# World Journal of Clinical Cases

World J Clin Cases 2021 February 6; 9(4): 764-998





#### **Contents**

Thrice Monthly Volume 9 Number 4 February 6, 2021

#### **MINIREVIEWS**

764 Chiari malformations in children: An overview

Spazzapan P, Bosnjak R, Prestor B, Velnar T

#### **ORIGINAL ARTICLE**

#### **Case Control Study**

774 Effect of hospital discharge plan for children with type 1 diabetes on discharge readiness, discharge education quality, and blood glucose control

Tong HJ, Qiu F, Fan L

#### **Retrospective Study**

784 Effect of biofeedback combined with high-quality nursing in treatment of functional constipation

Zhao X, Meng J, Dai J, Yin ZT

792 Radioactive 125I seed implantation for pancreatic cancer with unexpected liver metastasis: A preliminary experience with 26 patients

Li CG, Zhou ZP, Jia YZ, Tan XL, Song YY

# **Clinical Trials Study**

801 Biliary stent combined with iodine-125 seed strand implantation in malignant obstructive jaundice

Wang HW, Li XJ, Li SJ, Lu JR, He DF

#### **Observational Study**

812 Effects of different statins application methods on plaques in patients with coronary atherosclerosis

Wu X, Liu XB, Liu T, Tian W, Sun YJ

822 Usefulness of prenatal magnetic resonance imaging in differential diagnosis of fetal congenital cystic adenomatoid malformation and bronchopulmonary sequestration

Li Z, Lv YD, Fang R, Li X, Luo ZQ, Xie LH, Zhu L

### **CASE REPORT**

830 Reciprocal hematogenous osteomyelitis of the femurs caused by Anaerococcus prevotii: A case report

Daunaraite K, Uvarovas V, Ulevicius D, Sveikata T, Petryla G, Kurtinaitis J, Satkauskas I

838 Gastroduodenal intussusception caused by gastric gastrointestinal stromal tumor: A case report and review of the literature

Hsieh YL, Hsu WH, Lee CC, Wu CC, Wu DC, Wu JY

### Contents

# Thrice Monthly Volume 9 Number 4 February 6, 2021

847 Altemeier perineal rectosigmoidectomy with indocyanine green fluorescence imaging for a female adolescent with complete rectal prolapse: A case report

Yamamoto T, Hyakudomi R, Takai K, Taniura T, Uchida Y, Ishitobi K, Hirahara N, Tajima Y

854 Long-term survival in a patient with Hutchinson-Gilford progeria syndrome and osteosarcoma: A case

Hayashi K, Yamamoto N, Takeuchi A, Miwa S, Igarashi K, Araki Y, Yonezawa H, Morinaga S, Asano Y, Tsuchiya H

864 Recurrent medullary thyroid carcinoma treated with percutaneous ultrasound-guided radiofrequency ablation: A case report

Tong MY, Li HS, Che Y

871 "Bull's eye" appearance of hepatocellular adenomas in patients with glycogen storage disease type I atypical magnetic resonance imaging findings: Two case reports

Vernuccio F, Austin S, Meyer M, Guy CD, Kishnani PS, Marin D

878 Clinical characteristics and ABCC2 genotype in Dubin-Johnson syndrome: A case report and review of the literature

Wu H, Zhao XK, Zhu JJ

886 Adult-onset Still's disease evolving with multiple organ failure and death: A case report and review of the literature

Han ZB, Wu J, Liu J, Li HM, Guo K, Sun T

898 Open reduction and Herbert screw fixation of Pipkin type IV femoral head fracture in an adolescent: A case report

Liu Y, Dai J, Wang XD, Guo ZX, Zhu LQ, Zhen YF

904 Acute pancreatitis with pulmonary embolism: A case report

Fu XL, Liu FK, Li MD, Wu CX

912 Apert syndrome diagnosed by prenatal ultrasound combined with magnetic resonance imaging and whole exome sequencing: A case report

