

Case Report

Solitary metastasis from renal cell carcinoma in the anterior mediastinal lymph node

Satoru Moriyama¹, Motoki Yano^{1,2}, Hiroshi Haneda¹, Katsuhiro Okuda¹, Osamu Kawano¹, Yu Hikosaka^{1,3}, Risa Oda¹, Ayumi Suzuki¹, Ryoichi Nakanishi¹

¹Department of Oncology, Immunology and Surgery, Nagoya City University Graduate School of Medical Science, Nagoya, Japan; ²Division of Chest Surgery, Department of Surgery, Aichi Medical University, Nagakute, Japan; ³Department of Thoracic Surgery, Toyokawa City Hospital, Toyokawa, Japan

Received March 24, 2015; Accepted September 8, 2016; Epub October 15, 2016; Published October 30, 2016

Abstract: Solitary metastasis of renal cell carcinoma (RCC) in the mediastinal lymph nodes is rare in patients without lung metastasis. We herein report a case of RCC with solitary mediastinal lymph node metastasis. A mass in the anterior mediastinum was found in the chest computed tomography (CT) scan of an asymptomatic 43-year-old man. A mass on the right kidney was also revealed in an abdominal CT scan. The anterior mediastinal mass was removed. It was histologically diagnosed as a metastatic renal cell carcinoma of the anterior mediastinal lymph node. The patient subsequently underwent radical right nephrectomy and was diagnosed with renal cell carcinoma. Although the metastatic route from the right kidney to the mediastinal lymph node is unknown, solitary metastasis to the anterior mediastinal lymph node is possible.

Keywords: Solitary metastasis, renal cell carcinoma, anterior mediastinal lymph node

Introduction

Renal cell carcinoma (RCC) often metastasizes to the lung through a hematogenous route. Metastasis to the hilar and mediastinal lymph nodes usually occurs via a lymphogenous route from pulmonary metastatic lesions. Solitary metastasis to a mediastinal lymph node is uncommon in patients without lung metastasis. We herein report a rare case of RCC with solitary mediastinal lymph node metastasis in a patient without lung metastasis.

Case report

An asymptomatic 43-year-old man was referred to our institution due to a mass in the left hilum that was detected on a chest radiograph. He had a medical history of hypertension and had smoked one pack per day for twenty years. The results of a physical examination and laboratory analyses (including urinalysis) were unremarkable. Chest computed tomography (CT) revealed a well-defined mass of 4 × 3 cm in the anterior mediastinum towards the left hilum. It

was enhanced by contrast medium and was adjacent to the left pulmonary artery (**Figure 1A**). There were no other radiological abnormalities on the patient's chest CT. Magnetic resonance imaging (MRI) revealed an area of low-signal intensity on T1-weighted images and high-signal intensity on T2-weighted images.

A whole body Fluorine-18-2-fluoro-D-glucose positron emission tomography/CT (FDG-PET/CT) study (**Figure 2**) revealed intense focal FDG uptake [standard uptake value (SUV) max = 15.9] in the anterior mediastinum and focal uptake (SUV max = 13.7) in the right kidney. The right renal mass was 2.5 × 2.3 cm in size and was well-defined and enhanced on abdominal CT (**Figure 1B**). None of the patient's serum levels of tumor markers were elevated.

The anterior mediastinal mass was preoperatively diagnosed as a thymic epithelial tumor or a neurogenic tumor derived from the left phrenic nerve or vagus nerve. The renal tumor was preoperatively diagnosed as an early-stage RCC. The anterior mediastinal mass was resect-

Solitary mediastinal lymph node metastasis from RCC

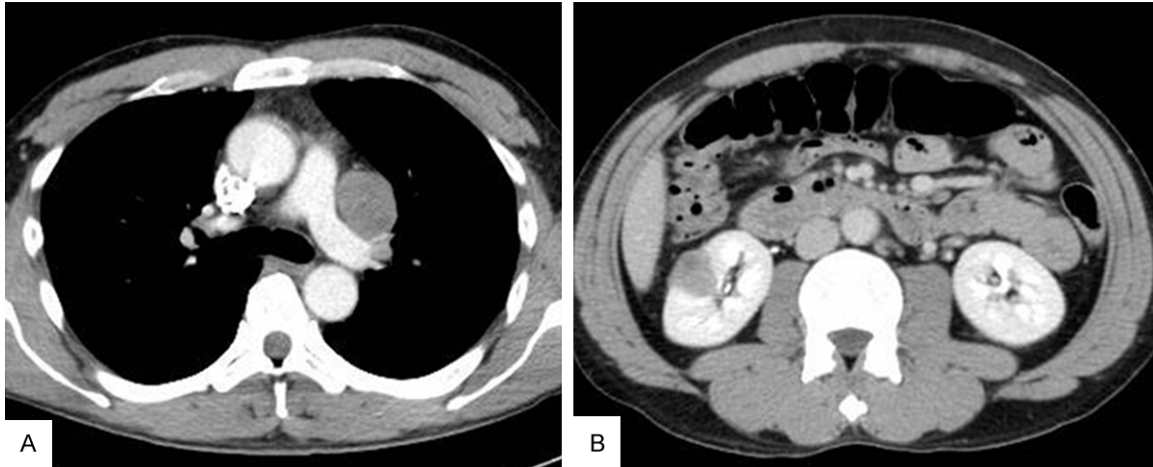


Figure 1. Enhanced chest and abdominal computed tomography. Enhanced chest computed tomography revealed a mass adjacent to the left pulmonary artery (A). Enhanced abdominal computed tomography revealed a tumor that was enhanced in the right kidney (B).



