

## Case Report

# Simultaneous multiple primary cancers with concomitant inflammatory myofibroblastic tumor: a case report

Xingyu Lv<sup>1,2</sup>, Jianming Ye<sup>3</sup>, Guangyi Jiang<sup>1,2</sup>, Yifan Wang<sup>1,2</sup>, Jisheng Lv<sup>4</sup>, Yong Wang<sup>1</sup>

<sup>1</sup>Department of General Surgery, <sup>2</sup>Key Laboratory of Laparoscopic Technology of Zhejiang Province, Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang, China; <sup>3</sup>Department of Thoracic Surgery, Jinhua People's Hospital, Jinhua, Zhejiang, China; <sup>4</sup>Department of Anesthesiology, Jinhua People's Hospital, Jinhua, Zhejiang, China

Received February 17, 2020; Accepted March 27, 2020; Epub May 1, 2020; Published May 15, 2020

**Abstract:** Multiple primary cancers are of rare occurrence. Most multiple primary cancers are metachronous multiple primary cancers, while simultaneous multiple primary cancers are rare. Inflammatory myofibroblastic tumors are rare. Inflammatory myofibroblastic tumor occurs most frequently in children and young adults. Herein, we report a rare case of simultaneous multiple primary cancers and inflammatory myofibroblastic tumor. A 44-year-old woman was admitted for a breast mass evaluation. The patient was positive for antinuclear, anti-mitochondrial, and anti-RO52 antibodies. Breast magnetic resonance imaging revealed a right breast mass. After neoadjuvant chemotherapy, modified radical mastectomy was performed. Postoperative histopathology revealed an invasive ductal carcinoma. Two months later, computed tomography revealed a nodule in the right upper lobe and ground-glass opacity in the lower lobe of the lungs. Lobectomy and lobe biopsy were performed. Postoperative histopathology revealed that the mass in the right upper lobe was an inflammatory myofibroblastic tumor and the right lower lobe lesion was an invasive adenocarcinoma. Immunohistochemistry of the inflammatory myofibroblastic tumor revealed negativity for anaplastic lymphoma kinase. At the 4-month follow-up, the patient showed good recovery. The etiology of multiple primary cancers and inflammatory myofibroblastic tumors is still unknown; in this case, we believe that autoimmune factors are the main cause of multiple primary cancers with concomitant inflammatory myofibroblastic tumor. Tissue biopsy is needed to ensure correct diagnosis of multiple primary cancers and inflammatory myofibroblastic tumor. Surgery-based comprehensive therapy is recommended. The prognosis is favorable and regular follow-up is necessary.

**Keywords:** Inflammatory myofibroblastic tumor, multiple primary cancers, primary breast cancer, primary lung cancer

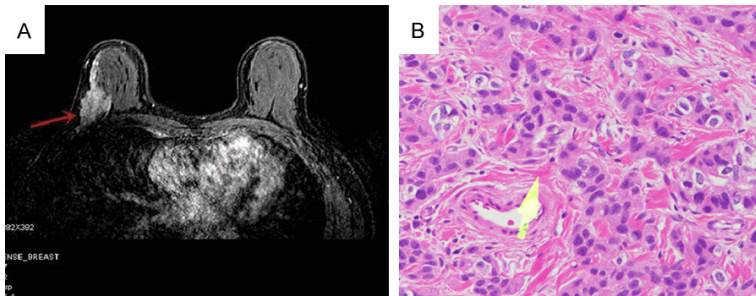
### Background

Multiple primary cancers (MPCs) were not recognized until the 1890s, and were first defined by Warren and Gates in 1932 [1]. The diagnostic criteria for MPCs are as follows: (1) at least two tumors proven malignant in an individual patient; (2) each malignancy has identified pathology; (3) the possibility of one being a metastasis of the other must be ruled out. In 1961, Moertel proposed that if MPCs are diagnosed within 6 months, they are simultaneous MPCs; if MPCs are diagnosed after more than 6 months, they are metachronous MPCs [2].

