

ลักษณะทางรังสีวิทยาของมะเร็งปอดชนิด *Bronchioloalveolar cell carcinoma* ในเขตภาคเหนือ

Radiographic Features of Bronchioloalveolar Carcinoma in Northern Thai people.

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Abstract

Purpose: To find incidence and describe the radiographic features of bronchioloalveolar carcinoma (BAC) in northern Thai people.

Materials and methods: After institutional review board approval, 55 patients who were pathological diagnosed BAC during 7 years (1999 - 2006) were reviewed. Only 30 patients (15 men and 15 female, mean age 58.6 years, range 39 – 77 years) were available for chest radiographs or CT images and included. We retrospectively studied each radiographic presentation and determined percentage of them.

Results: An incidence of BAC was about 8.74% among all primary lung cancers in northern Thai people. We found a solitary pulmonary nodule or mass 36.67%, solitary air-space consolidation (pneumonic pattern) 16.67%, multiple lesions with nodular predominant 30% and multiple lesions with air-consolidation predominant 16.67%. Most solitary lesion located in peripheral lung (90.1%) and had low density on chest radiograph (83.33%). The pleural tail sign was discovered only on CT images. An indolent course of disease and origination of tumor from a scar-like lesion were also seen. Metastasis to the rib, spine, and brain were also seen in this study.

Conclusion: BAC in the north showed various radiographic patterns that the most frequently feature was a solitary lesion, mainly nodule/mass. All multiple lesions showed large consolidation and multiple nodules throughout the lungs. Many previously radiographic characters were observed in this study, especially a low density nodule and peripheral distribution.

Keyword: CT, Chest radiograph, lung cancer, Bronchioalveolar cell carcinoma

Abbreviation: CT = Computed tomography; BAC = Bronchioalveolar cell carcinoma,
BAL = Bronchoalveolar lavage

บทคัดย่อ

วัตถุประสงค์: เพื่อให้ทราบถึงอุบัติการณ์การเกิดมะเร็งปอดชนิด bronchioloalveolar carcinoma (BAC) ในเขต ภาคเหนือและลักษณะทางรังสีวิทยาของโรคนี้

วัสดุและวิธีการ: เมื่อได้รับการอนุมัติจากกรรมการของคณะฯ ให้ทำการศึกษาข้อมูลเริ่มจากปี พ.ศ. 2542 ถึง 2549 (8ปี) รวบรวมผู้ป่วยได้ 55 รายที่ได้รับการวินิจฉัยทางพยาธิวิทยาและคงเหลือเพียง 30 รายที่สามารถศึกษาภาพรังสีได้เป็นผู้ป่วยชาย 15 ราย และหญิง 15 ราย อายุเฉลี่ย 58.6 ปี (ระหว่างช่วงอายุ 39-77 ปี) นำมาศึกษา ลักษณะทางรังสีวิทยาที่พบและร้อยละของลักษณะทางรังสีดังกล่าว

ผลการศึกษา: อุบัติการณ์การเกิดมะเร็งปอดชนิด BAC พบถึงร้อยละ 8.74 ของมะเร็งปอดชนิดปฐมภูมิ ทั้งหมดในเขตภาคเหนือ โดยพบลักษณะของก้อนเดี่ยวในปอดมากที่สุดถึงร้อยละ 36.67 พบ solitary airspace consolidation (pneumonic pattern) ร้อยละ 16.67 ในกลุ่มภาพรังสีทรวงอกที่พบพยาธิสภาพหลายชนิดนั้น กลุ่มที่มีก้อนในปอด เป็นลักษณะเด่นพบร้อยละ 30 ส่วนที่มี air consolidation เป็นลักษณะเด่นพบร้อยละ 16.67 ตำแหน่งที่พบบ่อยใน ปอดส่วนใหญ่อยู่นอก (periphery ร้อยละ 90.1) และมักพบเป็น low density area บนภาพรังสีทรวงอก (ร้อยละ 83.33) ลักษณะ pleural tail sign จะพบจากภาพเอกซเรย์คอมพิวเตอร์ (CT) เท่านั้น การศึกษารังสีนี้พบว่าระยะ เวลาการดำเนินโรคจะช้า โดยมักเริ่มจากการเป็น scar มาก่อน ผู้ป่วยของเราตรวจพบการแพร่กระจายไปยังกระดูก ซีโครง กระดูกสันหลังและสมองด้วย

