OPINION REVIEW

4280 Role of monoclonal antibody drugs in the treatment of COVID-19
Ucciferri C, Vecchiet J, Falasca K

MINIREVIEWS

4286 Review of simulation model for education of point-of-care ultrasound using easy-to-make tools
Shin KC, Ha YR, Lee SJ, Ahn JH

4303 Liver injury in COVID-19: A minireview
Zhao JN, Fan Y, Wu SD

ORIGINAL ARTICLE

Case Control Study

4311 Transanal minimally invasive surgery vs endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: A retrospective analysis
Shen JM, Zhao JY, Ye T, Gong LF, Wang HP, Chen WJ, Cai YK

4320 Impact of mTOR gene polymorphisms and gene-tea interaction on susceptibility to tuberculosis

Retrospective Cohort Study

4331 Establishment and validation of a nomogram to predict the risk of ovarian metastasis in gastric cancer: Based on a large cohort
Li SQ, Zhang KC, Li JY, Liang WQ, Gao YH, Qiao Z, Xi HQ, Chen L

Retrospective Study

4342 Predictive factors for early clinical response in community-onset Escherichia coli urinary tract infection and effects of initial antibiotic treatment on early clinical response
Kim YJ, Lee JM, Lee JH

4349 Managing acute appendicitis during the COVID-19 pandemic in Jiaxing, China
Zhou Y, Cen LS

4360 Clinical application of combined detection of SARS-CoV-2-specific antibody and nucleic acid
Meng QB, Peng JJ, Wei X, Yang JY, Li PC, Qu ZW, Xiong YF, Wu GJ, Hu ZM, Yu JC, Su W

4370 Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients
Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular carcinoma  
Zhang YH, Su B, Sun P, Li RM, Peng XC, Cai J

Clinical study on the surgical treatment of atypical Lisfranc joint complex injury  
Li X, Jia LS, Li A, Xie X, Cui J, Li GL

Application of medial column classification in treatment of intra-articular calcaneal fractures  
Zheng G, Xia F, Yang S, Cui J

Optimal hang time of enteral formula at standard room temperature and high temperature  
Lakananurak N, Nalinthassanai N, Suansawang W, Panarat P

Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer  
Liu J, Wang Y, Yu Y

Global analysis of daily new COVID-19 cases reveals many static-phase countries including the United States potentially with unstoppable epidemic  
Long C, Fu XM, Fu ZF

Left atrial appendage aneurysm: A case report  
Belov DV, Moskalev VI, Garbuzenko DV, Arefyev NO

Twenty-year survival after iterative surgery for metastatic renal cell carcinoma: A case report and review of literature  
De Raffele E, Mirarchi M, Casadei R, Ricci C, Brunocilla E, Minni F

Primary rhabdomyosarcoma: An extremely rare and aggressive variant of male breast cancer  
Satala CB, Jung I, Bara TJ, Simu P, Simu I, Vlad M, Szodorai R, Gurzu S

Bladder stones in a closed diverticulum caused by Schistosoma mansoni: A case report  
Alkhamees MA

Cutaneous ciliated cyst on the anterior neck in young women: A case report  
Kim YH, Lee J

Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high-dose combination cytotoxic chemotherapy: A case report  
Kim HB, Lee HJ, Hong R, Park SG
Contents

World Journal of Clinical Cases

Semimonthly Volume 8 Number 19 October 6, 2020

4494 Acute amnesia during pregnancy due to bilateral fornix infarction: A case report
Cho MJ, Shin DI, Han MK, Yum KS

4499 Ascaris-mimicking common bile duct stone: A case report
Choi SY, Jo HE, Lee YN, Lee JE, Lee MH, Lim S, Yi BH

4505 Eight-year follow-up of locally advanced lymphoepithelioma-like carcinoma at upper urinary tract: A case report
Yang CH, Weng WC, Lin YS, Huang LH, Lu CH, Hsu CY, Ou YC, Tung MC

