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Spontaneous regression of incidentally diagnosed bronchial squamous cell lung carcinoma after severe bronchitis: A case report

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Abstract

Spontaneous regression of lung cancer is exceptionally rare. But there have been several intriguing cases reported in early and even advanced stages of lung cancer. Although the exact mechanism remains to be elucidated, the inflammation and immunologic response have been suggested as one of the means of spontaneous regression. Chronic inflammation is generally known to induce and aggravate tumorigenesis, but the relationship between cancer and inflammation highly depends on the contexts. Here, we present a case of a 60-year-old male ex-smoker who complained of recurrent hemoptysis, cough, and purulent sputum. The initial chest CT scan revealed diffuse bronchial thickening and an endobronchial mass-like lesion in the left lingular segment. The bronchoscopic and pathological findings also suggested a diagnosis of squamous cell carcinoma with severe mucosal inflammation. He was treated with antibiotics for the bronchitis during the first 1 week and his symptoms markedly improved. After 3 weeks, he underwent a follow-up examination. Chest computed tomography and bronchoscopy revealed the significant improvement of the bronchial narrowing and mucosal edema. Biopsy was performed several times around the lesion where the tissue was initially taken. However, the pathological results showed only chronic inflammation of bronchi, not cancer cells. Fortunately, there was no recurrence of lung cancer in follow-up chest computed tomography or bronchoscopy for almost 5 years. In this case, the incidentally diagnosed bronchial squamous cell carcinoma disappeared after severe inflammatory reaction of the bronchial wall. The clinician should remind the risk of early lung cancer accompanied with bronchitis in high-risk patients of lung cancer and also be aware that although it is very rare, the lesions could spontaneously regress.

Keywords

Spontaneous neoplasm regression, lung neoplasms, inflammation, carcinoma, squamous cell

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Background

The standard definition of spontaneous regression (SR) is the partial or complete disappearance of a malignant tumor in the absence of treatment.[1] Although SR of cancer is extremely rare and the incidence of SR is approximately one in every 60,000 to 100,000 cancer patients, certain clinicians can have a chance to experience this intriguing phenomenon.[2] The mechanism of SR remains to be elucidated, but the inflammation and immunologic reaction have been considered as one of the means of SR.[3,4] Here, we present a case of a patient who had suppurative inflammation and superficial squamous cell carcinoma, which spontaneously regressed in the left lingular segment.

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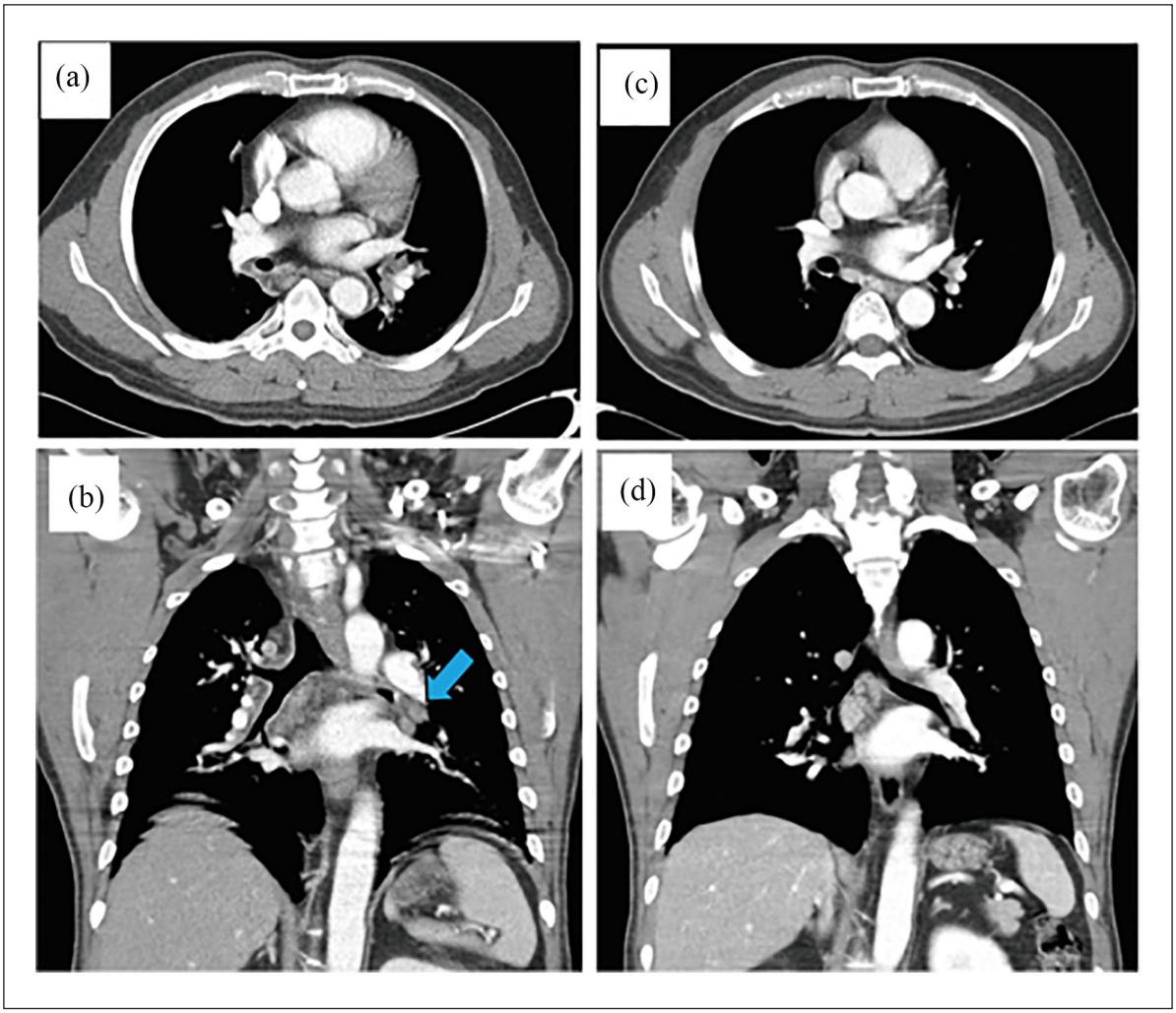