สรุป: BAC ที่พบในเขตภาคเหนือมีลักษณะทางรังสีได้หลากหลาย ซึ่งส่วนใหญ่จะเห็นเป็นก้อนในปอด ตั้งแต่องค์เดียวหรือหลายก้อน สามารถพบร่วมกับ consolidation ขนาดใหญ่และก้อนจำนวนมากกระจายอยู่ทั่วทั้งปอดได้ ลักษณะสำคัญทางรังสีที่เคยรายงานก่อนหน้านี้พบได้จากการศึกษานี้โดยเฉพาะลักษณะที่สำคัญคือ low density nodule และกระจายตัวทางด้านนอกของเนื้อปอด

Introduction:

Bronchioloalveolar carcinoma (BAC) is a rare subtype of lung adenocarcinoma, comprising less than 4% of all reported lung cancer⁽¹⁾, and characterized by growth of the malignant cells along the alveolar or terminal bronchiolar wall and using the lung framework as stroma (lepidic-growth). It has no invasion into the under stroma, blood vessels, or pleura⁽²⁾. According to the World Health Organization categorization (WHO), BAC has three histologic types which are nonmucinous, mucinous, and mixed nonmucinous and mucinous or indeterminate^(2, 3). The clinical hallmark is bronchorrhea in late presentation of diffuse BAC^(4, 5). Despite the extensively described features of BAC on both plain radiography and computed tomography worldwide, the features of BAC in Thai's population, which commonly present in the late stage of disease, have not yet been reviewed. This prompted us to study the incidence

and radiological features of pathological diagnosed BAC cases in our hospital, which are representative patients of the Northern Thai.

Materials and methods:

After institutional review board approval, 55 patients who were pathological diagnosed BAC during 8 years (1999- 2006) were reviewed. Only 30 patients (15 men and 15 female, mean age 58.6 years, range 39-77 years) were available for chest radiographs or CT images and included. We retrospectively studied each radiographic presentation and determine percentage of them.

Radiological evaluation:

All available radiographs were reviewed by 3 radiologists (KU, JE, SS) to determine the presenting radiographic patterns of BAC. The radiographic

features, mainly base on conventional chest film, were classified as solitary lesion or multiple lesions.

The solitary lesion group consisted of a pulmonary nodule or mass and solitary lung consolidation. A well-defined round or oval opacity in the lung with ≤ 3 cm in diameter was defined as pulmonary nodule ⁽⁶⁾, while size of mass was > 3 cm in diameter. Recorded findings included location (lobe and peripheral or central regions), size, margin, presence of intralesional cavity (focal area of low attenuation within the lesion), pleuropulmonary tail sign (an untapered straight or undulating line extending from a peripheral pulmonary lesion and terminating in a small triangular density at the pleura⁽⁷⁾). The central located lesions were defined as lesions within the medial one third of the hemithorax.

Focal air space consolidation (pneumonic pattern) was defined as homogeneous increased pulmonary attenuation that obscured the broncho-vascular margins with the possibility of an air bronchogram. In this group, we searched for air bronchogram, intralesional cavity, and fissure bulging, as well.

Other associated findings such as adenopathy, pleural effusion, and bony thorax metastasis were also studied. Evidence of distant metastasis from other radiologic investigations and interesting findings from chest CT scans were also recorded.

Results:

An incidence of BAC was about 8.74% among all primary lung cancers in northern Thai people. We found a solitary pulmonary nodule or mass 36.67%, solitary air-space consolidation (pneumonic pattern) 16.67%, multiple lesions with nodular predominant 30%, multiple lesions with air-consolidation predominant 16.67%. Diagram 1 showed distribution of the solitary lesion that were solitary mass-5, solitary nodule - 6 and solitary air-space consolidation (pneumonic pattern) - 5.

Main solitary lesion located in peripheral lung (90.1%) and had low density on chest radiograph (83.33%, Fig 1) and proven by CT as pseudocavity pattern in 2 cases (Fig 1 & 2). All lesions have characteristic irregular or spiculate border (81.8%). Two cases confirmed that this tumor is slow growing, which time to detection lesion is about 36 and 48 months. Air bronchogram is also observed in pneumonic group (Fig 3). The pleural tail sign was discovered only on CT images. CT chest showed incomplete surrounding ground-glass opacity (incomplete CT halo sign) in 66.67%.

