Transcatheter arterial embolization with trisacryl gelatin microspheres (Embosphere®) leads to life-threatening tumor lysis syndrome in a rectal carcinoid patient with hepatic metastases

Yuan-Hao Lo1, Ming-Tsun Tsai2, Chen-Yu Kuo3, Wen-Sheng Liu2,4,5, Rheun-Chuan Lee4,6, Yi-Chen Yeh4,7, Chung-Pin Li3,4, Jinn-Yang Chen2,4 and Yee Chao4,8

1Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, Taipei; 2Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei; 3Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei; 4National Yang-Ming University, School of Medicine, Taipei; 5Division of Nephrology, Department of Medicine, Taipei City Hospital, Zhong-Xing Branch, Taipei; 6Department of Radiology, Taipei Veterans General Hospital, Taipei; 7Department of Pathology and Laboratory Medicine, Taipei Veterans General Hospital, Taipei; 8Cancer Center, Taipei Veterans General Hospital, Taipei, Taiwan
Correspondence to: Wen-Sheng Liu. Email: robertliu2001@yahoo.com

Abstract
The incidence of gastrointestinal carcinoids appears to be increasing, and the rectum is the third most common location. Transcatheter arterial embolization (TAE) with trisacryl gelatin microspheres (Embosphere®) has been reported as an effective method for hepatic metastases of rectal carcinoids. Complications are uncommon and usually of minor consequence. We report an unusual case of a 34-year-old man with tumor lysis syndrome following TAE with Embosphere® in a patient with multiple hepatic metastases of a rectal carcinoid. Early detection and effective treatment are essential for this rare but potentially catastrophic complication.

Keywords: Transcatheter arterial embolization, tumor lysis syndrome, trisacryl gelatin microspheres, rectal carcinoid tumors

Submitted November 2, 2011; accepted for publication May 26, 2012
On physical examination, a huge mass was palpable in the upper abdomen. There was no ascites or signs of encephalopathy. On the day of admission, laboratory results showed hemoglobin 11.3 g/dL, platelet count 207,000/mm³, alanine aminotransferase (ALT) 37 IU/L, aspartate aminotransferase (AST) 35 IU/L, albumin 3.9 g/dL, total bilirubin 0.57 mg/dL, lactate dehydrogenase (LDH) 402 IU/L, creatinine 0.8 mg/dL, potassium 4 mmol/L, and prothrombin time 13.5 s. The Child-Pugh class was A.

On unenhanced and contrast-enhanced CT, there were more than 20 hepatic tumors in both lobes, with the largest being >18 cm in diameter (Fig. 1a and b). Hepatic angiography was performed via a right femoral artery approach (Fig. 2a and b). A 4-French catheter and a 2.7-French microcatheter were used for celiac trunk and superselective hepatic (segmental and subsegmental) angiography, respectively, revealing multiple tumor stains in both hepatic lobes. TAE was performed by injection of 2 mL 100–300 μm Embosphere particles in the left hepatic artery’s supplying branches and 2 mL 100–300 μm, 2 mL 300–500 μm Embosphere particles injection in the right hepatic artery’s supplying branches until there was sluggish hepatic arterial flow. The coil shown in the picture (Fig. 2) was placed during the procedure of Yttrium-90 therapy. Coil embolization of the right gastric artery and gastroduodenal artery could avert reflux and thereby decrease the risk of gastric ulcer during Yttrium-90 therapy.

Three days after TAE, the patient complained of general fatigue and poor appetite. He also became oliguric. Laboratory tests showed ALT 430 IU/L, AST 1910 IU/L, total bilirubin 7.63 mg/dL, LDH 16300 IU/L, creatinine 6.54 mg/dL, potassium 7 mmol/L, phosphorous 10.7 mg/dL, calcium 6.2 mg/dL, and uric acid 13.4 mg/dL.
As the patient developed hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia, and acute renal failure, the diagnosis of acute tumor lysis syndrome was made. He was first treated with 0.9% saline hydration, then alkalinization of urine with sodium bicarbonate, allopurinol for hyperuricemia, kalimate, and calcium gluconate for hyperkalemia were applied 3 days after TAE. However, anuria developed and he received emergency hemodialysis. Rasburicase was applied for hyperuricemia on the fifth day after TAE.

After intensive care, the patient gained satisfactory recovery of both renal and hepatic functions on day 68 after TAE. Laboratory tests showed ALT 16 IU/L, AST 16 IU/L, total bilirubin 0.58 mg/dL, creatinine 0.79 mg/dL, BUN 12 mg/dL, potassium 3.9 mmol/L, and prothrombin time 12.6 s. Follow-up unenhanced CT scan on day 34 after TAE showed large areas of necrosis (Fig. 3).

Because of disease progression 1 year later, TAE was performed once more with Embosphere® after prevention for tumor lysis syndrome (adequate hydration and the usage of rasburicase). Neither tumor lysis syndrome nor acute renal failure occurred after this procedure. Finally, the patient died of progressive disease 4 months after the second TAE.

Discussion

Carcinoid tumors are morphologically and biologically heterogeneous neuroendocrine tumors that have malignant potential. They are most commonly found in the gastrointestinal tract, with the rectum as the third most common location (6). In the United States, the age-adjusted incidence of colorectal carcinoid tumors is about 1 in 100,000, and the incidence of rectal carcinoid tumors has increased about 10-fold over the last 35 years (7). Rectal carcinoid tumors also present with metastasis in 4–18% of cases (8).