Chen L, Huang FX

919 Application of neoadjuvant chemotherapy combined with an otinib in occult breast cancer: A case report and review of literature

Zhang Y, Wu D, Zhao B, Tian XL, Yao TC, Li F, Liu WF, Shi AP

927 Atypical presentation of shoulder brucellosis misdiagnosed as subacromial bursitis: A case report

Wang FS, Shahzad K, Zhang WG, Li J, Tian K

935 Retroperitoneal teratoma resection assisted by 3-dimensional visualization and virtual reality: A case report

П

Liu T, Chen K, Xia RM, Li WG

943 Renal failure and hepatitis following ingestion of raw grass carp gallbladder: A case report

Zhou LN, Dong SS, Zhang SZ, Huang W

# World Journal of Clinical Cases

#### **Contents**

# Thrice Monthly Volume 9 Number 4 February 6, 2021

951 Pheochromocytoma as a cause of repeated acute myocardial infarctions, heart failure, and transient erythrocytosis: A case report and review of the literature

Shi F, Sun LX, Long S, Zhang Y

960 Immediate implant placement in combination with platelet rich-fibrin into extraction sites with periapical infection in the esthetic zone: A case report and review of literature

Fang J, Xin XR, Li W, Wang HC, Lv HX, Zhou YM

Acute inferior wall myocardial infarction induced by aortic dissection in a young adult with Marfan 970 syndrome: A case report

Zhang YX, Yang H, Wang GS

976 Primary nonkeratinizing squamous cell carcinoma of the scapular bone: A case report

Li Y, Zuo JL, Tang JS, Shen XY, Xu SH, Xiao JL

983 Fertility-sparing surgeries without adjuvant therapy through term pregnancies in a patient with low-grade endometrial stromal sarcoma: A case report

Gu YZ, Duan NY, Cheng HX, Xu LQ, Meng JL

992 Isolated interrupted aortic arch in an adult: A case report

Dong SW, Di DD, Cheng GX

III

#### Contents

# Thrice Monthly Volume 9 Number 4 February 6, 2021

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Editorial Board Member of World Journal of Clinical Cases, Salim R Surani, MD, MPH, MSHM, FACP, FCCP, FAASM is Chair of Critical Care at Corpus Christi Medical Center, Adjunct Clinical Professor of Medicine, Department of Pulmonary, Critical Care and Sleep Medicine at Texas A&M University, and Program Director of the Pulmonary Fellowship Program at Bay Area Medical Center, Corpus Christi. His training and education involved fellowship in Pulmonary Medicine at Baylor College of Medicine, Master's in Public Health, & Epidemiology from Yale University, and Master's in Health Management from University of Texas, Dallas. Having authored more than 250 peer-reviewed articles and written several books and book chapters. (L-Editor: Filipodia)

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CASE REPORT

# Recurrent medullary thyroid carcinoma treated with percutaneous ultrasound-guided radiofrequency ablation: A case report

Meng-Ying Tong, Hu-Sha Li, Ying Che

**ORCID number:** Meng-Ying Tong 0000-0001-7723-8306; Hu-Sha Li 0000-0002-3004-0658; Ying Che 0000-0002-0044-4168.

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Meng-Ying Tong, Hu-Sha Li, Ying Che, Department of Ultrasound, First Affiliated Hospital of Dalian Medical University, Dalian 116011, Liaoning Province, China

Corresponding author: Ying Che, MD, PhD, Professor, Department of Ultrasound, First Affiliated Hospital of Dalian Medical University, No. 222 Zhongshan Road, Dalian 116011, Liaoning Province, China. cheying@dmu.edu.cn

#### Abstract

#### **BACKGROUND**

Treatment for neck lymph node metastases after adequate initial surgery in medullary thyroid carcinoma (MTC) has been controversial. Ultrasound (US)guided radiofrequency ablation (RFA) has been widely used in recurrent welldifferentiated thyroid carcinoma. Here, we report for the first time the use of RFA in a patient with recurrent MTC.

