KAWASAKI MED. J. VOL. 9 : NO. 3, 197-202 (1983)

# Intra-Atrial Tumor Embolus in Hepatocellular Carcinoma

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*Accepted for Publication on April 19, 1983*

**ABSTRACT.** A case of hepatocellular carcinoma with a massive tumor embolus in the right atrium is reported. Although hepatocellular carcinoma often invades into portal and hepatic vein and may extend into the inferior vena cava, it is rare that the tumor grows out to fill the right atrium. The literature on the intracardiac metastasis of hepatocellular carcinoma as well as other carcinomas is reviewed.

**Key words : Tumor embolus — Heart — Hepatocellular carcinoma**

Hepatocellular carcinoma (HCC) often invades into the portal and hepatic vein system. Its extention into the major branches of either venous system or the inferior vena cava occurs on occasion, and may clinically be recognized by a sudden increase of portal vein pressure or so-called Budd-Chiari syndrome.[1,2] It is a rather rare phenomenon that the tumor growth extends up to the heart and fills the right atrium. In fact, out of 78 autopsy cases of HCC experienced at the Kawasaki Medical School Hospital between 1974 and 1982, only one case had an intra-atrial tumor growth, causing a sudden death. This rarity led us to review the literature in order to know the real incidence of such growth. The present communication describes our experience and summarizes a result of the literature review on the intracardiac metastasis of hepatocellular carcinoma as well as the other carcinomas.

## CASE REPORT

A 48-year-old man had been apparently well until October 1981, when a routine check-up disclosed liver dysfunction. About a month later, abdominal fullness developed and gradually aggravated so that he became dyspneic when he laid down. General fatigue was severe. He was admitted to the Kawasaki Medical School Hospital on January 19, 1982. Physical examination revealed a marked abdominal distention which hindered a palpation of the liver and spleen. There were no icterus, anemia, spider angiomata or palmar erythema. The lung-liver border was at the fifth rib. No heart murmur was audible. The lower extremities were free of edema or varicosities. Serum protein was 6.9 g/dl (Alb. 3.5 g/dl, Glb. 3.4 g/dl), Blood sugar 98 mg/dl,

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Bil. 0.7 mg/dl, γ-GTP 120 IU/l, GPT 36 IU/l, GOT 78 IU/l, LDH 281 IU/l, α-fetoprotein $1.4 \times 10^4$ ng/ml, HBs-Ag S/N 220.0 (+), and ICG 22.0%. Abdominal echography and computed tomographic scan disclosed a large mass involving right lobe of the liver and chest x-ray revealed multiple nodules in the right lung. Futraful and krestin, as well as krestin and picibanil were given. Hospital course was troubled by pneumonia and ascites. On February 23, he complained of abdominal pain and became shocky. A large amount of blood was aspirated through a nasogastric tube. Next day, urine output decreased and he died of respiratory failure.

## PATHOLOGICAL FINDINGS

The post-mortem examination showed two liter of bloody ascites. The liver weighed 3,750 g and right lobe was almost completely replaced by a hemorrhagic tumor, measuring $17 \times 14 \times 14$ cm (Fig. 1). The remaining of the hepatic tissue showed an appearance of cirrhosis (type Z of Nagayo-Miyake's classification, and micronodular type of international classification). The tumor infiltrated directly into omentum which was adherent to the antero-superior portion of the liver, on the one hand and partially into the diaphragm on the other. Tumor invaded into the portal vein, obstructing the lumen with a thrombus which extended down to 6 cm below the hilus. Through hepatic veins bilaterally, it grew out to the lumen of inferior vena cava. Upwards, it further extended into right atrial cavity where a $4 \times 2.5 \times 3.0$ cm mass was

