Pneumonectomy-Sparing NSAID Therapy for Pulmonary Inflammatory Myofibroblastic Tumor

Sofia Ghani, MD, Arpita Desai, MD,† Saraswati Pokharel, MD,‡ Todd Demmy, MD§, and Grace K. Dy, MD**

CASE REPORT

A 50-year-old female previous smoker presented with a chief complaint of hemoptysis. A computed tomography (CT) scan of the chest with and without contrast revealed a lobulated 1.6 cm mass in the left upper lobe bronchus. Fluorodeoxyglucose-positron emission tomography CT imaging showed no other evidence of systemic disease and her Eastern Cooperative Oncology Group performance status was 0. Bronchoscopy with biopsy revealed that the mass consisted of atypical spindle cells. The patient then underwent bronchoscopy for cauterization of the bleeding tumor and thoracoscopic left upper lobe sleeve lobectomy with lymph node dissection. Histopathology of the tumor was consistent with inflammatory myofibroblastic tumor (IMT), measuring 2.5 cm (Fig. 1). Immunohistochemistry was strongly positive for vimentin and focally positive for smooth muscle actin. Cytokeratin AE1/3, S-100, desmin P63, ALK-1, CD34, and BCL-2 were negative. No *ALK* or *ROS1* gene rearrangements were observed. After 3 months, CT angiography with three-dimensional virtual bronchoscopic reconstructions showed no bronchial stricture, intraluminal disease or extraluminal pathology. Repeated surveillance bronchoscopy, performed 7 months postoperatively, revealed a 2 mm nodule located 1 cm distal to the carina (Fig. 2*A*). Pathological analysis confirmed recurrent IMT morphologically identical to the original tumor. Immunohistochemical staining and ALK translocation analysis were not repeated. CT of the chest with and without contrast revealed postsurgical changes in the left lung with some irregularity and lobulation of the left main stem bronchus but without any evidence of local recurrence or metastasis. Treatment options offered to her at another institution were left complete pneumonectomy or local ablative therapy. The latter, however, was concerning for potentially accelerating recurrence from thermal injury.[1] The patient thus agreed to treatment with celecoxib 200 mg twice a day orally. Subsequent bronchoscopy after 2 months showed residual erythema in the area of the previous biopsy without any raised lesion/nodularity (Fig. 2*B*). Repeated bronchoscopy 8 months after initial bronchoscopy showed complete resolution with normal mucosa and no erythema. CT scan of the chest with contrast done at the time revealed no evidence of recurrent disease. Patient discontinued celecoxib 2 months after the second bronchoscopy, completing a 12-month course of treatment.

DISCUSSION

IMT is a rare entity that is composed of myofibroblastic proliferation interposed with inflammatory cell infiltrate that affects multiple organs including the lungs. In approximately 70–80% of cases affecting the lung, it is clinically asymptomatic, whereas in others, it usually presents with cough, hemoptysis, or as a solitary pulmonary nodule.[2] A recent study found that IMTs harbor, in addition to *ALK* rearrangement, other rearrangements in kinase genes, such as *ROS1* and *PDGFR*β.[3] Cyclooxygenase-2 enzyme and vascular endothelial growth factor expression in IMTs contribute to their growth, rationalizing the use of Nonsteroidal anti-inflammatory drugs, which can induce tumor regression through disruption of the vascular endothelial growth factor signaling pathway.[4] Although surgical resection is generally reserved for tumors that are localized, unresectable IMTs have been successfully treated with steroids, NSAIDs and ALK-inhibitors, such as crizotinib,[5] which was not an option in the absence of identifiable *ALK* or *ROS1* gene rearrangements. In our patient, the NSAID celecoxib proved beneficial in the management of local recurrence as an alternate to high-risk surgery, such as pneumonectomy. Case studies on NSAID therapy in IMT's are scarce but have a common inference that NSAID's induce durable remissions and responses persist after ceasing therapy with the longest reported response being 4 years in a patient with pancreatic head IMT. NSAID therapy should be entertained as an alternative for treating unresectable or recurrent IMT. Our patient achieved an excellent response to celecoxib for a locally recurrent IMT, thus avoiding the morbidity of a major surgery. She continues to be clinically asymptomatic 2 months after ceasing celecoxib administration. Surveillance bronchoscopy will be performed within the first 6 months after discontinuation of celecoxib.