Figure 1. Initial and follow-up chest CT findings: (a) The initial transverse CT scan revealed diffuse bronchial wall thickening and luminal narrowing of the lobar and segmental bronchi. (b) The initial coronal CT scan revealed a 7.7 mm diameter mass-like lesion suggesting endobronchial tumor in a left lingular bronchus (arrow) and enlargement of multiple mediastinal LNs enlargement. (c) On the follow-up transverse CT scan, the bronchial wall thickening had significantly improved. (d) On the follow-up coronal CT scan, previous mass-like lesion and mediastinal LNs significantly decreased.

Case presentation

A 60-year-old male was referred to the hospital due to hemoptysis, cough, and purulent sputum production for 2 weeks. He had suffered from diabetes mellitus for 12 years and was on an oral hypoglycemic agent. He was a 30 pack-year ex-smoker. On initial examination, his heart rate was 90 beats/min; the blood pressure was 120/80 mmHg, the respiratory rate was 22/min, and the body temperature was 37.2°C. Chest computed tomography (CT) revealed diffuse bronchial wall thickening and luminal narrowing in the lobar and segmental bronchi of the left lung, suggestive of endobronchial tumor spread and severe bronchitis. Lymph nodes (LNs) 1L, 7, and 9R were enlarged, suggesting metastasis or reactive changes related to infectious causes such as bronchitis (Figure 1(a) and (b)). Bronchoscopy showed the bronchial narrowing and edematous bronchial mucosa with suppurative inflammation of the lingular segment (Figure 2(a)). Bronchoscopic biopsy was conducted to reveal the infectious pathogens and evaluate malignancy. Five pieces of tissue were taken without significant post-biopsy bleeding. Unexpectedly, the pathology report demonstrated moderate-to-severe suppurative bronchitis and a few atypical cell clusters with nuclear pleomorphism and prominent nucleoli. Thorough pathology review concluded that it was consistent with squamous cell carcinoma (Figure 2(b) and (c)). Immunohistochemistry revealed that the epithelial cells were positive for p63 and CK5/6, and the Ki-67 index was 50% (Figure 2(d)–(f)). Alpha-hemolytic streptococcus was detected in sputum culture. Both acid-fast bacillus (AFB) stain and culture of sputum and bronchial washing were negative. Following pathology review, we finally diagnosed him as an incidental squamous lung carcinoma and severe bronchitis.

