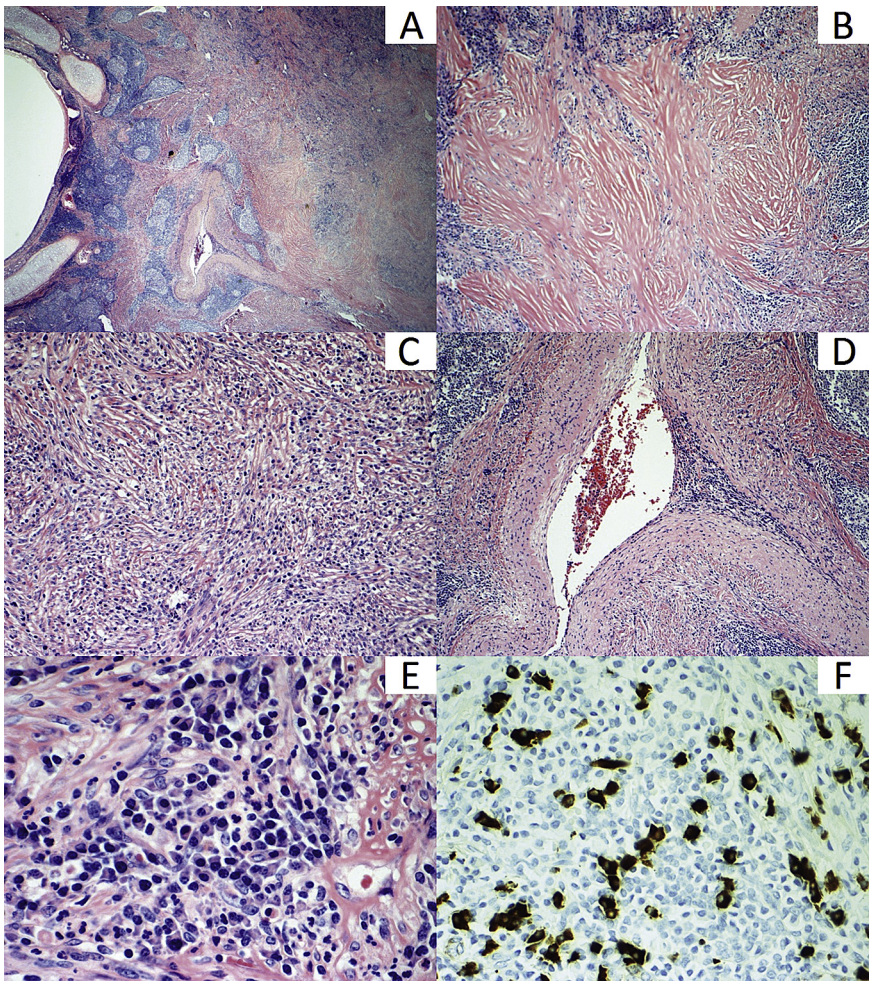

Fig 3. (A) Low-power view of mass showing collagenous fibrosis with admixed inflammatory cells. (Hematoxlyin and eosin [H&E], ×40.) (B) Areas of fibrosis consisting of dense collagen. (H&E, ×200.) (C) Areas of fibrosis with higher cellularity consisting of inflammatory cells and spindle cells with a vague storiform growth pattern. (H&E, ×200.) (D) Blood vessels showing partial obliteration by the fibroinflammatory process. (H&E, ×200.) (E) Inflammatory cell infiltrate containing numerous plasma cells. (H&E, ×400.) (F) Plasma cells were positive for immunoglobulin G4 (IgG4) in numbers greater than 50 per single high-power field. (IgG4 immunostain, ×400.)

suggest inflammation rather than malignancy. Surgical lung biopsy is currently the most specific method of diagnosis and should be correlated with clinical, radiologic, and laboratory findings.

The authors thank Erlin Daley, BA, for editorial assistance.

References

1. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4-related sclerosing disease. Eur Respir J 2012;39:180–6.
2. Inoue D, Zen Y, Abo H, et al. Immunoglobulin G4-related lung disease: CT findings with pathologic correlations. Radiology 2009;251:260–70.
3. Deshpande V, Zen Y, Chan JK, et al. Consensus statement on the pathology of IgG4-related disease. Mod Pathol 2012;25:1181–92.
4. Matsui S, Hebisawa A, Sakai F, et al. Immunoglobulin G4-related lung disease: clinicoradiological and pathological features. Respirology 2013;18:480–7.
5. Zen Y, Inoue D, Kitao A, et al. IgG4-related lung and pleural disease: a clinicopathologic study of 21 cases. Am J Surg Pathol 2009;33:1886–93.
6. Inoue T, Hayama M, Kobayashi S, et al. Lung cancer complicated with IgG4-related disease of the lung. Ann Thorac Cardiovasc Surg 2013; Apr 11: http://dx.doi.org/10.5761/atcs.cr.12.02208.

FEATURE ARTICLES

Multiple Lung Adenocarcinomas Associated With Von Hippel-Lindau Disease

Koei Ikeda, MD, PhD, Hironobu Osumi, MD, Kentaro Matsuishi, MD, Eri Matsubara, MD, Kousuke Fujino, MD, Hidekatsu Shibata, MD, PhD, Kentaro Yoshimoto, MD, PhD, Kenji Shiraishi, MD, PhD, Takeshi Mori, MD, PhD, and Makoto Suzuki, MD, PhD

Department of Thoracic Surgery, Graduate School of Medical Science, Kumamoto University, Kumamoto, Japan

Lung adenocarcinoma has never before been reported to be associated with von Hippel-Lindau (VHL) disease. Here, we report a case of VHL disease in a patient who had metachronous multiple lung adenocarcinomas. The

Accepted for publication Nov 25, 2013.

