Chemoembolization of Hepatocellular Carcinoma with Drug-Eluting Beads Complicated by Interstitial Pneumonitis

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ABSTRACT

Transarterial chemoembolization has proven benefit in the treatment of unresectable hepatocellular carcinoma (HCC). Commonly reported symptoms following chemoembolization with or without drug-eluting beads include abdominal pain, nausea, and low-grade fever, which typically limited resolve within a few days. A recent study comparing traditional chemoembolization versus chemoembolization with drug-eluting beads demonstrated similar survival between the two techniques, but improved tolerability when the drug-eluting beads were used. This case report describes a patient with unresectable HCC undergoing chemoembolization with drug-eluting beads. The post-procedure course was complicated by interstitial pneumonitis secondary to shunting of the drug-eluting beads containing doxorubicin to both lungs via tumor vasculature. This case highlights the relationship between the number and size of the tumors to be treated, arteriovenous shunting within the liver/tumors, and the size of the embolization particles.

KEYWORDS: Hepatocellular cancer, transarterial chemoembolization

CASE REPORT

The patient is a 55-year-old man with hepatitis C who was diagnosed with locally advanced, unresectable HCC 6 months ago. The patient presented with weight loss and abdominal discomfort, and further evaluation revealed extensive liver tumors involving more than 50% of both lobes of the liver. He had no ascites at presentation. At the time of consult, he was a Child-Turcotte-Pugh B, and his ECOG performance status was 0. His α -feto-protein (AFP) level was >400. The patient presented 2 months after the initial consult and various treatment options for locally advanced HCC were discussed. The patient elected to undergo transarterial chemoembolization after discussion of the potential benefits and risks of

the procedure, including a relatively high risk of hepatic failure following chemoembolization.

Hepatic artery angiography revealed multiple hepatic masses involving both lobes of the liver (Fig. 1). Selective chemoembolization of the right hepatic artery was performed with drug-eluting beads (LC Bead 300–500 micron/50mg doxorubicin). Four tumors in the right lobe of the liver were treated. No evidence of hepatopulmonary shunt was noted during the procedure. Postembolization angiography demonstrated residual right hepatic lobe tumor perfusion and extensive left hepatic lobe tumor blush replacing much of the left hepatic lobe.

The patient tolerated the chemoembolization well and was discharged from the hospital 3 days after

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Figure 1 Early (A) and delayed (B) hepatic angiography reveals multifocal hepatocellular carcinoma with the largest tumor in the right hepatic lobe.

the procedure. On follow-up, the patient's AFP decreased to 200. Three months later, the left hepatic lobe was chemoembolized with drug-eluting beads (LC Bead 100–500 micron/50 mg doxorubicin). Near the end of the procedure, hepatopulmonary shunting was noticed. The patient was discharged home 3 days after the procedure in stable condition. After several days, the patient was readmitted to the emergency room complaining of shortness of breath. A computed tomography (CT) pulmonary angiogram was performed, revealing extensive bilateral pulmonary interstitial infiltrates (Fig. 2). The patient was treated with steroids and antibiotics. The patient responded to the treatment (Fig. 3), and his clinical symptoms improved.

DISCUSSION

HCC is said to be the fifth most common cancer among men and the eighth in women world-wide.¹ HCC is more common in Asia, southern Africa, and the Far East

and is less common in northern Europe, the United States, and Australia. In the United States, the annual number of cases exceeds 16,000. The majority (60–80%) of patients presenting with HCC are not amenable to curative surgical resection or transplantation due to various reasons, including size of the primary tumor, extrahepatic metastasis, comorbid conditions, and extent of the underlying liver disease. These patients are potentially candidates for alternate modes of treatment such as ablative or transcatheter therapies.

Initial case reports of chemoembolization with lipiodol showed reduced tumor growth but often resulted in acute liver failure. Survival was not significantly improved.² Later, a survival benefit from chemoembolization versus best supportive care was demonstrated in 2 randomized clinical trials.^{3,4} Chemoembolization with drug-eluting beads has the potential advantage of increasing local, effective drug delivery with the reduction in systemic bioavailability of the chemotherapy. Randomized controlled studies have shown better patient

Figure 2 Axial (A) and coronal (B) computed tomography (CT) scans of the chest reveal diffuse, bilobar airspace disease. These findings were new since prior chest CTs.

Figure 3 There is marked improvement in the bilateral airspace disease. (A) Chest X-ray at clinical presentation. (B) Follow-up study.

tolerance to chemoembolization with drug-eluting beads compared with conventional chemoembolization. There appears to be significantly less liver toxicity and a reduction in clinical adverse events.^{5,6}

LC Beads are a hydrogel-composed microspheres, produced from polyvinyl alcohol, that are biocompatible, hydrophilic, nonresorbable, and precisely calibrated. The LC beads are used in combination with doxorubicin for locally advanced unresectable HCC and with irinotecan for treating metastatic colon cancer to the liver. HCC has a tendency to invade the portal and hepatic veins. This may result in the formation of arteriovenous shunting through the tumor vasculature. Although LC beads are available in many sizes, the smaller particles are more susceptible to reaching the lungs via the arteriovenous shunts.