After treatment with antibiotics for 7 days, his symptoms significantly improved. Three weeks later, he underwent

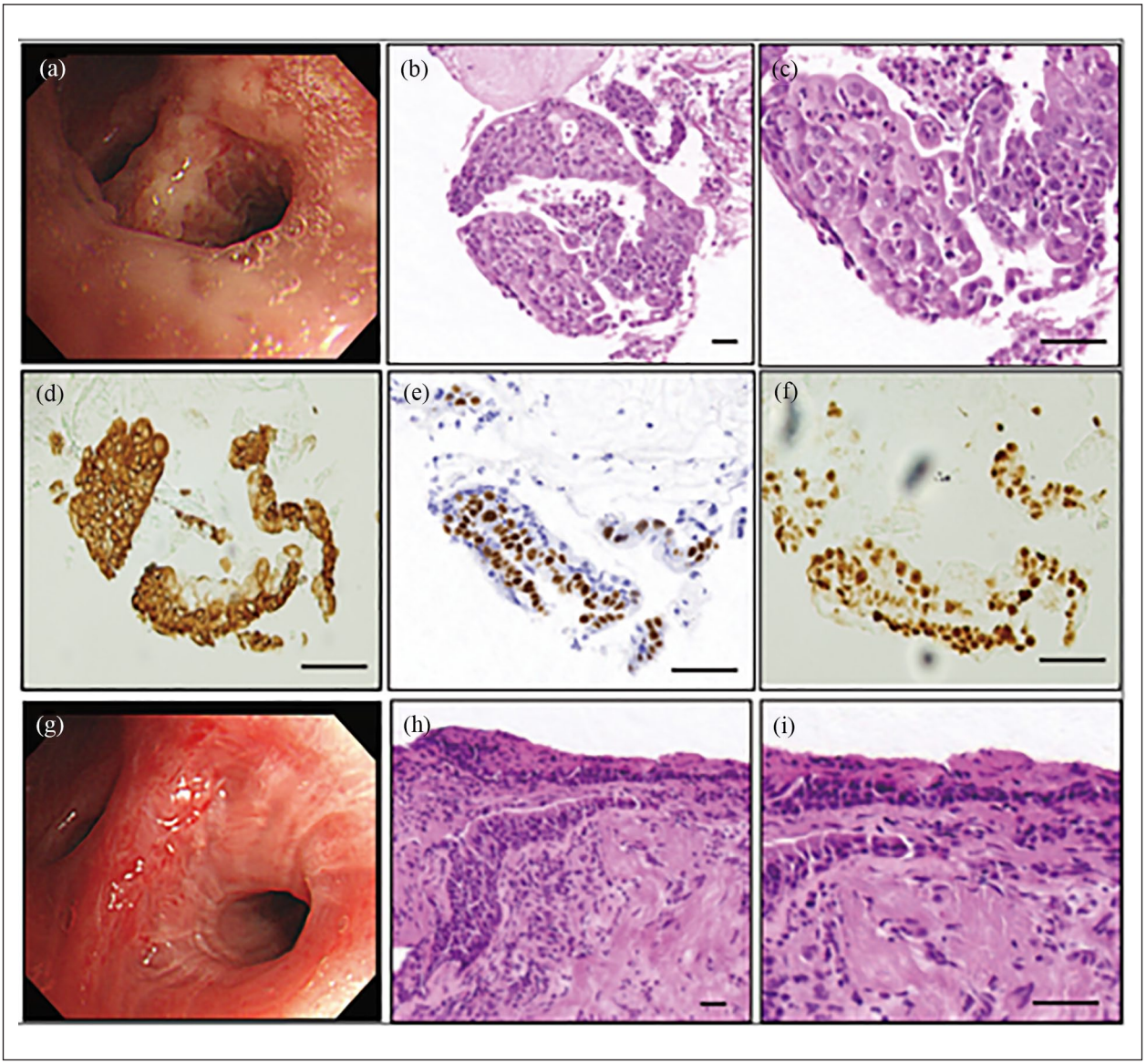

Figure 2. Initial and follow-up bronchoscopic and pathological findings. (a) Initial bronchoscopy revealed bronchial narrowing and edematous bronchial mucosa with suppurative inflammation of the lingular segment. (b and c) Hematoxylin and eosin staining of the initial biopsy reveal moderate-to-severe suppurative bronchitis and a few atypical cell clusters consistent with squamous cell carcinoma. (d) Immunohistochemistry of cytokeratin 5/6 in initial biopsy specimen. (e) Immunohistochemistry of p63 in initial biopsy specimen. (f) Immunohistochemistry of Ki-67 in initial biopsy specimen. (g) Follow-up bronchoscopy revealed less inflammation, and mucosal edema and redness. (h and i) Hematoxylin and eosin staining of the follow-up biopsy show regenerative epithelium and chronic inflammation without malignant cells. Scale bar: 50 μm.

