Clinical report

CyberKnife for hepatocellular carcinoma: the first case report in Thailand

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Background: CyberKnife is a frameless image-guided robotic system for stereotactic body radiotherapy. It can deliver an accurate and concentrated radiation beam to intracranial and extracranial targets for benign, malignant and some non-neoplastic conditions.

Objective: To report the first hepatocellular carcinoma (HCC) treated with CyberKnife at Ramathibodi Hospital.

Patient and methods: A 73-year-old man with a large right lobe hepatocellular carcinoma was treated with CyberKnife with the total dose of 4500 cGy in three fractions.

Results: Two weeks after CyberKnife, he developed radiation induced liver damage (RILD). The patient was admitted for observation and supportive treatment. He was discharged with much improvement of symptoms. Abdominal MRI taken 1 and 3 months after the CyberKnife revealed a significant reduction in size of HCC. His serum alpha fetoprotein was also decreased from 833 ng/mL to 12 ng/mL.

Conclusion: The present robotic radiosurgery was an effective alternative treatment for HCC. Early detection and proper supportive care was very important to decrease the morbidity from this serious radiation.

Keywords: CyberKnife, hepatocellular carcinoma, stereotactic body radiation therapy.

In mid-1990s, the CyberKnife robotic radiosurgery system (CK) was developed based on concepts of Lars Leksell’s radiosurgery by Adler et al. [1, 2]. Its prototype device was installed at Stanford, USA in 1994. In 2001, the American Food and Drug Administration (FDA) approved the CyberKnife for the treatment of lesions “anywhere in the body where radiation treatment is indicated”. To date, more than 100 CyberKnives have been installed worldwide.

In Thailand, the CyberKnife (Accuracy Inc, Sunnyvale, USA) was installed at Ramathibodi Hospital at Bangkok in January 2009. Figure 1 shows the first CyberKnife in Thailand. Here, we report initial results of the first patient with hepatocellular carcinoma (HCC) who was treated with CyberKnife in Thailand.

Case report
A 73-year-old man with underlying ischemic heart disease, renal insufficiency, hypertension, and diabetes presented with abdominal discomfort in November 2008. Physical examination was significant only with hepatomegaly. Liver function tests show total bilirubin, 0.4 ng/dL, direct bilirubin 0.2 mg/dL, aspartate aminotransferase, 35 U/L, alanine aminotransferase, 43 U/L, alkaline phophatase, 127 U/L, gamma glutamyl transpeptidase, 128 U/L, and alpha fetoprotein, 833 ng/mL. Abdominal MRI revealed a 8.6x5.6x6.2 cm mass at the right lobe of liver (Fig. 2). In accordance with these findings, the patient was diagnosed as HCC.
Because of many underlying diseases and a large tumor, he was not a candidate for surgery. Transarterial chemoembolization (TOCE) was attempted, but it failed due to severe stenosis of the celiac trunk. CyberKnife was selected. He received a total dose of 4,500 cGy in three fractions for three consecutive days to the hepatic mass. The patient could tolerate radiation very well, and no complication was reported during three days of CyberKnife. However, two weeks later, the patient developed jaundice, malaise and loss of appetite. Liver function tests showed elevation of alkaline phosphatase, 561 U/L, aspartate aminotransferase, 213 U/L, alanine aminotransferase, 271 U/L, gamma glutamyl transpeptidase, 642 U/L, total bilirubin, 6.9 ng/dL, and direct bilirubin 5.8 mg/dL. Other laboratory tests were within normal limits. According to these findings, radiation induced liver damage (RILD) was suspected. The patient was admitted for observation and supportive treatment. He was discharged with improvement of symptoms. Abdominal MRI taken 1 and 3 months after the CyberKnife revealed a reduction in HCC size (Fig. 3). After three month follow up, his alpha fetoprotein decreased from 833 ng/mL to 12 ng/mL, and liver enzymes decreased to normal levels. Regular liver function test and imaging follow up is planned to monitor for complication to response after radiation.
CyberKnife is a frameless image-guided robotic whole body stereotactic radiosurgery system. The system consists of a 6-MV lightweight linear accelerator, a computer controlled robotic arm, a pair of X-ray imager target locating system, and a computer workstation. The compact 6-MV LINAC mounted on the robotic manipulator that can position and point the LINAC with 6 degrees of freedom, permits a much wider range of beam orientation than other conventional radiation devices [1-3]. CyberKnife can be corrected for patient’s position change during the real-time treatment with an accuracy of 1.1±0.3 mm, computer tomography (CT) with a 1.25 mm computer tomography (CT) slice thickness [4-6]. It has been used to treat intracranial and extracranial lesions, such as AVM, trigeminal neuralgia, tumors of the brain, spine, lung, liver, prostate, head/neck area, etc [6-10].

HCC is the fifth most common tumor. Worldwide, it is responsible for nearly a million deaths annually. In Thailand, HCC is still a large health problem due to high incidence and more advanced forms of the disease. The implementation of the CyberKnife could be an alternative option for HCC treatment. To date, many medical centers have started using CyberKnife to treat primary or metastatic liver cancers with early encouraging results. Choi et al. [11] reported 31 HCC patients treated with CyberKnife. The overall response rate was 71.9% and the median survival for small HCC and advanced HCC was 12 months and eight months, respectively. No patient experienced grade-4 toxicity. Reports about the complication after the CyberKnife treatment in HCC are difficult to find due to its short clinical experience.

Radiation-induced liver damage (RILD) was also called radiation hepatitis. It is rare but a serious complication in hepatic irradiation. It was defined as anicteric or elevated transaminases. The anicteric is defined as RIDL with elevation of alkaline phosphatase level at least two-fold and non-malignant ascites (classic RIDL) [12]. The RIDL with elevated transaminases is define as elevated at least five-fold of the upper limit of normal or of pre-treatment level (Grade-3 or -4 hepatic toxicity of Common Toxicity Criteria Version 2.0 by the National Cancer Institute, USA) (non-classic RIDL) [13], in the absence of documented progressive disease. Our patient had jaundice and elevated alkaline phosphatase and transaminases within two weeks after completed radiation. It is most likely that these abnormal presentations were from the direct radiation injury of the liver. It is important to follow patients after hepatic irradiation and identify any RILD. Early detection and proper supportive care are very important for decreasing the morbidity and mortality from this serious complication.

The authors declare no conflict of interest.

References


