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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Hepatology* (*WJH*, *World J Hepatol*) is to provide scholars and readers from various fields of hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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Two-stage hepatectomy with radioembolization for bilateral colorectal liver metastases: A case report

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Abstract

BACKGROUND

Two-stage hepatectomy (TSH) is a well-established surgical technique, used to treat bilateral colorectal liver metastases (CRLM) with a small future liver remnant (FLR). However, in classical TSH, drop-out is reported to be around 25%-40%, due to insufficient FLR increase or progression of disease. Trans-arterial radioembolization (TARE) has been described to control locally tumor growth of liver malignancies such as hepatocellular carcinoma, but it has been also reported to induce a certain degree of contralateral liver hypertrophy, even if at a lower rate compared to portal vein embolization or ligation.

CASE SUMMARY

Herein we report the case of a 75-year-old female patient, where TSH and TARE were combined to treat bilateral CRLM. According to computed tomography (CT)-scan, the patient had a hepatic lesion in segment VI-VII and two other confluent lesions in segment II-III. Therefore, one-stage posterior right sectionectomy plus left lateral sectionectomy (LLS) was planned. The liver volumetry estimated a FLR of 38% (segments I-IV-V-VIII). However, due to a more than initially planned, extended right resection, simultaneous LLS was not performed and the patient underwent selective TARE to segments II-III after the first surgery. The CT-scan performed after TARE showed a reduction of the treated lesion and a FLR increase of 55%. Carcinoembryonic antigen and CA 19.9 decreased significantly. Nearly three months later after the first surgery, LLS was

Checklist (2016).

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performed and the patient was discharged without any postoperative complications.

CONCLUSION

According to this specific experience, TARE was used to induce liver hypertrophy and simultaneously control cancer progression in TSH settings for bilateral CRLM.

Key Words: Trans-arterial; Radioembolization; Two-stage hepatectomy; Colorectal liver metastases; Selective internal radiation therapy; Yttrium90; Case report

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Core Tip: Two-stage hepatectomy and trans-arterial radioembolization (TARE) are usually used in advanced stage primary liver malignancies. In this case report, two-stage hepatectomy and TARE were combined, for the first time, to treat a patient with bilateral colorectal liver metastases and a small future liver remnant. In particular, TARE was performed to induce liver hypertrophy and at the same time to control tumor growth between stages, thus reducing the risk of tumor progression.

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INTRODUCTION

Two-stage hepatectomy (TSH) has been traditionally advocated for bilateral colorectal liver metastases (CLRM) that could not be resected in a single operation^[1]. In TSH, when the future liver remnant (FLR) is considered not enough, contralateral portal vein ligation (PVL) or embolization (PVE) can be performed in the first stage to increase FLR volume. However, 25%-40% of patients will not undergo the second stage due to insufficient liver hypertrophy and/or progression of disease^[2]. Trans-arterial radioembolization (TARE) consists of the selective intra-arterial administration of microspheres loaded with a radioactive compound – usually yttrium90 – and has been shown to control tumor growth and to induce liver hypertrophy especially in patients with primary liver cancer. More recently, it has been shown to be effective also in CLRM setting^[3]. However, the combination of these two techniques has never been explored before.

CASE PRESENTATION

Chief complaints

A 75-year-old female patient presented herself with mild abdominal pain.

History of present illness

Ultrasonography and abdominal computed tomography (CT) detected three unknown hepatic lesions in segment VI-VII ($n = 1$) and segment II-III ($n = 2$), respectively. The lesion of the right lobe seemed to infiltrate the right hepatic vein whereas the other two confluent lesions in segment II-III showed a particular intrabiliary growth pattern (Figure 1).

History of past illness

The patient had undergone endoscopic removal of a sigmoid polyp cancer (T1NxMxR0) 3 years before.

