

Clinical Observation of Treatment with Ar-He Targeted Cryoablation in Liver Tumor

Huazhi Song, Fengtao Yi, Ying Liu, Guoqing Yao

Centre of Ar-He knife, Wuhan General Hospital, Guangzhou Military area of PLA, Wuhan 430070

Abstract Objective To investigate the local effect, adverse reaction and complications of Ar-He targeted cryoablation. **Method** Using local anesthesia, under B-ultrasonography or computer tomography monitoring, 255 patients with primary hepatocellular carcinoma and 21 patients with metastatic liver carcinoma underwent percutaneous Ar-He targeted cryoablation treatment. **Results** In 276 patients, 213 patients were followed up for more than 12 months. The one-year survival rate was 70.9% (151 cases). Hepatic hemorrhage occurred in 7 cases (2.5%), liver pain in 97 cases (35.1%), fever in 118 cases (42.8%). **Conclusion** Percutaneous Ar-He targeted cryoablation was an effective, safe and reliable method for patients with liver tumor.

Key Words Liver tumor; Ar-He knife; Cryotherapy

The Ar-He targeted cryoablation for patients with primary hepatocellular carcinoma or with metastatic liver carcinoma has been in use in China for over 5 years. It has been shown to be an effective method of destruction of primary and metastatic liver tumors, especially for those with unresectable advanced liver tumors^[1]. Here we presented our study of 276 patients with primary and metastatic liver tumors who underwent percutaneous Ar-He targeted cryoablation treatment.

DATA AND METHODS

Clinical data

Between August 2000 and December 2003, 276 patients (age ranged 13~75, averaging 49 years old; 233 males and 43 females; 219 patients with primary hepatocellular carcinoma, 36 patients with primary cholangiocarcinoma, 21 patients with metastatic liver adenocarcinoma) with liver tumors underwent percutaneous Ar-He targeted cryoablation treatment. The tumor size ranged from 23.8 mm×18.1 mm to 130.0 mm×120.0 mm in diameter (averaging 65 mm×48 mm). 27 cases combined clinically with jaundice, 129 cases with abdominal pain, 61 cases with ascites, 39 cases with portal cancer emboli, 7 cases suffered from metastatic lung tumors. 83 cases no symptom. Liver function levels of 163 patients were Child A, 93 patients were Child B, and 20 patients Child C. In all patients, AFP levels of 172 patients were over 400 ng/ml, 67 patients were between 100 ng/ml and 400 ng/ml, in 37 patients was below 100 ng/ml.

Equipment

Cryocare surgery system made in US, with 4 especially cryoprobes made as 2、3、5、8 mm in diameter; TOSHIBA SSA-220A ultrasonic diagnostic apparatus.

Methods

Blood routine, blood coagulation function, liver function and renal function were tested before operation. Corresponding treatment was given if the results of blood tests above were abnormal. Cryoablation can't be started until the results became normal. One day before operation, according to the size, shape, and localization of tumor in liver, the localization and depth of the cryoprobes were determined using B-ultrasonography and computer tomography guidance technique, and marked on the patient's skin. Fast 12 h before operation and diazepam IM at 30 min before operation.

According to different localization of tumors in liver, patients take supine, prone or lateral recumbent position. Venous passage was established, electrocardiographic monitoring system was set up, and oxygen inhalation was given if necessary. Operative instruments such as surgical knife handle, blade suture and suture needle were prepared.

According to preoperative localization, the route of entry and depth was again confirmed using B-ultrasonography or CT. After local anesthesia, a small incision on the patient's skin was made. Under B-ultrasonography or CT monitoring, the cryoprobes were inserted into each targeted area. The patients, whose tumor size were below 30 mm in

diameter, were asked to hold inhaling during operation, so that the cryoprobes were accurately inserted into the targeted area.

