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Case Report

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A Case of Hepatocellular Carcinoma Treated with Mid-Infrared Rays

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Abstract

A 61-year-old man suffering from hepatocellular carcinoma was treated with Mid-Infrared rays (MIFR) irradiation. The patient was diagnosed with hepatocellular carcinoma at a hospital referred by his primary doctor, with markedly elevated values of tumor markers, and started oral administration of molecular target drugs. Initially, the tumor marker decreased once, but increased again 6 months after the start of therapy. Following the increase, the patient started MIFR irradiation therapy at our institution. After that, according to our instructions, the molecular target drug was tapered off (1/2, then 1/4), and finally oral administration was discontinued, and only MIFR irradiation therapy was performed. From the 12th month after the start of MIFR irradiation therapy, the tumor marker has maintained the reference value, and the growth of the tumor has disappeared in the abdominal CT imaging examination.

Keywords: Hepatocellular Carcinoma, PIVKA II, Mid-Infrared Rays

1. Case Presentation

The patient was a male hepatitis B virus carrier and was being treated for diabetes and hyperlipidemia by his primary doctor. At the age of 61, he had a weight loss of 8 kg and back pain, and was referred to the hospital by his family doctor, where he was diagnosed with hepatocellular carcinoma. He started taking a molecular target drug (lenvatinib mesylate 4 mg 2 tablets/day) prescribed by the referring hospital. After that, he was treated with MIFR irradiation therapy at our institution.

2. Therapeutic Process and Result

The therapeutic process is shown in Table 1 and Fig. 1, and the abdominal CT images are shown in Figures 2, 3, and 4. In Table 1 and Fig.1, the values of tumor markers (PIVKA II), the doses of prescribed molecular target drug, and the number of MIFR irradiation treatments are shown by month (the month of treatment start is 1). The therapeutic process is shown in months from the start of treatment.

Month/Year	Number of Months	PIVKA II (mAU/mL)	Dosage	Times of MIFR irradiation	CT examination
Oct-20	1	287,744	1/1		2020.10.28
Nov-20	2		1/1		
Dec-20	3	273	1/1		
Jan-21	4	250	1/1		
Feb-21	5	270	1/1		
Mar-21	6	7,847	1/1		
Apr-21	7	12,591	1/1		
May-21	8	24,171	1/1	6	2021.05.06
Jun-21	9	57,630	1/1	12	
Jul-21	10	52,307	1/1	11	

Aug-21	11	53,927	1/2	6	
Sep-21	12	27,541	1/2	9	
Oct-21	13	18,091	1/4	8	
Nov-21	14	29,918	1/4	7	
Dec-21	15		0	8	
Jan-22	16	39,105	0	4	
Feb-22	17		0	6	
Mar-22	18		0	7	
Apr-22	19	56	0	6	
May-22	20		0	6	
Jun-22	21	43	0	5	
Jul-22	22	32	0	4	
Aug-22	23		0	2	
Sep-22	24		0	3	
Oct-22	25	33	0	3	
Nov-22	26		0	2	
Dec-22	27		0	3	
Jan-23	28	30	0	3	2023.01.26
Feb-23	29		0	3	
Mar-23	30		0	2	
Apr-23	31		0	2	
May-23	32	37	0	2	