Conventional chemoembolization leading to adult respiratory distress syndrome (ARDS) has been reported.⁷ In this retrospective analysis, ARDS was diagnosed in 4 patients following transcatheter arterial embolization or chemoembolization. All patients had large (≥ 5 cm) and hypervascular HCC, and there was pulmonary lipiodol deposition on computed tomography (CT). Interestingly, none of these patients exhibited arteriovenous shunting angiographically. Other studies have revealed similar clinical toxicity, and they have implicated hepatic vein tumor invasion,⁸ large doses of Ethiodol[®] (> 20 cc; Savage Laboratories, Medford, NY),^{9,10} and treatment via the inferior phrenic arteries.¹¹

An early radioembolization study suggested that radiation pneumonitis may become a complication from yttrium-90 intraarterial delivery when the lung shunting (as assessed by Tc-MAA scan) is above 13%.¹² A recent article reported on 58 patients who underwent yttrium-90 glass microsphere radioembolization with a cumulative radiation dose > 30 Gr. None of these patients developed clinical or radiologic findings of radiation

pneumonitis.¹³ The current practice for most interventional radiologists is to limit the lung radiation dose to 30 Gr per treatment session and 50 Gr per lifetime when using glass microspheres, and to not offer therapy with resin microspheres when the lung shunt fraction is $> 20\%$.

The treatment for chemical pneumonitis is largely supportive. A pulmonary consultation is warranted. The prognosis for these patients is dependent on many factors, including comorbid pulmonary conditions.

REFERENCES

1. Bosch FX, Ribes J, Díaz M, Cléries R. Primary liver cancer: worldwide incidence and trends. *Gastroenterology* 2004; 127(5, Suppl 1):S5–S16
2. A comparison of lipiodol chemoembolization and conservative treatment for unresectable hepatocellular carcinoma. Groupe d'Etude et de Traitement du Carcinome Hépatocellulaire. *N Engl J Med* 1995;332(19):1256–1261
3. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology* 2002;35(5):1164–1171
4. Llovet JM, Real MI, Montaña X, et al; Barcelona Liver Cancer Group. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. *Lancet* 2002;359(9319):1734–1739
5. Lammer J, Malagari K, Vogl T, et al; PRECISION V Investigators. Prospective randomized study of doxorubicin-eluting-bead embolization in the treatment of hepatocellular carcinoma: results of the PRECISION V study. *Cardiovasc Intervent Radiol* 2010;33(1):41–52
6. Dhanasekaran R, Kooby DA, Staley CA, Kauh JS, Khanna V, Kim HS. Comparison of conventional transarterial chemoembolization (TACE) and chemoembolization with doxorubicin drug eluting beads (DEB) for unresectable hepatocellular carcinoma (HCC). *J Surg Oncol* 2010;101(6): 476–480

7. Wu GC, Perng WC, Chen CW, Chian CF, Peng CK, Su WL. Acute respiratory distress syndrome after transcatheter arterial chemoembolization of hepatocellular carcinomas. *Am J Med Sci* 2009;338(5):357–360
8. Kwok PC, Lam TW, Lam CL, Lai AK, Lo HY, Chan SC. Rare pulmonary complications after transarterial chemoembolisation for hepatocellular carcinoma: two case reports. *Hong Kong Med J* 2003;9(6):457–460
9. Chung JW, Park JH, Im JG, Han JK, Han MC. Pulmonary oil embolism after transcatheter oily chemoembolization of hepatocellular carcinoma. *Radiology* 1993;187(3):689–693
10. Matsumoto K, Nojiri J, Takase Y, et al. Cerebral lipiodol embolism: a complication of transcatheter arterial chemoembolization for hepatocellular carcinoma. *Cardiovasc Intervent Radiol* 2007;30(3):512–514
11. Choi CS, Kim KH, Seo GS, et al. Cerebral and pulmonary embolisms after transcatheter arterial chemoembolization for hepatocellular carcinoma. *World J Gastroenterol* 2008;14(30):4834–4837
12. Leung TW, Lau WY, Ho SK, et al. Radiation pneumonitis after selective internal radiation treatment with intraarterial ⁹⁰yttrium-microspheres for inoperable hepatic tumors. *Int J Radiat Oncol Biol Phys* 1995;33(4):919–924
13. Salem R, Parikh P, Atassi B, et al. Incidence of radiation pneumonitis after hepatic intra-arterial radiotherapy with yttrium-90 microspheres assuming uniform lung distribution. *Am J Clin Oncol* 2008;31(5):431–438