CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 77 (2020) 147–151

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Liver metastasis from pancreatic neuroendocrine tumors after pancreaticoduodenectomy successfully treated by radiofrequency ablation combined with transcatheter arterial embolization: A case report

Kazuhiko Hashimoto [a,*], Taku Yasumoto [b], Yujiro Fujie [a], Junya Fujita [a], Tadashi Ohnishi [a]

[a] Department of Surgery, NTT West Osaka Hospital, 2-6-40, Karasugatsuji, Tennouji-ku, Osaka City, 543-8922, Japan
[b] Department of Interventional Radiology, Miyakojima IGRT Clinic, 1-16-22, Miyakojimahondori, Miyakojima-ku, Osaka City 534-0021, Japan

ARTICLE INFO

Article history:
Received 24 October 2020
Received in revised form 26 October 2020
Accepted 27 October 2020
Available online 1 November 2020

Keywords:
Pancreatic neuroendocrine tumors
Liver metastasis
Radiofrequency ablation
Transcatheter arterial embolization
Case report

ABSTRACT

BACKGROUND: Surgical resection is the first-choice treatment for operable liver metastases from pancreatic neuroendocrine tumors (pNETs). However, radiofrequency ablation, transcatheter arterial chemoembolization, and interventional radiology are expected to control local disease activity and improve survival rates in patients not eligible for surgery.

PRESENTATION OF CASE: A 54-year-old woman underwent pancreaticoduodenectomy for treatment of an 80-mm-diameter pancreatic head tumor. Histologically, the pancreatic tumor was diagnosed as a nonfunctional pNET (G2). At 38 months postoperatively, abdominal computed tomography showed two 15-mm-diameter liver tumors in segment 3 and segment 5/6, respectively. The patient requested nonsurgical treatment. Therefore, radiofrequency ablation combined with transcatheter arterial embolization was performed for the liver metastases. No complications occurred after the therapy. She was alive without recurrence at the time of this writing (33 months after the liver metastasis therapy, 74 months after the operation).

DISCUSSION: Although interventional radiology and radiofrequency ablation should be very carefully performed after pancreaticoduodenectomy or biliary reconstruction, our patient showed a good response to treatment without serious complications.

CONCLUSION: This report details our experience in treating liver metastasis from a pNET after pancreaticoduodenectomy. The metastasis was successfully treated by radiofrequency ablation combined with transcatheter arterial embolization.

1. Introduction

Pancreatic neuroendocrine tumors (pNETs) are rare tumors, occurring at an incidence of 3.65 per 100,000 individuals per year [1] and accounting for 1%–2% of all pancreatic neoplasms [2]. pNETs are a heterogeneous group of tumors with variations in their clinical presentation, tumor biology, and prognosis [2].

The treatment strategy for liver metastases is described in the European Neuroendocrine Tumor Society (ENETS) guidelines [3]. Surgery is recommended for simple liver metastases and bilobar liver metastases, and multidisciplinary treatment is recommended for bilobar sporadic liver metastases. Therefore, surgical resection is the first-choice treatment for operable liver metastases from pNETs. However, radiofrequency ablation (RFA), transcatheter arterial chemoembolization (TACE), and interventional radiology (IVR) are expected to control local disease activity and improve survival rates in patients not eligible for surgery.

We herein report a case of liver metastasis from a pNET that was successfully treated by RFA combined with transcatheter arterial embolization (TAE) and present a review of the literature. This work has been reported in line with the SCARE 2018 criteria [4].

2. Presentation of case

A 54-year-old woman underwent pancreaticoduodenectomy for treatment of a pancreatic head tumor. The maximal diameter of the resected tumor specimen was 80 mm (Fig. 1a). Histopathological examination of the pancreatic tumor led to a diagnosis of a nonfunctional pNET (G2, fT3N0M0, Stage II) (Fig. 1b). Immunohistochemical staining revealed positivity for cytokeratin and

* Corresponding author. Present address: Department of Surgery, NTT West Osaka Hospital, 2-6-40, Karasugatsuji, Tennouji-ku, Osaka City, 543-8922, Japan.
E-mail address: Kazunta19@aol.com (K. Hashimoto).

