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Bronchial mucoepidermoid carcinoma: A case report

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ABSTRACT

INTRODUCTION: Bronchial localization of Mucoepidermoid carcinoma (MEC) is rare. The precise nature of these neoplasms is not yet clear and little is known on the histogenesis and pathogenesis of the disease. Here we present a case of a bronchial MEC with a detailed pathological, immunohistochemical, and molecular analysis.

PRESENTATION OF A CASE: A 46 years old Caucasian male patient was referred to our Unit for fever, non productive cough and dyspnea lasting for two months. The chest CT scan evidenced an 8-mm intraluminal lesion in the left main bronchus, in correspondence of the origin of the lingular segmental bronchus. Multiple biopsies were performed through bronchoscopy, and the diagnosis of a mucoepidermoid carcinoma of the lung was obtained. A left upper lobectomy was performed. The histopathological examination confirmed the preoperative diagnosis and stage (pT1N0M0). No further therapies were employed, given the stage of the disease. The patient is presently free of disease, approximately three years after surgery.

DISCUSSION: The treatment of MECs is usually surgical by traditional or sleeve lobectomy, performed with an open or video-assisted technique, with the aim of an R0 resection. In this stage the prognosis is excellent. Conversely, high grade tumors seems to be particularly aggressive, even more than other NSCLC.

CONCLUSIONS: Low grade type of Bronchial MEC, as our case, is often characterized by an optimal clinical management and prognosis. The lack of EGFR sensitizing mutations does not preclude the use of TKIs, which may be extremely useful in patients non responsive to other therapies.

1. Introduction

Mucoepidermoid carcinoma (MEC) is a common neoplasia of the salivary glands, initially described by Stewart et al. in 1945 [1]. It was reported for the first time in bronchi by Smetana et al. in 1952, and since then a few cases have been further described, given his relative rarity [2].

The precise nature of these neoplasms is not yet clear and little is known on the histogenesis and pathogenesis of the disease. This is probably due to its rarity and the small number of studies published, focusing on its molecular aspects. Here we report a case of a bronchial mucoepidermoid tumor with a detailed pathological, immunohistochemical, and molecular analysis, as well as a review of the current literature on the histogenic and molecular characteristics of the disease.

2. Case report

A 46 years old Caucasian male patient was referred to our Unit in November 2013 for fever, non productive cough and dyspnea lasting for two months. The personal and family history was unremarkable; He was a former tobacco smoker (1.75 pack years).

On physical examination it was evidenced a left latero-cervical lymph node swelling, and the presence of crackles in the lower left pulmonary field. Routine blood tests evidenced neutrophil leukocytosis, elevated C-reactive protein (CRP 17.58 mg/dL) and erythrocyte sedimentation rate (ESR 115/h). The serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9), cytokeratin fragment 19 (CYFRA 21-1), and neuron specific enolase (NSE) were all within normal range. The radiography of the chest evidenced an area of inflammatory consolidation in correspondence of the left mid-lower pulmonary fields. Subsequently a contrast chest CT scan was performed which evidenced an 8-mm

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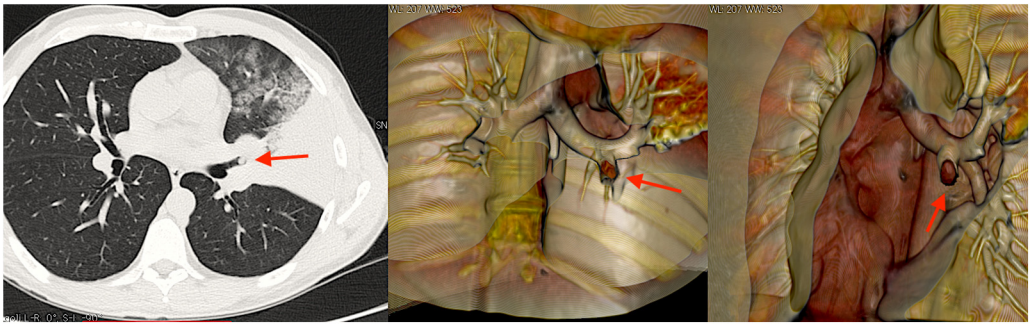

Fig. 1. (A–C) Computed tomography (CT) scan show an intraluminal lesion in the left main bronchus, in correspondence of the origin of the lingular segmental bronchus.