Table 1: Therapeutic Process

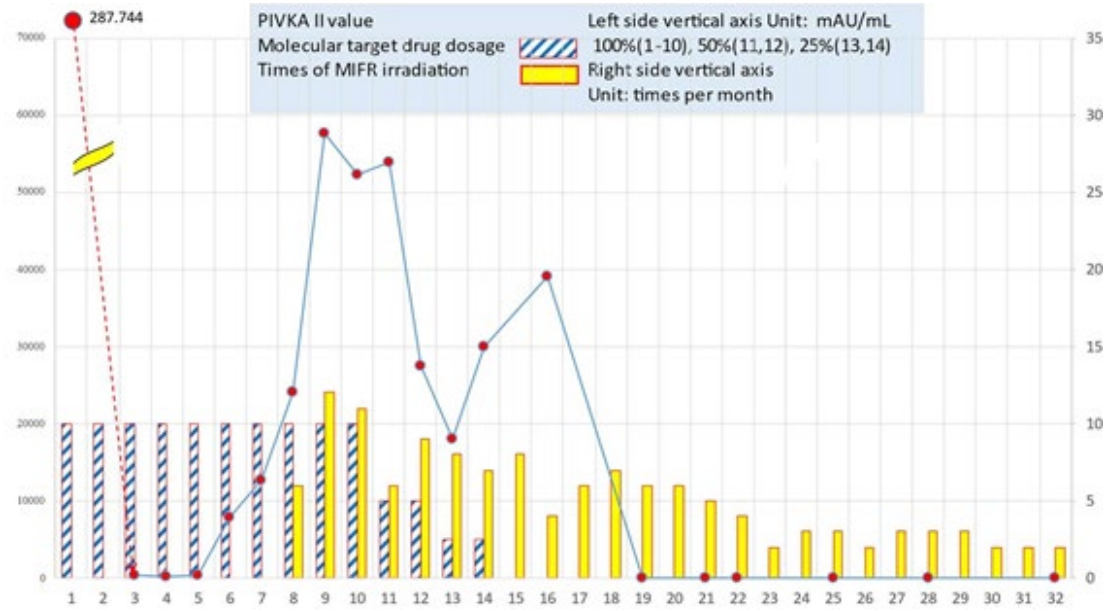


Figure 1: Therapeutic Process (PIVKA II value, Molecular target drug dosage, Times of MIFR irradiation)