https://doi.org/10.1016/j.ijscr.2020.10.130

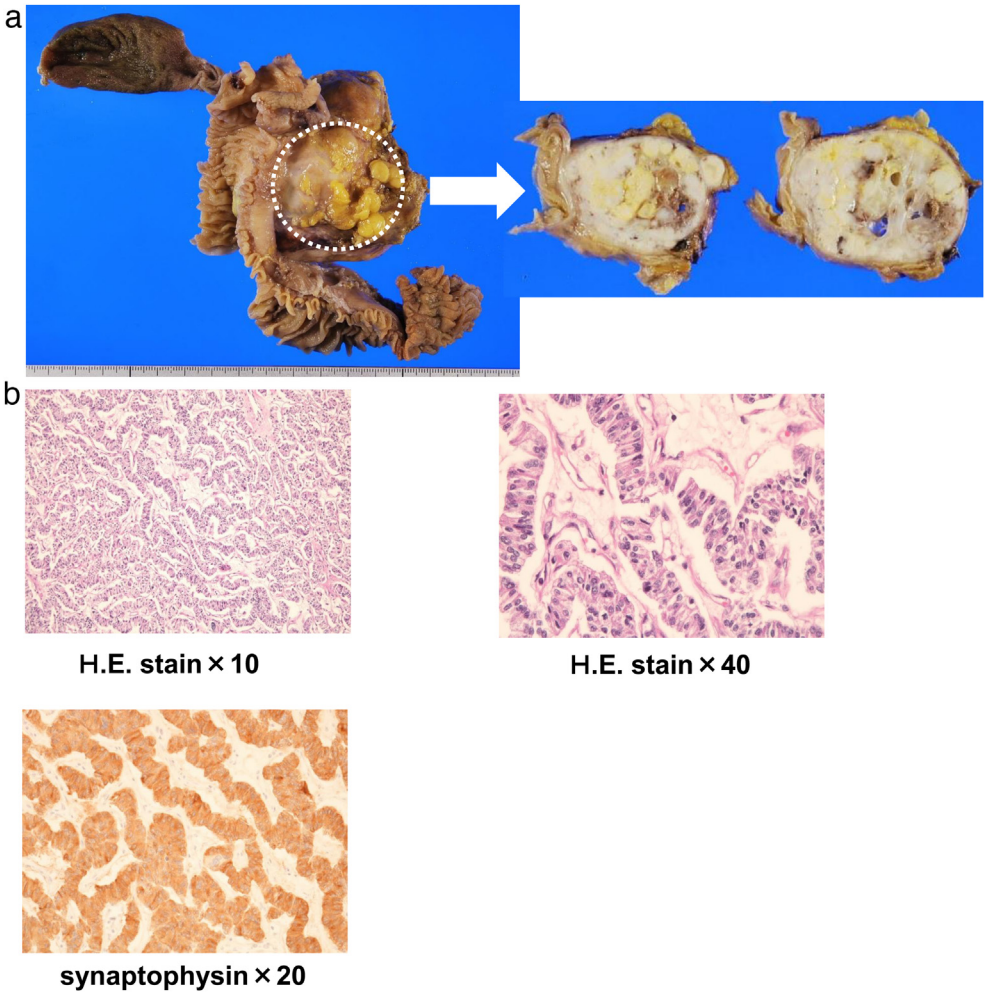

Fig. 1. (a) Resected specimen: The maximum tumor size was 80 mm in diameter. (b) Histopathological findings: The tumors were histologically, the pancreas tumor was diagnosed as the nonfunction pancreas neuroendocrine tumors (pNETs, G2). Immunohistochemical staining showed that the tumor lesions were synaptophysin positive.

synaptophysin and negativity for p53. No postoperative complications occurred.