4512 Spontaneous resolution of idiopathic intestinal obstruction after pneumonia: A case report
Zhang BQ, Dai XY, Ye QY, Chang L, Wang ZW, Li XQ, Li YN

4521 Successful pregnancy after protective hemodialysis for chronic kidney disease: A case report
Wang ML, He YD, Yang HX, Chen Q

4527 Rapid remission of refractory synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome in response to the Janus kinase inhibitor tofacitinib: A case report
Li B, Li GW, Xue L, Chen YY

4535 Percutaneous fixation of neonatal humeral physeal fracture: A case report and review of the literature
Tan W, Wang FH, Yao JH, Wu WP, Li YB, Ji YL, Qian YP

4544 Severe fundus lesions induced by ocular jellyfish stings: A case report
Zheng XY, Cheng DJ, Lian LH, Zhang RT, Yu XY

4550 Application of ozonated water for treatment of gastro-thoracic fistula after comprehensive esophageal squamous cell carcinoma therapy: A case report
Wu DD, Hao KN, Chen XJ, Li XM, He XF

4558 Germinomas of the basal ganglia and thalamus: Four case reports
Huang ZC, Dong Q, Song EP, Chen ZJ, Zhang JH, Hou B, Lu ZQ, Qin F

4565 Gastrointestinal bleeding caused by jejunal angiosarcoma: A case report
Hui YY, Zhu LP, Yang B, Zhang ZY, Zhang YJ, Chen X, Wang BM

4572 High expression of squamous cell carcinoma antigen in poorly differentiated adenocarcinoma of the stomach: A case report
Wang L, Huang L, Xi L, Zhang SC, Zhang JX

4579 Therapy-related acute promyelocytic leukemia with FMS-like tyrosine kinase 3-internal tandem duplication mutation in solitary bone plasmacytoma: A case report
Hong LL, Sheng XF, Zhuang HF

4588 Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report
Zhang X, Gu X, Li JG, Hu XJ
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4595</td>
<td>Severe hyperlipemia-induced pseudoerythrocytosis - Implication for misdiagnosis and blood transfusion: A case report and literature review</td>
<td>Zhao XC, Ju B, Wei N, Ding J, Meng FJ, Zhao HG</td>
</tr>
<tr>
<td>4603</td>
<td>Novel brachytherapy drainage tube loaded with double 125I strands for hilar cholangiocarcinoma: A case report</td>
<td>Lei QY, Jiao DC, Han XW</td>
</tr>
<tr>
<td>4615</td>
<td>Primary hepatic myelolipoma: A case report and review of the literature</td>
<td>Li KY, Wei AL, Li A</td>
</tr>
<tr>
<td>4624</td>
<td>Endoscopic palliative resection of a giant 26-cm esophageal tumor: A case report</td>
<td>Li Y, Guo LJ, Ma YC, Ye LS, Hu B</td>
</tr>
<tr>
<td>4633</td>
<td>Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review</td>
<td>Long X, Zhang L, Cheng Q, Chen Q, Chen XP</td>
</tr>
<tr>
<td>4644</td>
<td>Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report</td>
<td>Cai X, Yu JJ, Tian H, Shan ZF, Liu XY, Jia J</td>
</tr>
<tr>
<td>4660</td>
<td>Bochdalek hernia masquerading as severe acute pancreatitis during the third trimester of pregnancy: A case report</td>
<td>Zou YZ, Yang JP, Zhou XJ, Li K, Li XM, Song CH</td>
</tr>
<tr>
<td>4667</td>
<td>Localized primary gastric amyloidosis: Three case reports</td>
<td>Liu XM, Di LJ, Zhu JX, Wu XL, Li HP, Wu HC, Tuo BG</td>
</tr>
<tr>
<td>4676</td>
<td>Displacement of peritoneal end of a shunt tube to pleural cavity: A case report</td>
<td>Liu J, Guo M</td>
</tr>
<tr>
<td>4681</td>
<td>Parathyroid adenoma combined with a rib tumor as the primary disease: A case report</td>
<td>Han L, Zhu XF</td>
</tr>
</tbody>
</table>
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Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report

Xing Zhang, Xin Gu, Jia-Gen Li, Xian-Jie Hu

CASE REPORT

Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report

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Author contributions: Zhang X and Hu XJ admitted the patient and performed the surgery; Gu X was the pathologist who made the diagnosis and analyzed and interpreted the pathological findings; Zhang X reviewed the literature and contributed to manuscript drafting; Zhang X and Li JG revised the manuscript; All authors approved the final version of the manuscript to be submitted.