#### CASE SUMMARY

We report the case of a 56-year-old woman with cervical lymph node metastases of MTC. Four years previously, she had undergone a total thyroidectomy and neck lymph node dissection. A neck US revealed many enlarged nodes during the follow-up period. Moreover, the serum calcitonin jumped to 198.17 pg/mL, which strongly indicated the recurrence of MTC. Subsequently, two metastatic lymph nodes were confirmed by US-guided fine-needle aspiration-cytology and fineneedle aspiration-calcitonin, and then the patient was treated with RFA. Four months later, the neck US and a contrast-enhanced US showed obvious shrinkage in the ablation zones, and the serum calcitonin dropped to 11.80 pg/mL.

#### **CONCLUSION**

This case suggests that RFA may be an effective and safe treatment for local recurrent MTC.

Key Words: Medullary thyroid carcinoma; Radiofrequency ablation; Lymph node metastasis; Calcitonin; Fine-needle aspiration; Case report

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864

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Core Tip: Adequate surgery is the mainstay of treatment in medullary thyroid carcinoma. However, neck lymph node metastases after adequate initial treatment are present in a majority of cases. So far, treatment for neck lymph node metastases after adequate initial surgery in medullary thyroid carcinoma has been controversial. Radiofrequency ablation, which is considered a moderate approach between secondary surgery and surveillance, may be attempted for these recurrent patients. This case suggests that radiofrequency ablation may be an effective and safe treatment for local recurrent medullary thyroid carcinoma.

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# INTRODUCTION

The prevalence of medullary thyroid carcinoma (MTC) accounts for approximately 3% to 5% of all thyroid malignancies[1] in sporadic (85% of cases) or hereditary (15% of cases) form<sup>[2]</sup>. MTC is more aggressive and progressive than well-differentiated thyroid carcinoma and is characterized by early lymph nodal metastases[1,3,4]. Adequate surgery is the mainstay of treatment in MTC. However, neck lymph node metastases after adequate initial treatment are present in the majority of cases<sup>[5,6]</sup>. In these cases, a second surgical treatment can be considered, but its real therapeutic role is controversial because of the absence of randomized trials comparing reoperation to observation alone. In patients without infiltration of vital neck structures or symptomatic lesions, reoperation may lead to overtreatment and consequential complications<sup>[7,8]</sup>. Active surveillance management, as an alternative, is not acceptable for many anxious patients. Therefore, radiofrequency ablation (RFA), which is considered a moderate approach between surgery and surveillance, may be attempted for these recurrent patients.

Ultrasound (US)-guided tumor ablation has become a mature treatment for recurrent differentiated thyroid carcinoma<sup>[9]</sup>. However, to the best of our knowledge, no case has been published that elucidates the efficacy and safety of RFA in local recurrent MTC. We herein describe the outcome of recurrent MTC with neck lymph node metastases treated by RFA in a patient who refused to undergo a second surgery.

# CASE PRESENTATION

#### Chief complaints

A 56-year-old female presented to the department of ultrasound with recurrent MTC.

# History of present illness

The patient was diagnosed with sporadic MTC at the age of 51. She presented a hypoechoic solid nodule that was approximately 0.5 cm × 0.4 cm in the left thyroid gland with no pain, diarrhea, flushing or any other specific symptom. The preoperative serum calcitonin was 1165.97 pg/mL. The patient was then treated with total thyroidectomy with central neck dissection and modified left lateral neck dissection. The nodule was pathologically confirmed to be MTC. Nine of fourteen metastatic lymph nodes were found in the excised lymphoid adipose tissue at the left cervical level II-IV, VB and VI (Table 1). Three months after surgery, the serum calcitonin dropped to 11.86 pg/mL (Figure 1).

