

Stage 1a Non-Small Cell Lung Cancer Detected by Assaying Autoantibodies to Tumor Antigens

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PURPOSE

Lung cancer is the leading cause of cancer deaths worldwide. Early detection is difficult given the lack of an easy, inexpensive screening method and insensitivity and nonspecificity of current imaging methods. We report that testing for autoantibodies (AABs) to tumor antigens can help with early identification of malignant lung nodules.

METHODS

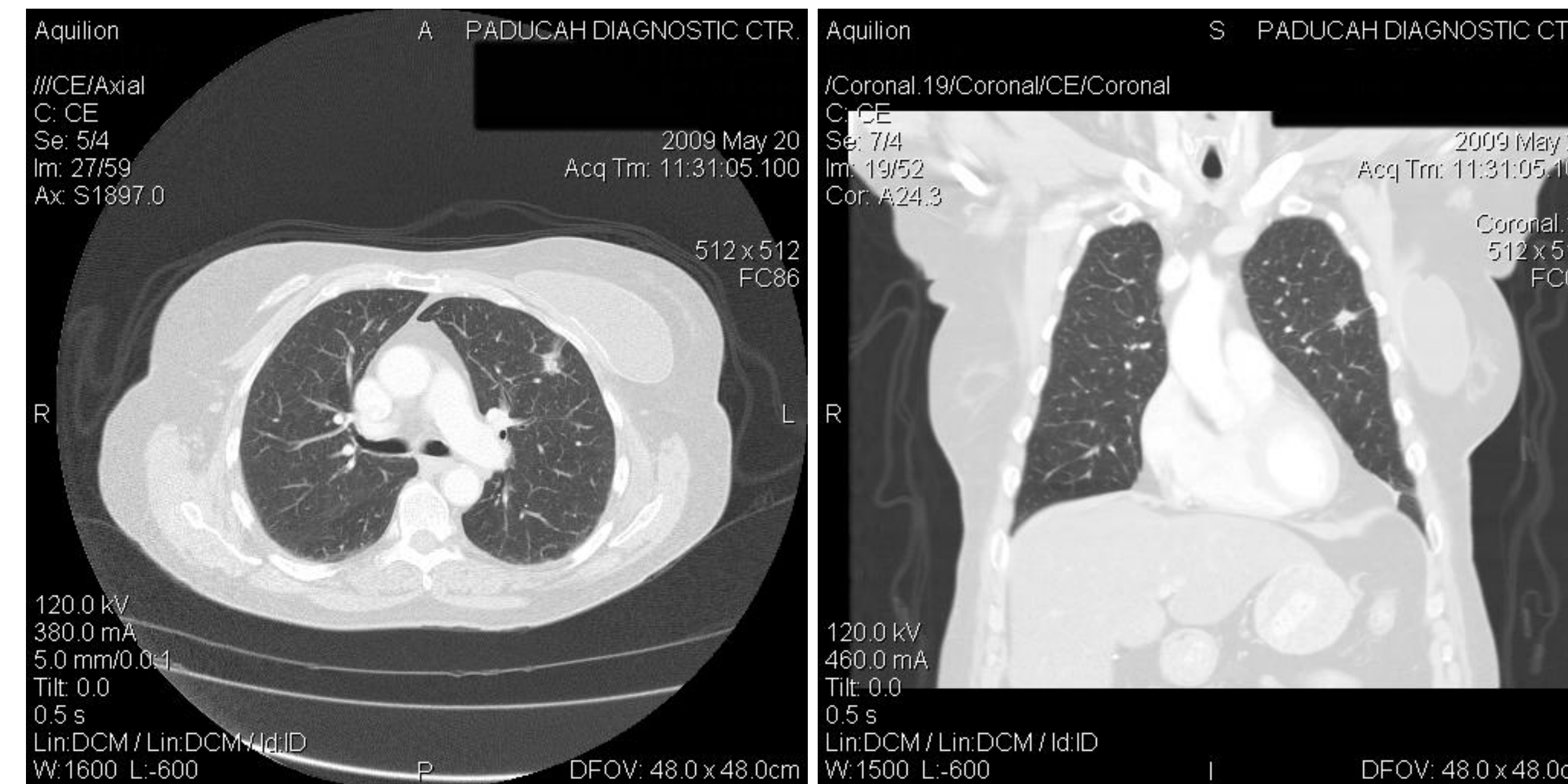
A 69 year old female with a 30 pack-year smoking history presenting with cough, congestion and some pleuritic pain was found to have a spiculated non-calcified, 15 mm nodule in the left upper lobe suspicious for malignancy or an inflammatory process, and she was treated with antibiotics. The patient had an unremarkable physical exam and normal postbronchodilator pulmonary function. Her father died of lung cancer.