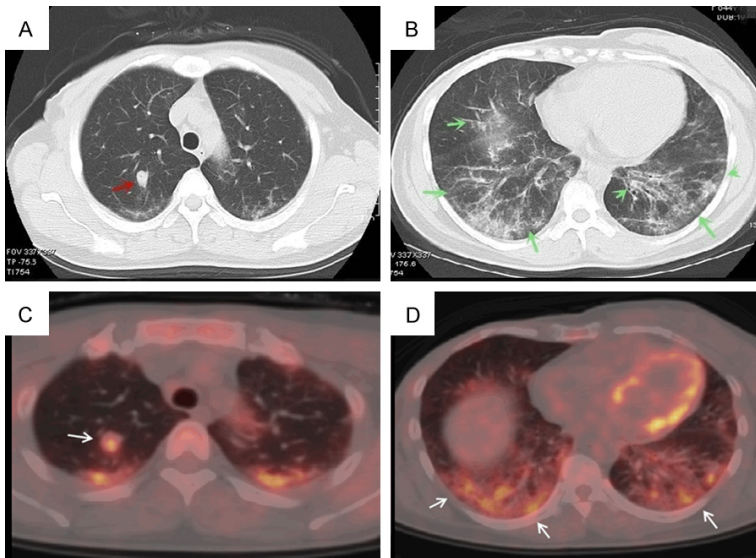
The World Health Organization classified inflammatory myofibroblastic tumors (IMTs) as a distinct entity in 1994 [3]. IMT is a rare mass-forming lesion characterized by fibroblastic or myofibroblastic spindle cell proliferation with varying degrees of inflammatory cell infiltration and intermediate biologic potential [4].

The diagnosis of MPCs and IMT is currently very precise owing to the development in imaging equipment and pathology examinations [5]. The incidence of MPCs in cancer patients is 0.5-10% [6], with most MPCs being metachronous MPCs, while simultaneous MPCs are rare

## Multiple primary cancers and a tumor



**Figure 1.** A. Breast magnetic resonance imaging revealed a right breast mass (arrow). B. Pathology after surgery showing a right breast invasive ductal carcinoma (magnification,  $\times 200$ ) (arrow).



**Figure 2.** Chest computed tomography reveals a high-density nodule in the right upper lobe (A) and ground glass opacity (GGO) in the lower lobe of the lung (B) (arrow). Positron-emission tomography/computed tomography showing the lung nodule (C) and GGO (D) with elevated standardized uptake values (arrow).



**Figure 3.** Resected specimen of tumor in the right upper lobe.

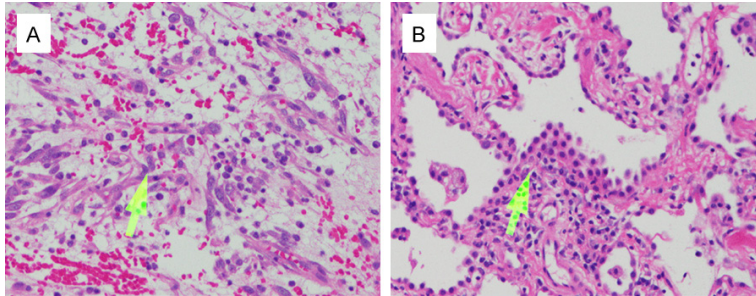
[7]. The worldwide incidence of IMT is 0.04-0.7% [8]. IMT occurs most frequently in children and young adults [9]. Herein, we provide a rare case of simultaneous double primary cancers with concomitant IMT in a 44-year-old woman; to the best of our knowledge, this is the first such reported case.

### Case presentation

In September 2018, a 44-year-old woman with no remarkable medical history or family history of malignancy was admitted to evaluate a breast mass; she reported 5 kg weight loss in 3 months. She was positive for antinuclear antibody (ANA), anti-mitochondrial antibody (AMA) and anti-R052 antibodies. Ultrasonography revealed a 4.7-cm  $\times$  1.9-cm hypoechoic tumor in the upper outer quadrant of the right breast. Breast magnetic resonance imaging (**Figure 1A**) revealed a 5.0-cm  $\times$  2.0-cm right breast mass. Ultrasound-guided core needle biopsy revealed a right breast invasive ductal carcinoma. The patient underwent right-sided modified radical mastectomy in October 2018. Postoperative histopathology (**Figure 1B**) revealed a right breast invasive ductal carcinoma. The postoperative course was uneventful; the patient began to receive adjuvant chemotherapy.