The size of the ice ball and the relationship between the ice ball and blood vessels or bile duct in the targeted area was monitored with B-ultrasonography or CT during operation. Once the ice ball is near blood vessels or bile duct, freezing must be stop at once and re-thawed should be started immediately. Generally speaking, the ice ball near blood vessels can't damage the blood vessel. The author treated the tumor proximity to vena cava inferior, when the tumor had been frozen by the ice ball, the temperature of vena cava inferior was normal. During operation, the changes of patients' respiration, blood pressure and pulse should be closely measured. Stop freezing immediately and give treatment if something abnormal. When cryotherapy ended, the cryoprobes were withdrawn, hemostat packed, suture and gauze given and then patients were fixed with abdominal belt.

After operation, patients were kept in bed for 12 hours and their blood pressure and pulse were measured once every half an hour for six hours,

routine treatment with antibiotic, hemostat and hepatinica were given. Hydration treatment was given for those with wide range of freeze.

RESULTS

In all 276 patients, 213 cases have been followed up for over 12 months. The one-year survival rate was 70.9% (151/213). 129 cases was accompanied with abdominal pain, 98 patients of which liberated. Ascites in 46 of 61 patients regressed; in the 93 patients of child B of liver function, 63 patients became Child A (67.7%), and 6 cases out of 20 cases with child C of liver function became the child B. In 172 cases whose AFP > 400 ng/ml re-examined after operation, the AFP level in 79 cases remained more than 400 ng/ml, 57 cases became between 100 ng/ml and 400 ng/ml, and 36 cases decreased to <100 ng/ml. The tumors size decreased 10~20 mm in 76 cases (table 1, 2), decreased about 30 mm in 52 cases, no change in 62 cases and in 23 cases enlarged compared with that before operation



Fig.1 Before cryoablation

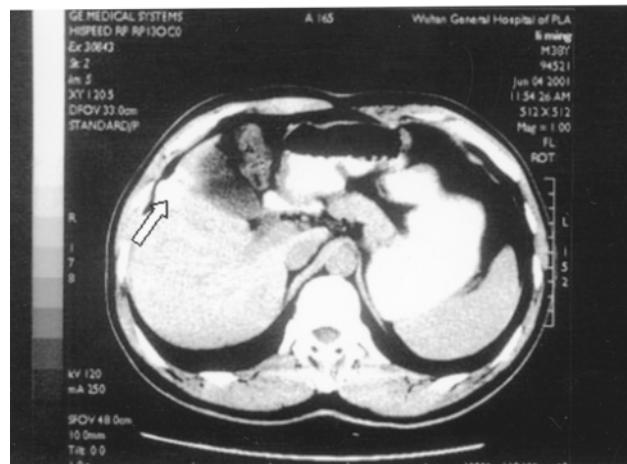


Fig. 2 3 years after cryoablation

DISCUSSION

Indications and contraindications^[2]

Indications: The massive type of primary liver carcinoma ($D \leq 10\text{cm}$); Multi-foci of primary liver carcinoma are not over 3 foci. Multi-foci of metastatic carcinoma are not over 5 foci. The size of every focus is not larger than 4cm; Those combined with locality metastatic foci outside liver which can be operated or cryoablated.

Contraindications: The tumor proximity to or

invasion of bile duct or blood vessels; Multi metastatic foci and diffuse liver carcinoma; The range of tumors is larger than 70% of liver; Patients combined with serious hepatic cirrhosis, hypersplenism, history of pre-existing hemorrhage of portal vessel and risk of bleeding; Patients can't undergo operation because of heart, lung and renal function are abnormal Blood coagulation function is abnormal.

Determination of cryoablation range

The cryoablation range of tumors has positive

correlation with prognosis. We study some references^[3]: the cryoablated range should be 1~2cm in diameter larger than tumor size. In fact, it is difficult to do so because of the tumor's size or multiple. For single tumor and its size was smaller than 50 mm in diameter, with normal hepato-renal function, the ice ball should be larger than 60 mm. If the tumor size was larger than 50 mm, especially with abnormal hepato-renal function, the size of ice ball should not be larger than that of the tumor. Otherwise normal hepatic tissues may be damaged and hepatic or renal function failure may easily happen after operation. If the tumors size was larger than 100 mm, it's better to cryoablate twice cycles (2/3 for the first cycle and 1/3 for the second cycle a week later). If tumors near diaphragmatic or hepatic surface, the size of ice ball should not be larger than that of tumor, or the ice ball may crack and liver hemorrhage may occur. Cryoablate once for all that are less than 4 foci and cryoablate fractionally for over 5 foci.