follow-up bronchoscopy to re-evaluate the endobronchial lesions. Fortunately, the mucosal edema with purulent inflammation had markedly improved and only mucosal edema and redness remained (Figure 2(g)). Several times of biopsy were performed around the lesion where the initial tissue was taken. Interestingly, the second pathology report showed only mild chronic inflammation without cancer cells (Figure 2(h) and (i)). Follow-up CT demonstrated a significant improvement of overall bronchial wall thickening (Figure 1(c)) and the decrease in the size of enlarged mediastinal LNs (Figure 1(d)). At the same time, the positron emission tomography (PET) scan showed no evidence of malignancy (Figure 3(a) and (b)). We performed bronchoscopy or chest CT scan regularly for almost 5 years. Last chest CT scan performed at about 5 years after initial diagnosis showed no recurrence of squamous cell cancer (Figure 3(c)). The last bronchoscopic finding was also non-specific and the cytology of bronchoalveolar lavage showed no malignant cell (Figure 3(d)).

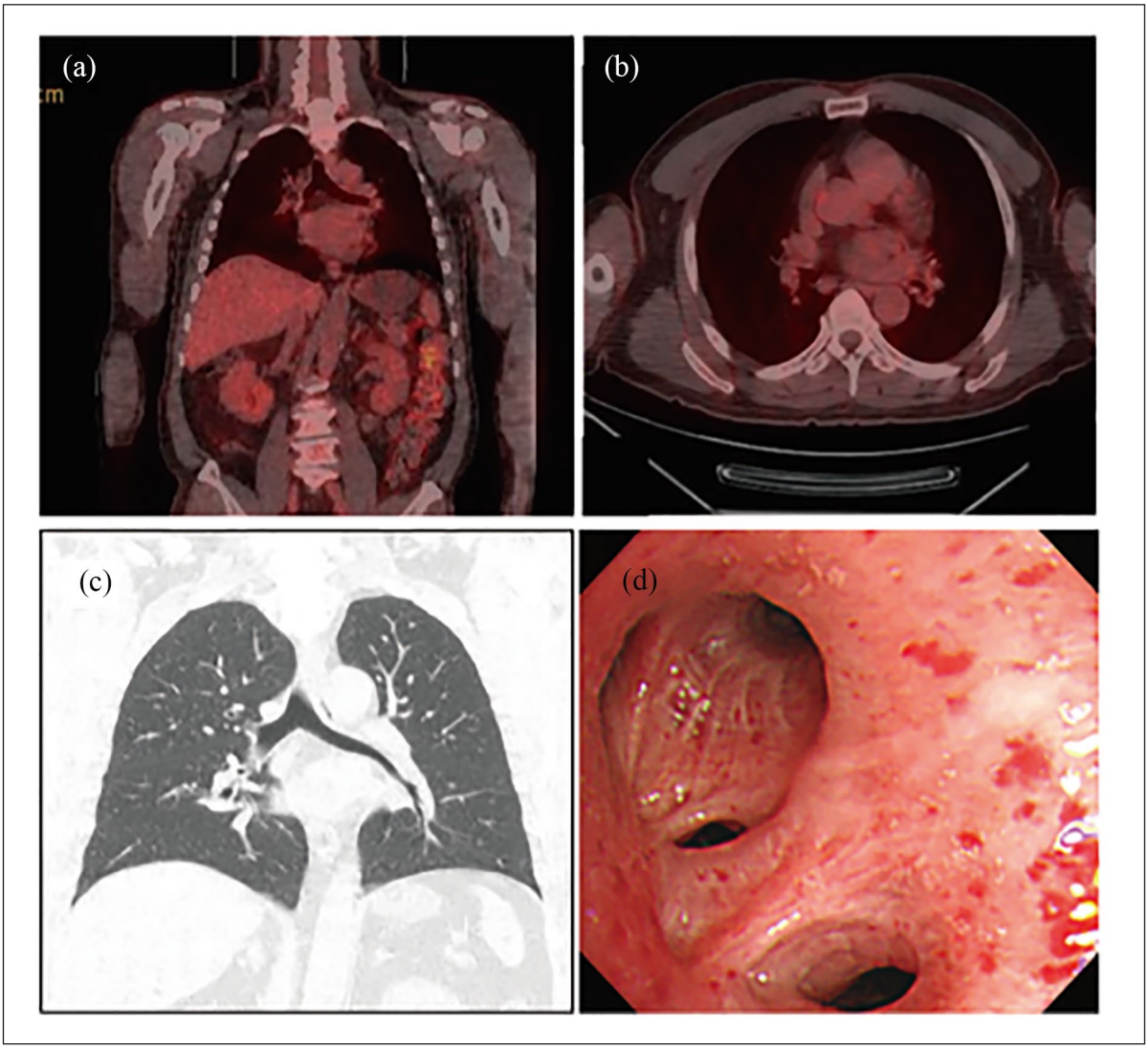

Figure 3. Initial PET-CT scan, last chest CT scan, and bronchoscopic finding. (a and b) Initial PET-CT scan showed no hypermetabolic lesion. (c) Last chest CT scan performed at about 4 years after initial diagnosis showed no recurrence of squamous cell cancer. (d) Last bronchoscopic finding was normal.

Discussion

Natural history of early squamous cancer lesion in the bronchus has been hardly studied because it usually does not cause any symptom and it can only be diagnosed by bronchoscopic biopsy.[5] Most of superficial endobronchial squamous cancer lesions are detected incidentally by bronchoscopic investigation for other respiratory diseases such as pneumonia, bronchitis, and other lung mass in smokers. While bronchial dysplasia can be normalized without further progression to lung cancer,[6] SR of cancer is extremely rare and there are less than 30 cases of SR of pathologically confirmed lung cancer.[2,3] There are several possible mechanisms of SR such as apoptosis, differentiation, hormonal effect, and inhibition of telomerase or angiogenesis.[7,8] In addition, immunoglobulin, inflammation, and immune responses are main feasible factors.[7,8] But the precise mechanism of SR is still controversial and remains to be revealed.[3,7,8]

Lung cancer can co-exist with many inflammatory diseases such as pneumonia, bronchitis, and chronic obstructive pulmonary disease, especially in smokers.[9,10] These pulmonary diseases involve acute or chronic inflammation of the lung parenchyma or interstitium.[11] Most lung cancer patients experience some episodes of pneumonia and bronchitis during cancer treatment. In general, chronic inflammation is known to induce and aggravate tumorigenesis.[12,13] However, the effects of inflammation and immune response on lung cancer remain on the debate and they might vary greatly depending on the context.[14] The chronic inflammation following exposure to carcinogens such as asbestos and beryllium is a risk factor of lung cancer.[15] However, the immunologic response of cytotoxic CD8+ T cells stimulated by immune checkpoint inhibitors can kill the cancer cells.[16,17]