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Abstract

BACKGROUND
Esophageal cancer is one of the most common causes of cancer-related death. Some patients with esophageal cancer have distant metastases at the time of diagnosis, but metastasis to the thyroid gland (MTG) and multifocal thyroid lesions alone are extremely rare.

CASE SUMMARY
In this case report, we present a case of a 69-year-old male with esophageal MTG. The patient visited our hospital for a routine body check-up, which revealed multifocal nodules in his thyroid lobes and enlarged cervical lymph nodes. A fine needle aspiration biopsy showed malignancies in both thyroid lesions and lymph nodes. The patient was initially diagnosed with primary bilateral thyroid cancer that spread to his lymph nodes, and a total thyroidectomy was performed. The histology showed MTG and therefore, a diagnostic work-up was implemented to determine the primary tumor. A fluorine-18-deoxyglucose positron emission tomography scan showed that the lower part of the esophagus and the lymph nodes in the neck, chest, and abdomen were involved. An esophagogastrscopy and corresponding pathology revealed distal esophageal squamous cell carcinoma. The esophageal MTG diagnosis was confirmed with pathological immunohistochemistry.

CONCLUSION
This case report highlights the difficulty in diagnosing esophageal MTG. Patients may have no malignancy history and be asymptomatic. Further diagnostic procedures are necessary after MTG is confirmed by cytology or histology, and
the final diagnosis should be made according to the identification of the primary malignancy combined with pathological immunohistochemistry findings.

Key Words: Esophageal squamous cell carcinoma; Metastasis; Thyroid gland; Thyroidectomy; Lymph nodes; Case report

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Core Tip: Metastasis to the thyroid gland (MTG) from esophageal cancer is rare, and only a few sporadic cases have been reported thus far. This study reports the findings of esophageal squamous cell carcinoma MTG in a 69-year-old man who presented for a routine checkup. The patient underwent bilateral thyroidectomy. The histology showed MTG. A diagnostic work-up was implemented and revealed metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement. He was administered four rounds of chemotherapy and is well 1 year after the diagnosis. Our findings will be of importance for diagnosing this rare condition.

INTRODUCTION

Esophageal cancer is the ninth most common cancer worldwide, with 572034 new cases estimated in 2018, and the sixth leading cause of cancer-related death, with 508585 cases[1]. Esophageal cancer distant metastases most commonly occur in the liver, followed by the lungs, bones, and brain[2]. Metastasis to the thyroid gland (MTG) is rare, with reported in surgical series ranging from 1.4% to 3.0%[3]. Esophageal malignancies are relatively rare sources of the thyroid metastases, compared to kidney and lung malignancies, and are only seen in 9% of patients with MTG[4]. In the clinical setting, secondary thyroid tumors only present without concurrent primary cancer symptoms or known malignancy histories in patients with MTG, and this situation can perplex physicians. We present the case of a patient with metastatic esophageal squamous cell carcinoma (ESCC) of a thyroid gland, which was initially misdiagnosed as primary thyroid cancer with cervical lymph node metastasis. After a thyroidectomy, esophageal MTG was confirmed by a fluorine-18-deoxyglucose positron emission tomography (FDG-PET-CT) combined with pathological immunohistochemistry.

CASE PRESENTATION

Chief complaints

An ever healthy 69-year-old Chinese male patient was hospitalized after a routine check-up that showed malignancy-suspected nodules in his bilateral thyroid lobes and enlarged cervical lymph nodes on both sides.