intraluminal lesion in the left main bronchus, in correspondence of the origin of the lingular segmental bronchus (Fig. 1 a–c). The lesion showed a smooth tissue enhancement and determined atelectasis of the lingular segment, as well as ground glass opacities in the apico – posterior segment of the upper lobe (Fig. 2). Multiple biopsies were performed through bronchoscopy, and the diagnosis of a mucoepidermoid carcinoma of the lung was obtained. The lesion presented mucin-secreting, squamoid and transitional cells, with minimal pleomorphism and mitotic figures. Immunohistochemical positivity was found for CK5 and CK7, while CK-20, S-100, SMA and TTF1 were negative. The staging process was completed with a total body CT scan and a PET/CT scan which showed no lymphatic or distant metastasis. The patient underwent a left upper lobectomy and mediastinal lymphadenectomy through left anterolateral thorachotomy. The histopathological examination of the specimen confirmed the preoperative diagnosis and stage (pT1N0M0), as well as the oncological radicality of the surgical procedure. No further therapies were employed, given the stage of the disease. The patient is presently free of disease, approximately three years after surgery.

3. Discussion

Mucous and serous glands of the respiratory tract can be occasionally involved in the arousal of neoplasms. The most frequent types are the MECs (more than 50%), adenoid cystic carcinomas (ACCs) and epithelial-mioepithelial carcinomas (EMCs) [3]. According to the World Health Organization (WHO) classification of tumors, these neoplasms constitute a distinct group of lung malignancies, and account for less than 1% of all lung cancers [3]. MEC is the most common subtype accounting for 0.1–0.2% of all lung cancers [4].

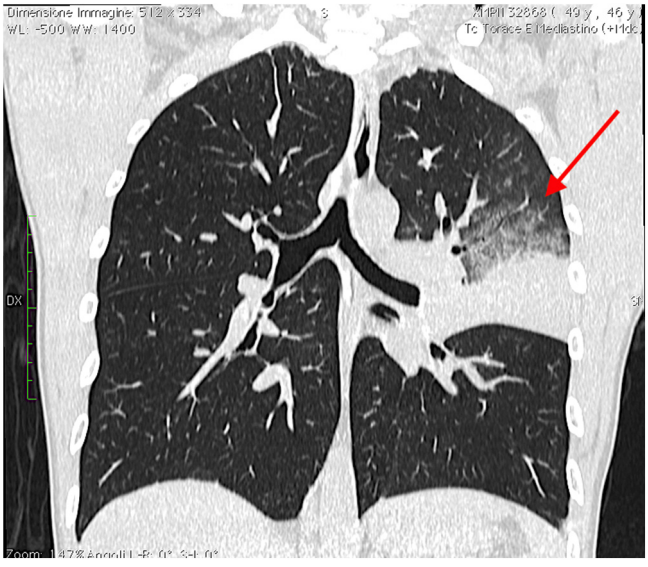

Fig. 2. Computed tomography (CT) scan showed a smooth tissue enhancement and determined atelectasis of the lingular segment, as well as ground glass opacities.

MEC affects generally patients younger than those affected by the most common non small cell lung cancers (NSCLC), as happened in our case [5]. In a series of 56 cases published by Yousem et al., more than 50% of the sufferers were under the 30 years of age, while in that of Li et al., the mean age was 34 years [6]. Mean ages were between 50 and 55 years in other reports; it seems that high grade MEC occurs more frequently in older patients, in comparison to low grade MEC [4,7,8]. No clear sex predilection has been ruled out, as well as no precise correlation with smoking habits or familiar predisposition.

These neoplasms mainly involve the lobular or segmental bronchi, often causing complete or partial atelectasis of the corresponding distal parenchyma, with subsequent obstructive irritation and inflammation. This pattern determines the arousal of the typical clinical manifestations of the disease, like cough, wheezing, hemoptysis, fever, and pneumonia [4,8]. The signs and symptoms often last for months or years, given the slow development of MECs, and symptomatic treatments can only offer temporary or no improvements. Nevertheless, cases of rapid progression have been described [9].

Chest X-ray and CT scan are the main imaging tools for the evaluation of MECs. The tumors are generally well circumscribed, round, oval or lobulated masses. Signs of bronchial stenosis or obstruction are frequent: distal bronchial dilatation, mucoid impaction, postobstructive pneumonia, air trapping, atelectasis, peripheral lucency, etc [10]. MECs resulted markedly enhanced in CT scans obtained after administration of intravenous contrast medium, and the attenuation coefficient was generally greater to that of the chest wall musculature; nevertheless, cases of mild enhancement have been described [10]. These features should be taken into account in the differential diagnosis between MECs and other commoner lung malignancies. Nevertheless, differential diagnosis with other tumors like carcinoids or adenosquamous carcinoma may be radiologically challenging. In our case areas of associated ground glass tissue have been evidenced on CT, but they were easily attributed to the obstructive consequences of the tumor.