At 38 months postoperatively, abdominal dynamic computed tomography revealed two 15-mm-diameter highly enhanced liver tumors in the early phase; one was present in segment (S) 3, and the other was present in S5/6 (Fig. 2). The patient requested nonsurgical treatment. Therefore, RFA combined with TAE was performed for treatment of the liver metastases. Abdominal angiography showed tumor staining in S3 and S5/6, and TAE was performed (Fig. 3). The right common femoral artery was punctured, and a 4-Fr sheath was placed under fluoroscopic guidance. Celiac and common hepatic angiography using a 4-Fr angiographic catheter (RC-09; Medikit, Tokyo, Japan) showed tumor staining in S3 and S5/6 in the liver. Selective segmental TAE using a gelatin sponge (Gelpart; Nippon Kayaku, Tokyo, Japan) was then performed with a 1.9-Fr microcatheter (Tellus; Asahi Intecc, Nagoya, Japan) introduced through the angiographic catheter. The procedure was completed after confirming disappearance of the tumor staining on common hepatic angiography.

One day after the TAE procedure, the metastatic liver tumors in S3 and S5/6 were punctured by a radiofrequency electrode (VIVA RF generator system; STARmed, Goyang, Korea) under computed tomography (SOMATOM Definition AS Open 64; Siemens, Munich, Germany) fluoroscopic guidance, and RFA was performed to treat the two metastatic liver tumors (Fig. 4). No severe complications occurred after the combination therapy of TAE and RFA.

The patient was not treated with chemotherapy or molecularly targeted drugs in accordance with her wishes. Follow-up computed tomography revealed no recurrence after treatment by RFA combined with TAE (Fig. 5). She was alive without recurrence at the time of this writing (33 months after the liver metastasis therapy, 74 months after the pancreaticoduodenectomy).

3. Discussion

pNETs frequently cause multiple organ metastases. The most common are liver metastases, which occur at a frequency of 30–40% [5,6]. The incidence of synchronous and metachronous liver metastases is 84% and 16%, respectively [7].

Guidelines for the treatment of liver metastasis from NETs have been published in Europe [3] and the United States [8], where many such cases occur, and the treatment is carried out in accordance with these guidelines. The ENETS guideline [3] states that liver metastasis is determined by the spread of the lesion: simple (unilobar or limited), complex (bilobar), or diffuse. In general, hepatectomy is the first choice for patients with simple and complex patterns of liver metastasis. There is no indication for surgical treatment for liver metastases with extrahepatic lesions, and systemic drug therapy is generally the treatment of choice in such patients. However, when reduction of hepatic metastases may alleviate excess hormonal symptoms and improve the prognosis, the

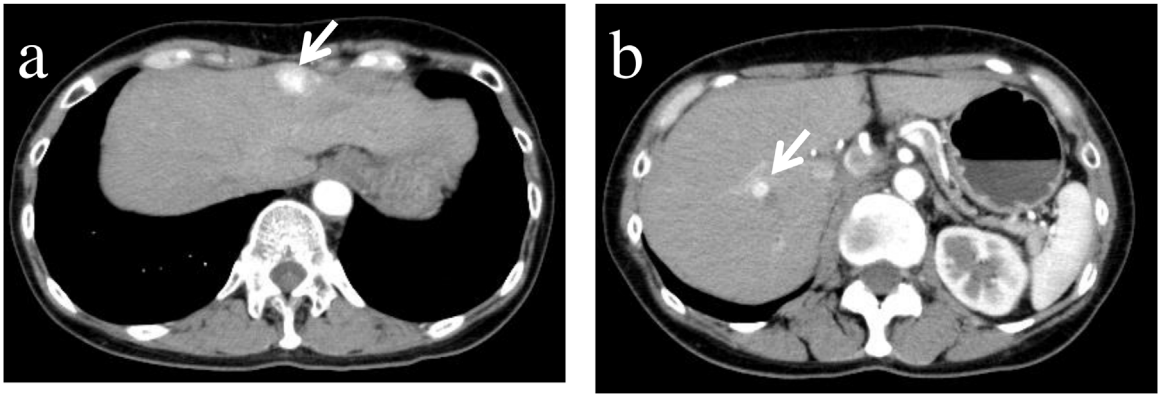

Fig. 2. Abdominal dynamic CT scans shows highly enhanced liver tumors in early phase, one 15 mm in diameter in S3 (a) and the other 15 mm in diameter in S5/6 (b).