Many different kinds of treatments have been reported to be effective in hepatic metastases of carcinoid tumors, including somatostatin analogues, alpha-interferon, chemotherapy, radiofrequency ablation, liver embolization alone or with chemotherapy (chemoembolization), cytoreductive surgery, and liver transplantation (1–4). Liver embolization, as part of a multimodality treatment protocol, may lead to partial radiological response as well as symptomatic improvement of disabling endocrine symptoms (2–4, 9).

Several types of particles have been used in TAE, including trisacryl gelatin microspheres (Embosphere®). Embosphere® particles are not degradable and are more homogenous of size than particles previously used (e.g. polyvinyl alcohol or gel-foam). Granberg et al. have reported that TAE with Embosphere® particles is a safe and effective treatment for patients with metastatic carcinoid tumors (4). Our patient with metastatic carcinoid tumors underwent superselective TAE with Embosphere® particles, however, tumor lysis syndrome developed after the treatment. To our knowledge, this is the first reported case of tumor lysis syndrome after TAE with Embosphere® for metastatic carcinoid tumors.

Most cases of tumor lysis syndrome occur after treatment of hematopoietic malignancies (10). However, it may occur, albeit rarely, after TAE of solid tumors. Hsieh et al. reported a few cases that developed tumor lysis syndrome after TAE of hepatocellular carcinomas. Larger tumor size is one of the risk factors (11). In our patient, there were more than 20 metastatic carcinoid tumors in both lobes of the liver, with the largest one being >18 cm in diameter. Moreover, vessel occlusion by Embosphere® particles may be more permanent because they are non-degradable.

The frequency of tumor lysis syndrome is increasing among patients who have tumors that used to be only rarely associated with this complication. It occurs when tumor cells release their contents into the blood, leading to hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia (10). Deposition of uric acid and calcium phosphate crystals in the renal tubules can cause acute renal failure. Standard treatment includes the correction of electrolyte imbalance and acidosis. Adequate intravenous hydration is essential to prevent acute renal failure. Allopurinol can be used for hyperuricemia but may cause serious allergic reactions. Recombinant urate oxidase (rasburicase) is an effective alternative for lowering uric acid levels. If patients fail to respond to medical treatment, urgent hemodialysis is indicated (12).

The cause of a high attenuation rim around the necrotic masses is not clear (Fig. 3). Lipiodol was not mixed with Embosphere®. Furthermore, contrast medium retention was also less likely as CT was performed on day 34 after TAE. One possible explanation is dystrophic calcification after tissue necrosis (13).

In conclusion, TAE for hepatic metastases of carcinoid tumors is a feasible treatment that may give relief of symptoms. Tumor lysis syndrome is an uncommon but potentially catastrophic complication that should always be considered and treated immediately when it occurs.
ACKNOWLEDGEMENTS

This work was supported by grants from the Taipei Veterans General Hospital (VGH 100C-178) and from the National Science Council (NSC 98-2314-B-075-029). The authors also thank the Division of Experimental Surgery of the Department of Surgery, Taipei Veterans General Hospital for their assistance.

REFERENCES

1. Sutcliffe R, Maguire D, Ramage J, et al. Management of neuroendocrine liver metastases. Am J Surg 2004;187:39–46
2. Carrasco CH, Charnsangavej C, Ajani J, et al. The carcinoid syndrome: palliation by hepatic artery embolization. Am J Roentgenol 1986;147:149–54
3. Schell SR, Camp ER, Caridi JG, et al. Hepatic artery embolization for control of symptoms, octreotide requirements, and tumor progression in metastatic carcinoid tumors. J Gastrointest Surg 2002;6:664–70
4. Granberg D, Eriksson LG, Welin S, et al. Liver embolization with trisacryl gelatin microspheres (Embosphere™) in patients with neuroendocrine tumors. Acta Radiol 2007;48:180–5
5. Rand T, Loewe C, Schoder M, et al. Arterial embolization of unresectable hepatocellular carcinoma with use of microspheres, lipiodol, and cyanoacrylate. Cardiovasc Intervent Radiol 2005;28:313–8
6. Wang AY, Ahmad NA. Rectal carcinoids. Curr Opin Gastroenterol 2006;22:529–35
7. Modlin IM, Oberg K, Chung DC, et al. Gastroenteropancreatic neuroendocrine tumours. Lancet Oncol 2008;9:61–72
8. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer 2003;97:934–39
9. Loewe C, Schindl M, Cejna M, et al. Permanent transarterial embolization of neuroendocrine metastases of the liver using cyanoacrylate and lipiodol: assessment of mid- and long-term results. Am J Roentgenol 2003;180:1379–84
10. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med 2011;364:1844–54
11. Hsieh PM, Hung KC, Chen YS. Tumor lysis syndrome after transarterial chemoembolization of hepatocellular carcinoma: case reports and literature review. World J Gastroenterol 2009;15:4726–8
12. Davidson MB, Thakkar S, Hix JK, et al. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. Am J Med 2004;116:546–54
13. Avci Z, Alioglu B, Canan O, et al. Calcification of the gastric mucosa associated with tumor lysis syndrome in a child with non-Hodgkin lymphoma. J Pediatr Hematol Oncol 2006;28:307–10

© 2012 The Foundation Acta Radiologica
This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/2.0/), which permits non-commercial use, distribution and reproduction in any medium, provided the original work is properly cited.