

CASE REPORT

Principles of biopsy in suspected lung cancer: priority still based on invasion in the era of targeted therapy?

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ABSTRACT

There are multiple ways to obtain a biopsy for patients with suspected lung cancer under clinical circumstances. Diagnostic goals described previously in literature should be achieved preferably by using the safest, least invasive, and least costly biopsies. Insight into molecular profile and era of targeted therapy challenged the previous concepts on tumor biopsy. Distinct principles of biopsy should be revisited to adopt the advances in clinical research. A 53-year-old gentleman with 10-year history of dust exposure consulted to our hospital because of bloody sputum. PET/CT scanning revealed a 3.2-centimeter mass with an increased ¹⁸F-FDG uptake in right upper lung lobe, metabolically active lesions in multiple stations of mediastinal or bilateral hilar lymph nodes and an intramuscular nodule in the left gluteus maximus. He underwent transthoracic core needle biopsy of the lung mass, resection of intramuscular nodule, bronchoscopy and right upper lung lobectomy in sequence. The final diagnosis was considered as systemic lipid deposition. Principles of biopsy in suspected lung cancer should be prioritized in sequence based on weight in clinical management, acquisition of tissue, invasion, efficiency and cost.

KEY WORDS

Lung cancer; biopsy; principle; management

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Introduction

Tumor biopsy is an essential part of the diagnostic workup and sound therapeutic decision making in oncology. For patients with suspected lung neoplasms, diagnosis and staging of the tumor are paramount to direct an optimal treatment plan (1,2). There are multiple ways to obtain a biopsy for patients with suspected lung cancer under clinical circumstances. Percutaneous, endoscopic, incisional, and excisional biopsies have different indications, invasion, accuracy, and efficacy (2,3). These sampling techniques should be properly selected or planned in reasonable sequence on a specific case. Principles of biopsy described previously in literature were based on the safety, invasion, and cost (3,4). As the development of individualized treatment in clinical oncology, molecular profile was imperative in lung cancer

patient management. Molecular selection triumphed clinical selection in the era of targeted therapy (5,6). Histological classification, molecular examination, screening for clinical trials, and establishment of tissue bank required more and more tissue (5,7-10). Therefore, principles of biopsy for suspected lung cancer have to be revisited in the era of targeted therapy. We reported a patient with suspected lung cancer undergoing various biopsy techniques.

Case presentation

A 53-year-old gentleman consulted to our hospital because of bloody sputum. He experienced 10-year dust exposure in previous occupation, and was diagnosed with diabetes mellitus five years ago. As a smoker with 80 pack-year cigarette history, he presented blood-streaked sputum one month ago, and the symptom was persistent. Physical examination revealed no significant signs. Laboratory tests including complete blood count, biochemistry profile and tumor markers (CYFRA, SCC, and CEA) were within normal range. PET/CT scanning showed a mass in the anterior segment of right upper lung lobe, with 3.2 centimeters in diameter, and the maximum standard uptake value (SUV) achieved 5.5. Metabolically active lesions were