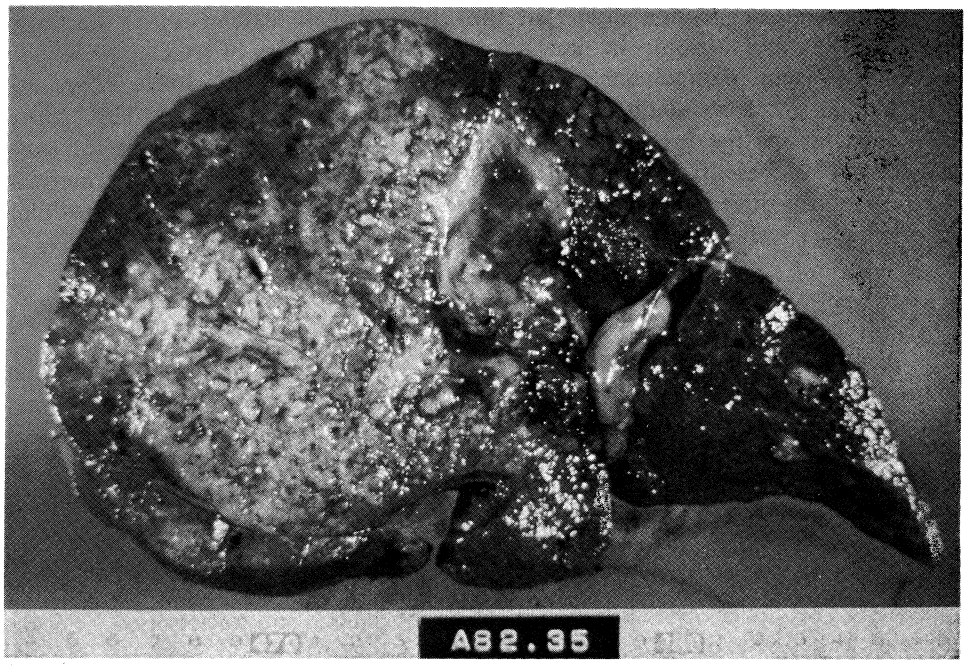


Fig. 1. Section of the liver showing hepatocellular carcinoma mainly involving the right lobe. Note the micronodular cirrhosis in the remaining tissue.

formed (Fig. 2). It completely impacted at tricuspid valve (Fig. 3), but was apparently free from endocardial surface. Slender stalks were present on the

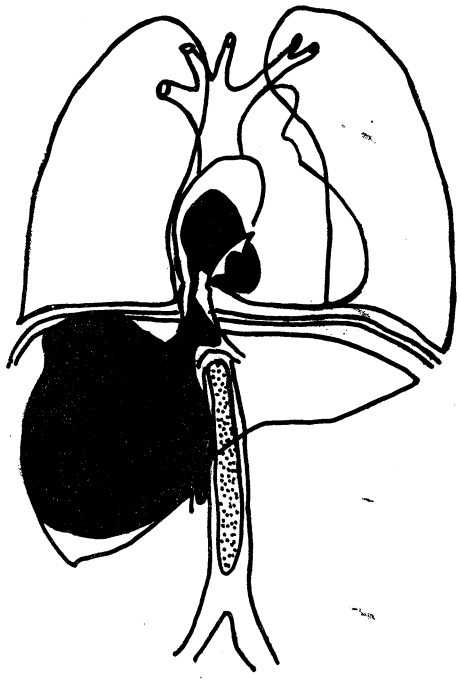

Fig 2. Extension of hepatocelluar carcinoma.