After the initial treatment, the patient was followed up with neck US, serum calcitonin and carcinoembryonic antigen every 3-6 mo. During the follow-up, an enlarged lymph node (0.4 cm × 0.3 cm) with no visible hilum at left level VI was detected by the neck US in the 9th mo. A similar lymph node (0.5 cm × 0.4 cm) appeared in the left supraclavicular fossa in the 44th mo. In addition, many lymph nodes at the right cervical level II-III and left level V became enlarged. Serum

865

Table 1 Pathology of cervical lymph nodes in the initial surgery			
Level	Number of metastasis	Total number	
Left II	1	3	
Left III	1	1	
Left IV	1	3	
Left VB	0	0	
Left VI	6	7	
Total	9	14	

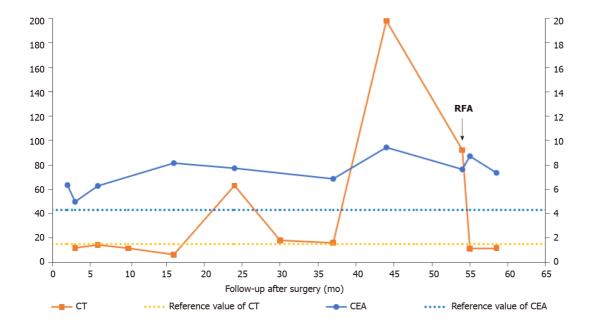


Figure 1 Changes of serum calcitonin and carcinoembryonic antigen levels at each follow-up visit after the initial surgery. The dashed lines indicate reference values. CEA: Carcinoembryonic antigen; CT: Calcitonin; RFA: Radiofrequency ablation.

calcitonin jumped to 198.17 pg/mL in the 44th mo. Afterwards, serum calcitonin remained at a high level, which was significantly higher than the reference (Figure 1). The serum carcinoembryonic antigen level had been relatively stable since the initial surgery. The abdominal and lung computed tomography scan revealed no suspicious metastasis.

# Physical examination

She presented with no lump or tenderness in the neck. Trachea was in the middle of the neck.

#### Laboratory examinations

After the recurrent signs occurred, the patient visited our department for further diagnosis and treatment in the 54th mo. Serum calcitonin was increased at 92.18 pg/mL (normal range: < 15 pg/mL).

# Imaging examinations

We performed the neck US on the patient, finding six morphologically suspicious lymph nodes. To identify the lymph nodes that harbored metastatic lesions, we conducted US-guided fine-needle aspiration (FNA) on these six nodules. The results of FNA-cytology and FNA-calcitonin are displayed in Table 2. Four of the nodes turned out to be reactive hyperplasia nodes, whereas the other two revealed suspicious malignancy. Moreover, the FNA-calcitonin values of these two suspicious lymph nodes were significantly higher (2000 pg/mL) than the others indicating metastatic lesions.

Table 2 Results of fine-needle aspiration-cytology and fine-needle aspiration-calcitonin			
Location/level (size)	Cytological pathology	FNA-calcitonin, pg/mL	
Right/II	Reactive hyperplasia	< 2.00	
Right/III	Reactive hyperplasia	< 2.00	
Left/V (5.0 mm × 3.0 mm)	Reactive hyperplasia	< 2.00	
Left/V (7.9 mm × 4.1 mm)	Reactive hyperplasia	< 2.00	
Left/VI <sup>1</sup>	No tumor cell found	> 2000	
Left/supraclavicular fossa <sup>1</sup>	A few epithelioid cells	> 2000	

<sup>&</sup>lt;sup>1</sup>Metastatic lymph nodes suggested by both fine-needle aspiration (FNA)-cytology and FNA-calcitonin.

#### FINAL DIAGNOSIS

Postoperative recurrent MTC with metastatic lymph nodes of left VI and left supraclavicular fossa.