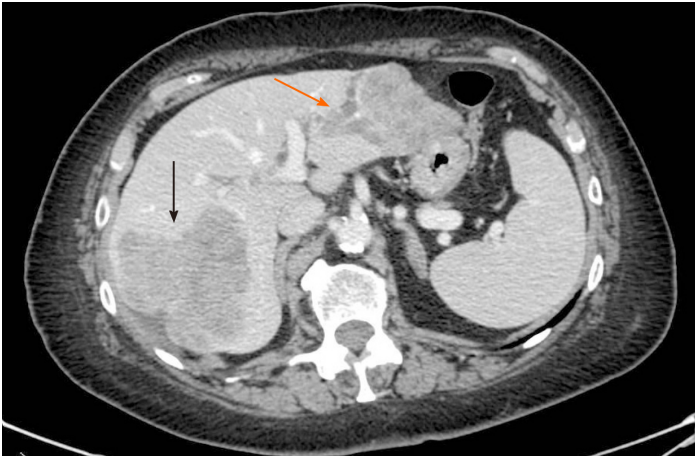


Figure 1 Pre-operative computed tomography-scan. The lesion occupying the right posterior segments of the liver (black arrow) and two other confluent lesions in the left lobe with intrabiliary growth pattern (orange arrow).

Personal and family history

She suffered from hypertension and hypoparathyroidism. She had no family history of cancer.

Physical examination

The patient had a good performance status. Physical examination was unremarkable with vital signs within the normal range of values. No jaundice was observed.

Laboratory examinations

Liver function tests were normal and tumor markers were increased (carcinoembryonic antigen, CEA = 3284.9 ng/mL; CA 19-9 = 703.9 U/mL).

Imaging examinations

Esophagogastroduodenoscopy and colonoscopy were negative. According to liver volumetry, total functional liver volume (TFLV) measured 1635 mL and FLR (segments I-IV-V-VIII) 621 mL, with a resulting FLR/TFLV of 38%.

FINAL DIAGNOSIS

The final diagnosis of the presented case was suspected bilateral hepatic metastases from colorectal cancer.

TREATMENT

The operation started with a minimally invasive approach, but it was converted to open surgery due to diaphragm infiltration by the lesion located in the right liver. Intraoperative ultrasound showed that part of segment VIII was also involved. After detachment of the lesion from the diaphragm and its suture, a portal branch of segment V was ligated during parenchymal transection. Given the wider than initially planned hepatic surgery (segments V-VI-VII + part of segment VIII) and the difficulties encountered during the first resection, left lateral sectionectomy (LLS) was postponed. As a bridge treatment, TARE was chosen in order to control locally the disease while waiting for FLR increase. According to the CT-scan performed 10 d after surgery, FLR measured 632 mL. A small intrabdominal fluid collection was incidentally detected close to the surgical site as well as an ischemic area in segment V. The patient was discharged home on postoperative day 14, without major complications. The final diagnosis, based on histopathology of surgery specimen, was adenocarcinoma from colorectal cancer (KRAS and BRAF wild-type). TARE was carried out 11 d after discharge and realized with a single treatment (200 Gy) of Selective Internal Radiation (SIR) spheres (Sirtex Medical, Sydney, Australia) without any post-procedural complications (Figure 2). Forty-seven days after TARE, the

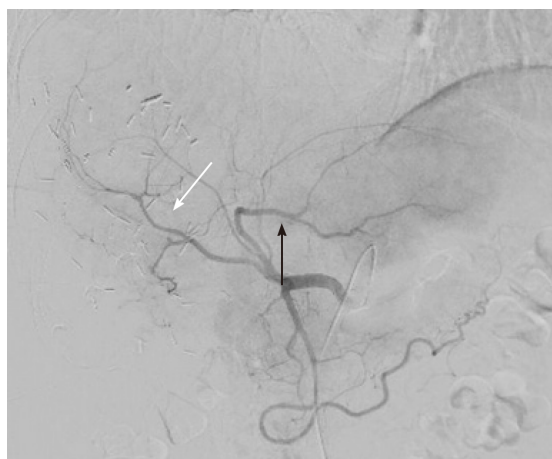


Figure 2 Arterial vascular anatomy during trans-arterial radioembolization procedure treating the tumor lesion in segments II-III (black arrow). The angiography also showed the remaining right anterior portal pedicle (white arrow).