Flexible bronchoscopy represents the main diagnostic tool for MECs, because it allows direct visualization of the lesions and biopsies, although extraluminal or peripheral lesions cannot be assessed by bronchoscopy. In our case, given the rich vascularity of the lesion, we preferred to perform biopsies through rigid bronchoscopy, in order to avoid hemorrhagic complications.

The gross aspect of MECs is very similar to that described in our case. An oval or round shape, hard – elastic consistency, smooth margins and yellowish – tan colour are the main macroscopic features of the tumors, along with their mixed solid and cystic appearance [7,10]. Microscopically, the epithelial component of

low grade tumors presents mucin-secreting, squamoid and transitional cells. Cystic and solid areas can be seen; the former can be full of mucin and the latter show frequently small glands, tubules and cysts. Keratinization is exceptional, as well as invasion into the pulmonary parenchyma [4,7,10]. The high grade counterpart presents areas of solid growth, with atypia, mitotic activity and necrosis, and may be difficult to distinguish from lung adenosquamous carcinomas; TTF-1 is a useful marker to this scope as it is frequently positive in the latter tumors and always negative in MECs [8,11].

Immunohistochemistry has been employed, not only for differential diagnosis, but also for determining the histiogenesis of MECs. Older publications immunohistochemically established that the tumors arise in the excretory duct of the salivary glands and this finding was confirmed also in lung lesions [12,13]. However, myoepithelial participation was evidenced in other studies [14]. The issue was more recently addressed by Sanchez-Mora et al., who performed an ultrastructural and immunohistochemical study on 16 surgically resected MECs, and demonstrated that they arise in the duct of the submucosal bronchial gland, without any myoepithelial participation [7].

Only a few studies have been performed in the field of the genetic molecular alterations of MECs. The mutations of the EGFR gene are the better described ones, because of their role in the use of targeted therapies with tyrosin kinase inhibitors (TKIs) in lung adenocarcinomas harboring EGFR gene mutations [15]. EGFR mutations are rare in lung or salivary MECs [16,17], and lacked in our case. Nevertheless, clinical responses to TKIs have been described also in tumors lacking sensitizing EGFR mutations, which present at (11:19) traslocation with an associated CRTC1-MAML2 fusion oncogene [18]. The latter seems to be of primary importance in patients in whom a targeted therapy is under consideration and it would be interesting to assess its role also in other lung cancer subtypes. Interestingly the translocation leads to up-regulation of the EGFR ligand amphiregulin, and several NSCLC cell lines have been demonstrated to be amhiregulin-sensitive to gefitinib [19,20].

The treatment of MECs is usually surgical by traditional or sleeve lobectomy, performed with an open or video-assisted technique, specially for low grade early stage lesions [3,8]. The main aim of surgery should always be an R0 resection. Cases of preoperative radiotherapy and/or chemotherapy have been described in the treatment of more aggressive or not radically resected cases [11]. Nevertheless, the effectiveness of this methods is not clear neither in the preoperative nor in the postoperative setting[8]. This makes all what we mentioned before about the employment of TKIs extremely interesting. The prognosis is excellent in low grade early stage tumors as that of our patient, treated with R0 surgery alone. Conversely, high grade tumors seems to be particularly aggressive, even more than other NSCLC.

4. Conclusions

Bronchial MEC is a rare tumor of the lung that affects young and middle-aged patients, without predilection of sex. It comprises a low grade type, often characterized by an optimal clinical management and prognosis, as occurs in our case, and a rarer high grade counterpart with more aggressive features. The current immunohistochemical evidence suggests that MECs origin from the glandular duct of the bronchial submucosal glands. The lack of EGFR sensitizing mutations does not preclude the use of TKIs, which may be extremely useful in patients non responsive to other therapies.

Authors states that the work has been reported in line with the SCARE criteria [21].

Conflicts of interest

None.

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The study sponsors had no such involvement.

Ethical approval

Whether approval by Instituitional Board has been given for this case report.

Consent

Informed consent was abtained from the patient; all authors ensure that all text and images alterations to protect anonymity do not distort scientific mean of the manuscript.

Author contribution

Giorgio C. Ginesu: Writing paper.
Michele Barmina: Writing paper.
Panagiotis Paliogiannis: Writing paper.
Maria L Cossu: data analysis.
Claudio F. Feo: Text edit.
Francesca Addis: data collection.
Trombetta Matilde: data anlysis.
Alberto Porcu: text edit.

Guarantor

Giorgio C. Ginesu.

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