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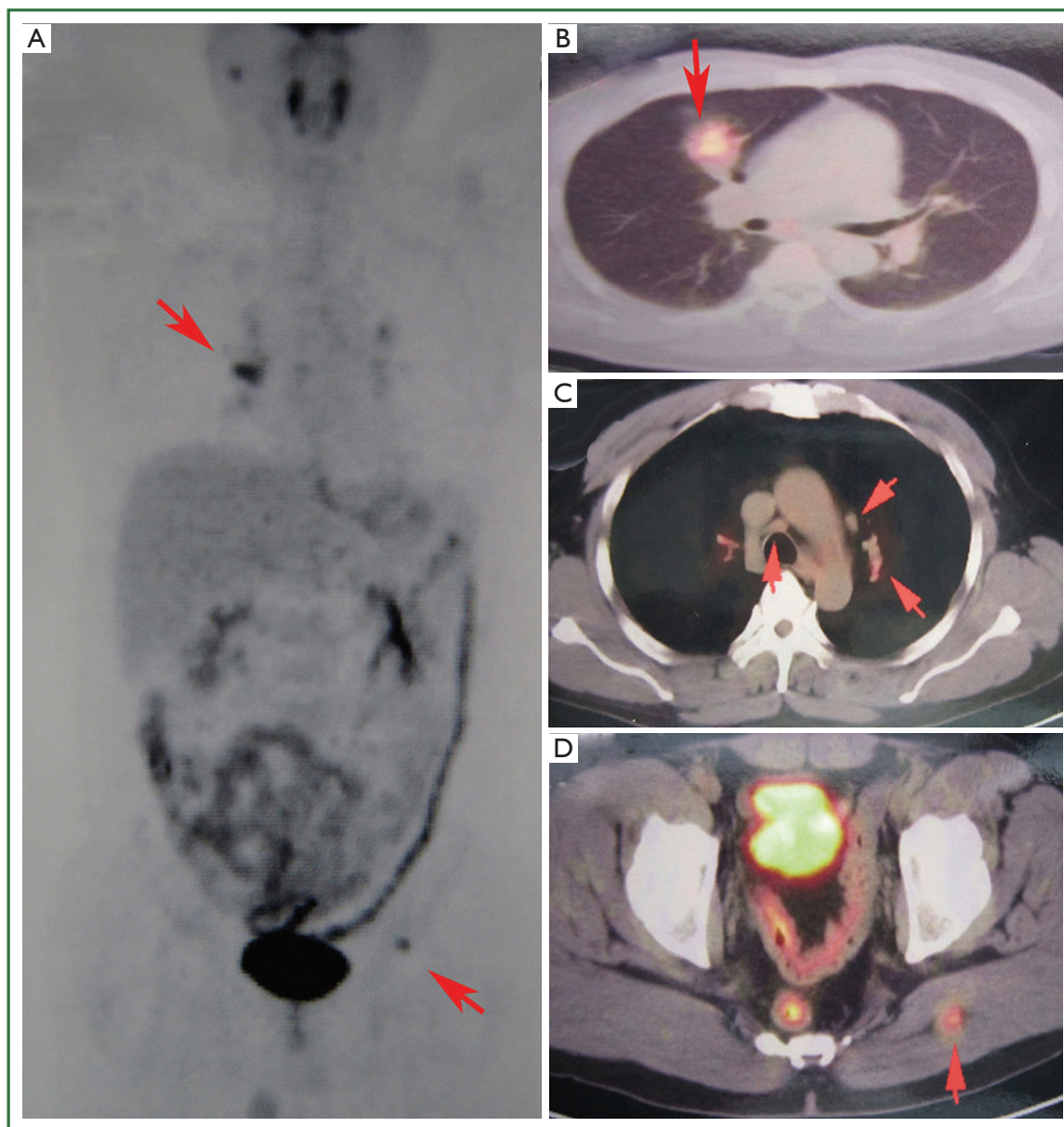


Figure 1. PET/CT scanning. A. overview; B. a lobulated mass with an increased ^{18}F -FDG uptake in the right upper lung lobe; C. mediastinal and hilar lymph nodes; D. intramuscular nodule in the left gluteus maximus. The red arrows refer to suspected lesions.

also detected in multiple stations of mediastinal or bilateral hilar lymph nodes, and an intramuscular nodule in the left gluteus maximus (Figure 1). Due to lung cancer was suspected clinically, he underwent transthoracic core needle biopsy of lung lesion on the date of hospitalization. Blood clot and phagocytic cells were detected in pathological examination (Figure 2A,B). One week later he underwent resection of intramuscular nodule, aggregation of foamy histiocytes and surrounding fibrosis plus calcification was detected pathologically (Figure 2C,D). The following bronchoscopy also revealed non-malignancy (Figure 3A,B). Finally, right upper lung lobectomy was performed after a 3-week stay in hospital. The final diagnosis was considered

as systemic lipid deposition (Figure 3C,D). Clinical data of the patient was from the electronic medical record database of the Guangdong Lung Cancer Institute (GLCI). The study was approved by the Institutional Review Boards of Guangdong General Hospital (GGH). Informed consent was obtained from the patient.