Serial followup CT showed stable findings at 3 months, and decreased size from 15x13 mm to 12x11 mm at 6 months.

PET/CT revealed the nodule to have an SUV of 2.2, with no other foci of uptake. Because of the decreasing size and low FDG avidity, conventional guidelines indicated continued imaging follow-up.

Due to our high suspicion for malignancy, we tested serum for the presence of autoantibodies to tumor antigens known to have implications in lung cancer (*EarlyCDT™-Lung*, Oncimmune USA LLC, DeSoto, KS).¹⁻⁵ This assay detects a panel of six AABs (Annexin 1, CAGE, GBU4-5, NY-ESO-1, p53 and SOX2) specific for tumor-associated antigens.

RESULTS



Chest CT showing irregularly bordered, noncalcified nodule in the anterior segment of the left upper lobe measuring 12 x 11 mm, decreased in size from 15 x 13 mm on previous scan. PET showed SUV of 2.2, suggesting inflammatory disease.

Test	Units	Result	Cutoff
Annexin 1 AAb	RU	5.6434	6.89
CAGE AAb	RU	3.4798	4.05
GBU4-5 AAb	RU	4.5256	4.28
NY-ESO-1 AAb	RU	2.0006	3.43
p53 AAb	RU	4.4326	5.42
SOX2 AAb	RU	3.6554	3.71

EarlyCDT-Lung showed an elevated AAb level above cutoff for GBU4-5, indicating the patient is at high risk of having a lung cancer. A left upper lobectomy revealed a 23 mm well-differentiated adenocarcinoma. Margins were clear by >10 mm. Hilar and mediastinal nodes were negative (stage Ia). The patient is currently doing well with no evidence of disease.

DISCUSSION

The presence of autoantibodies to tumor antigens correlates highly with the presence of cancer and can predate the visibility of the tumor on imaging.⁶ While frequently useful in diagnosis, CT is limited by low specificity in small nodules, and PET is limited by low sensitivity in small or less metabolically active nodules. Here we used complementary testing, CT along with the *EarlyCDT-Lung* blood test, which had an impact on medical decision making and taken in conjunction with all the other tests led to earlier resection of an early stage lung cancer.

CONCLUSIONS

A physician must be highly suspicious of malignancy before deciding to biopsy the lung. In this case, the appearance on imaging was not absolutely indicative of cancer, and the *EarlyCDT-Lung* result increased our confidence that the lesion was malignant, leading to resection. *EarlyCDT-Lung* can advance the field by improving on the predictive value of CT and PET, and lead to earlier resection of malignant nodules.

REFERENCES

- Robertson JFR, et al. Autoantibodies in early breast cancer. *J Clin Oncol* 2005; 23(16S):549.
- Chapman C, et al. Autoantibodies in breast cancer: their use as an aid to early diagnosis. *Ann Oncol* 2007; 18:868-873.
- Chapman CJ, et al. Autoantibodies in lung cancer: possibilities for early detection and subsequent cure. *Thorax* 2008; 63:228-233.
- Murray A, et al. Technical validation of an autoantibody test for lung cancer. *Ann Oncol* 2010; 21:1687-1693.
- Boyle P, et al. Clinical validation of an autoantibody test for lung cancer. *Ann Oncol*, Epub July 2010, doi: 10.1093/annonc/mdq361.
- Zhong L, et al. Profiling tumor-associated antibodies for early detection of non-small cell lung cancer. *J Thor Oncol* 2006;1: 513-519.