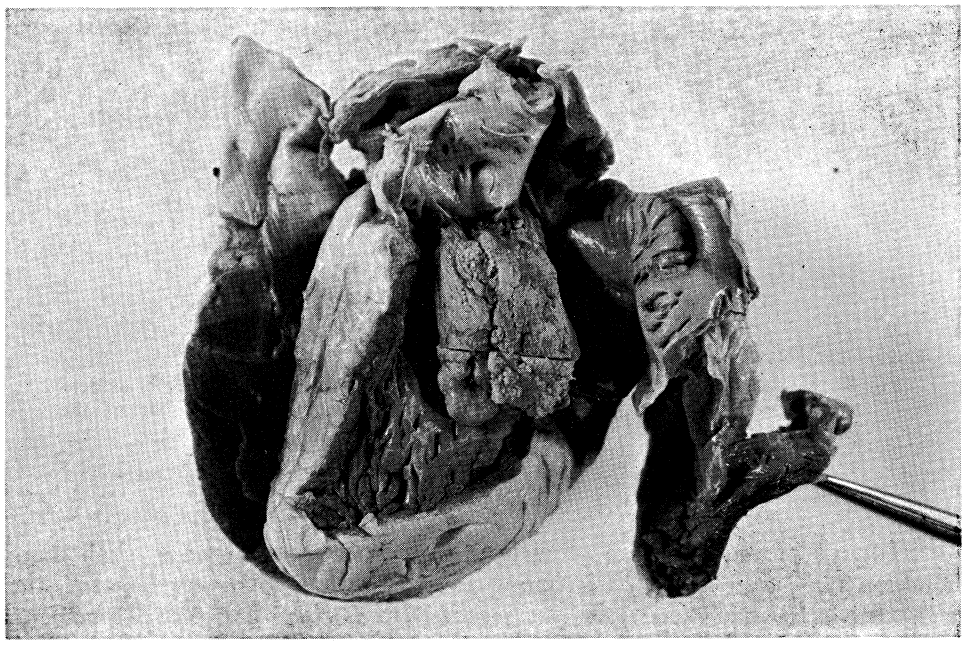

Fig. 3. The tumor embolus resting on the tricuspid valve.

tumor masses both of the right atrium and of the inferior vena cava as if the former had been the extension of the latter, but they were, in fact, discontinuous from each other. The lower portion of the inferior vena cava was completely obstructed by the tumor embolus with subsequent thrombus formation. Minute metastatic foci were found scattered in the lungs, and peritoneal surface including Douglas pouch. No apparent rupture of the tumor was discernible in any portion of the peritoneal surface. Esophageal varices were moderate in degree without a rupture. Stomach showed numerous petechial hemorrhages. Histological examination of the tumor in liver tissue showed mixed trabecular and giant cell type of hepatocellular carcinoma (Edmondson III–IV), which was mostly necrotic. Regenerative nodules in the remaining liver tissue in places showed massive coagulation necrosis, suggestive of terminal ischemia. The mass in the right atrium consisted of lobulated HCC which maintained sinusoidal structure, remniscent to the tumor in the liver (Fig. 4). The surface of the mass was covered by the endothelium and continuous to that of sinusoidal structure in the tumor. There was no adhesion or invasion to the endocardium.

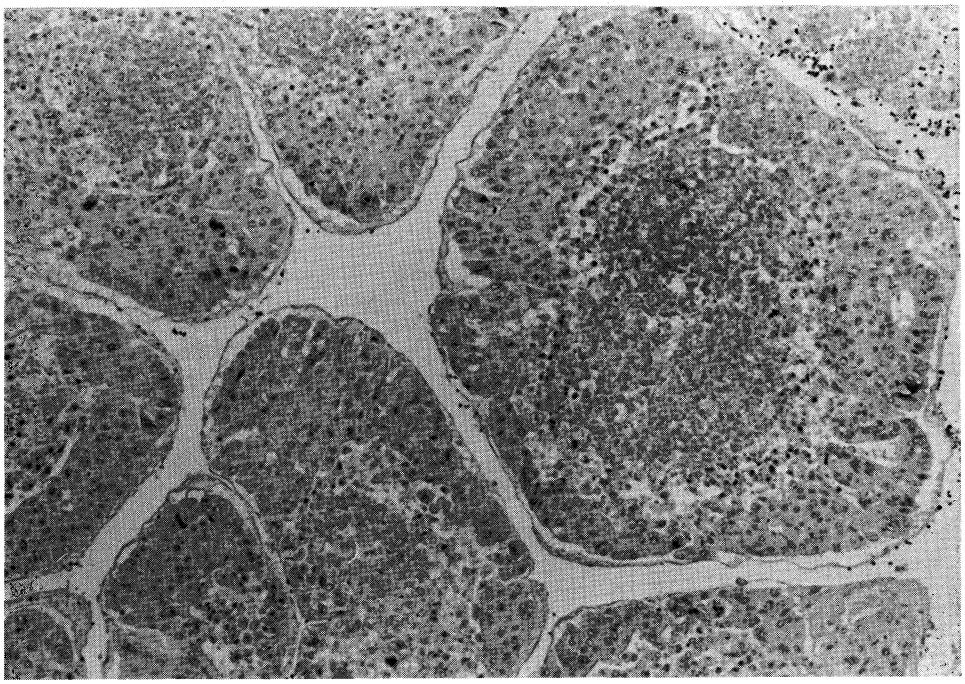

Fig. 4. A superficial portion of the tumor embolus. Sinusoidal structure is evident and the endothelium within the tumor embolus is continuous to that of the surface. (H-E, ×100)