History of present illness

The patient was asymptomatic and received the treatment for the first time at our hospital.

History of past illness

The patient had an unremarkable past history except for diabetes and hypertension.

Physical examination

Physical examination revealed a 3.0 cm firm thyroid mass in the right thyroid lobe, and swollen neck lymph nodes were palpated on both sides.
Laboratory examinations
The laboratory test results were normal for free triiodothyronine level (6.21 pmol/L, normal range 3.28-6.47 pmol/L), free thyroxine level (10.23 pmol/L, normal range 7.64-16.03 pmol/L), and thyroid-stimulating hormone level (1.79 mIU/L, normal range 0.51-5.91 mIU/L). The tumor markers levels were all in normal range.

Imaging examinations
Ultrasonography revealed multiple Thyroid Imaging Reporting and Data System 4c nodules in bilateral thyroid lobes (Figure 1). Neck contrast-enhanced computed tomography (CT) scan indicated multifocal disease in the thyroid lobes and enlarged cervical lymph nodes on both sides (Figure 2).

Further diagnostic work-up
The patient underwent a fine needle aspiration (FNA) biopsy of the thyroid lesions and neck lymph nodes, which showed malignant tumor cells in both (Figure 3).

FINAL DIAGNOSIS
The final diagnosis of MTG from ESCC was based on the immunohistochemical panel after thyroidectomy.

TREATMENT
The patient received a total thyroidectomy plus bilateral level VI lymph nodes dissection. The permanent section revealed metastatic squamous cell carcinoma in the thyroid gland. Therefore, further diagnostic procedures were performed to determine the primary carcinoma. A chest CT scan revealed mediastinal nodal involvement, and an abdominal ultrasound was negative. A postoperative FDG-PET-CT was performed, which showed that the lower part of the esophagus and the lymph nodes in the neck, chest, and abdomen were all involved (Figure 4). The patient underwent an esophagogastroscope, and a lesion was noted in the distal esophagus, in which squamous cell carcinoma was confirmed by biopsy (Figure 5A). Immuno-histochemistry of the thyroid lesions was consistent with features of metastatic ESCC (Figure 5B-H). The patient received four rounds of adjuvant chemotherapy of oxaliplatin combined with 5-fluorouracil every 3 wk and then withdrew due to the side effects.

OUTCOME AND FOLLOW-UP
He was followed up every 3 mo after discharge. At present, he is on traditional Chinese medicine and feels well 1 year after the diagnosis.

DISCUSSION
Although rare, esophageal MTG does occur. Physicians should keep in mind that it is necessary to perform further examinations of the cervical region when malignant, multifocal lesions in the thyroid gland are noted. MTG needs to be considered as a differential diagnosis, even in patients with no prior history of malignancy. MTG is generally regarded to result from the spread of a primary tumor by a hematogenous route. Despite its rich blood supply, the thyroid is a rare site for metastatic disease. This phenomenon is due to fast arterial flow that prevents cancer cell adhesion, and the high oxygen saturation and iodine content of the thyroid gland inhibit the growth of malignant cells\(^3\). The incidence of MTG is low and amounts to 2%-3% of all malignant tumors of the thyroid\(^5\). The most common primary malignancies that can metastasize to the thyroid gland are renal cell cancer, followed by lung cancer and breast cancer\(^6\). MTG from esophageal cancer is extremely rare, and only a few sporadic cases have been reported in the literature thus far\(^7-10\). To our knowledge, there has been no reported case of metastasis of esophageal cancer to the thyroid gland and widespread involvement of distant lymph nodes at the same time.
Metastatic disease that involves the thyroid gland may pose a diagnostic challenge. At presentation, MTG may share similarities with primary thyroid tumors, and most patients are asymptomatic\(^1\). MTG may be the sole presentation, without any primary tumor-related symptoms or previous malignancy history. This patient with MTG lacked symptoms of advanced-stage esophageal cancer like dysphagia, weight loss, and chest pain. The thyroid masses and neck nodal involvement were the only positive findings at the initial imaging and physical examination before the surgery. The fine needle aspiration cytology did not reveal MTG as well. Preoperative fine
Zhang X et al. Metastasis of esophageal carcinoma to thyroid

Figure 4  Fluorine-18-deoxyglucose positron emission tomography-computed tomography fused transaxial images (A-C) and maximum intensity projection (D). A and C: They show the uptake nodal focus (center of crossing); B: It shows an enlarged lymph node (center of crossing) and esophageal lesion (white arrow); D: It shows widespread lymph node involvement (orange arrows) and an esophageal lesion (white arrow).

