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Original Article

Evaluation of clinicopathological characteristics and prognosis of lung ınvasive mucinous adenocarcinomas based on computed tomography (CT) findings

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Abstract

Aim: The aim of our study is to evaluate the cases with invasive mucinous adenocarcinoma (IMA) detected separately from lung adenocarcinoma in the 2015 WHO classification and to associate the clinicopathological findings and evaluate their prognostic significance based on computed tomography (CT) findings.

Materials and Methods: The materials of patients who underwent resection from January 1 2011 to June 31 2019 at our hospital were reviewed after archive screening and those belonging to the Invasive mucinous adenocarcinoma group were determined according to the WHO 2015 classification. Clinical and radiological data of the cases were collected. Tumors were classified as solitary or pneumonic type based on CT findings, and the data obtained were compared statistically.

Results: Based on CT findings (pneumonic and solitary), pathological T stages were significantly different between the two groups. Based on CT findings, pneumonic type-IMA was associated with a more advanced stage ($p<0.001$) and worse prognosis than solitary type-IMA. In addition, while pneumonic type IMA has a higher rate of aerogenous spread (STAS), there was no statistically significant relationship between other clinicopathological findings.

Conclusion: Invasive mucinous tumors can be created with different CT images. Based on CT findings, evaluation of invasive mucinous adenocarcinoma before surgical resection may be useful in predicting prognosis.

Keywords: Computed tomography; invasive mucinous adenocarcinoma; lung cancer; prognosis

INTRODUCTION

Lung cancer is a major cause of cancer-related deaths worldwide. The most common pathological subtype of Non-Small Cell Carcinoma (NSCLC) is adenocarcinoma, the prevalence of which has been increasing. Invasive mucinous adenocarcinoma (IMA), formerly known as mucinous bronchioloalveolar carcinoma (BAC), has taken its place as a separate category in the 2015 WHO classification due to its different clinical, radiological, pathological and genetic features (1-5). IMAs make up approximately 2-10% of lung adenocarcinomas (6).

It has been shown that more aggressive compared to other subtypes of lung adenocarcinomas (7). Although they may have relatively low incidence (accounting for only 2-5% of all lung adenocarcinomas (ADCs)), several previous studies have proved the unique characteristics of IMAs that show significant differences from invasive non-mucinous ADCs in terms of clinical, pathologic, genomic, and prognostic aspects (4,8-11). Histologically, tumor cells contain abundant intracytoplasmic mucin and show goblet and/or columnar cell morphology with small, basal located nuclei (Figure 1). Characteristically, the nuclear atypia is absent or very low (Figure 2). Except for solid growth pattern of IMA, other patterns (acinar, papillary, micropapillary and lepidic) can be seen in heterogeneous associations just like non-mucinous tumors.

IMA also has a different progress pattern, compared with other subtypes of adenocarcinoma. In IMA, lymph node and distant metastasis are much less common than in other subtypes of adenocarcinoma (3,4,12). However, the aerogenous spreading and satellite lesions frequently occur in patients with IMA (8). In addition, a number of studies (1,12-14) have demonstrated that the clinicopathological results of IMA are closely related to computed tomography findings based on CT findings. Therefore, the present study investigated the association between clinicopathological features of primary lung IMA based on CT findings.

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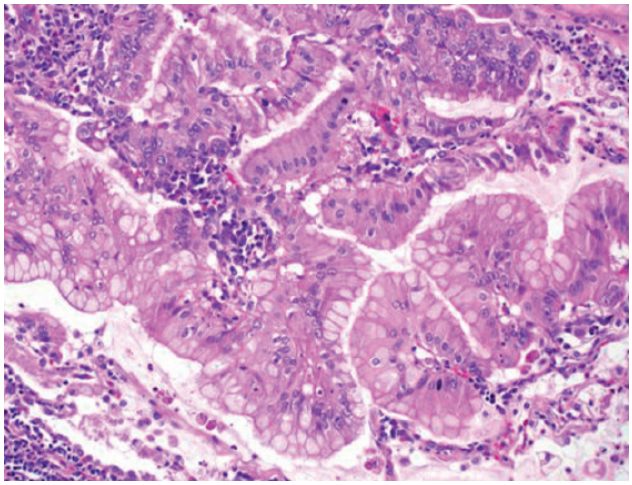