The multiple lesions consisted with 9 cases of multiple lung nodules and 5 cases of a large area of air-space consolidation with multiple nodules (Fig 4). All cases of multiple nodules scattered in both lungs and ranged from 0.5 to 2 cm in diameter. In contrast with the solitary group, most nodules had

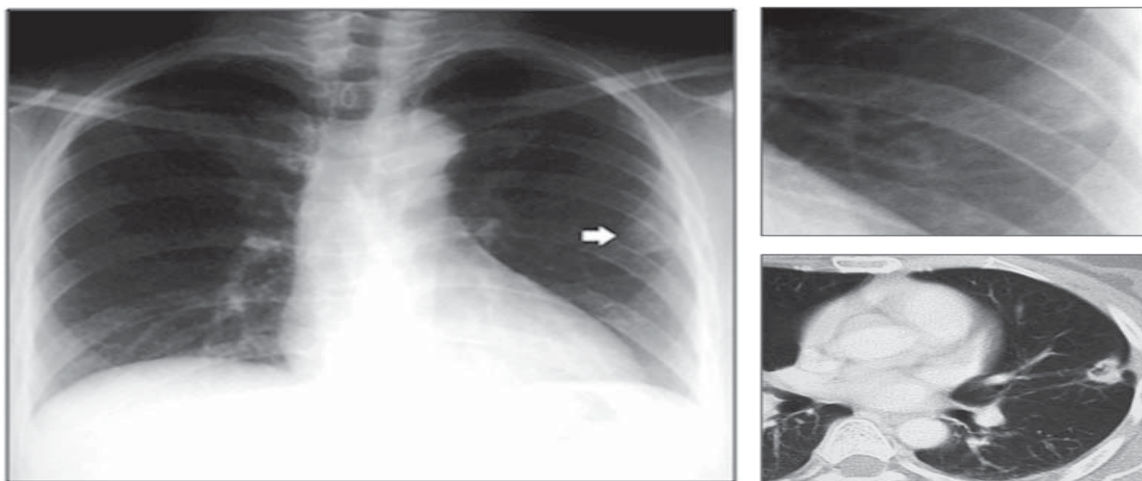


Figure 1 a, b, c: BAC - solitary nodule pattern. Fig 1a, Chest radiograph PA upright of a 42 - year - old woman with no symptom shows a 1.5 - cm low density pulmonary nodule at the periphery of the left mid lung zone (arrow) and closed up lesion on Fig 1b, spot film. Fig 1c, Chest CT reveals a cavity within this nodule. Also note presence of the pleural tail sign.

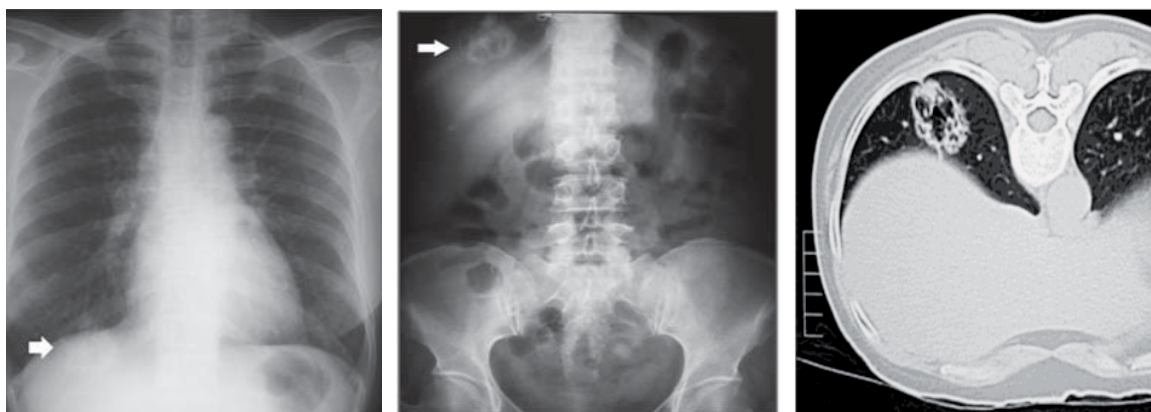


Figure 2 a, b, c: BAC – solitary mass pattern. Fig 2a, Chest film PA upright of a 56 – year – old woman shows an irregular mass with cavities at the right lung base, which is more clearly seen on the plain abdomen (Fig 2b). Chest CT (Fig 2c) demonstrates a cavitary mass with bubble radiolucencies of pseudocavity and presence of pleural tail at its anterior and posterior aspect.

well defined and smooth margin (77.8%). Small intranodular cavity was detected 66.7% (Fig 5). CT chest was available in 3 cases of air-space group that revealed air bronchogram, CT angiogram sign and low attenuation of lung consolidation. A crazy - paving pattern was found in only one case.