Discussion

The reported case was clinically diagnosed as advanced lung cancer based on imaging data. There were several candidate lesions for biopsy, and various biopsy techniques with different

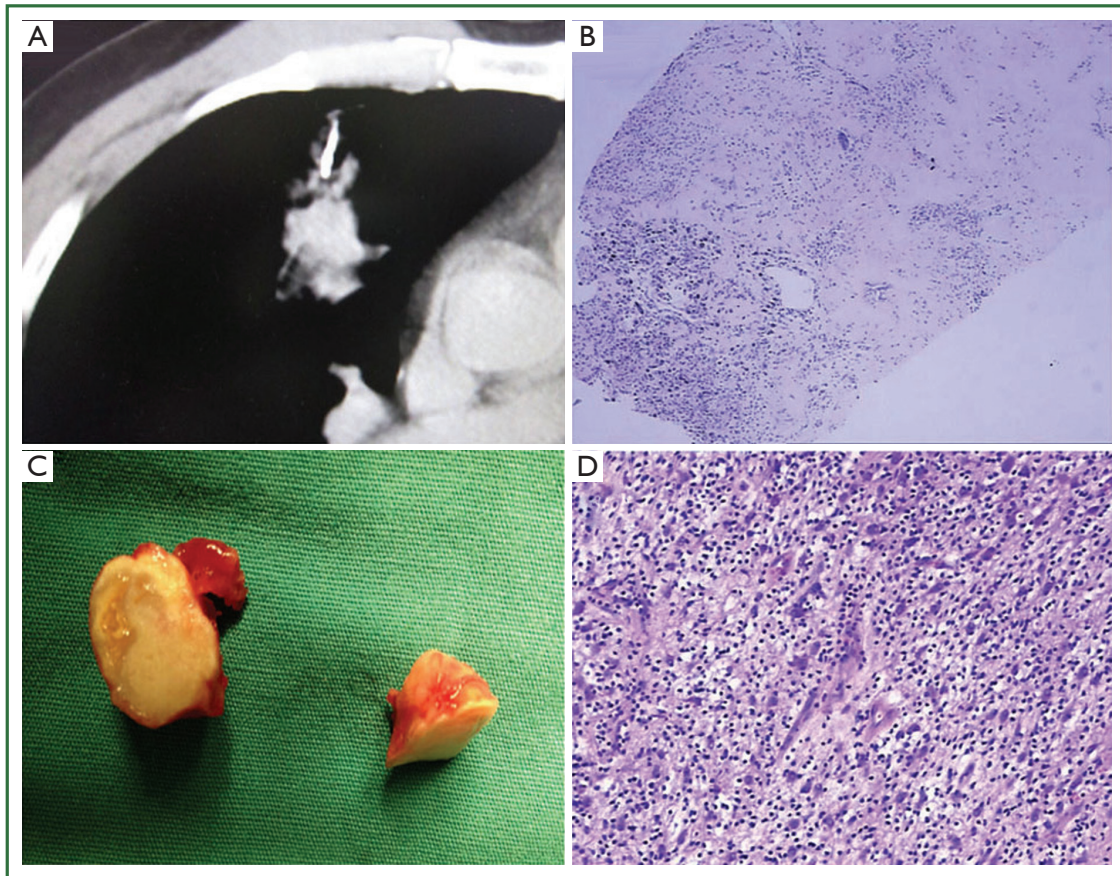


Figure 2. Needle biopsy of lung mass and intramuscular nodule resection. A. CT-guided biopsy with core needle directed to the mass in right upper lung lobe; B. histopathologic photomicrograph of needle biopsy showed blood clot and aggregation of phagocytic cells; C. surgical resection of intramuscular nodule in the left gluteus maximus. HE, $\times 40$; D. histopathologic photomicrograph of intramuscular nodule revealed local aggregation of foamy histiocytes, part of obsolete hemorrhage, and surrounding fibrosis plus calcification. HE, $\times 200$.