Figure 1. Histological sections showing basale-localized, pale cytoplasmic goblet and columnar cells. (Hematoxylin and eosin stain; original magnification x200)

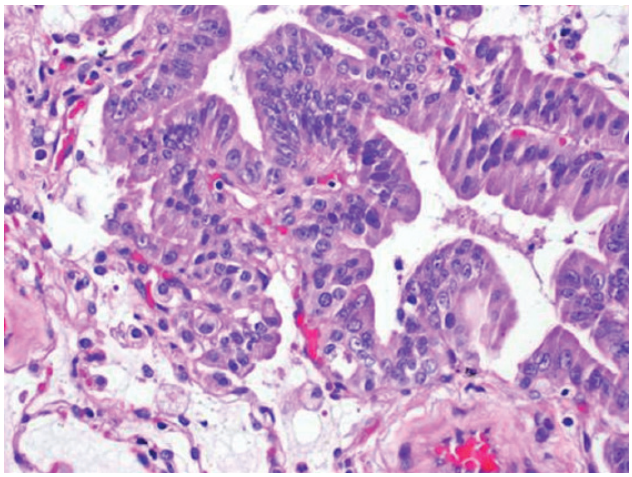

Figure 2. Histological sections showing invasive mucinous carcinoma with very low nuclear atypia (Hematoxylin and eosin stain; original magnification x400)

MATERIALS and METHODS

We reviewed all records of patients undergoing lung resection between January 1 2011 to June 31 2019 at Yedikule Chest Diseases and Thoracic Surgery Hospital and included cases with invasive mucinous adenocarcinoma. We compared the clinicopathological findings of 46 patients included in our study with the preoperative CT findings.

In this study, we evaluated invasive mucinous adenocarcinoma according to the new classification of lung adenocarcinoma by the International Society for Lung Cancer Research (5). Tumor size along the long axis, histologic subtype, lymph node metastasis, lymphatic permeation, vascular invasion, pleural involvement, and aerogenous spread were evaluated. Lymphatic invasion was evaluated as positive when tumor cells were recognized in the lymphatic lumen. Vascular invasion was evaluated as positive when tumor cells were recognized in the lumen of a blood vessel. Pleural involvement was defined as positive when tumor cells extended beyond the elastic layer of the pleura after Elastica van Gieson staining. STAS was evaluated as positive when tumor cells were recognized in the pulmonary alveolus.