An indolent course of disease and origination of tumor from a scar-like lesion were also seen (Fig 6). Adenopathy were seen in all groups, except the solitary pneumonic group, while pleural effusion found in all, except the solitary nodule group. Metastasis to the rib, spine, and brain were also seen in this study in solitary air-space consolidation and multiple lesion groups.

Discussion:

The number of bronchioloalveolar carcinoma (BAC) case diagnosed at Maharaj Nakorn Chiang Mai hospital in the past 8 (1999-2006) years were 55 cases, which represented 8.74% of all primary lung cancers. The incidence of BAC in our study is higher than W.L. Read et al. study, reported less than 4% ⁽¹⁾ and also higher than incidence from the national cancer institute of Thailand during 2003-2005 ⁽⁸⁾. In 2005 the incidence of BAC was very high and about 6.15% of the total bronchogenic carcinoma. The higher incidence of lung cancer in the north than other Thai regions ⁽⁸⁾ and improved diagnosis technology could be influence factors of difference incidence of BAC between our study and others.

BAC is rare subtype of lung adenocarcinoma that malignant cells raised along the alveolar walls and pure lepidic growth without stromal, vascular and pleural invasion and indolent course ⁽²⁾. WHO has classified BAC into three histologic types:- nonmucinous, mucinous, and indeterminate (mixed nonmucinous and mucinous). Atypical adenomatous hyperplasia (AAH) was added in WHO classification as premalignant lesion since 2004 ⁽²⁾. All of these pathological patterns have closely associated to the radiological findings ^(2, 9, 10).

Liked the prior reports ^(4, 5, 10, 11), the solitary nodule / mass was the commonest pattern (53.33%) and followed by the multiple metastatic tumor liked pattern. The multiple lesions with consolidation form had prevalence equal to the solitary consolidation pattern, about 16.67%. In solitary nodule group, most of them were located periphery (90.9%), especially in the RUL. Another interesting finding in this study was that most of the nodular lesions appeared as a low density nodule on chest radiograph (83.3%). It was shown by CT as intratumoral pseudocavities, since nodule still had cystically dilated neoplastic glands or patent of intranodular bronchi and bronchioles ⁽⁹⁾. The pathological change of pure lepidic growth without alveolar wall collapse demonstrated as pure ground-glass opacity on CT image, while if there were some alveolar walls collapsed, it would corresponded to heterogeneous, low attenuation nodules on the images ⁽⁹⁾.

Adenocarcinoma, particularly BAC is well recognized to be one of scar tumors with the possible etiologic relationship with chronic inflammation (4, 12, 13). We also found one case that the tumor originated from a previous scar (Fig 6). There were two cases that the tumor doubling time over two years, confirmed that BAC is slowly growth (4, 5, 11, 14). To our knowledge, no explanation of this phenomenon was yet given.

Pleural tail sign is the result of desmoplastic reaction to the peripherally located tumor, which produces thickened fibrous stands radiating from the tumor out along the interlobar septa to the pleural surface (15). This finding was observed only on CT images, not on the chest radiograph. Be carefully, pleural tail sign is nonspecific and maybe found in various chronic granulomatous pneumonias such as chronic tuberculosis, nocardiosis, and blastomycosis (15).

We categorized a solitary contiguous area of lung consolidation as a solitary lesion, whether it involved more than one lobe. This pattern could be further subtype into localized (involved less than 1 lobe) or diffuse coalescent form ⁽¹¹⁾. Most of consolidative pattern are a mucinous histologic subtype and this radiograph could not be distinguished from infectious pneumonia ⁽¹⁰⁾. However, Aquino et al ⁽¹⁶⁾ had point out that a consolidation when associate with coexisting nodule (by CT scan) or a peripheral distribution of the consolidation should suggest a diagnosis of BAC.