performance characteristics may apply. One lesion would be selected as the prioritized target in clinical practice. Scientific arrangement in biopsy selection should refer to available principles. The existing biopsy concepts were established in the age of cyto-toxic chemotherapy, and were based on the safety, invasion, and cost (3,4). As the oncology developed into the era of individualized treatment, tumor biopsy aimed to meet not only evidence of malignancy, but also molecular profiling and translational study. The presented patient initially underwent CT guided transthoracic core needle biopsy on lesion in the right upper lung lobe. It was a minimally invasive procedure for this case (11,12). And the maneuver was efficacious as it was conducted on the date of hospitalization. But core needle biopsy failed to establish a diagnosis on this case, although its safety was observed afterwards. Even the needle biopsy of lung lesion could detect malignancy; the pathological staging of the disease would not achieve. Thus, core needle biopsy on lung mass could not direct the whole management of the patient, and should not be the priority in biopsy sequence. There was a similar story

with bronchoscopy in this patient. Both core needle biopsy and bronchoscopy may face a dilemma in subsequent management in that acquisition of tissue for molecular profiling, or slides for trial screening would not fulfill. For the surgical resection of intramuscular nodule in the gluteus maximus, the procedure determined if the disease was classified as stage IV with solitary distant metastasis. Because the gluteus maximus was not a common metastatic site of lung cancer, confirmation of the intramuscular nodule was pivotal in subsequent management (13-15). Therefore, biopsy of intramuscular nodule held the highest weight in diagnosis and treatment. And, the surgical specimen could fulfill the molecular profiling, meet clinical trials screening or provide additional tissue for tissue bank establishment. With regard to safety and efficacy, the excisional procedure would have to be conducted in operation room; registration for operation may prolong the patient's stay in hospital, but its safety was proved and should be on the top of biopsy options for this patient. Lobectomy in this case was more invasive, more costly and time consuming, when compared