#### TREATMENT

After identification of the metastatic lymph nodes (Figure 2A and 2E) by US-guided FNA, we performed RFA on them. The RFA and postoperative contrast-enhanced ultrasound (CEUS) was performed using the LOGIQ E9 Ultrasound System (GE Healthcare, Chicago, IL, United States) with a 9L linear array transducer (6-15 MHz). The ultrasound was conducted using a unipolar RF generator (VIVA RF generator, VRS01; STAR Med Co., Ltd., Korea) and an 18-gauge internally cooled electrode with a 7-mm active tip (VIVA RF Electrode; STAR Med Co., Ltd.). The procedure was performed by a US interventional physician with 15 years of experience in RFA treatment. Briefly, 1% lidocaine was injected for local anesthesia on the puncture point. To prevent thermal injury, saline was injected to isolate the target ablation zone with surrounding tissue, including the trachea, recurrent laryngeal nerves, and supraclavicular nerves (Figure 2B and 2F). Then, the electrode tip was inserted into the lesions (Figure 2C and 2G), fixed at their centers and kept motionless during the ablation procedure. After a short period, transient hyperechoic zones consisting of vapor were observed at the electrode tip (Figure 2D and 2H). During the procedure, the RF generator monitored the temperature at the electrode tip. The power was automatically reduced once the temperature reached 60 °C.

#### OUTCOME AND FOLLOW-UP

Following the RFA procedure, we immediately performed US and CEUS on the patient. The US revealed two hyperechoic ablated zones that covered the metastatic lesions completely, and CEUS confirmed no enhancement in them (Figure 3A and 3B). No major complications such as intolerable pain, hematoma or nerve injury occurred during or after the treatment. One month after RFA, the patient's serum calcitonin level dropped to 11.40 pg/mL. Four months later, the neck US and CEUS showed obvious shrinkage in the ablation zones (Figure 3C and 3D), and the serum calcitonin remained at 11.80 pg/mL.

# DISCUSSION

In this case, we described for the first time the effective use of RFA in the treatment of recurrent MTC with cervical lymph node metastases. The action of RFA, performed with hydrodissection and spot-ablation techniques, performs the main role in coagulating the nodes. After absorption of necrotic tissue, significant shrinkage of metastatic lymph nodes coupled with marked clinical improvement in metastasisrelated symptoms was observed. Remarkably, no nerve injuries or inflammatory

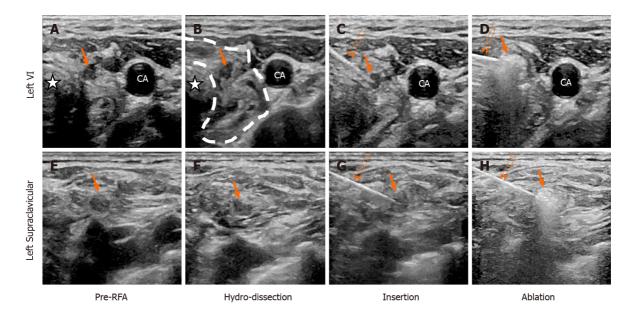


Figure 2 Ultrasound-guided radiofrequency ablation process. A-D: Lymph nodes at left level VI; E-H: Lymph nodes at left supraclavicular fossa; A and E: Ultrasound (US) images of pre-radiofrequency ablation (RFA); B and F: US images of the hydrodissection process. Saline was injected to form an edema zone (circled by the dashed line), isolating the target ablated zones with nerves, trachea (marked with star) and skin; C and G: US images of insertion with the electrode tip; D and H: US images of the radiofrequency ablation procedure. The single arrows point to the lymph nodes of the target. The double arrows point to the RF electrode. CA: Carotid artery.

