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Case Report

A CASE OF "MICROINVASIVE CARCINOMA OF THE BRONCHUS"

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Summary

Deciding on a treatment approach for early stage lung cancer (0-1) is sometimes difficult because of uncertainties regarding the depth of tumour invasion and its margins. Even with advanced technology, such as endobronchial ultrasound and autofluorescence bronchoscopy, it is often difficult to be precise. In this currently discussed case, treatment of a 61-year-old female patient with early stage IA lung cancer could not proceed for such reasons. Fortunately, timely surgical intervention allowed preservation of lung function and the patient is now under close surveillance.
Key words: autofluorescence bronchoscopy, lung cancer, surgery

Introduction

Lung cancer is among the leading causes of cancer-related deaths – its five-year survival rate is lower than 10% [1]. Most diagnosed cases are in advanced stages and palliative chemotherapy is the only feasible treatment [2]. A fundamental tool in diagnostic endobronchial procedures for lung cancer is bronchoscopy. New technologies like autofluorescence bronchoscopy have been introduced in clinical practice to improve the visibility of premalignant and malignant lesions. The most important applications of this innovation are in diagnosing severe dysplasia, carcinoma in situ (CIS), and microinvasive carcinoma (MIC). When investigating conditions like these, the professional competency of bronchoscopists and pathologists is essential. Such conditions, combined with the overall result of these diagnostic techniques determine the treatment approach: either surgery, endobronchial treatment or follow up only. In the following report, we present a case of MIC of the bronchus with challenging diagnostic and therapeutic difficulties.

Case presentation

The presented patient is a 61-year-old woman, who suffers from chronic obstructive pulmonary disease (COPD). Her occupation is in the clothing manufacturing industry. When first presented, she was on dual bronchodilator inhaled therapy at home and was a smoker at the time, with a consumption of half a pack

per day for over 30 years. She had undergone an oophorectomy in the past due to a cyst and was also on additional therapy with simvastatin 10 mg once per day and aspirin protect 100 mg once per day.

During a regular visit to her pulmonologist she complained of cough and bloody spots in the sputum. Physical examination revealed prolonged expiration and single wheezing sounds. Functional tests showed the following data: oxygen saturation (SatO2) 95%; heart rate 70 bpm; blood pressure 100/70 mm Hg; forced expiratory volume for 1 second (FEV1) – 1.4 l, 70% of predicted value. No suspicious changes were seen on postero-anterior (PA) chest X-ray (Figure 1).

Figure 1. PA chest roentgenography. Pulmonary emphysema

The patient refused bronchoscopy at first but agreed one month later. Meanwhile, a computed tomography (CT) scan of the chest was performed (Figure 2).

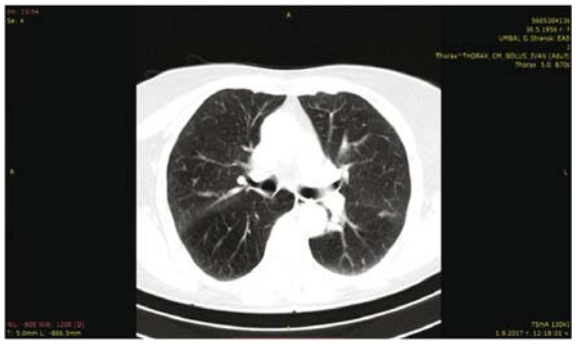

Figure 2. Chest CT scan. Pulmonary emphysema

The CT scan was negative, with only pulmonary emphysema observed. During bronchoscopy, we used two modes of investigation: white light and autofluorescence mode. The former was a standard bronchoscopy, while the latter showed normal epithelium in green and abnormal in magenta. The initial section of the bronchus for the 6th left lung segment was infiltrated and fluorescence positive (Figure 3).

The biopsies revealed high grade dysplasia and CIS (Figure 4).