In this case, the findings of the initial CT, bronchoscopy, and pathology strongly suggested squamous cell lung cancer.

However, follow-up examinations performed after the treatment for severe bronchitis showed no evidence of malignancy. Since there might be considerable inter-observer variability between pathologists in the assessment of the pre-invasive lesions,[5] the possibility that the initial lesion was severe dysplasia or squamous cell metaplasia accompanied by inflammation of bronchial epithelial cell cannot be completely excluded. However, after the pathology review of this case, it was concluded that the initial lesion was early squamous cell carcinoma without stromal invasion.

Healing process of epithelial wound contains mucosal denudation, epithelial restitution, and the recruitment of immune cells.[18] Severe bronchitis may also cause epithelial denudation and immunologic reactions in the bronchial mucosa.[19] In the process, the damaged mucosa and adjacent early cancerous lesions can be removed and replaced with new epithelium.

There are a few case reports with the remission of stage I squamous lung cancer located in the lung parenchyma.[20,21] In this case, we presented a patient with SR of early bronchial squamous cell carcinoma after severe bronchitis for the first time.

Conclusion

In certain cases of early squamous lung cancer, careful pathology reviews and longitudinal examinations may be required for exact diagnosis and proper treatment. Furthermore, clinicians should consider the risk of early lung cancer accompanied with bronchitis in high-risk patients of lung cancer and also think of the possibility that the lesions could spontaneously regress.

Author contributions

C.C. contributed to conceptualization, supervision, and writing. C.-S.L. contributed to pathological diagnosis and slide review. G.Y. and Y.K. contributed to reviewing and editing. All authors approved the submitted version and agreed to be personally accountable for the authors' own contributions.

Availability of data and materials

All data generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case was obtained from Clinical Research Ethics Committee of Chungnam National University Hospital. Institutional review board (IRB) file number is 2015-07-001-002.

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Informed consent

Written informed consent was obtained from the patient for publication of this report and any accompanying images.

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