*Department of Medicine, Roswell Park Cancer Institute, Buffalo, New York; †Department of Medicine, SUNY Buffalo, Buffalo, New York; ‡Department of Pathology, Roswell Park Cancer Institute, Buffalo, New York; and §Department of Thoracic Surgery, Roswell Park Cancer Institute, Buffalo, New York.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Arpita Desai, MD, Department of Medicine, SUNY, Buffalo, New York 14215. E-mail: arpitade@buffalo.edu

DOI: 10.1097/JTO.0000000000000574

ISSN: 1556-0864/15/1009-0e89

REFERENCES

1. Lee SH, Kim SH, Lee JY, et al. Inflammatory myofibroblastic tumor: A possible complication of percutaneous radiofrequency ablation for hepatocellular carcinoma. *Korean J Radiol* 2009;10:635–640.
2. Cerfolio RJ, Allen MS, Nascimento AG, et al. Inflammatory pseudotumors of the lung. *Ann Thorac Surg* 1999;67:933–936.

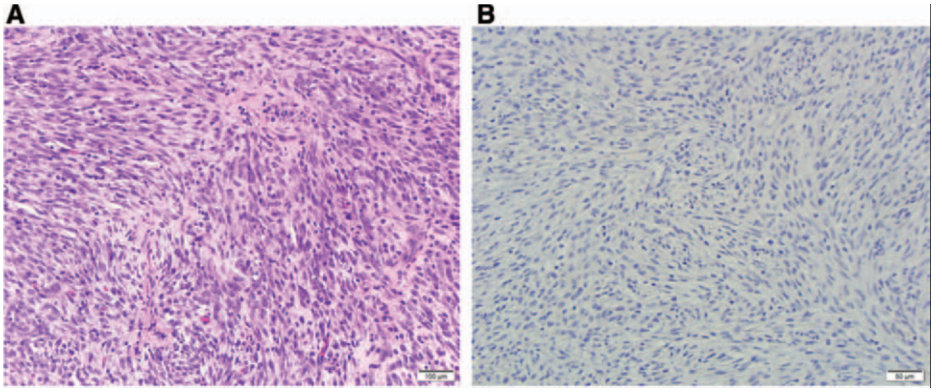

FIGURE 1. *A*, Atypical spindle cells and inflammatory infiltrate (H&E stain); 200× magnification. *B*, Negative ALK immunohistochemical expression.

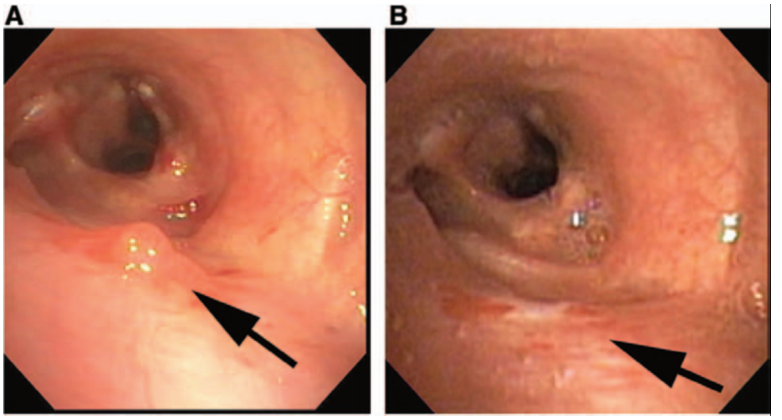

FIGURE 2. *A*, Nodular recurrence (biopsy confirmed) on initial surveillance bronchoscopy. *B*, Residual erythema postcelecoxib treatment with no pathological evidence of recurrence.

3. Lovly CM, Gupta A, Lipson D, et al. Inflammatory myofibroblastic tumors harbor multiple potentially actionable kinase fusions. *Cancer Discov* 2014;4:889–895.
4. Applebaum H, Kieran MW, Cripe TP, et al. The rationale for nonsteroidal anti-inflammatory drug therapy for inflammatory myofibroblastic tumors: A Children's Oncology Group study. *J Pediatr Surg* 2005;40:999–1003; discussion 1003.
5. Butrynski JE, D'Adamo DR, Hornick JL, et al. Crizotinib in ALK-rearranged inflammatory myofibroblastic tumor. *N Engl J Med* 2010;363:1727–1733.