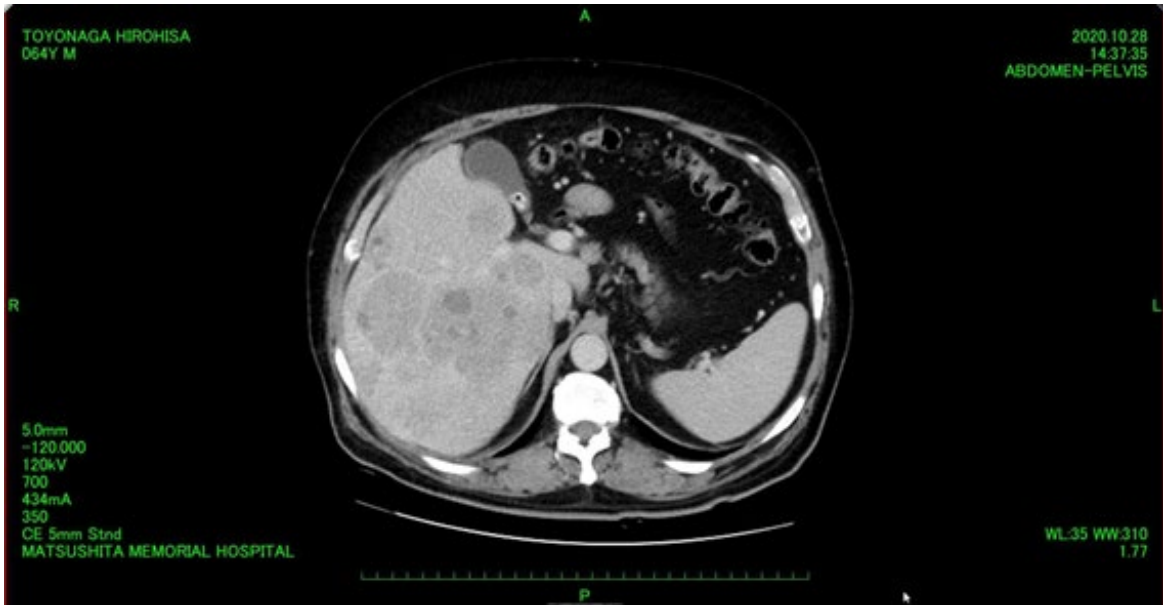


Figure 2: Abdominal CT Image (2020 10 28) at the Time of Diagnosis

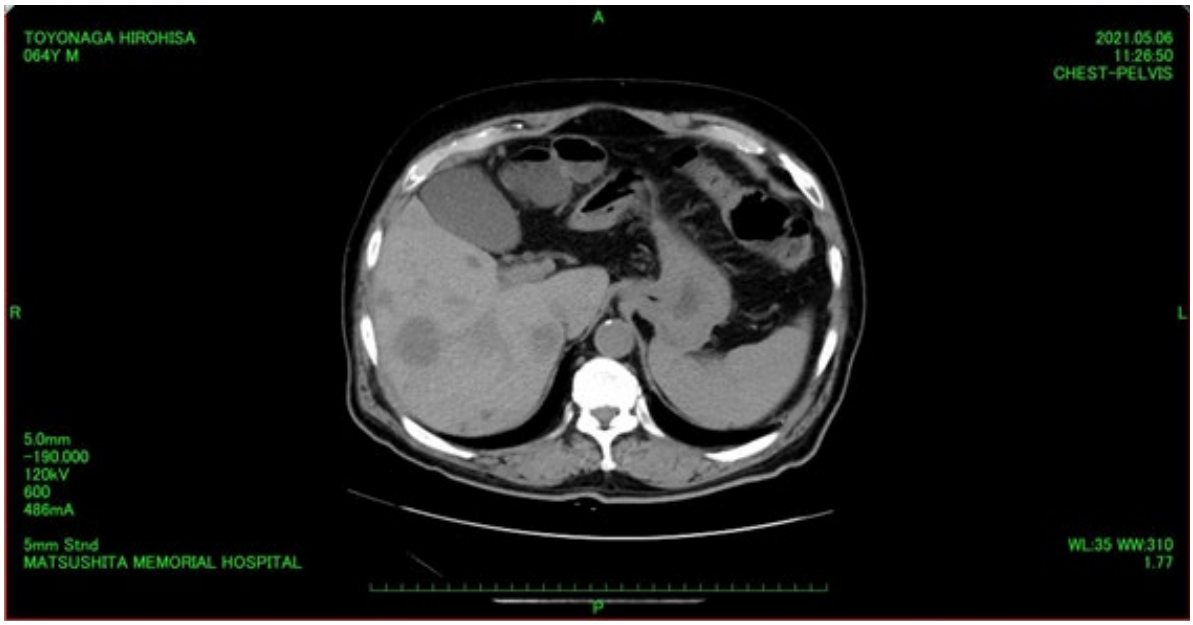


Figure 3: Abdominal CT Image (2021 05 06) 8 Months After Starting Oral Treatment

When he was diagnosed with hepatocellular carcinoma at the referral hospital, the tumor marker PIVKA II value was 287,744 mAU/mL (Table 1, Fig. 1), and most of the liver was occupied by tumor cells on the abdominal CT image (Fig. 2). He was immediately prescribed a molecular target drug (lenvatinib mesylate 4 mg 2 tablets/day) at the referral hospital and started taking it. The PIVKA II values decreased once, but after 6 months, the PIVKA II values began to increase again at which point he visited us to receive MIFR irradiation therapy. The therapy was immediately started three times a week (8th month). In addition to MIFR irradiation treatment, oral administration of the prescribed molecular target drug was continued because a tendency toward tumor necrosis was observed in abdominal CT images (Fig. 3).

At 4 months after the start of irradiation treatment (11th month), suppression of the increase in PIVKA II value began to be observed along with severe diarrhea which is a side effect of the continued molecular target drug, so the molecular target drug was halved (administered every other day). Two months later (13th month), a decrease in PIVKAII value was observed, confirming the effectiveness of MIFR irradiation treatment, and the molecular target drug was reduced to 1/4 of the original dosage. One month later, an increase in the PIVKA II value was confirmed, but it was judged to be apoptosis due to MIFR irradiation treatment, and oral administration of the molecular target drug was discontinued (15th month).

One month after discontinuation (month 16), the PIVKA II value increased further, but the good quality of life continued, and the other blood test results were favorable. It was judged to be the apoptotic effect of MIFR irradiation treatment. Therefore, MIFR treatment was continued without resuming the administration of the molecular target drug. Three months later (19th month), the PIVKA II value dropped sharply to reference value and has remained at reference value since then. Along with this, the frequency of MIFR irradiation treatment was gradually reduced.

Currently, MIFR irradiation treatment is performed once every two weeks for the purpose of preventing recurrence. Twenty-two months after starting MIFR radiation therapy (28th month), the patient is doing well and leading a normal life. Tumor necrosis was observed on the abdominal CT image (Fig. 4).

