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Chemoembolic lobectomy: imaging findings of hepatic lobar volume reduction after transcatheter arterial chemoembolization

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ABSTRACT
Hepatic lobar atrophy-hypertrophy complex formation is an uncommonly reported sequella of hepatic arterial embolotherapy procedures. Whereas radiation-induced hepatic lobar ablation has been described after intra-arterial therapy with yttrium-90 microspheres, this phenomenon has not been reported after transcatheter arterial chemoembolization. Here, we report a case of prominent hepatic lobar atrophy with contralateral lobar hypertrophy after chemoembolization and suggest a mechanism by which arterial embolization contributes to the volumetric response.

Key words: • *chemoembolization* • *liver* • *atrophy* • *hypertrophy* • *lobectomy*

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Recently, there has been much interest in the concept of radiation-induced hepatic lobar ablation with marked volumetric loss and contralateral compensatory lobar hypertrophy (1–3). This phenomenon, termed radiation lobectomy, has been described to occur after yttrium-90 (^{90}Y) microsphere radioembolization and has been associated with high rates of tumor response and improved long-term patient survival in preliminary investigations (1). At present, the causative relationship between the administered radiation dose and the volumetric change is unknown, and the degree to which vascular embolization contributes to the observed changes remains uncertain. We recently encountered a striking case of hepatic lobar atrophy-hypertrophy complex formation after transcatheter arterial chemoembolization that suggests a possible contribution of arterial embolization to the volumetric response, which we present herein.

Case report

A 50-year-old man with a history of type 2 diabetes mellitus, hypertension, and hepatitis B virus liver disease was referred to interventional radiology for liver-directed therapy for the treatment of biopsy-proven hepatocellular carcinoma (HCC). The patient initially presented for assessment after screening computed tomography (CT) scan demonstrated a 4-cm right hepatic lobe mass, which was confirmed as HCC by image-guided core needle biopsy. Metastatic disease was ruled out with a chest CT and bone scan. The patient evaluation demonstrated an Eastern Cooperative Oncology Group performance status of zero (4), and the lab examination showed normal synthetic liver function (total bilirubin 0.9 mg/dL, albumin 4.2 g/dL, and prothrombin time 10.0 s). The initial α-fetoprotein level was only slightly elevated, measuring 15.5 ng/mL. Treatment options were discussed, and transcatheter arterial chemoembolization was elected for local tumor control.

Subsequently, the patient underwent drug eluting bead chemoembolization using 300–500-micron LC beads (Angiodynamics; Queensbury, New York, USA) loaded with 50 mg doxorubicin and mixed with 50 mg cisplatin and 20 mg mitomycin C in suspension. For chemoembolization, a standard right common femoral artery approach was used to position a 5 French reverse curve catheter in the celiac artery. The chemoembolic material was administered through a 2.8 French microcatheter placed coaxially in a segmental distribution via a right hepatic artery ascending branch (Fig. a) to a static angiographic endpoint. The patient had an uneventful post-procedure hospital course and was discharged 24 hours after treatment.

The patient follow-up included serial CT scans and lab assessment, which were performed initially at one month post-procedure and then at approximately three-month intervals. Although the one-month post-