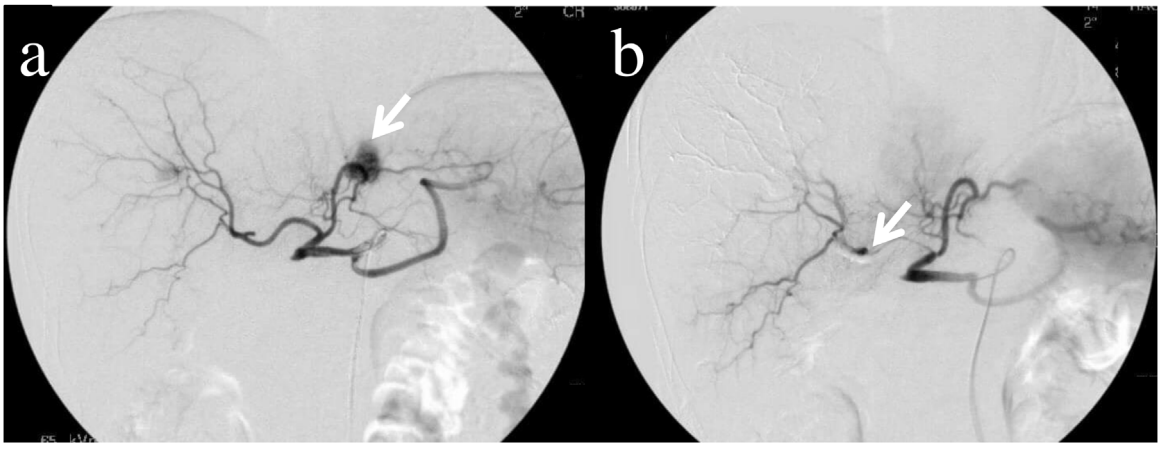

Fig. 3. Abdominal angiography showed tumor staining in S3 (a) and S5/6 (b), and TAE was performed.

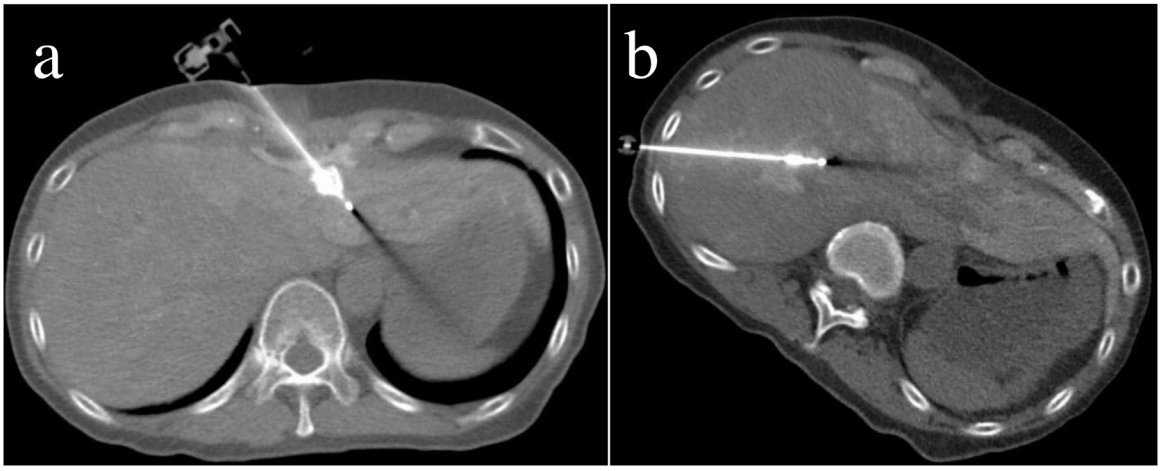

Fig. 4. Tumors of S3(a) and S5/6 (b)liver were punctured by RFA needle and RFA was performed. No serious complications were observed after the therapy.

standard treatment options are tumor reduction surgery, hepatic arterial embolization, and molecularly targeted agents.

RFA is a good form of local therapy for G1/G2 pNETs with a limited number of metastases of ≤3 cm (specifically, ≤14 metastases and a tumor volume of ≤20% of the total liver) [5]. RFA is effective in relieving tumor-related symptoms; unlike surgical resection, however, it has not been shown to prolong survival. The ENETS guideline [3] states that RFA provides 10–11 months of symptomatic relief in about 70% of patients. In some cases, complete tumor removal, which would have been difficult to achieve by surgery alone, can be achieved by RFA combined with surgical resection. Complications of RFA, which occur in <5% of patients, include pain, bleeding, pneumothorax, and liver abscesses [9,10]. The risk of liver abscesses is high after pancreaticoduodenectomy and biliary reconstruction, and caution should be exercised.