patient underwent a new CT-scan showing a 32% reduction of the confluent lesion in segment II-III, with a surprisingly final FLR volume of 980 mL (FLR increase = 55%, FLR/TFLV = 77%) (Figure 3). CEA and CA 19.9 decreased to 93.7 ng/mL and 92.5 U/mL, respectively. After resolution of the abdominal collection by percutaneous drainage, we planned the second stage of surgery and 3 mo later after the first operation, the patient underwent LLS.

OUTCOME AND FOLLOW-UP

The postoperative course was uneventful. The patient did not receive any adjuvant chemotherapy and almost two years after the first surgery is still alive and free of disease.

DISCUSSION

According to this specific experience, TARE was used for the first time, combined with classical TSH, to control cancer progression between stages, waiting for adequate liver hypertrophy before the second resection.

TARE has been already shown to produce effective liver parenchyma hypertrophy in patients with primary hepatic malignancies treated with lobar 90Y radioembolization therapy^[4]. After TARE, however, compared to PVE/PVL, the hypertrophy is radiation-induced rather than caused by embolization and is reached at a slower rate. According to a recent systematic review^[5], the median kinetic growth rate of the contralateral lobe for patients underwent lobar TARE for CRLM was 0.8% per week compared to 6.1% of PVE. Despite a slower increase, however, a hypertrophy of 26%-47% was obtained at time intervals ranging from 44 d to 9 mo^[4], of similar magnitude to that observed after PVE. In addition, Birgin *et al*^[5] found that up to 84% of patients affected by primary and secondary hepatic malignancies had a local tumor control following TARE and about 30% of unresectable tumors underwent hepatic resection.

Review of the literature, including only studies of patients submitted to hepatectomy for CRLM after preoperative TARE ($n = 18$)^[6-18] (Tables 1 and 2), showed that even though many of them comprised bilateral distribution of CRLM^[18-20], only Pardo *et al*^[21] reported a “two-stage resection” in 10 patients, 7 of whom underwent associating liver partition and portal vein ligation for staged hepatectomy (ALPPS), probably from the cohort of Justinger *et al*^[22]. In this latter study, resectability of ALPPS + TARE was 85.7%. Increase of FLR in CRLM patients was reported only in few studies^[22,23]. In our report, TARE to segment II-III led to a FLR increase of 55%, probably induced by the combined regenerative effect produced by the first liver resection, similar to what happens in ALPPS procedure, and by TARE itself. If a larger FLR hypertrophy was required, the role of TARE in combination also with classical portal vein occlusion techniques such as PVE/PVL or ALPPS, could have been

Table 1 Review of the literature including patients submitted to preoperative trans-arterial radioembolization for colorectal liver metastases