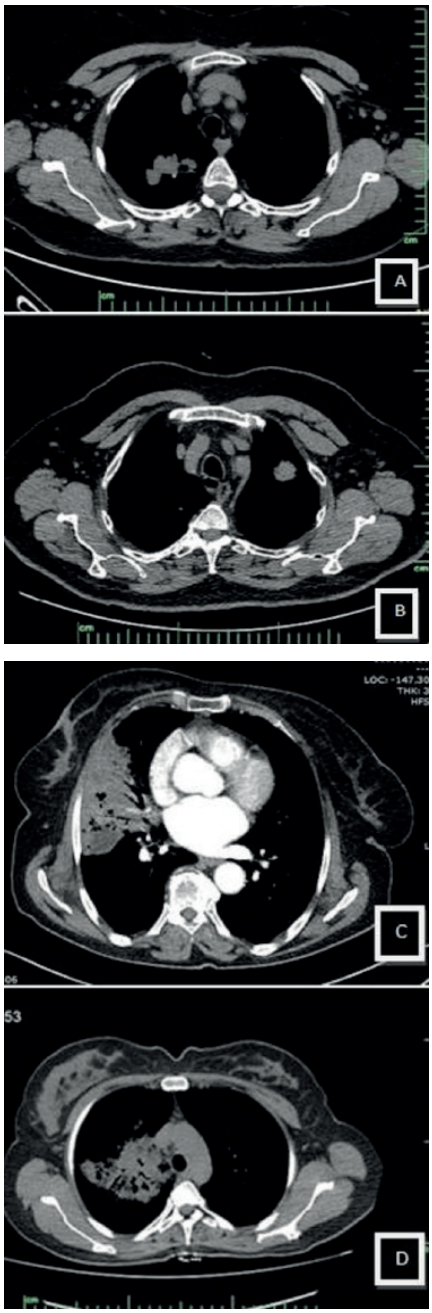

Figure 3. (A, B) Computed tomography findings for solitary-type tumors on lung; (C, D). Computed tomography findings for pneumonic-type tumors on lung

Evaluation of CT Findings

Based on preoperative CT findings, we classified the tumors into two types: (1) solitary type, in which the shadows represented solitary nodules or masses (Figure 3A,B), and pneumonic type (Figure 4A), in which the shadows represented consolidation with or without air bronchogram that occupied extensive areas of the lung lobe. The CT findings of this type of tumor are similar to those of pneumonia (Figure 4B)

According to CT findings, chi-square test was used to analyze the relationship between solid and pneumonic

subtypes and clinicopathological features, p<0.05 value was considered statistically significant. All statistical analyses were performed using SPSS 22.0 (Chicago, IL, USA).

RESULTS

Clinicopathological Characteristics

Forty-six IMAs cases were included in the study. Table 1 shows the clinicopathological characteristics of the patients according to the IMA subtypes based on CT findings. Of these patients, 26 were female (56.5%) and 20 were male (43.5%), and the median age was 60.67 years (ranging from 37 to 80 years old). Tumor diameter in the resection materials were measured between 0.8 cm and 14 cm (average diameter 4.48cm). Pathological tumor stage were determined as pT1 in seventeen cases, pT2 in fourteen cases, pT3 in six cases and pT4 in nine cases. STAS) were detected in 52.1% (24/46) of patients. Lymphatic invasion were observed in 14 cases (30.4%). Pleural invasion were observed in 15 cases (32.6%). Vascular invasion were observed in 6 cases (13.1%). Lymph node metastasis was observed in 9 cases (19.6%).

Based on the CT findings, pathologic T stages significantly differed between the two grups of patients with IMA. The pneumonic type was associated with a higher (pT3+pT4) pathological stage because of its relatively large tumor size (p<0.001). Among the clinical findings, the pneumonic type was associated with a higher proportion of symptoms (p=0.004) and smoking history (p=002).

Table 1. Clinicopathologic characteristics of tumor type based on computed tomography findings

Characteristics	Total n (%)	Pneumonic type (n)	Solid type (n)	P value
Total of patiens	46			
Age	range 37-80	5	12	**0.723**
	median 60.67	10	19	
Gender				**0.334**
Female	26	10	16	
Male	20	5	15	
Diamater				**0.064**
3cm<	18	3	15	
3cm ≥	28	12	16	
Location				**0.923**
Upper/middle	25	8	17	
Lower	21	7	14	
Vasculer invasion				
Yes	6	3	3	**0.330**
No	40	12	28	
Pleural involvement				**0.550**
Yes	15	4	11	
No	31	11	20	
Lymphatic invasion				**0.327**
Yes	14	6	8	
No	32	9	23	
Aerogenous spread (STAS)				***0.001**
Yes	24	13	11	
No	22	2	20	
Pathological stage				***0.001**
pT1-pT2	29	4	25	
pT3-pT4	17	11	6	
Lymph node metastasis				**0.398**
N0	37	11	26	
N1+N2	9	4	5	
Smoking history				***0.002**
Yes	19	11	8	
No	27	4	23	
Symptom				
Yes	36	14	22	**0.085**
No	10	1	9	

*** Chi square test p value**

Moreover, in our series, STAS was seen commonly cases with pneumonic-type, only two patient with pneumonic-type showed negative aerogenous spread (p=0.001).

