Surgical Oncology 24 (2015) 258–263

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

How should we manage small focal pure ground-glass opacity nodules on high-resolution computed tomography? A single institute experience

Masafumi Yamaguchi [a, *], Akio Furuya [b], Makoto Edagawa [a], Kenichi Taguchi [c], Shinichiro Shimamatsu [a], Gouji Toyokawa [a], Ryo Toyozawa [a], Kaname Nosaki [a], Fumihiko Hirai [a], Takashi Seto [a], Mitsuhiro Takenoyama [a], Yukito Ichinose [a]

[a] Department of Thoracic Oncology, National Kyushu Cancer Center, Japan
[b] Department of Diagnostic Imaging and Nuclear Medicine, National Kyushu Cancer Center, Japan
[c] Department of Pathology, National Kyushu Cancer Center, Japan

ARTICLE INFO

Article history:
Received 8 June 2015
Received in revised form
24 July 2015
Accepted 9 August 2015

Keywords:
Pure ground-glass opacity nodules
Lung adenocarcinoma

ABSTRACT

Background: Although the detection of pure ground-glass opacity (p-GGO) nodules on high-resolution chest computed tomography (HRCT) often implies a diagnosis of lung adenocarcinoma, the management of p-GGO nodules remains under discussion.
Objective: To assess the correlation between the radiological and pathological diagnoses of small p-GGO on HRCT.
Patients and methods: This is a single-institution retrospective study. We analyzed 89 consecutive patients, including 33 patients with resected p-GGO nodule(s) equal or less than 20 mm in maximal diameter on axial images of HRCT.
Results: Thirty-nine patients underwent locoregional treatment (Treatment group), including surgical resection in 33 and stereotactic body radiation therapy in six. The remaining 50 patients were observed (Observation group) using periodic chest HRCT. The median follow-up time was 30.4 (4.9–102.5) months in the Treatment group and 44.8 (0.4–1125.8) months in the Observation group. During the follow-up period, the p-GGO nodules increased in size in eight patients over a median of 20.6 (12.1–50.6) months, with increased attenuation in three patients over a median of 20.6 (12.1–50.6) months, and either decreased in size or disappeared in four patients over a median of 6.9 (2.0–11.2) months. Thirty-three patients with 47 nodules underwent surgical resection, including 41 adenocarcinomas, one neuroendocrine tumor, three cases of atypical adenomatous hyperplasia and two benign lesions. The frequency of invasive adenocarcinoma was higher among the larger p-GGO nodules.
Conclusions: Careful observation and decision making with respect to the timing of intervention in cases of p-GGO nodules are warranted.

1. Introduction

Recent progress and the spread of computed tomography (CT) for use in clinical screening for lung cancer has resulted in a higher rate of detection of small lung nodules, including so-called pure ground-glass opacity (p-GGO) nodules, compared to that achieved with conventional chest radiography [1,2]. Pulmonary p-GGO nodules are defined as lesions showing hazy increased attenuation that does not obliterate the underlying bronchial or vascular structures on high-resolution CT [3]. The incidence of p-GGO nodules has been reported to range from 6% to 12% of all CT-detected pulmonary nodules in the usual screening setting [4,5]. Many clinicians face difficulties in treating patients with these asymptomatic and occasionally detected nodules for the following reasons: 1) the clinical course of p-GGO nodules is generally thought to be indolent [6,7]; 2) obtaining a radiological diagnosis of

* Corresponding author. 3-1-1, Notame, Minami-ku, Fukuoka City 811-1395, Japan.
E-mail address: yamaguchi.m@nk-cc.go.jp (M. Yamaguchi).

http://dx.doi.org/10.1016/j.suronc.2015.08.004
0960-7404/

these lesions is quite difficult, as even fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) often fails to distinguish p-GGO nodules from malignant tumors [8,9]; 3) since p-GGO nodules are generally small in size, it is technically difficult to perform a biopsy via fiberoptic bronchoscopy or computed tomography guidance in most cases, and surgical resection alone often provides the actual diagnosis [10]; 4) the radiological-pathological concordance of p-GGO nodules is non-specific, and many reports suggest the possibility of malignancy, such as adenocarcinoma, non-malignant lesions, such as those of atypical adenomatous hyperplasia (AAH), or other benign diseases [6,7,11–17].

In this context, we herein report our series of patients with p-GGO and discuss the possible timing of clinical intervention.

