Granulomatous Inflammation Mimics Disease Progression in Patients with Anaplastic Lymphoma Kinase Fusion Positive Non-Small Cell Lung Cancer: A Case Series

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Background

ALK TKIs are the standard of care treatment for patients with advanced ALK fusion positive NSCLC. As with any treatment, rare adverse events may not be observed until long after the clinical trials have ended.

Methods

Here we describe a series of cases from our clinic in which patients with advanced *ALK* fusion positive NSCLC developed granulomatous inflammation while receiving treatment with an ALK TKI.

Results

Patient 1 is a 46-year-old white male who underwent curative-intent treatment with concurrent chemo-radiation therapy for stage IIIA lung adenocarcinoma. *ALK* rearrangement was detected by FISH. He developed metastatic disease and was treated with crizotinib and later alectinib. After more than 11 years on ALK TKIs he was found to have newly FDG-avid cervical, thoracic, and upper abdominal lymph nodes on PET. A biopsy of an FDG-avid right supraclavicular lymph node revealed non-necrotizing granulomatous inflammation without evidence of malignancy. He was started on prednisone. Repeat PET after 6 weeks of this treatment showed decreased FDG avidity in most lymph nodes.

Patient 2 is a 62-year-old white male who underwent upfront resection of a stage IIIA lung adenocarcinoma. At the time of surgery he was found to have pleural metastases, upstaging his disease to IVA. He was started on combination chemo-immunotherapy. The immunotherapy was dropped after 1 cycle when DNA- and RNA-based sequencing on the resection specimen revealed the presence of an *EML4-ALK* fusion. He received another 3 cycles of chemotherapy before his treatment was changed to alectinib. A PET after about 3 months on alectinib showed newly FDG-avid right supraclavicular and mediastinal lymph nodes. An excisional biopsy of an FDG-avid right supraclavicular lymph node did not show any evidence of malignancy but did show necrotizing granulomatous inflammation. He was started on prednisone. Repeat PET after

3 weeks of this treatment showed decreased size and FDG avidity of the mediastinal lymph nodes.

Patient 3 is a 44-year-old white female who underwent upfront surgery for a stage IIIA lung adenocarcinoma. The peri-bronchial surgical margin and 9 of 16 lymph nodes removed were involved with adenocarcinoma. RNA-based sequencing on the initial biopsy specimen revealed the presence of an *EML4-ALK* fusion. She received 4 cycles of adjuvant chemo-immunotherapy. PET done at the conclusion of this therapy showed a recurrent FDG-avid mass at the site of the prior surgical resection. Disease recurrence was suspected and she was started on alectinib. PET after about 2 months on alectinib showed stable size and FDG avidity of the previously seen lung mass. A CT-guided biopsy of the mass did not show any evidence of malignancy but did show non-necrotizing granulomatous inflammation. She developed dyspnea on exertion. Alectinib was held and prednisone was started. Subsequent CT showed decreasing size and eventual resolution of the lung mass. Her symptoms slowly improved and prednisone was tapered over a period of 6 months.

Conclusion

Patients with advanced *ALK* fusion positive NSCLC being treated with ALK TKIs can develop granulomatous inflammation that mimics disease progression on imaging. Prednisone appears to be an effective treatment.