Multiple pulmonary nodules or a combination of both nodules and consolidation were categorized as multiple lesions pattern, this pattern may be called as diffuse pattern ^(5, 10, 11). In our study, these nodules are rather uniform in sized and distribution throughout both lungs, supporting the multicentric origin theory of the disease ⁽⁵⁾. We did not found any finding to differ between multiple nodules from BAC and from extrathoracic pulmonary metastasis.

Many previously described CT scan findings of BAC were also observed in this study such as pleural indentation or pleural tail, ground-glass opacity surrounding the lesion (CT halo sign), pseudocavity, cavity, and air bronchogram in the solitary pattern; low attenuation consolidation, CT angiogram sign, fissure bulging, and air bronchogram in the pneumonic pattern. A crazy-paving pattern is also seen at the periphery of one of our multiple lesions with consolidation form predominate case. We had difference in percentage of each finding when compared with the prior reports ^(9, 17-19). These could be from 1) most of cases were advanced cancer, 2) small number of BAC cases, although we had highest incidence in Thailand and 3) poor database collecting (film loss) and difference of CT technique. As improved technology in picture archiving and communicating system (PACS) and radiologic information system (RIS) to keep images and data, these will help us to continue studying BAC, deeply.



Figure 3 a, b. BAC - pulmonic pattern. Chest film PA upright (Fig 3a) and lateral (Fig 3b) show airspace consolidation at the basal segment of right lower lobe with tubular radiolucencies of air bronchogram (arrow).

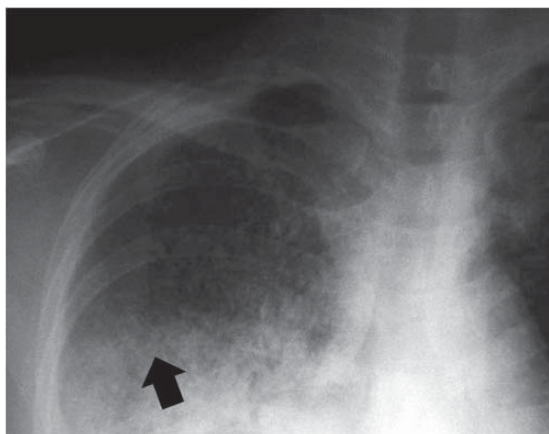


Figure 4: Chest film PA upright of a 45 - year - old woman shows airspace consolidation in the right middle and lower lung fields with multiple tiny nodules in the remaining lungs. Note 7th right posterior rib destruction (arrow).



Figure 5: Chest film PA upright of the 51 - year - old man demonstrates multiple circumscribed nodules in both lungs. Some nodules have small cavities (arrow).

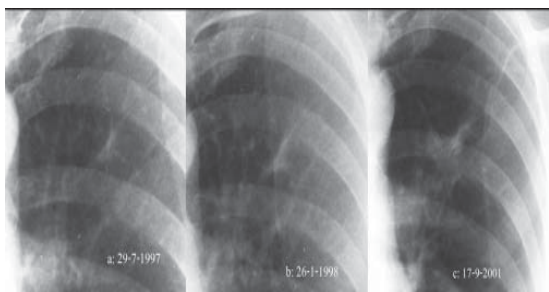


Figure 6 a, b, c: Serial chest radiographs of a 68 - year - old man. Initially, there was a scar - liked opacity in the left upper lobe (Fig 6a). Note gradual enlargement of the lesion to be a spiculated nodule (Fig 6c) within 4 - years, later.

Conclusion:

BAC in our people is not uncommon (8.74% of all primary lung cancer) and had various radiographic presentations that the most frequently pattern was a solitary lesion, mainly nodule/mass. Multiple lesions composed of both consolidation and multiple nodules throughout lungs in different scale. Many previously described typical radiographic findings had been observed in this study. We found that the combined low density nodule with peripheral distribution was characteristic pattern of BAC on chest radiograph.