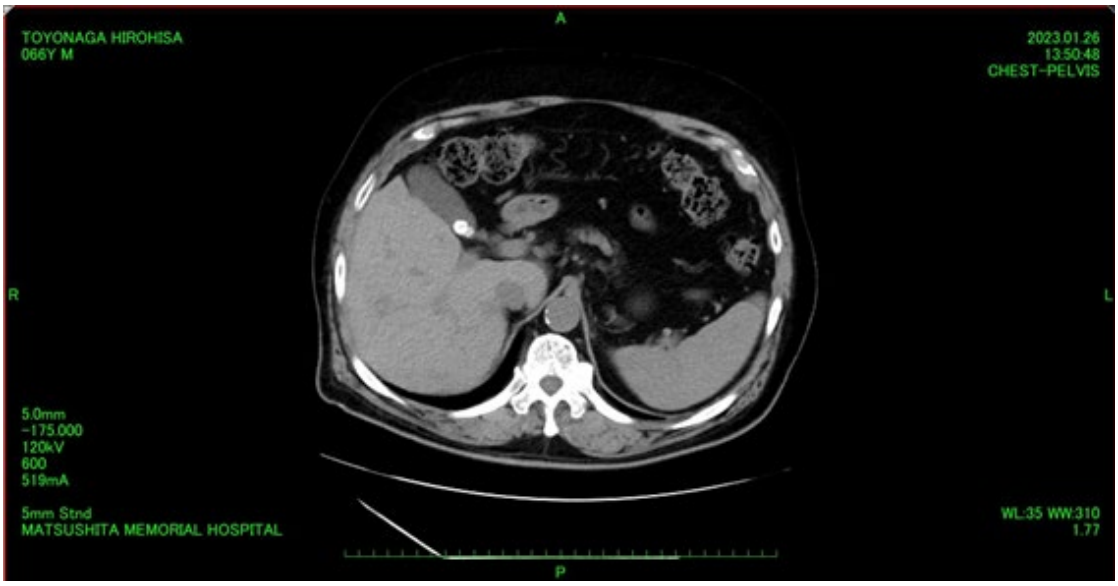


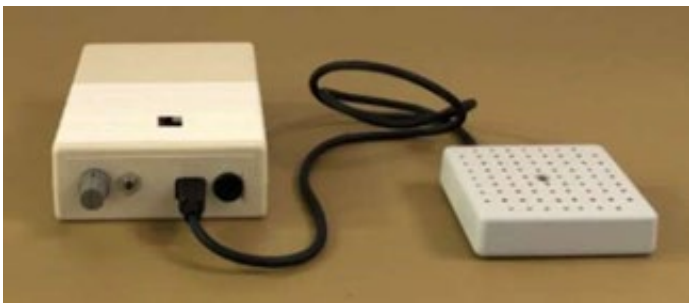
Figure 4: Abdominal CT Image (2023 01 26) 28 Months After Starting Oral Treatment

3. Materials/Methods

3.1 MIFR Irradiation Apparatus

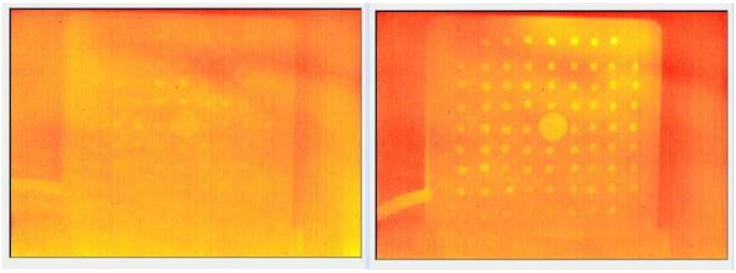
MIFR irradiation apparatus was developed under the guidance of the late Dr. Hiroki Shima (SHIMA Institution for Quantum Medicine, the first director). As shown in Fig. 5, it consists of part A for selecting a reference frequency and part B for emitting MIFR. Part B contains a polystyrene sheet as a filter. Fig. 5 shows MIFR irradiation images of part B taken with a near-infrared camera with a sensitivity of 3 to 6 μm (manufactured by Vision Sensing Co., Ltd., Osaka, Japan). The left side of MIFR irradiation images shows the off state, and the right side shows the on state. The light in the on state indicates that MIFR around 4.8 μm are emitted due to the effect of the filter. In MIFR radiation treatment, the part B is applied to the affected area and its surroundings.

MIFR Irradiation Apparatus



Part A (DxWxH : 16x10x3.8cm3) Part B (DxWxH : 8x8x2cm3)

MIFR Irradiation Images



OFF state ON state

Figure 5: Apparatus and Images

3.2 MIFR Irradiation Therapy

About 10 MIFR irradiation apparatus are used on the affected area of cancer and its surroundings, and one treatment is performed for about 1 hour. The number of times of treatment is determined according to the patient's condition and situation (including visits and possible treatment schedules) and severity. Usually, treatment is given 3 times a week at the beginning, and the frequency of treatment is gradually reduced as the disease condition improves.

4. Discussion

We reported that MIFR irradiation induces apoptosis of prostate cancer cells in vitro and that the wavelength of this irradiation is 4.8 μm [1,2]. The patient with hepatocellular carcinoma was treated using the MIFR irradiation apparatus developed based on this. The goal of anticancer drug therapy is for cancer cells to stop growing and enter an apoptotic state. This time, we experienced a case in which MIFR irradiation treatment was used in combination with anticancer drug therapy, and then MIFR irradiation treatment alone was effective, although anticancer drugs alone could not achieve the goal.

We performed MIFR irradiation treatment on a hepatocellular carcinoma patient, and observed the suppression of hepatocellular carcinoma growth and disappearance due to apoptosis through the course of PIVKA II value [3]. and the abdominal CT images.