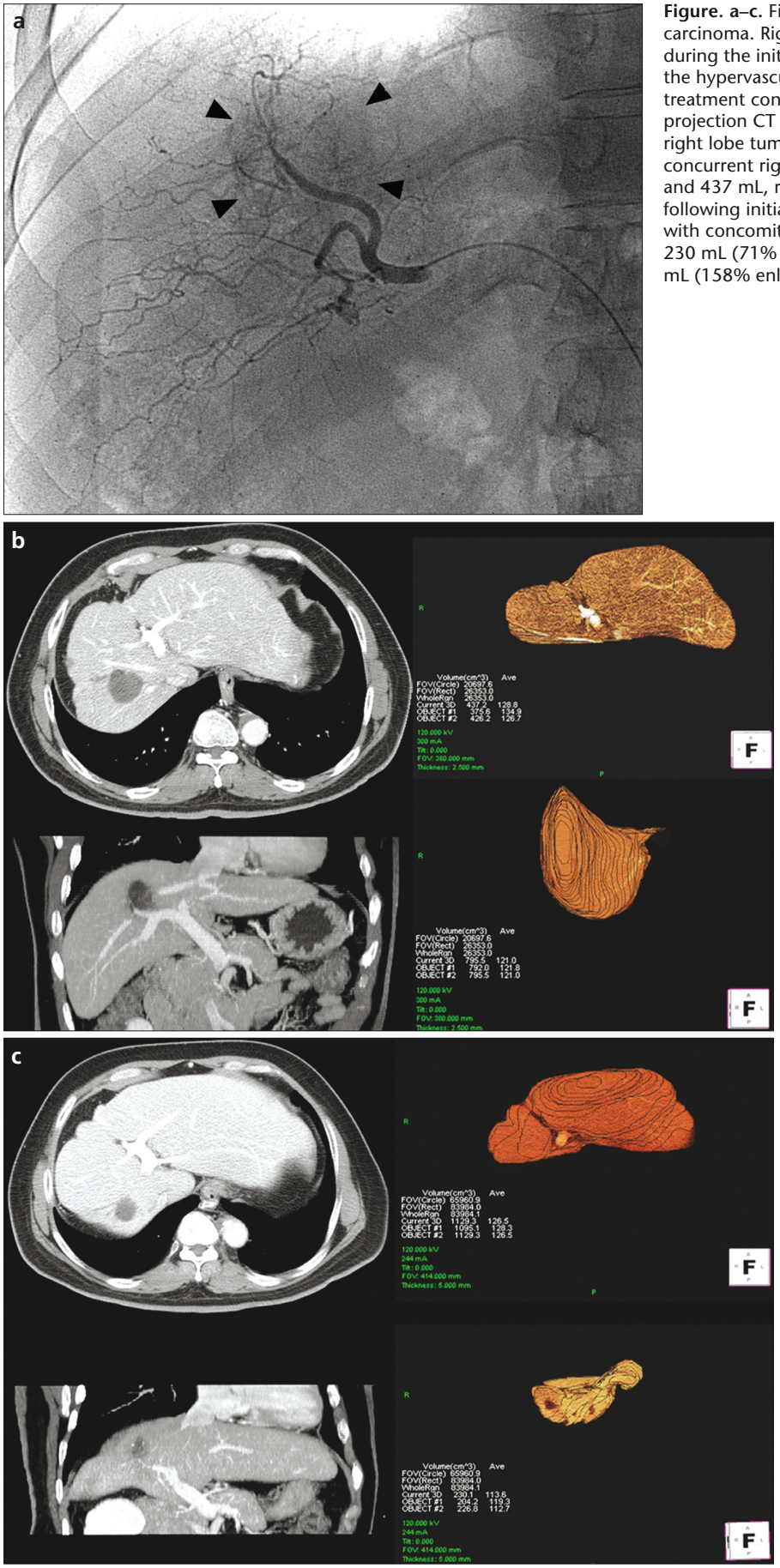

Figure. a–c. Fifty-year-old man with right lobe hepatocellular carcinoma. Right hepatic arteriogram **(a)** performed during the initial chemoembolization procedure showing the hypervascular tumor *(arrowheads).* One month post-treatment contrast-enhanced axial and maximum intensity projection CT scans **(b)** demonstrating low attenuation in the right lobe tumor, which indicates treatment response. The concurrent right and left hepatic lobe volumes were 796 mL and 437 mL, respectively. CT scan **(c)** obtained 35 months following initial therapy revealing complete tumor response with concomitant marked progressive right lobe atrophy to 230 mL (71% reduction) and left lobe hypertrophy to 1129 mL (158% enlargement).

treatment CT scan showed good tumor response (Fig. b), the patient underwent two additional right hepatic lobe chemoembolization treatment sessions at three months (again using drug eluting beads) and seven months (a 20-mL volume of cisplatin, doxorubicin, and mitomycin C solution mixed 1:1 with emulsifying iodized oil) after the initial therapy due to local residual and/or recurrent tumors. Additionally, because vague areas of atypical right hepatic lobe contrast enhancement were evident in the 12-month follow-up imaging, the patient underwent a right hepatic lobe biopsy, which demonstrated chemotherapy-related parenchymal fibrosis and a giant cell response without neoplasm. Surveillance imaging was continued, and a CT scan performed 35 months (Fig. c) following the initial chemoembolization demonstrated marked temporal changes in hepatic lobar volumes, including right lobe atrophy with concomitant left lobe hypertrophy. Concomitantly, a complete tumor response was evident based on necrosis criteria, and the laboratory analysis indicated that the enlarged left lobe functionally compensated for the shrunken right lobe, as evidenced by the maintenance of liver synthetic function (total bilirubin 1.6 mg/dL, albumin 3.5 g/dL, prothrombin time 13.7 s). The patient is currently alive with excellent performance status 38 months following the initial chemoembolization.