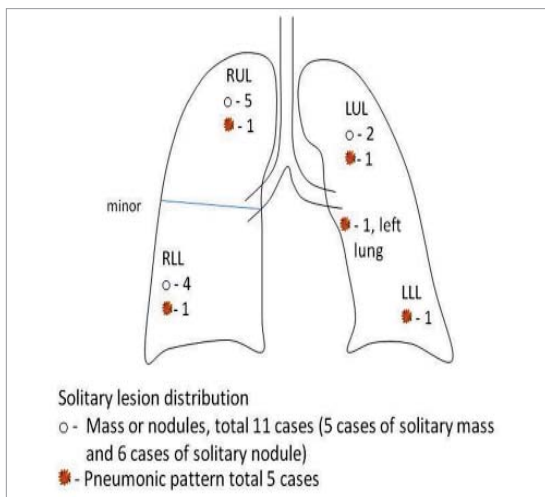


Diagram 1: Location of solitary lesion in each lobe. Solitary lesion distribution:

- - Mass or nodule, total 11 cases (5 cases of solitary mass and 6 cases of solitary nodule).
- - Pneumonic pattern, total 5 cases.

Reference:

1. Read WL, Page NC, Tierney RM, et al. The epidemiology of bronchioloalveolar carcinoma over the past two decades: analysis of the SEER database. Lung Cancer. 2004 Aug;45(2):137-42.
2. Travis WD, Garg K, Franklin WA, et al. Evolving concepts in the pathology and computed tomography imaging of lung adenocarcinoma and bronchioloalveolar carcinoma. J Clin Oncol. 2005 May 10;23(14):3279-87.
3. Histological typing of lung tumours. Tumori. 1981 Aug;67(4):253-72.
4. Epstein DM. Bronchioloalveolar carcinoma. Semin Roentgenol. 1990 Jan;25(1):105-11.
5. Miller WT, Husted J, Freiman D, et al. Bronchioloalveolar carcinoma: two clinical entities with one pathologic diagnosis. AJR Am J Roentgenol. 1978 May;130(5):905-12.
6. Erasmus JJ, Connolly JE, McAdams HP, et al. Solitary pulmonary nodules: Part I. Morphologic evaluation for differentiation of benign and malignant lesions. Radiographics. 2000 Jan-Feb;20(1):43-58.
7. Hill CA. "Tail" signs associated with pulmonary lesions: critical reappraisal. AJR Am J Roentgenol. 1982 Aug;139(2):311-6.
8. National Cancer Institute. Cancer registry. Bangkok : The Institute, 2005.
9. Gaeta M, Barone M, Caruso R, et al. CT-pathologic correlation in nodular bronchioloalveolar carcinoma. J Comput Assist Tomogr. 1994 Mar-Apr;18(2):229-32.
10. Hsu CP, Chen CY, Hsu NY. Bronchioloalveolar carcinoma. J Thorac Cardiovasc Surg. 1995 Aug;110(2):374-81.
11. Hill CA. Bronchioloalveolar carcinoma: a review. Radiology. 1984 Jan;150(1):15-20.
12. Delarue NC, Anderson W, Sanders D, et al. Bronchiolo-alveolar carcinoma. A reappraisal after 24 years. Cancer. 1972 Jan;29(1):90-7.
13. McNamara JJ, Kingsley WB, Paulson DL, et al. Alveolar cell (bronchiolar) carcinoma of the lung. J Thorac Cardiovasc Surg. 1969 May;57(5):648-56.
14. Marcq M, Galy P. Bronchioloalveolar carcinoma. Clinicopathologic relationships, natural history, and prognosis in 29 cases. Am Rev Respir Dis. 1973 Apr;107(4):621-9.
15. Shapiro R, Wilson GL, Yesner R, et al. A useful roentgen sign in the diagnosis of localized bronchioloalveolar carcinoma. Am J Roentgenol Radium Ther Nucl Med. 1972 Mar;114(3):516-24.
16. Aquino SL, Chiles C, Halford P. Distinction of consolidative bronchioloalveolar carcinoma from pneumonia: do CT criteria work? AJR Am J Roentgenol. 1998 Aug;171(2):359-63.
17. Akata S, Fukushima A, Kakizaki D, et al. CT scanning of bronchioloalveolar carcinoma: specific appearances. Lung Cancer. 1995 Jun;12(3):221-30.
18. Im JG, Han MC, Yu EJ, et al. Lobar bronchioloalveolar carcinoma: "angiogram sign" on CT scans. Radiology. 1990 Sep;176(3):749-53.
19. Kuhlman JE, Fishman EK, Kuhajda FP, et al. Solitary bronchioloalveolar carcinoma: CT criteria. Radiology. 1988 May;167(2):379-82.