When preparing for the fourth cycle of adjuvant chemotherapy in December 2018, the patient underwent routine chest computed tomography (CT). CT revealed a 1.5-  $\times$  1.5-cm high-density nodule in the right upper lobe (**Figure 2A**) and ground-glass opacity (GGO) in the lower lobe of the lung (**Figure 2B**). Positron emission tomography-computed tomography (PET/CT) confirmed the lung nodule (**Figure**

## Multiple primary cancers and a tumor



**Figure 4.** Pathology after surgery showing an inflammatory myofibroblastic tumor (A) in the right upper lobe and an invasive adenocarcinoma (B) in the right lower lobe (magnification,  $\times 200$ ) (arrow).

2C) and GGO (Figure 2D) with elevated standardized uptake values, indicating malignancy. After multidisciplinary discussion, video-assisted thoracoscopic wedge resection of right upper lobe and right lower lobe biopsy were performed in December 2018. Surgical findings of the right upper lobe showed a circumscribed multinodular mass with a white fleshy cut surface (Figure 3). Postoperative histopathology revealed that the right upper lobe mass was an IMT (Figure 4A) and the right lower lesion was an invasive adenocarcinoma (Figure 4B). Immunohistochemistry of the IMT showed CD38 (+); CD138 (-); CK7 (-); ALK (-); SMA (-); Vimentin (+); Actin (-); Ki-67 (10%); and p53 (-). The patient showed uneventful recovery and continued to receive adjuvant chemotherapy. At the 4-month follow-up, the patient showed good recovery without any metastasis or recurrence.

### Discussion and conclusion

The etiologies of MPCs and IMT are both unclear. The possible etiology of MPCs include genetic defects [10] and autoimmune factors [11]. The etiology of IMT may be infectious [12], traumatic [13], or autoimmune syndromic [14]. Approximately 50% of IMTs show a cytogenetic translocation involving *ALK* on chromosome 2p23, resulting in *ALK* overexpression [15]. In this case, immunohistochemistry of IMT showed *ALK* negativity. There was no family history of cancer, infection, or trauma. However, ANA, AMA, and anti-RO52 antibodies were positive. Therefore, we speculate that autoimmune factors were the main cause of MPCs with concomitant IMT.

Although PET/CT is commonly used to differentiate between benign and malignant tumors,

false-positive results are inevitable [16]. In this case, postoperative histopathology demonstrated that the mass in the right upper lobe, diagnosed preoperatively as malignancy on PET/CT, was an IMT. Therefore, tissue biopsy is needed to ensure correct diagnosis of MPCs and IMT.

The treatment is different for MPCs and metastatic and recurrent cancers [17]. Metastatic and recurrent cancers are mainly treated with non-surgical palliative care. However, MPCs are mainly treated with surgery-based comprehensive therapy (radical surgery combined with chemotherapy or radiotherapy). Surgery with complete excision remains the primary treatment for IMT, although no real consensus regarding IMT treatment exists [18]. In the present case, the patient was diagnosed with coexistent simultaneous MPCs and IMT. Therefore, surgery-based comprehensive therapy was performed.

MPC prognosis is better than that of recurrent and metastatic cancers [19]. IMT prognosis is generally favorable, and regular follow-up is necessary [20]. Therefore, the patient has been advised to undergo reexaminations every 3 months; we will continue to follow-up this patient.

To our knowledge, simultaneous double primary cancers with concomitant IMT are rare. The etiology is still unknown; in this case, we believe that autoimmune factors are the main cause of MPCs with concomitant IMT. Surgery-based comprehensive therapy is recommended. The prognosis is favorable and regular follow-up is necessary. More studies are needed to clarify whether there is a deeper association between MPCs and IMT.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Yong Wang, Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, Zhejiang, China. Tel: +86-0571-87951111; Fax: +86-0571-88981358; E-mail: 3313023@zju.edu.cn