4.1 Start of MIFR Irradiation Treatment

At the beginning of oral administration of the molecular target drug, the PIVKA II value became the reference value. This is thought to be because the molecular target drug exerted its effect and suppressed the proliferation of cancer cells. However, 6 months after the start of oral administration, the PIVKA II value increased, which was considered to be due to the recurrence of hepatocellular carcinoma. MIFR irradiation treatment was then started at our institution, but since a tumor was observed in the abdominal CT image (Fig. 2), oral administration of the molecular target drug was continued.

4.2 Decrease in the Molecular Target Drug

PIVKA II values increased further after initiation of combination therapy (9 months). Despite continued oral administration of the molecular target drug that were effective at the beginning, no improvement in symptoms was observed. However, since the increase in PIVKA II value was suppressed, the oral dose of the molecular target drug was halved (administered every other day) taking into account the effect of MIFR irradiation treatment (11th month). It was then confirmed that the PIVKA II value decreased sharply, and the administration of the molecular targeted drug was reduced to 1/4 (13th month) of the original dosage.

4.3 Growth Inhibition of Hepatocellular Carcinoma

As can be seen from the course of treatment (Table 1, Fig. 1), the PIVKA II value increased sharply once (9th month), but thereafter the increase was suppressed (11th month). When it was confirmed that the PIVKA II value had leveled off (11th month), the oral dose of the molecular target drug was halved (administered every other day). It is thought that the adverse effects of side effects caused by the molecular target drug were avoided and the effect of MIFR irradiation treatment improved. Furthermore, when the subsequent decrease in PIVKA II value was confirmed (13th month), the oral dose of the molecular target drug was further reduced to 1/4.

4.4 Judgment of Apoptosis

Growth suppression was confirmed by MIFR irradiation treatment, but an increase in PIVKA II value was observed again (14th month). At this time, the patient's condition was good, so it was determined that it was not a recurrence of hepatocellular carcinoma but an apoptotic effect due to MIFR irradiation treatment. Then oral administration of the molecular target drug was discontinued (15th month). One month after the discontinuation, the PIVKA II value increased further, but the good quality of life continued, and the results of blood tests other than the PIVKA II value were also good. The judgment remained unchanged, and MIFR irradiation treatment was continued while oral administration of the molecular target drug was discontinued.

4.5 Growth and Apoptosis of Hepatocellular Carcinoma

Focusing on the PIVKA II value from the course of treatment (Table 1, Fig. 1), it increased by 33,459mAU/mL from the 8th to the 9th month, and increased by 11.872mAU/mL from the 13th to the 14th month. Comparing the amount of increase between the two, the latter is about 1/3 of the former. Since the amount of increase is clearly small, it is presumed that the state of hepatocellular carcinoma differs between the former and the latter. That is, the former is presumed to be the growth (recurrence) of hepatocellular carcinoma, and the latter is due to apoptosis.

From the 14th to the 16th month (2 months), it increased to 9,187mAU/mL (4,593.5/month). Compared to the amount of increase (11,872) in the 13th and 14th months, the increasing trend during the 2 months is about 1/2 or less on average for 1 month. This is not recognized as a growth (recurrence) of hepatocellular carcinoma. The increase in PIVKA II values from 13 to 16 months is considered to be due to enhanced apoptosis of hepatocellular carcinoma.

4.6 Continuation of MIFR irradiation treatment

Subsequently, MIFR irradiation treatment alone was continued, and the PIVKA II value was within the reference range (19th month). And MIFR irradiation treatment was given to the patient once or twice a week. The PIVKA II values remained within the reference range, the patient was in good condition, and the abdominal CT image at 28 months showed no hepatocellular carcinoma.

4.7 Judgment by Tumor Marker

Based on this example, it is considered necessary to consider how to understand the tumor marker (PIVKA II value) not only from the perspective of cancer cell proliferation but also from the perspective of cancer cell apoptosis.

5. Conclusion

We experienced a case in which MIFR irradiation therapy was effective in treating hepatocellular carcinoma. The patient received oral administration with a molecular target drug immediately after being diagnosed, and this initially showed therapeutic effects. However, due to recurrence, MIFR irradiation treatment was started at our institution. After that, the oral administration of the molecular target drug was discontinued, and the positive effects were obtained only with MIFR irradiation treatment.

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Author Contributions

J.S wrote this report. S.I. assisted in the editing of figures and the description of materials and methods.

Author Information

The authors declare no competing financial interests. Correspondence and requests for materials should be addressed to Junko Shima

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