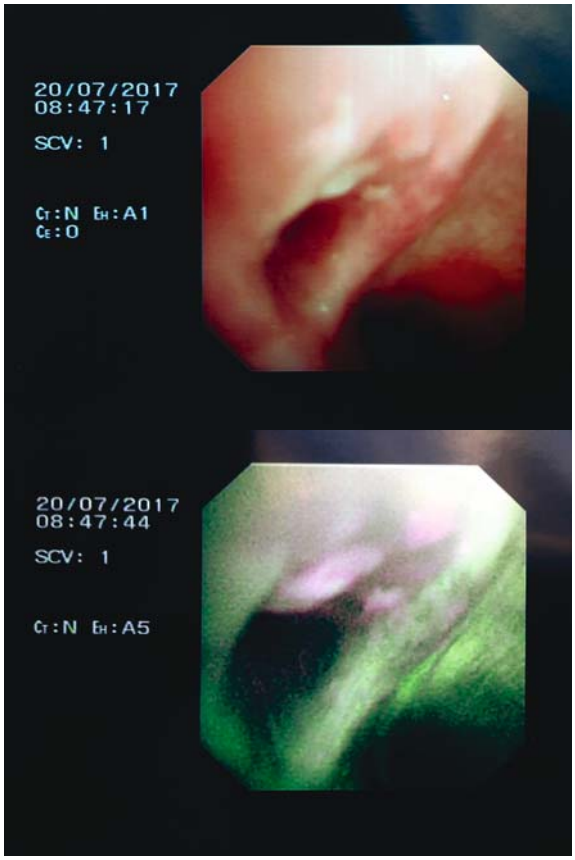

Figure 3. White light and autofluorescence bronchoscopy. Infiltration of the bronchus for VI segment on the left

Immunohistochemistry was p63 (+ve) and thyroid transcription factor 1 (TTF1) (-ve). Bronchoscopy was repeated and the biopsies were consistent with the above results. Discussion about treatment options included an endobronchial approach – electrosurgery, which would preserve lung function. Ultimately, conventional surgery was favoured and low lobectomy was performed. The histology of the removed lobe demonstrated squamous lung cancer with keratinisation, infiltration of the resection line and no metastasis in the regional lymph nodes. It was defined as stage IA.

Six months after the procedure, the patient was found to be in good condition with the following test results: SatO2 97%; heart rate – 71/ bpm; FEV1 – 1.21 l; 60% of predicted value. PA chest X-ray is shown on figure 5.

The only treatment prescribed was a double inhaled bronchodilator. Follow-up bronchoscopy revealed no abnormal changes.

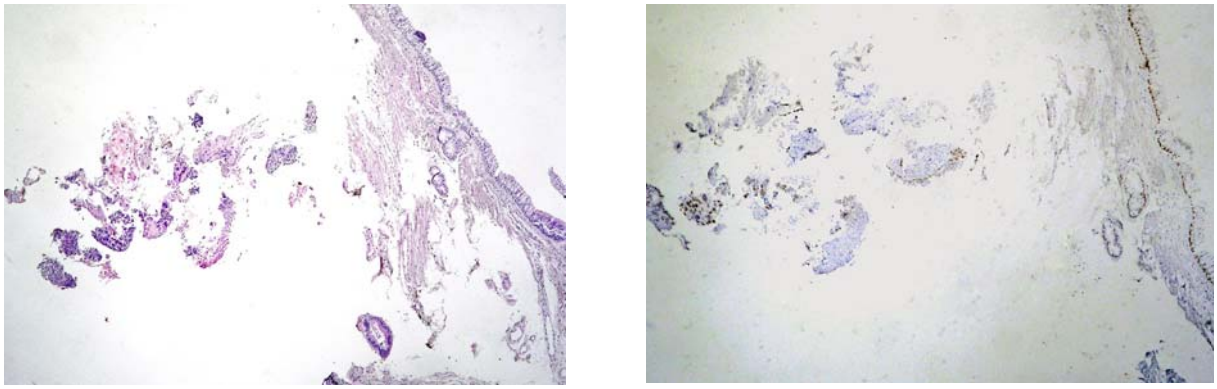

Figure 4. HE 40X. Endobronchial biopsy
*High grade dysplasia was evident in some tissue fragments HE, 40x. Nuclear positivity for p63 was evident in the dysplastic epithelium. IHC p63, 40x

Figute 5. PA chest roentgenography after the surgery. Left low lobectomy

Discussion

Based solely on the findings from endoscopy, the discussed lesion can be qualified as early-stage lung cancer.