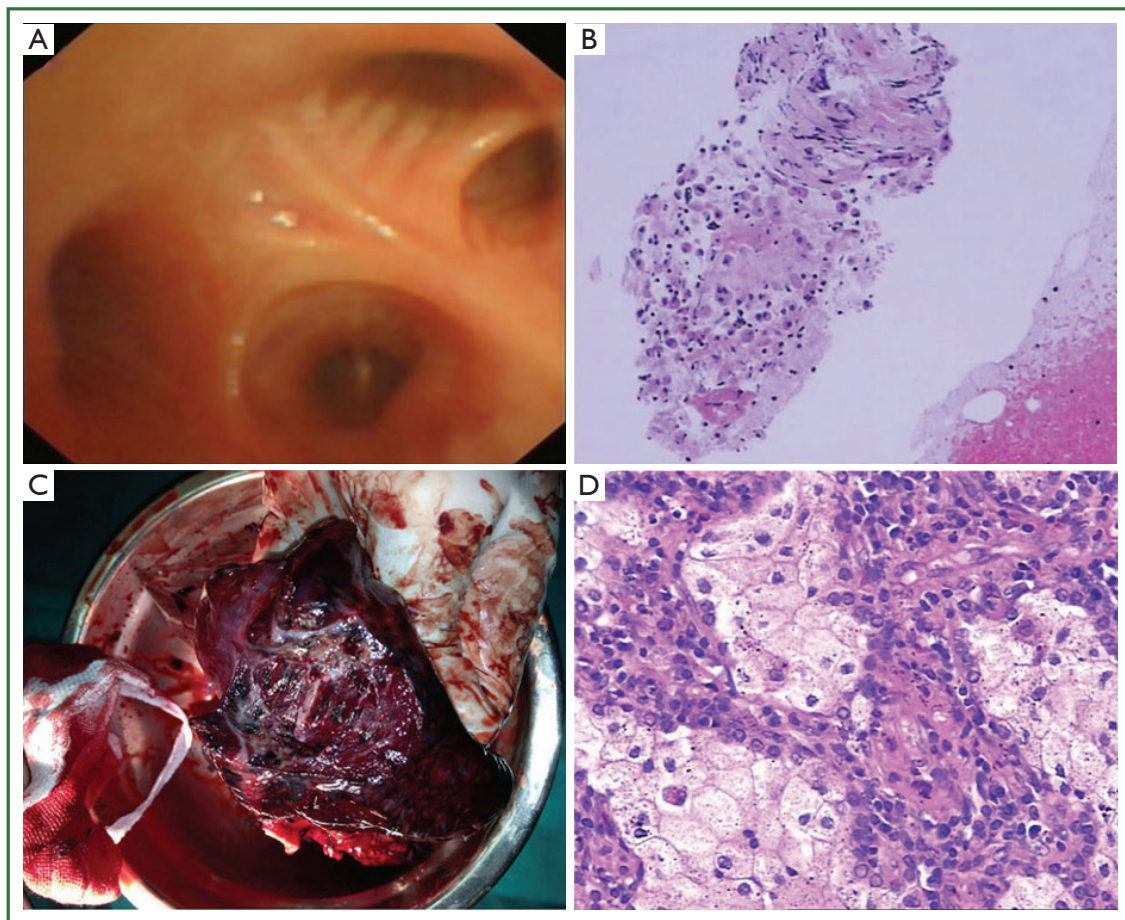


Figure 3. Bronchoscopy and right upper lung lobectomy. A. endoscopic view of right upper bronchus; B. histopathologic photomicrograph of endoscopic biopsy found fibrous tissue and a small amount of tissue cell aggregation, part of cells with hemosiderin and lipid phagocytosis. HE, $\times 200$; C. surgical resection of right upper lung mass; D. histopathologic photomicrograph of resected lung mass demonstrated aggregation of frothy histiocytes in alveolar cavity, inflammatory cell infiltration, and proliferation of fibrous tissue. HE, $\times 200$.

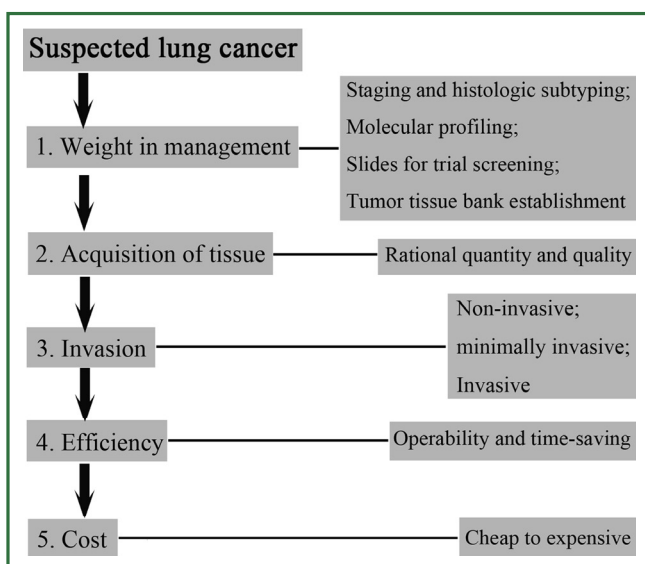


Figure 4. Proposed algorithm in tumor biopsy.

with the aforementioned biopsy techniques, but the procedure produced the largest tissue and determined the final diagnosis.

Based on the above discussion, we could propose principles of biopsy in suspected lung cancer into five items (Figure 4). Item I, weight in whole management. For a patient with suspected malignancy, clinical doctors should plan the framework of following management, evaluate the weight of available biopsic techniques for management, and select a key biopsy site. Item II, acquisition of tissue. The biopsy technique should provide tissue with rational quantity and quality to support the whole management. Item III, invasion. Progress on instruments and techniques provide increased patient comfort, excellent cosmetic results and minimal morbidity (4). Biopsy in surgical way could be prioritized when it became a determinant to clinical management. Item IV, efficiency. An efficacious biopsy could shorten the stay in hospital before reach a sound therapeutic decision. Item V, medical cost. The affordability for specific biopsy technique should be taken into account. Evaluation of

Table 1. Evaluation of various techniques based on biopsy principles.

Technique	I	II	III	IV	V
Needle biopsy in lung lesion	poor	poor	good	good	good
Resection of intramuscular nodule	good	moderate	good	moderate	good
Bronchoscopy	poor	poor	good	good	good
Lobectomy	poor	good	poor	poor	poor

Note: I, weight in whole management; II, acquisition of tissue; III, invasion; IV, efficiency; V, medical cost.

four biopsy techniques performed on the reported patient was summarized in Table 1. Surgical resection of intramuscular nodule should be the prioritized biopsic technique for this patient.

Conclusions

Principles of biopsy in suspected lung cancer should be based on weight in clinical management, acquisition of tissue, invasion, efficiency and cost as priority in sequence.

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