Management and prevention of complications

Management of complications^[4]: In all 276 patients, 97 cases (35.1%) have pain of hepatic area, 9 cases (3.3%) have pleural effusions, 118 cases (42.8%) were accompanied with fever, 13 cases (4.7%) with myohemoglobinuria. One of 7 cases with hemorrhagic shock, which is the most serious complications, died of long time shock and renal function failure. Hemorrhagic shock may be related with abnormal blood coagulation mechanism, which existed in all 7 cases. Once hemorrhagic shock happened, blood transfusion and hemostat should immediately be given. Hepatic arteriography and hepatic artery embolism was especially effective method for patients with emergent hemorrhagic shock. If hepatic artery embolism can't prevent hemorrhage or it is no condition to do this treatment, laparotomy must be done to find out the location of hemorrhage and to suture and press the wound or to ligate hepatic artery. Other complications such as fever and hepatic pain can be managed with corresponding treatment. Example: the fever with temperature above 38.5°C can give dexamethasone 5 mg IV, the reactive pleural effusions, which may be due to diaphragmatic harm in cryoablation of tumor near diaphragmata, should be thorax drainage when liquid is over 500 ml. Myohemoglobinuria begins one day after operation and lasts about 3 days, which can be combined with re-

nal function failure. It may be related with the large range of cryoablation and with damage of normal hepatic-tissue. Myohemoglobinuria should immediately be given hydration and basic urine treatment. It should be given to observe closely the change of urine and examine renal function, urine routine, electrolyte and blood gas analysis everyday, and to prevent necrosis of renal tubule.

Prevention of complications: Hemorrhagic shock is the most serious complications in patients underwent Ar-He targeted cryoablation^[5,6].

We take some steps to prevent the hemorrhagic shock (1)Blood coagulation mechanism was assessed before operation, give corresponding treatment if abnormal, blood glucose level in patients with diabetes mellitus should be controlled to the normal range. (2) Controlling the range of cryoablation. Because the ice ball cracking can induce hemorrhage of liver, especially for the tumor located on the surface of liver. (3) The numbers of inserted cryoprobes can't be over 3 at one time. (4) The cryoprobes were withdrawn after temperature is over 5°C. Otherwise it is easy to induce damaging of hepatic capsular and hemorrhaging.

The treatment by Ar-He target cryoablation is especially effective for patients with liver tumors. It is of great significance to alleviate patients' pain, prolong patients' lifetime and improve patients' life quality. Ar-He target edcryoablation has advantage of less hurt, less hemorrhage and less serious side effect. It is advisable in extensive clinical practice.

REFERENCES

1. Wang Senming, Zhang Jiren, Peng Qiuping, et al. The treatment of irresectable liver tumors by percutaneous targeted Ar-He cryoablation. *International Journal of Cancer Therapy*, 2000,3(1):16-18
2. Zhang Jiren(chief editor). The technique of treating tumors by targeted Ar-He cryoablation. Hongkong: Pioneer Bioscience publishing Co, 2003. 28-110.
3. Mala T, Frich L, Aurdal, L, et al. Hepatic vascular inflow enhance tissue destruction during cryoablation of porcine liver. *J Surg Res*, 2003 Dec, 115(2): 265-271.
4. Saranton T, Bilchick A, Ramming KP, et al. Complications of hepatic cryosurgery. *Semin Surg Oncol*, 1998, 14(2): 156-162.
5. Cha C, Lee FT, Jr, Rikkers LF, et al. Rationale for the combination of cryoablation with surgical resection of hepatic tumors. *J Gastrointest Surg*, 2001, 5:206-213.
6. Song HZ, Yi FT, Zhang YX. Treatment of liver tumors by targeted Ar-He Cryoablation. *International Journal of Modern Cancer Therapy*, 2000, 5(1): 26-29.