## DISCUSSION

Tumors of the heart are of rarity and metastatic tumors are much more common than the primary.[3,4] Among patients with malignant neoplasm, the incidence of cardiac metastases was reported to range from 10 to 20 percent, which is 20 to 40 fold greater than the primary cardiac tumors of both

benign and malignant nature. In 1960, Hanfling[5] divided metastatic cardiac tumors into four groups according to the site of the involvement ; namely, 1) pericardial, 2) epicardial and myocardial, 3) endocardial and 4) chamber involvement (tumor embolism). First two groups are observed more commonly. Pericardial involvement usually arises from retrograde lymphatic spread or direct extension from intrathoracic neoplasm. Therefore, lung and breast are the common primary organs. In our experience of 78 HCC cases, there were two cases with pericardial involvement. Myocardial involvement was most often hematogenous. No metastasis in this fashion has been experienced in our HCC cases. Endocardial and chamber involvement is uncommon. In our literature review, only one case of endocardial implantation was reported in hepatocellular carcinoma. The chamber involvement was subdivided into three by their route of extension. The tumor may grow as an extension from superior vena cava. Examples are carcinomas of the lung, lymphomas, and carcinomas of the thyroid gland. The left atrium may be invaded from tumor extension through the pulmonary veins. This is commonly seen in carcinomas of the lung. Tumor involving the inferior vena cava may extend up to the right atrium.[3,6] Such tumors are commonly from the kidney and liver. Other tumors such as testicular teratoma, chondrosarcoma, leiomyosarcoma, reticulum cell sarcoma and leukemia are also known to cause such involvement.[3] Needless to say, our case was an example of the third type.

In so far as hepatocellular carcinoma is concerned, a few reports[7–16] have been appeared on the tumor embolism within the right atrium. In addition to his own case, Culpepper and von Haam[7] reviewed 3 cases of intra-atrial growth of HCC in the literature. Gregory[8] added 5 cases from the literature. Other sporadic case reports[11–15] are present. Studies of larger series of HCC indicates its incidence around 1-3% and a probable increase in these days.

Gustafson[9] found two such examples among their 62 cases of HCC (3%). Edmondson and Steiner[10] also found one of such cases out of 65 HCC they examined (1.5%). In Japan where HCC is more common than the western countries, Nakashima et al.[16] experienced ten out of 233 necropsied HCC cases (4.29%). This figure seems little too high. Their review of the data in the annual registries of autopsies disclosed the incidence of tumor embolism in the heart by HCC to be 0.67% between 1965 and 1975 and 1.8% for the year 1975. They commented that intra-atrial tumor growth is on the increase because of the prolonged survival of the patient resulted from early diagnosis and therapeutic progression. Okuda[17] clinically observed one such growth out of the 134 Japanese cases with HCC.

Clinical features of this condition were also clearly described by Hanfling.[5] They may have no clinical manifestations. Murmur of stenosis, soft heart sound of poor quality and the superior and inferior vena cava syndrome may be observed. Kato et al.[13] emphasized that the major signs of intra-atrial metastasis are the changes of heart murmur, dyspnea, syncope and shock which are evoked by patients' postural change. Five cases with sudden death and 9 cases with dyspnea developing on the change of the posture were, in fact, reported. Nakashima et al.[16] in contrast, reported that only one of ten patients with HCC developed sudden syncope and hypotension on the change of body

position.

Lastly, the cause of shock in our own case was not due to tumor impaction itself. Clinical history seems to suggest the following sequence of event.

Gastrointestinal bleeding developed in the terminal stage, which was manifested by abdominal pain and blood extraction through nasogastric tube. Then, the ischemic change or mechanical trauma due to cardio-pulmonary resuscitation have resulted in the rupture of the tumor stalk in the right atrium and impaction of the main mass at the tricuspid valve.

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