Discussion

The liver atrophy-hypertrophy complex represents the hepatic regenerative response following parenchymal injury (5). This process may occur due to any liver disease that induces atrophy, including biliary, portal vein, and hepatic vein obstruction. The subsequent restorative process involves cel-

lular hyperplasia, which occurs as a result of growth factor and cytokine production (including hepatocyte growth factor, transforming growth factor α, and interleukin 6), signaling pathway initiation (including nitric oxide and mitogen activated protein kinase pathways), and transcription factor activation (including NF-κb, AP-1, and STAT3), leading to hepatocyte proliferation (5). Hepatic lobar atrophy-hypertrophy complex formation is a well-described sequela of portal vein embolization (PVE) but has been less commonly reported and analyzed after hepatic arterial embolotherapy procedures (1, 6–8).

Recent studies that investigated the effects of ^{90}Y radioembolization on the liver have shown that this therapy may result in changes in the hepatic parenchymal volume, including ipsilateral lobar atrophy and contralateral lobar hypertrophy, as well as the induction of liver fibrosis and portal hypertension (7). The term "radiation lobectomy" has been proposed to describe the use of internal brachytherapy radiation to obliterate tumor-containing liver tissue on a lobar level with concomitant hypertrophy of the non-radiated hepatic lobe. Investigators have recently described the findings of radiation lobectomy in a cohort of 20 patients with primary liver malignancies (1). In the reported series, radiation lobectomy occurred with an incidence of at least 6%, and a median cumulative dose of 132 Gy resulted in a 52% median volumetric reduction in the treated right lobes, with a median 40% compensatory volumetric increase in the untreated left lobes. Radiation lobectomy was associated with good clinical outcomes, with tumor objective response rates ranging from 55–70% and 90%, for size and necrosis criteria, respectively.

Transcatheter arterial chemoembolization represents a recognized locoregional therapy for hepatocellular carcinoma with proven survival benefits (9, 10). Similar to radioembolization, this therapy utilizes the discrepancy in blood supply between hypervascular neoplastic tissue, which derives the majority of its blood supply from the hepatic artery, and non-cancerous liver parenchyma, which is predominantly perfused by the portal vein, to administer a targeted tumor therapy consisting of a combination of chemotherapeutic and embolic agents (11–13). Embolic materials slow the blood flow through the tumor and sequester chemotherapy agents to achieve high localized drug concentrations within the tumor, which then act through specific cellular mechanisms to induce cell death (11). Tumor necrosis rates following chemoembolization have been reported to range from 60–100% (12). Unlike radioembolization, marked parenchymal atrophy in the treated lobes has not been reported following chemoembolization.

The mechanism by which ispilateral hepatic lobar atrophy and contralateral hypertrophy are induced after intra-arterial chemoembolization remains unknown. In PVE, these volumetric alterations are explained based on the diversion of a significant portion of the hepatic blood supply from the portal vein away from the diseased liver toward the non-diseased future liver remnant, culminating in contralateral regeneration and hypertrophy of non-embolized hepatic parenchyma. We speculate that the similar changes observed after chemoembolization in our case could be related to the greater dependence of the cirrhotic liver on the hepatic artery. It is known that a decrease in portal venous blood flow in the setting of cirrhosis results in an increase in hepatic arterial flow in a phenomenon termed the hepatic arterial buffer response (14). Given these changes in hepatic hemodynamics, it is possible that with the appropriate degree of hepatic arterial dependence and lack of portal venous flow, arterial embolization may induce volumetric changes in the liver similar to PVE when arterial flow is shunted from a diseased hepatic lobe to a non-tumorous lobe. Despite the single case experience presented herein, this hypothesis is corroborated by the more significant volumetric changes observed herein as compared to a study that reported volumetric changes following hepatic arterial coil embolization in non-diseased livers, in which the mean reported degrees of atrophy and hypertrophy were 10% and 37%, respectively. It is notable that a biopsy of the treated right hepatic lobe after three chemoembolization sessions revealed evidence of hepatic fibrosis, suggesting at least a partial role for chemotherapy-induced liver scarring in the atrophy process. However, given the use of embolic microspheres and the static angiographic chemoembolization endpoint, we believe that the role of embolization is a more important factor in the development of the observed volumetric changes. Finally, it should be mentioned that the similar hemodynamic alterations in the cirrhotic liver might explain the observed volumetric changes in radiation lobectomy but with radiation-induced liver fibrosis causing arterial diversion as opposed to arterial embolization, given the generally less embolic nature of ^{90}Y microspheres.

In both radiation lobectomy and our case of chemoembolic lobectomy, the observed imaging changes were associated with improved patient survival. A 40.6% five-year survival rate has been reported for cases of hepatocellular carcinoma with radiation lobectomy (1), and our patient remains alive and well 38 months following chemoembolization. At present, uncertainty remains concerning the true pathophysiology and natural history of hepatic lobectomy after intra-arterial therapy. Further investigations of this phenomenon, including its incidence, contributing factors, relationship with hepatic arterial and portal venous hemodynamics, and association with clinical outcome, are vital to achieving a better understanding of this condition.

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