Ref.	Year	Type of study	Pts included, <i>n</i>	CRLM ¹ , <i>n</i> (%)	Tumor location (<i>n</i>)	Bilobar <i>n</i> (%)	Prior resection, <i>n</i> (%)	Resectability, <i>n</i> (%)
Gray <i>et al</i> ^[18]	2001	HAI <i>vs</i> HAI + TARE in unresectable CRLM; RCT	74	36 (48.6)	Colon (29), rectum (7)	36/36 (100)	0	1/36 (2.8)
Lim <i>et al</i> ^[6]	2005	TARE after failure of FU in unresectable CRLM; prospective	30	30 (100)	NA	NA	0	1/30 (3.3)
Sharma <i>et al</i> ^[7]	2007	TARE + FOLFOX4 in unresectable CRLM; prospective (phase I)	20	20 (100)	Right colon (4), sigmoid (5), rectum (4), other colon sites (7)	NA	0	2/20 (10)
Cosimelli <i>et al</i> ^[19]	2010	TARE in unresectable CRLM; prospective (phase II)	50	50 (100)	Colon (41), rectum (9)	35/50 (70)	12/50 (24.0)	2/50 (4.0)
Hendlishz <i>et al</i> ^[8]	2010	FU <i>vs</i> TARE + FU in unresectable CRLM; RCT	44	21 (47.7)	NA	NA	NA	1/21 (4.8)
Brown <i>et al</i> ^[9]	2011	TARE <i>vs</i> CHT <i>vs</i> no therapy before hepatectomy; case-control	840	16 (1.9)	NA	NA	NA	16/16 (100)
Whitney <i>et al</i> ^[10]	2011	TARE in unresectable liver disease; retrospective	44	15 (34)	Rectum (15)	0	0	1/15 (6.7)
Vouche <i>et al</i> ^[11]	2013	TARE in unresectable liver disease; retrospective	83	8 (9.6)	NA	0	0	1 (12.5)
Wang <i>et al</i> ^[20]	2013	TARE before liver resection for CRLM; retrospective	24	24 (100)	Sigmoid (1), rectum (1), other colon sites (1), unknown (21)	1/3 (33.3)	0	3/24 (12.5)
Henry <i>et al</i> ^[12]	2015	TARE before liver resection for metastatic cancer; retrospective	9	4 (44.4)	NA	NA	0	4/4 (100)
Justinger <i>et al</i> ^[22]	2015	TARE in marginally resectable CRLM; retrospective	13	13 (100)	Right colon (2), sigmoid (4), rectum (7)	9/13 (69.2)	7/13 (53.8) ²	11/13 (84.6)
Moir <i>et al</i> ^[13]	2015	TARE in unresectable liver disease; retrospective	44	22 (50)	NA	NA	NA	4/22 (18.2)
Maleux <i>et al</i> ^[14]	2016	TARE in unresectable CRLM; NA	88	71 (80.6)	NA	58/71 (81.6)	10/71 (14.0)	1/71 (1.4)
Lewandowski <i>et al</i> ^[23]	2016	TARE in unresectable right-sided liver disease; retrospective	13	1 (7.6)	NA	0	NA	1/1 (100)
Wright <i>et al</i> ^[15]	2017	TARE in unresectable liver disease; retrospective	465	6 (1.2)	NA	NA	NA	6/6 (100)
van Hazel <i>et al</i> ^[16]	2016	FOLFOX6 <i>vs</i> FOLFOX6 + TARE ± Bevacizumab; RCT	530	267 (50.3)	Left colon (141), right colon (72), rectum (45), other colon sites (7), unknown (2)	NA	NA	38/267 (14.2)
Pardo <i>et al</i> ^[21]	2017	TARE before liver resection or transplantation; retrospective	100	30 (30)	NA	44/100	7/30 (23.3) ²	30/30 (100)
Wasan <i>et al</i> ^[17]	2017	FOLFOX <i>vs</i> FOLFOX + TARE; RCT	1103	554 (50.2)	Colon (421), rectum (116), unknown (17)	NA	NA	56/554 (10.1)

¹Treated with transarterial radioembolization.²Associating liver partition and portal vein ligation for staged hepatectomy. CHT: Chemotherapy; CRLM: Colorectal liver metastases; FU: Fluorouracil; HAI: Hepatic artery infusion; NA: Not available; RCT: Randomized controlled trial; TARE: Transarterial radioembolization.

explored. However, in this case, TARE was preferred over PVE or PVL since segment IV had to be preserved being part of the FLR. Furthermore metastasis in segment II-III could have progressed leading to the drop out of the patient. On the other side, the risk of proceeding with a second simultaneous hepatectomy or ALPPS was deemed too high. Last but not least, from the oncological point of view, this strategy may allow surgeons, without dealing with time issue, to select only patients with favorable tumor biology, according to radiological response after TARE^[12].

CONCLUSION

TARE in TSH setting may represent a viable option to increase resectability in patients with bilateral CLRM by stimulating liver hypertrophy and controlling locally the disease. Future larger, comparative studies may help answer the questions above.