The early stage non-small cell lung cancer (NSCLC) is defined as CIS – Tis N0 M0, stage 0 according to the International Association for Study of Lung Cancer (IASLC) staging system, or MIC. CIS includes the presence of signs of cellular atypia observed in the full thickness of the mucosa but not penetrating through the basement membrane. MIC features a few millimetres of bronchial invasion but none involving muscles and cartilages.

The timescale for progression from CIS to invasive carcinoma is considered to be 2 to 10 years. It is uncertain if all cases of CIS eventually progress to invasive carcinomas [3, 4].

Discussion on possible treatment options emphasised on endobronchial treatment like electrocoagulation to preserve lung function and the availability of a facility to carry out this procedure. Such treatment is only applicable when the lesion is less than 1 cm in length and the distant margin is visible [5, 6]. Autofluorescent bronchoscopy (AFB) findings suggested that the margins were evident (Figure 4). It is difficult, however, to be sure about the degree to which the bronchus was affected, even with a positron emission tomography (PET) scan and endobronchial ultrasound techniques [7].

Even at an early stage such tumours cause relatively high mortality rates. Some authors demonstrate a 5-year survival rate of 41% [8]. Daniels et al. (2013) consider 5-year survival to be about 50-60% even for stage I and II of lung cancer. These are high mortality rates, but they are caused by new cancers or metastatic diseases. In contrast, the prognosis of NSCLC CIS (stage 0) is excellent [9].

According to other existing findings, endobronchial treatment is not as effective as surgery in eradicating preinvasive lesions, but has the advantages of preserving lung tissue and carrying less operative risk [10].

It is difficult to establish the difference between a CIS and MIC-invasive carcinomas [11].

According to the 7th edition of IASLC tumor, node, metastasis (TNM) classification, the letter R can be used as a new descriptor to complement the already used TNM letters. The aim is to designate the presence or absence of a residual tumour at the site of the surgical resection line.

The designation R0 is used when the margins after resection are clean, both grossly and microscopically. When the margins are not involved macroscopically and only

microscopically, the designation is R1. When the margins are macroscopically and microscopically involved, the code letter is R2. If CIS is present in the resection lines histology, the qualifier (is) is added to R1. Ultimately, the prognosis of R1(is) at the margin of the bronchus is significantly better than any R1 prognosis [12].

In the 8th edition of the IASLC TNM, a new category-R(un) was proposed, to document an "uncertain resection". This means no evidence of residual disease. However, nodal assessment is not based on a sufficient number of recommended nodes for complete resection. The same is true in case of positivity of the most superior mediastinal node sampled [13].

In our case, the decided designation would be R1. The patient has recovered now and we will follow her up in the future.

There are a few withstanding questions regarding this case. The first one is about penetration of the tumour in the bronchial wall. In this case, the distinction between CIS and MIC was difficult.

The second question was whether the infiltration of the resection line by the tumour was significant to the prognosis. The R1 designation makes it seem like the resection is incomplete. Other authors think that the prognosis depends mostly on the N status and less so on the margin infiltration status [12]. Vallieres et al. (2011) discussed the approaches currently applied to such cases in a meeting of the International Staging Committee of the IASLC, where opinions on the matter were not uniform. The first suggested approach is to do nothing after the resection, only follow up bronchoscopy shortly after surgery. The second is a more aggressive approach, in which surgical sleeve resection and even pneumonectomy is proposed. Others recommend using adjuvant radiotherapy to the stump area. Photodynamic or autofluorescence-guided laser therapies in the area of interest are yet another option. The authors ultimately concluded that R1is does not affect the prognosis of the patient negatively and there is no evidence that additional treatment would be helpful.

In our case, the chosen approach is close follow-up with fluorescence bronchoscopy without other measures. The patient is currently in good condition 15 months after the surgery. The decision about the resection line was based on the surgeon's professional experience and the lack of strong agreement on the topic in the broader medical community.

Conclusions

The presented case is an example of early-stage lung cancer in which the treatment approach was disputable. It was difficult to establish the accurate size of the lesion through bronchoscopy and histology. Autofluorescence bronchoscopy proved to be of substantial help in the decision-making for the case we present.

Surgical treatment was effective, and so far there is no need for additional therapy.

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