Figure 2. Positron emission tomography. Positron emission tomography revealed the accumulation of fluorodeoxyglucose on the mass in the anterior mediastinum (SUV 15.9) (arrows) and a tumor in the right kidney (SUV 13.7) (dashed arrow).

ed using video-assisted thoracoscopic surgery (VATS). It was easily removed and did not involve the nerves. An intraoperative histological exam-

ination of a snap frozen specimen of the mediastinal lymph node resulted in a diagnosis of metastatic RCC. Mini-thoracotomy was immediately performed and mediastinal and hilar lymph node dissection was added. Tumor cells were only detected in the anterior mediastinal mass. The patient made an uneventful postoperative recovery. One month later, the patient underwent radical right nephrectomy. The diagnosis was RCC. A histological examination of the mediastinal tumor revealed findings that were compatible with metastatic renal cell carcinoma (Figure 3). The patient was given sunitinib as a postoperative adjuvant therapy. Single brain metastasis was discovered 9 months after the thoracotomy. The patient received everolimus as a second-line therapy and underwent surgical treatment for brain metastasis. Thereafter, brain recurrences occurred intermittently. The patient underwent additional surgical treatment, stereotactic radiotherapy and chemotherapy. It is currently 62 months since the first operation and the patient has had no recurrence of RCC.

Discussion

In the present report, a mass was located on the edge of the anterior mediastinum that was defined by the mediastinal division of the Japanese Association for the Research on the Thymus (JART). Thymic epithelial tumors are representative anterior mediastinal tumors. We initially diagnosed the anterior mediastinal

Solitary mediastinal lymph node metastasis from RCC

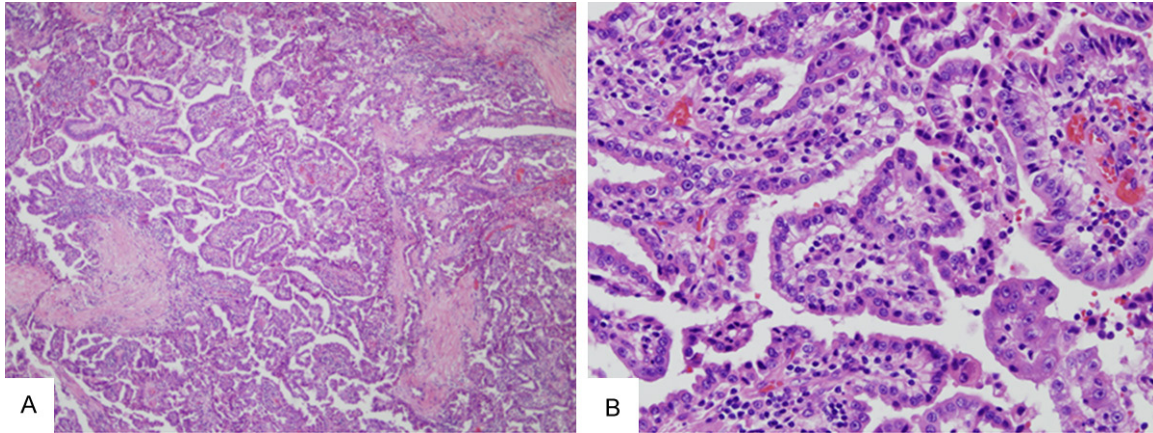


Figure 3. Pathological findings. (A) Histological examination of the anterior mediastinal tumor revealed that it was metastatic renal cell carcinoma (Hematoxylin and eosin staining, (A) low magnification: $\times 40$, (B) high magnification: $\times 200$).

mass as a thymoma or a neurogenic tumor derived from the left phrenic nerve or vagus nerve.

A total of 25-30% of RCC patients have metastases at their initial presentation [1]. The lung, bones, liver and brain are the common sites for distant metastases in RCC patients. Metastases to the mediastinal lymph nodes are usually found together with lung metastasis. The anterior mediastinum is a rare site of metastasis, particularly in a patient with no lung metastasis. There is only one case in the literature that describes metastasis to an anterior mediastinal lymph node from RCC at the time of the initial diagnosis [2].