Table 2 Review of the literature including patients submitted to preoperative trans-arterial radioembolization for colorectal liver metastases

Ref.	FLR increase %	Time TARE-surgery, median (range), mo	Type of hepatic resection (n)	Post-operative mortality %	Survival, median (range), mo	Disease free, median (range), mo	Recurrence after surgery, n (%)
Gray <i>et al</i> ^[18]	NA	NA	NA	0	96	NA	NA
Lim <i>et al</i> ^[6]	NA	NA	NA	NA	NA	22	1/1 (100)
Sharma <i>et al</i> ^[7]	NA	NA	LLS + S6 (1), RH + S3 (1)	NA	NA	NA	NA
Hendlish <i>et al</i> ^[8]	NA	NA	RH (1)	0	NA	1.5	1/1 (100)
Brown <i>et al</i> ^[9]	NA	6.5 (4-13)	NA	NA	NA	NA	NA
Whitney <i>et al</i> ^[10]	NA	NA	RT (1)	0	NA	24	1/1 (100)
Vouche <i>et al</i> ^[11]	NA	NA	RT (1)	0	NA	NA	NA
Wang <i>et al</i> ^[20]	NA	NA (4-9)	RH (2), LH + S6 (1)	0	NA	NA	NA
Henry <i>et al</i> ^[12]	NA	5 (2-8)	LLS (1), multiple wedge, HAI pump (1), RT + RFA (1), RT (1)	50	13 (0-27)	6.2 (1.8-10.5)	3/4 (75)
Justinger <i>et al</i> ^[22]	32.9 (ALPPS), 27.1 (no ALPPS)	2 (1-5)	RT (4), RH (5), mesohepatectomy (1), LT (1)	7.6	25 (12-38) ¹	NA	NA
Moir <i>et al</i> ^[13]	NA	4 (2-11)	NA	0	15 (11-19) ¹	NA	NA
Maleux <i>et al</i> ^[14]	NA	NA	S + RFA (1)	0	NA	NA	NA
Lewandowski <i>et al</i> ^[23]	15	1.6 (1-7)	RT (1)	0	4.8	NA	NA
Wright <i>et al</i> ^[15]	NA	9 (3-20)	RT (2), S (1), RH (3)	16.6	25 (NA)	NA	NA
van Hazel <i>et al</i> ^[16]	NA	NA	NA	0	NA	NA	NA
Pardo <i>et al</i> ^[21]	NA	NA	NA	10	NA	NA	NA
Wasan <i>et al</i> ^[17]	NA	NA	NA	3.6	NA	NA	NA

¹95% confidence interval. ALPPS: Associating liver partition and portal vein ligation for staged hepatectomy; HAI: Hepatic artery infusion; LH: Left hepatectomy; LLS: Left lateral sectionectomy; LT: Left trisectionectomy; RFA: Radiofrequency ablation; RH: Right hepatectomy; RT: Right trisectionectomy; S: Segmentectomy; NA: Not available.

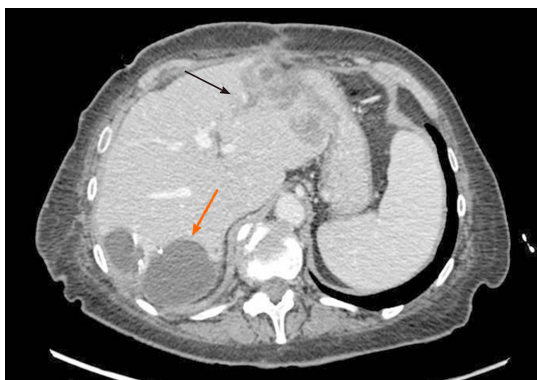


Figure 3 Computed tomography-scan performed one month after trans-arterial radioembolization. The reduction of the lesion of the left lobe and the intrabiliary growth pattern (black arrow). An intrabdominal fluid collection was found close to the surgical site (orange arrow).

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