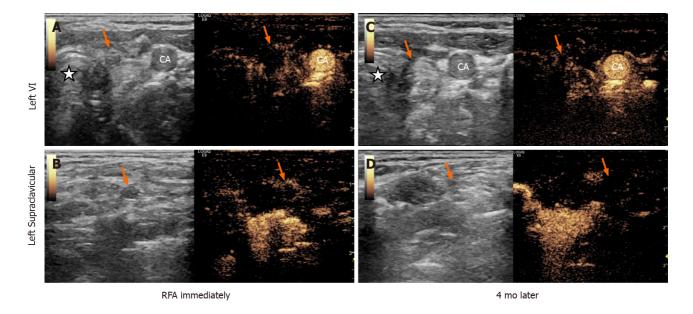


Figure 3 Images of ultrasound and contrast-enhanced ultrasound after the radiofrequency ablation. A and B: Images captured immediately after radiofrequency ablation (RFA); C and D: Images 4 mo after RFA. The arrows point to ablated lymph nodes. Pentagram (marked with star): Trachea. CA: Carotid artery.

changes induced by RFA were encountered, which is a critical advantage as compared to a secondary surgery.

RFA has been recently used to treat patients with metastatic lymph nodes from recurrent papillary thyroid carcinoma[10,11] and primary papillary thyroid microcarcinoma without cervical lymph node metastasis[12-15]. Complete disappearance of the whole lesion was reported in the majority of cases during the follow-up periods. In terms of safety, few major complications have been encountered, demonstrating the safety of RFA[11]. Therefore, RFA is an acceptable treatment to manage both primary papillary thyroid microcarcinoma and metastatic lymph nodes from papillary thyroid carcinoma in terms of efficacy and safety for nonsurgical candidates.

RFA for recurrent MTCs has not been reported in the literature. However, for the present case, in which the patient had undergone an initial complete surgery and then

postoperative lymph nodes metastasized, we decided to perform RFA on the patient for the following reasons. First, because the recurrent MTC did not appear to infiltrate vital neck structures or symptomatic lesions, reoperation may have led to overtreatment and produced negative complications[7,8]. Second, adhesions or inflammatory changes induced by the initial surgery may produce difficulties for the secondary surgery. Third, the patient was very anxious, and active surveillance management was deemed unacceptable. Fourth, the patient refused to undergo a second surgery.

To perform RFA, a critical issue is to accurately identify the metastatic lymph nodes. Calcitonin measurement in FNA washout has been suggested as a useful supplement to conventional FNA-cytology in patients with metastatic MTC or increased serum calcitonin<sup>[16-19]</sup>. The cut-off level for FNA-calcitonin has been reported to range from 10.4 to 67 pg/mL<sup>[19-22]</sup>. Specifically, Kihara et al<sup>[21]</sup> reported that when the cut-off value was 21.0 pg/mL, FNA-calcitonin had the highest sensitivity and specificity (nearly 100%), noting the contrast with approximately 45%-63% sensitivity of routine FNAcytology<sup>[23,24]</sup>. In this case, FNA-calcitonin of the lymph nodes at left level VI and left supraclavicular fossa were significantly higher (> 2000 pg/mL) than the other lymph nodes, despite the negative FNA-cytology result, indicating that these two lymph nodes were responsible for the persistent increase in serum calcitonin.

After identifying the metastatic lymph nodes, we conducted RFA on these two lesions. In our patient, after two insertions of an RF electrode using a spot ablation technique, the lesions were completely ablated as indicated by the postoperative CEUS and follow-up sonography evaluations. These imaging changes in the lesions were accompanied by a clinically significant decline in serum calcitonin values. Overall, this case provides evidence to support the mainstay role of RFA in the treatment of local recurrent MTC. As a local minimally invasive therapy, RFA is an acceptable treatment for managing metastatic lymph nodes in MTC in terms of efficacy and safety, which is necessary in prolonging disease-free survival time and delaying systemic therapy. Moreover, a greater number of patients and a long follow-up period should be employed to elucidate the long-term efficacy of RFA.

# CONCLUSION

To the best of our knowledge, this is the first case study of RFA in the treatment of local recurrent MTC. The effective and safe response suggests the possibility that RFA may be a novel option to control local recurrent MTC, warranting clinical verifications with larger sample sizes.

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869

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