IVR may also be effective for postoperative liver metastases from pNETs. Because liver metastases from pNETs are blood flow-rich lesions and >90% of the blood supply to the tumor comes from the hepatic artery [11], endovascular therapy (TACE, TAE) has been promoted. The effect of hepatic arterial embolization on liver

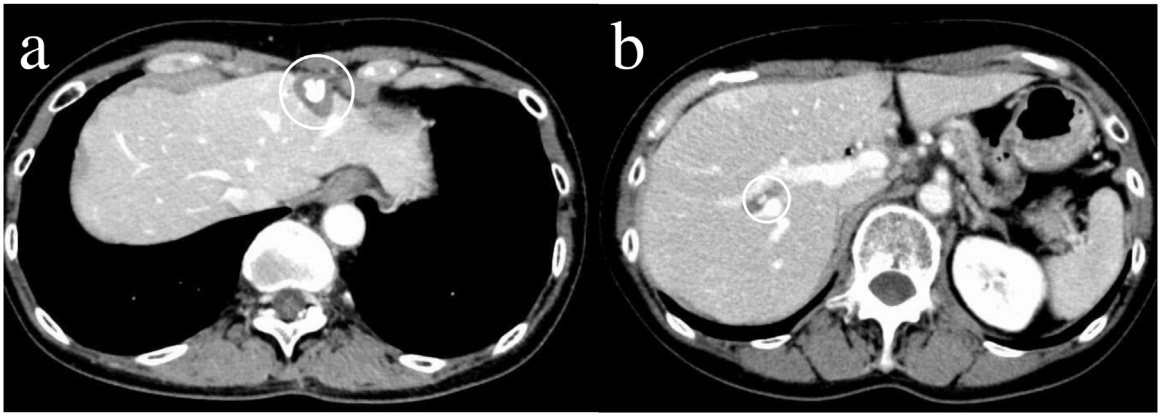

Fig. 5. 14 months after RFA combined with TAE, abdominal dynamic CT scans shows no recurrence of liver S3 (a), S5/6 (b) tumors.

metastases from NETs was first reported by Carrasco et al. [12] in 1986, and 95% of patients responded to the treatment with a median progression-free survival duration of 11 months.

The superiority of TACE over TAE is inconclusive. Gupta et al. [13] reported that in terms of the survival rate and tumor reduction, TACE was not superior to TAE for liver metastases of gastrointestinal origin but TACE was superior to TAE for liver metastases of pNET origin. With respect to liver metastases of gastrointestinal origin, the only randomized controlled trial comparing TACE and TAE showed no significant difference in the 2-year progression-free survival rate (38% and 44%, respectively). These results suggest that TACE may be more effective than TAE in the treatment of liver metastases of pNET origin than gastrointestinal origin [14]. However, TAE reportedly induces slightly less severe complications and should therefore be considered for patients with risk factors [15]. Additionally, cholangitis and liver abscesses are reportedly more frequent and more severe after TACE or TAE following pancreaticoduodenectomy and biliary reconstructive surgery, and caution should be exercised when treating recurrence after surgical resection.

Our patient had a complex pattern of liver metastasis from a pNET (G2) and was eligible for surgery; however, nonsurgical treatment was performed at her request. Because RFA is easily influenced by blood flow, we considered that RFA combined with TAE could expand the range of coagulation and improve the local control rate by controlling blood flow. Therefore, RFA combined with TAE was performed in this case. Although IVR (TACE, TAE) and RFA after pancreaticoduodenectomy or biliary reconstruction should be performed with caution because of the risk of liver abscess formation, our patient showed a good response to treatment without serious complications. It is necessary to accumulate more cases, including indications for specific treatments, and conduct further long-term follow-up studies.

4. Conclusion

Although IVR and RFA should be very carefully performed after pancreaticoduodenectomy or biliary reconstruction, our patient showed a good response to treatment without serious complications. This report details our experience in using RFA combined with TAE to treat liver metastasis from a pNET after pancreaticoduodenectomy.