Address correspondence to Dr Ikeda, Department of Thoracic Surgery, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto 860-8556, Japan; e-mail: koei@cg7.so-net.ne.jp.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2013.11.080

patient is a 64-year-old-woman with VHL disease. She underwent surgical resection of one adenocarcinoma and one atypical adenomatous hyperplasia. A second lung adenocarcinoma developed metachronously. A point mutation in the *VHL* gene was confirmed in DNA from a blood sample, and loss of heterozygosity at the *VHL* locus was detected in the lung adenocarcinoma. The *VHL* dysfunction may have a role in the development of multiple lung adenocarcinomas.

(Ann Thorac Surg 2014;98:1467–70)

Von Hippel-Lindau disease (VHL) is an autosomal dominant disorder that is characterized by various benign and malignant tumors in multiple organs. The most frequent examples of tumors associated with VHL disease are hemangioblastoma in the central nervous system, retinal hemangioblastoma, pheochromocytoma in the adrenal glands, renal cell carcinoma, and pancreatic islet cell tumors [1]. Von Hippel-Lindau disease is caused by mutation of the *VHL* tumor suppressor gene, which is located on chromosome 3p25-26 [2]. Numerous reports have indicated that chromosome 3p is frequently detected in lung cancer [3, 4] and several tumor suppressor genes, including *VHL*, are located in this region [5]. Recent advances in high-resolution computed tomography have increased the detection rate of multiple ground glass opacity nodules, which are often diagnosed as atypical adenomatous hyperplasia (AAH) or adenocarcinoma (AD) with a lepidic pattern, and which often have mutation in the epidermal growth factor receptor (*EGFR*) gene [6]. However, the molecular mechanisms that underlie the development of multiple lung nodules are unknown, as is knowledge of their genetic background.

In this report, we describe a case of VHL disease in a patient who had multiple lung ADs. In addition, we examined the significance of alteration in the *VHL* gene in the development of multiple lung nodules.

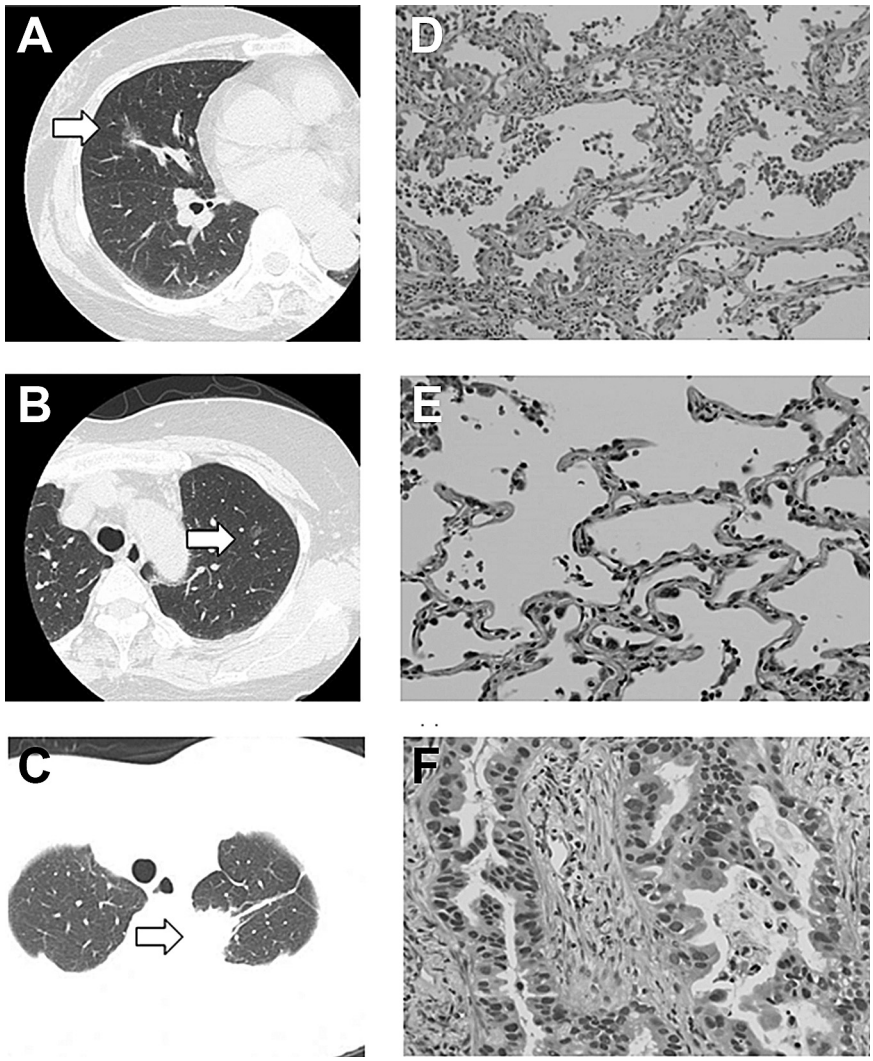

Fig 1. The findings from (A–C) computed tomography scans and from (D, E, hematoxylin-eosin stain, magnification ×100) pathology examination of the resected specimens and (F, hematoxylin-eosin stain, magnification ×400) the needle biopsy specimen are shown. (A, D) Adenocarcinoma (arrow) in the right middle lobe. (B, E) Atypical adenomatous hyperplasia (arrow) in the left upper lobe. (C, F) Adenocarcinoma (arrow) in the left upper lobe.