a heterozygous point mutation and deletion in exon 11 of c-KIT. A genetic analysis revealed a heterozygous point mutation and deletion in exon 11 of c-KIT.

**Experiences and lessons**

This case report excluded the diagnosis of metastases from GISTs using CT, ultrasound, esophagogastroduodenoscopy and colonoscopy. Additionally, a genetic analysis was used to confirm the tumor as a primary hepatic GIST.

**Peer review**

This case report verified the diagnosis using histological and genetic analyses. Furthermore, the patient underwent an extended sequential therapy consisting of surgery, imatinib mesylate, and sunitinib malate.

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