2. Patients and methods

A total of 2214 consecutive, redundant radiology reports of high-resolution chest computed tomography (HRCT) containing the words “pure ground-glass opacity” filed at National Kyushu Cancer Center between March 2006 and December 2012 were retrospectively reviewed. The term ground-glass opacity (GGO) was defined in this study as “hazy increased attenuation in the lung that does not obliterate the bronchial or vascular margins,” according to the Fleischner Society [18]. The p-GGO lesions included in this analysis were well-circumscribed, spherical and without any areas of consolidation or cavities (Fig. 1). The chest HRCT images were independently reviewed by a board-certified thoracic surgeon (M.Y.) and board-certified radiologist (F.A.) blinded to the patients' background information. Subsequently, two were discussed about the actual selection of p-GGO on HRCT, and finally identified 89 patients with p-GGO lesions equal to or less than 20 mm in maximal diameter on axial images; the medical records of these patients were subsequently reviewed.

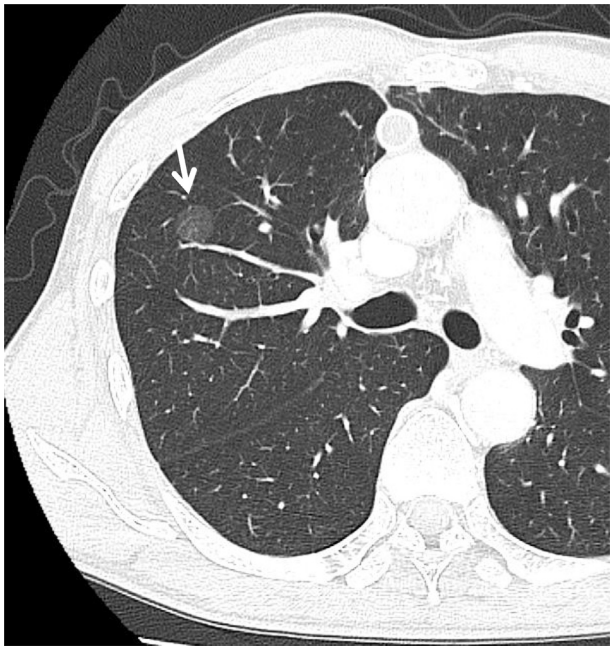

Fig. 1. A high-resolution CT appearance of the representative case of focal pure ground-glass opacity (p-GGO) in this analysis (arrow head). The p-GGO lesions included in this analysis were well-circumscribed, spherical and without any areas of consolidation or cavities.

The institutional review board and ethics committee reviewed and approved the study protocol. Written informed consent was obtained from all patients.

2.1. Image acquisition

The chest HRCT images were acquired using 16-detector (Aquilion16 LB, Toshiba CO., Tokyo, Japan) and 64-detector (Aquilion64 CXL, Toshiba CO., Tokyo, Japan) systems. Unenhanced spiral acquisitions were obtained from the thoracic inlet to the base of the lung, with the images reconstructed at slice reconstruction intervals of 1 and 5 mm. All studies were processed using a window level and width setting for lung parenchyma (level = −650, width = 1500) and the mediastinum (level = 35 HU, width = 450 HU).

2.2. Pathological analysis

The pathological analysis of the tumors was performed based on the 2004 WHO classification of cell types [1]. The classification of histological invasiveness of adenocarcinoma was determined based on the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma [19]. Briefly, adenocarcinoma in situ (AIS), formerly bronchioloalveoral adenocarcinoma (BAC), contains no invasive area with its size equal or less than 3 cm, while minimally invasive adenocarcinoma (MIA) contains equal or less than 5 mm invasive area within the tumor equal or less than 3 cm and invasive adenocarcinoma (IA) has more than 5 mm invasive area within the tumor equal or less than 3 cm.

In cases involving p-GGO with a diagnosis of lung cancer, the 7th edition of the tumor, node, metastasis (TNM) staging system for lung cancer was applied [2].

2.3. Selection of treatment

Since this was a retrospective analysis, the decision of the treatment, i.e., observation or application of local treatment including surgical resection or stereotactic radiotherapy was made by the each attending physician basis, however, basically surgical resection was selected for the nodules such as its size in maximal dimension over 15 mm, tumor location was just adjacent visceral pleura, or its apparent enlargement in size or identification of consolidation within the p-GGO during observation by HRCT. Generally, limited pulmonary resection, i.e. partial lung resection or segmentectomy was planned. Partial resection was applied in patients with p-GGO nodules adjacent to the visceral pleura with a maximal diameter within approximately 10 mm. When the p-GGO nodule was located near a central area, segmentectomy was performed in order to completely remove the lesion. Lobectomy was planned in cases in which 1) the p-GGO nodule was located in a central area and it was difficult to secure an adequate surgical margin or 2) multiple p-GGO nodules were detected in the same lobe. All surgical procedures were performed under video-assisted thoracic surgery.

The regimen of stereotactic body radiation therapy (SBRT) was selected according to the patient's age, physiological condition and wishes.

2.4. Statistical analysis

Comparisons of discrete variables between the two groups were made using the χ^2 test or Fisher's exact test, as appropriate. All statistical analyses were performed using the IBM SPSS Statistics 18 software package (SPSS Japan, an IBM company, Tokyo Japan).