## Multiple primary cancers and a tumor

### References

- [1] Warren S and Gates O. Multiple primary malignant tumors-a survey of the literature and statistical study. *Am J Cancer* 1932; 16: 358-414.
- [2] Demandante CG, Troyer DA and Miles TP. Multiple primary malignant neoplasms: case report and a comprehensive review of the literature. *Am J Clin Oncol* 2003; 26: 79-83.
- [3] Coindre JM. Histologic classification of soft tissue tumors (WHO, 1994). *Ann Pathol* 1994; 14: 426-7.
- [4] Gallego L, Santamarta TR, Blanco V, Garcia-Consuegra L, Cutilli T and Junquera L. Inflammatory myofibroblastic tumor of the lung and the maxillary region: a benign lesion with aggressive behavior. *Case Rep Dent* 2013; 2013: 879792.
- [5] Koutsopoulos AV, Dambaki KI, Datsaris G, Giannikaki E, Froudarakis M and Stathopoulos E. A novel combination of multiple primary carcinomas: urinary bladder transitional cell carcinoma, prostate adenocarcinoma and small cell lung carcinoma—report of a case and review of the literature. *World J Surg Oncol* 2005; 3: 51.
- [6] Zubaidi A. Multiple primary cancers of the colon, rectum, and the thyroid gland. *Saudi J Gastroenterol* 2008; 14: 202-5.
- [7] Lv M, Zhang X, Shen Y, Wang F, Yang J, Wang B, Chen Z, Li P, Zhang X, Li S and Yang J. Clinical analysis and prognosis of synchronous and metachronous multiple primary malignant tumors. *Medicine (Baltimore)* 2017; 96: e6799.
- [8] Panagiotopoulos N, Patrini D, Gvinianidze L, Woo WL, Borg E and Lawrence D. Inflammatory myofibroblastic tumour of the lung: a reactive lesion or a true neoplasm? *J Thorac Dis* 2015; 7: 908-11.
- [9] Dongel I, Yazkan R, Duman L, Ozturk O and Kapucuoglu FN. Huge inflammatory myofibroblastic tumor of pleura with concomitant nuchal fibroma. *Ann Thorac Surg* 2013; 96: 1461-4.
- [10] Cybulski C, Nazarali S and Narod SA. Multiple primary cancers as a guide to heritability. *Int J Cancer* 2014; 135: 1756-63.
- [11] Alsarkhi LK and Weber GF. Antiosteopontin autoantibodies in various types of cancer. *Oncol Rep* 2018; 40: 3879-89.
- [12] Androulaki A, Papathomas TG, Liapis G, Papaconstantinou I, Gazouli M, Goutas N, Bramis K, Papalambros A, Lazaris AC and Papalambros E. Inflammatory pseudotumor associated with Mycobacterium tuberculosis infection. *Int J Infect Dis* 2008; 12: 607-10.
- [13] Perera MT, Wijesuriya SR, Kumarage SK, Ariyaratne MH and Deen KI. Inflammatory pseudotumour of the liver caused by a migrated fish bone. *Ceylon Med J* 2007; 52: 141-2.
- [14] Gonzalez-Duarte A, Sullivan S, Sips GJ, Naidich T, Kleinman G, Murray J, Morgello S, Germano I, Mullen M and Simpson D. Inflammatory pseudotumor associated with HIV, JCV, and immune reconstitution syndrome. *Neurology* 2009; 72: 289-90.
- [15] Antonescu CR, Suurmeijer AJ, Zhang L, Sung YS, Jungbluth AA, Travis WD, Al-Ahmadie H, Fletcher CD and Alaggio R. Molecular characterization of inflammatory myofibroblastic tumors with frequent ALK and ROS1 gene fusions and rare novel RET rearrangement. *Am J Surg Pathol* 2015; 39: 957-67.
- [16] Zheng Z, Pan Y, Pan T and Li J. Coexistent pulmonary inflammatory pseudotumor and carcinoma in one patient: does positron emission tomography/computed tomography help. *Ann Thorac Surg* 2011; 91: e43.
- [17] Okada M, Tsubota N, Yoshimura M and Miyamoto Y. Operative approach for multiple primary lung carcinomas. *J Thorac Cardiovasc Surg* 1998; 115: 836-40.
- [18] Tomazic A, Gvardijancic D, Maucec J and Homan M. Inflammatory myofibroblastic tumor of the pancreatic head - a case report of a 6 months old child and review of the literature. *Radiol Oncol* 2015; 49: 265-70.
- [19] Nishimura Y, Komatsu S, Ichikawa D, Okamoto K, Shiozaki A, Fujiwara H, Murayama Y, Kuriu Y, Ikoma H, Nakanishi M, Ochiai T, Kokuba Y and Otsuji E. The clinical influence of double or multiple primary cancers on the prognosis of patients with gastric cancer. *Gan To Kagaku Ryoho* 2012; 39: 2301-3.
- [20] Ding D, Bu X and Tian F. Inflammatory myofibroblastic tumor in the head of the pancreas with anorexia and vomiting in a 69-year-old man: a case report. *Oncol Lett* 2016; 12: 1546-50.