Needle aspiration cytology is a reliable approach to establish the diagnosis. However, it has limitations with regard to distinguishing MTG from primary thyroid carcinoma. Therefore, this disease can confuse surgeons and masquerade the primary thyroid cancer metastases to cervical lymph nodes. Even after the thyroidectomy, the permanent section showed MTG. It was not an easy task to determine the primary tumor, and the work-up diagnostic procedures helped locate the primary tumor. After all other routine examinations are negative for the primary tumor, FDG-PET-CT usually is the final resort; in some patients, the primary tumors cannot be found[4]. Although the indication of surgery for metastatic thyroid carcinomas is uncertain and does not impact overall survival, in some patients with MTG, a total thyroidectomy is warranted[12-14]. Especially for MTG multifocal disease, a total thyroidectomy should be considered and may achieve control of the central neck[6]. Furthermore, definitive histology by surgical excision may be required to confirm the diagnosis[15].

The differential diagnoses of MTG of ESCC include primary squamous cell carcinoma (PSCC) of the thyroid and mucoepidermoid thyroid carcinoma (MEC). PSCC of the thyroid resembles anaplastic thyroid carcinoma in clinical presentation. Patients with PSCC of the thyroid present with rapidly increasing neck mass invading the adjacent structures. Besides patients’ history, immunohistochemical panel is useful in diagnosing MTG. PSCC as well as squamous carcinoma component in association with other thyroid carcinomas have been shown to be positive for paired box gene 8 (PAX-8) protein[16]. Like anaplastic thyroid carcinoma, PSCC shows a high frequency of P53 overexpression[17]. In this case, PAX-8 and P53 were negative. The microscopic features of multifocal tumor nests along the vessels found in this case indicate MTG as well. The immunohistology characteristics of MEC generally demonstrate positive for thyroid transcription factor-1 (TTF1) and thyroglobulin. In this case, TTF1 and thyroglobulin were both negative. Furthermore, the immunohistochemical staining was positive for CK5/6 and P40. Combined with the results of FDG-PET-CT and esophagogastroscopey, the diagnosis of MTG from ESCC was confirmed.

CONCLUSION

It is difficult to determine the primary tumor when patients with esophageal MTG are asymptomatic and have no previous malignancies. Further diagnostic procedures are
Figure 5 Fine needle aspiration cytology of the thyroid lesions stained with hematoxylin and eosin (× 200) and the immunohistochemical features. A: Permanent section of the esophagus stained with hematoxylin and eosin shows esophageal squamous cell carcinoma (× 200); B: Histology of MTG stained with hematoxylin and eosin shows multifocal tumor nests (orange arrow) (× 40); C: Immunohistochemical negative staining of metastasis to the thyroid gland (MTG) for thyroid transcription factor-1 (orange arrow) (× 200); D: Immunohistochemical negative staining of MTG for thyroglobulin (orange arrow) (× 200); E: Immunohistochemical positive staining of MTG for CK5/6 (orange arrow) (× 200); F: Immunohistochemical positive staining of MTG for P40 (orange arrow) (× 200); G: Immunohistochemical negative staining of MTG for (orange arrow) (× 200); H: Immunohistochemical negative staining of MTG for paired box gene 8 (orange arrow) (× 200).
necessary after MTG is confirmed by cytology or histology, and the final diagnosis should be made according to the identification of the primary malignancy combined with pathological immunohistochemistry findings.

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