Declaration of Competing Interest

The authors report no declarations of interest.

Funding

Nothing to declare.

Ethical approval

This study is exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors contribution

KH participated in the care of the patient including the operation and wrote the initial draft of the manuscript. TY participated in the care of the patient in the interventional radiological therapy.

YF, JF and TO participated in the surgery and revised the manuscript. TY, YF, JF and TO gave final approval of this paper to be published. All authors read and approved the final manuscript.

Registration of research studies

NA.

Guarantor

Kazuhiko Hashimoto, M.D., Ph.D.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We thank Angela Morben, DVM, ELS, from Edanz Group (https://en-author-services.edanzgroup.com/ac), for editing a draft of this manuscript.

References

[1] B. Lawrence, B.I. Gustafsson, A. Chan, et al., The epidemiology of gastroenteropancreatic neuroendocrine tumors, Endocrinol. Metab. Clin. North Am. 40 (1) (2011) 1–18, vii.
[2] S.A. Milan, C.J. Yeo, Neuroendocrine tumors of the pancreas, Curr. Opin. Oncol. 24 (1) (2012) 46–55.
[3] M. Pavel, D. O'Toole, F. Costa, et al., Vienna Consensus Conference participants. ENETS consensus guidelines update for the management of distant metastatic disease of intestinal, pancreatic, bronchial neuroendocrine neoplasms (NEN) and NEN of unknown primary site, Neuroendocrinology 103 (2) (2016) 172–185.
[4] R.A. Agha, M.R. Borrelli, R. Farwana, K. Koshy, A. Fowler, D.P. Orgill, For the SCARE Group, The SCARE 2018 statement: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. (60) (2018) 132–136.
[5] R.S. Chamberlain, D. Canes, K.T. Brown, et al., Hepatic neuroendocrine metastases: does intervention alter outcomes? J. Am. Coll. Surg. 190 (4) (2000) 432–445.
[6] I.M. Modlin, K.D. Lye, M. Kidd, A 5-decade analysis of 13,715 carcinoid tumors, Cancer 97 (4) (2003) 934–959.
[7] H. Nave, E. Mössinger, H. Feist, et al., Surgery as primary treatment in patients with liver metastases from carcinoid tumors: a retrospective, unicentric study over 13 years, Surgery 129 (2) (2001) 170–175.
[8] National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology, Available from:, 2019 http://www.nccn.org/professionals/physician_gls/PDF/sclcpdf.
[9] H. Mohan, P. Nicholson, D.C. Winter, et al., Radiofrequency ablation for neuroendocrine liver metastases: a systematic review, J. Vasc. Interv. Radiol. 26 (7) (2015) 935–942.
[10] K.S. Gurusamy, R. Ramamoorthy, D. Sharma, et al., Liver resection versus other treatments for neuroendocrine tumours in patients with resectable liver metastases, Cochrane Database Syst. Rev. 2009 (2) (2009) CD007060.
[11] C. Proye, Natural history of liver metastasis of gastroenteropancreatic neuroendocrine tumors: place for chemoembolization, World J. Surg. 25 (6) (2001) 685–688.
[12] C.H. Carrasco, C. Charnsangavej, J. Ajani, et al., The carcinoid syndrome: palliation by hepatic artery embolization, AJR Am. J. Roentgenol. l47 (1) (1986) 149–154.
[13] S. Gupta, M.M. Johnson, R. Murthy, et al., Hepatic arterial embolization and chemoembolization for the treatment of patients with metastatic neuroendocrine tumors: variables affecting response rates and survival, Cancer 104 (8) (2005) 1590–1602.
[14] F. Maire, C. Lombard–Bohas, D. O'Toole, et al., Hepatic arterial embolization versus chemoembolization in the treatment of liver metastases from well-differentiated midgut endocrine tumors: a prospective randomized study, Neuroendocrinology 96 (4) (2012) 294–300.
[15] F. Fiore, M. Del Prete, R. Franco, et al., Transarterial embolization (TAE) is equally effective and slightly safer than transarterial chemoembolization (TACE) to manage liver metastases in neuroendocrine tumors, Endocrine 47 (1) (2014) 177–182.