Ground glass opacity of the lung: The veil that needs lifting

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Disclosures: Abbas is a paid consultant for Boston Scientific, Inc, and Intuitive Surgical, Inc. Neither entity was involved in the preparation of the manuscript.

Received for publication Aug 6, 2017; accepted for publication Aug 28, 2017.

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J Thorac Cardiovasc Surg 2017;154:2100-1

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2017.08.095>

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Central Message

Residual GGOs after resection of lepidic adenocarcinoma may harbor underlying malignancy. If they progress, patients should be offered definitive therapy, with no expected adverse effect on survival.

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A ground glass opacity (GGO) on computed tomography is characterized by increased attenuation but preserved broncho-vascular markings, caused by fluid or cellular material filling the alveoli.^{1,2} Many GGOs are not malignant; however, benign GGOs often disappear within 3 months, whereas persistent ones are usually a manifestation of either preinvasive or invasive adenocarcinoma.³⁻⁵ Pulmonary adenocarcinoma is classified as preinvasive (including atypical adenomatous hyperplasia and adenocarcinoma in situ), minimally invasive adenocarcinoma, and invasive adenocarcinoma.⁶ There is supportive evidence that a step-wise linear progression exists from atypical adenomatous hyperplasia to adenocarcinoma in situ to invasive adenocarcinoma.⁷ It is estimated that GGOs are found in 0.2% to 0.5% of computed tomographic scans.⁸ Some of these GGOs enlarge or increase their solid component, whereas others remain “stable” for years. It is often a subject of debate whether a GGO should be surgically resected or safely watched.

Gao and colleagues⁹ describe a 70-patient retrospective study on the fate of residual GGOs after resection of a node-negative lepidic adenocarcinoma dominant tumor. End points for the study were GGO progression, need for local therapy for a GGO, and overall and disease-free survivals. Univariate analysis was conducted for factors associated with GGO progression and the need for treatment. Multivariate analysis was conducted for factors associated with GGO progression. Overall survival was 92.9%, but disease-free survival was 78.6%. Intervention for a progressing GGO was necessary in 15.7% of patients within a 4.1-year period. Greater dominant tumor size and initial GGO larger than 1 cm were associated with GGO progression. Neither growth of a GGO nor the need for intervention negatively affected overall survival. The article elegantly provides justification for focusing on only the most dominant lesion in patients with synchronous GGOs, rather than assuming metastatic disease.

A few drawbacks do exist. It is difficult to draw strong conclusions from the relatively small number of patients

overall (n = 70) and the small numbers who actually had progression (n = 21) or required treatment (n = 11). Also, the length of follow-up of only 4.1 years may be too short for a study on the natural history of a slowly growing disease. In a study of 122 pure GGOs in 89 patients with a median follow-up of 59 months, the median volume doubling time was 769 days, and 90% of the GGOs did not grow.¹⁰ Furthermore, for a disease that has been linked to genetic mutations especially in epidermal growth factor receptor, the most helpful idea for future studies would be to report on such mutations in the dominant tumor and subsequently biopsied GGOs.

The concern of Gao and colleagues⁹ about possibly overstaging in these cases will be dispelled by the 8th edition of the TNM classification for lung cancer.¹¹ This staging system recognizes that these GGO lepidic adenocarcinomas have distinctly different characteristics, excellent outcomes, and infrequent regional or distant metastasis. These tumors will be designated by the T category of the highest T lesion, the number or “m” in parentheses (#/m), and a collective N and M category. A histologic assessment of each GGO will not be required.¹² This simply means that multifocal GGOs will be considered multiple primaries and not metastatic, regardless of location or laterality.

A GGO has been likened to a veil that covers a portion of the lung. Like a veil, it hides an underlying secret, and this secret may be cancer. Similar studies that include genetic analysis and longer follow-up may shed light on why some of these lesions turn malignant. This will

undoubtedly help us learn when and how to lift this dark veil.

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