The metastatic pathway from the right kidney to the mediastinal lymph node is not clear. One lymphogenous route is via the thoracic duct. This may occur if there is retrograde flow to the peribronchial lymphatics from the thoracic duct due to its incompetence or the absence of valves [3]. Assouad et al. [4] reported that the renal lymphatics are always connected to the thoracic duct. Reflux from the thoracic duct during lymphangiography is found in 5-14% of all examined patients, probably due to valvular incompetence [5]. The other lymphogenous route is via the retroperitoneal lymphatics to the inferior pulmonary ligament that leads to the hilar and mediastinal lymph nodes [6]. A hematogenous route is also possible through lung metastasis from RCC [7]. Mediastinal lymph node metastases occur as a second step from pulmonary micrometastases. Pul-

monary metastases may sometimes be too small to be detected. In our case, although the patient later developed brain metastasis, we hypothesize that the metastatic route to the mediastinal lymph node was lymphogenous, either from the thoracic duct due to retrograde lymphatic flow or through the retroperitoneal lymphatics to the inferior pulmonary ligament, because no lung metastases were detected.

Solitary metastasis is identified at the initial diagnosis of RCC in 1-3% of patients [8]. Radical nephrectomy with the resection of solitary metastasis has been reported (depending on the site of metastasis) [9], because neither chemotherapy nor radiation therapy has proven effective in the treatment of metastatic disease. Immunotherapy, such as recombinant human interleukin-2 and interferon-alpha, has been effective, but the overall response rate in patients with metastatic RCC is only 15-20% [10]. Recently, targeted agents, either vascular endothelial growth factor inhibitors or mammalian target of rapamycin inhibitors, have shown encouraging results [11, 12]. However, surgical resection should be considered whenever complete surgical resection is possible [13, 14].

In conclusion, we experienced a rare case of solitary metastasis in the anterior mediastinal lymph node in a patient with renal cell carcinoma. Although the metastatic route from the right kidney to the mediastinal lymph node is not clear, solitary lymph node metastasis from extrathoracic neoplasms, including RCC, should

Solitary mediastinal lymph node metastasis from RCC

be considered in the differential diagnosis of anterior mediastinal masses.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Motoki Yano, Division of Chest Surgery, Department of Surgery, Aichi Medical University, 1-1 Yazakokarimata, Nagakute, 480-1195, Japan. Tel: +81- 561-62-3311; Fax: +81-561-63-6841; E-mail: motoki2ds@yahoo.co.jp

References

- [1] Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. *N Engl J Med* 1996; 335: 856-875.
- [2] Mattana J, Kurtz B, Miah A, Singhal PC. Renal cell carcinoma presenting as a solitary anterior superior mediastinal mass. *J Med* 1996; 27: 205-210.
- [3] Mcloud TC, Kalisher L, Stark P, Greene R. Intra-thoracic lymph node metastases from extra-thoracic neoplasms. *Am J Roentgenol* 1978; 131: 403-407.
- [4] Assoud J, Riquet M, Foucaut C, Hidden G, Delmas V. Renal lymphatic drainage and thoracic duct connections: implications for cancer spread. *Lymphology* 2006; 39: 26-32.
- [5] Rosenberger A, Adler O, Abrams HL. The thoracic duct: structural, functional, and radiologic aspects. *CRC Crit Rev Radiol Sci* 1972; 3: 523-541.
- [6] Wright FW. Enlarged hilar and mediastinal nodes (and especially lower right hilar node enlargement) as a sign of metastasis of a renal tumour. *Clin Radiol* 1977; 28: 431-436.
- [7] Kanzaki R, Higashiyama M, Okami J, Kodama K. Surgical treatment for patients with solitary metastasis in the mediastinal lymph node from renal cell carcinoma. *Interact Cardiovasc Thorac Surg* 2009; 8: 485-487.
- [8] Tolia BM, Whitmore WF. Solitary metastasis from renal cell carcinoma. *J Urol* 1975; 114: 836-838.
- [9] Thyavihally YB, Mahantshetty U, Chamara-janagar RS, Raibhattanavar SG, Tongaonkar HB. Management of renal cell carcinoma with solitary metastasis. *World J Surg Oncol* 2005; 3:48.
- [10] Bukowski RM. Natural history and therapy of metastatic renal cell carcinoma: the role of interleukin-2. *Cancer* 1997; 80: 1198-1220.
- [11] Escudier B, Porta C, Schmidinger M, Algaba F, Patard JJ, Khoo V, Eisen T, Horwich A. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014; 25: iii49-iii56.
- [12] Wagstaff J, Johes R, Hawkins R, Porfiri E, Pickering L, Bahl A, Brown J, Buchan S. Treatment patterns and clinical outcomes in patients with renal cell carcinoma in the UK: insights from the RECCORD registry. *Ann Oncol* 2016; 27: 159-165.
- [13] Thomas AA, Rini BI, Stephenson AJ, Garcia JA, Fergany A, Krishnamurthi V, Novick AC, Gill IS, Klein EA, Zhou M, Campbell SC. Surgical resection of renal cell carcinoma after targeted therapy. *J Urol* 2009; 182: 881-886.
- [14] Alt AL, Boorjian SA, Lohse CM, Costello BA, Leibovich BC, Blute ML. Survival after complete surgical resection of multiple metastases from renal cell carcinoma. *Cancer* 2011; 117: 2873-2882.