Among the pathological findings, no statistically significant associations were observed between lymph node metastasis, lymphatic invasion, vascular invasion, diameter or pleural involvement and the CT findings among the subtypes (Table 1). In our institution, lobectomy and systemic lymph node dissection was performed as standard surgical treatment for all cancer patients.

Recurrence was observed in solid type in two cases and pneumonic type in one case. All recurrences detected were intrathoracic metastasis such as lung metastasis, pleural extension and mediastinal lymph node metastasis. No cases of extrathoracic metastasis of IMA occurred in this group.

DISCUSSION

According to the International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) classification system for lung adenocarcinoma published in 2011, the adenocarcinomas formerly classified as mucinous BAC (15). In 2015, the World Health Organization (WHO) also classified IMA as an invasive adenocarcinoma subtype (13).

Some studies have reported a relationship between CT findings and the clinicopathological features of non-mucinous adenocarcinoma. However, there are fewer studies in terms of CT findings in IMAs with a specific adenocarcinoma subtype. Nie et al. (1) in a compared study with a solitary type, pneumonic type was found to be associated with high T stage, N stage, and pathological stage (p<0.001). We designed this study to determine our IMA cases according to the WHO 2015 classification and to compare clinicopathological data of IMA cases with pre-surgical CT (pneumonic and solid type) findings and to determine their prognostic significance.

IMAs, which account for 2%–10% of lung adenocarcinoma cases in the world were considered to be more malignant than other common subtypes of lung adenocarcinoma, such as lepidic and acinar subtypes (15-16). In IMAs, there are generally aerogenous spread, advanced disease, bronchoore and a faster disease course (17). IMAs tend to be multifocal, multi-layered, and bilateral, which may be reflecting increased aerogenous spread. However, lymph node and distant metastasis are much less common than other adenocarcinoma subtypes (12).

In our study, there was no statistically significant difference in terms of lymph node metastasis of our IMA patients. According to CT findings (pneumonic and solid) prognosis was found poorly, especially in pneumonic type patients. Statistically, CT findings showed that pneumonic type cases were associated with higher STAS, advanced pathological stage, and poor prognosis. Previous published reports have shown STAS to be an indicator of poor prognosis.

Although not statistically significant in our study, the rate of lymph node metastasis was found in pneumonic type (36%) more than solid type. In the similarly studies conducted by Watanabe and Nie et al., (8, 1) the rate of increased lymph node metastasis in pneumonic type has been shown to be a poor prognostic factor.

There are some differences in the results of previous studies on the prognosis of IMAs. Yoshizawa et al (17) reported that IMA had a high incidence of recurrence. However, some recent studies have shown that IMA has a favorable prognosis and may not be aggressive. (4,11) This suggests that IMAs can be classified into low to moderate cancer groups, as there are differences in survival rates.

LIMITATIONS

Our study has several limitations first, it was limited inherently by its retrospective design, and we might have had a selection bias. Second, this study was performed in a single institution and follow-up periods were variable. Clinical results were of limited importance because some patients had different postoperative follow-up and treatments. Meanwhile, the sample size of 46 patients is too small to confirm differences between IMA subgroups with different morphological features that do not reflect imaging features. Current findings need to be confirmed by further research with larger examples.

CONCLUSION

In conclusion, we classified the invasive mucinous adenocarcinoma into two subgroups according to CT findings, pneumonic and solid. These findings were useful in predicting prognosis before surgical resection. In addition to the advanced pathological stage, aerogenous spread was also important here. More validation studies are required to improve the preoperative and therapeutic strategies for invasive mucinous adenocarcinoma, formerly called mucinous BAC.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: Ethical approval (Study number:6.12.2019/2084) was obtained from the local ethics committee of the Istanbul Research and Training Hospital.

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