Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography findings in a pediatric mucoepidermoid carcinoma and differential diagnosis

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Abstract
An 11 years old boy was referred to our hospital. He complained for the last three months for intermittent cough and shortness of breath after exercise which worsened recently. Airways computed tomography (CT) showed an abnormal endobronchial tumor, obstructing the right main bronchus and also atelectasis in the upper lobe of the right lung. Bronchoscopy showed a wet on its surface mass obstructing the right main bronchus. Biopsy showed a mucoepidermoid carcinoma (MEC). The fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) scan showed in the sa-me area a mass with slightly increased ^{18}F-FDG uptake (maximum standardized uptake value, SUVmax: 3.8), without mediastinal lymph nodes involvement. The boy had thoracoscopic resection of the right upper lobe, right main bronchus and right inferior lobe bronchial sleeve anastomosis. Histological examination confirmed the diagnosis of a low to intermediate grade malignant MEC without lymph nodes metastases. The patient has been well and free from recurrence for 2 years postoperatively.

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Introduction

Mucoepidermoid carcinoma (MEC) is derived from salivary mucus glands and usually occurs in the parotid and submandibular salivary glands area. Bronchial MEC is a rare disease in children which comprises 30% - 70% of all bronchial tumors and 0.2% of all lung tumors [1]. Several reports have estimated that MEC represent about 0.1% to 0.4% of all newly diagnosed cancers, or 2.6 new cases per 1,000, 000 people per year [2], [3-5]. This tumor accounts for approximately 10% of the primary malignant pulmonary neoplasms in childhood [6]. Bronchial MEC is a low potential epithelial tumor characterized by intraluminal growth [3] and a combination of epidermoid, mucus-secreting and intermediate cells [7]. The clinical symptoms are nonspecific including dyspnea, cough, wheezing, heamoptysis or obstructive pneumonia. Early diagnosis, and surgical resection are important in children if the bulk of the remaining pulmonary parenchyma is preserved, so as thoracic deformity and functional morbidity of the lungs are minimized [6]. The diagnosis of MEC in children is usually delayed [1]. The best modality to first detect a tracheal lesions is CT [8]. Bronchoscopy with biopsy are recommended [9]. Only 2 pediatric bronchial MEC cases have been reported using fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) [6, 10]. We report and discuss such a case.

Case Report

An 11 years old boy was referred to our hospital for worsened intermittent cough and shortness of breath after exercise over a 3 months period with no significant past medical history. Symptoms were improved after antibiotic treatment. Computed tomography (CT) showed an abnormal endobronchial lesion obstructing the right main bronchus, the right upper lobe bronchus junction and also showed atelectasis of the superior lobe of the right lung (Figure 1). A bronchial foreign body or tumor was highly suspected. Physical examination demonstrated decreased right bronchial respiration

without wheezing. He had no tumor-related family history. Laboratory tests including peripheral blood counts and tumor markers including carcinoembryonic antigen (CEA), alpha fetoprotein (AFP) and carbohydrate antigens (CA) were within the normal range. Biopsy performed by the aid of bronchoscopy showed a mass covered with mucus in the right upper bronchus (Figure 2A), which was diagnosed as MEC. Then the patient was transferred to the Department of Thoracic Surgery, where a ^{18}FDG PET/CT scan showed a mass 1.7-1.4cm with increased uptake and maximum standardized uptake value, SUVmax: 3.8 (Figures 3A - 3B). Obstructive pneumonia and atelectasis in the right superior lobe were also observed without mediastinal lymphadenopathy. Two weeks after biopsy, the boy had thoracoscopic resection of the right upper lung, the right main bronchus and the right inferior lobe bronchial sleeve anastomosis. Histological examination showed a combination of epidermoid cells, mucus-secreting cells and intermediate cells which confirmed the diagnosis of low-intermediate grade malignant MEC with tumor-free surgical margins and no lymph node involvement (Figure 2B). Immunohistochemical staining was positive for cytokeratin, P63 and CD117 with Ki-67 (3%+). The patient was feeling well and was free from recurrence as he was examined by us 2 years later.

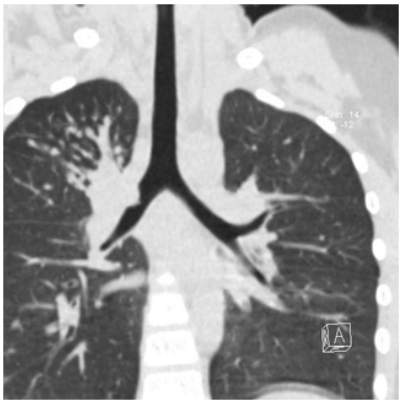

Figure 1. In computed tomography, the airways showed an endobronchial tumor obstructing the right main bronchus with "cut-off" sign.

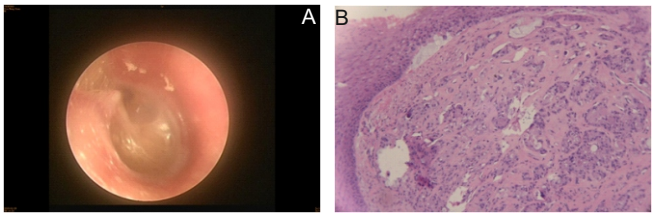

Figure 2. Endoscopic inspection revealed a polypoid mass obstructing the bronchus of the right upper lobe (A). Pathology showed a combination of epidermoid cells, mucus-secreting cells and intermediate cells (100×) (B), with positive cytokeratin 5, 7 (not shown) with Ki-67 （3%+） indicating the diagnosis of low-intermediate grade mucoepidermoid carcinoma.

Discussion

There have been 38 cases ranging in age from 3 to 15 years, average age 9 years (mean and standard deviation : M±SD= 9±3), described in the literature [1, 3, 6, 7, 9-30] and only 2 of them were diagnosed by PET/CT scan [6, 10]. Of the 38 cases described in the literature, there is a slight male predominance of MEC in children 1.2:1 (21/17). The initial clinical symptoms of bronchial MEC are mostly nonspecific indicating obstruction, such as dyspnea, cough and rarely hemoptysis or atelectasis [13, 16, 17] as in our case. Clubbing, wheezing and recurrent colds have also been reported [31]. However, some patients have no symptoms and the diagnosis is made incidentally [10]. Recurrent pneumonia, persistent cough and hemoptysis are the most common presenting manifestations. Because tumors that originate in trachea are rare in children, 7 out of the 38 patients were initially misdiagnosed as having asthma [1, 9, 13, 16, 17, 24] and 11/38 cases had cough as first symptom, as also in our case [3, 6, 13, 14, 20, 22, 23, 25, 32-34]. Atelectasis, chest pain, shortness of breath, wheezing, recurrent pneumonia and fever were reported in 7 cases [1, 3, 11, 12, 15]. Most of the cases with pediatric MEC reported in the literature were from China (10 cases), USA (9) and Japan (5). Other 10 countries reported 1-2 cases each. The grade of malignancy was predominately low (31/38 cases), intermediate (4 cases) or high (3 cases). The size of the tumor when first diagnosed, as measured in 14/38 cases, varied from 1.2-8.7cm^2 (mean 3.1cm^2) and maximal diameter varied from 0.8-2.5cm (mean 3.5cm^2). Because of the nonspecific respiratory symptoms, diagnosis of bronchial MEC was reported to be delayed from 2 weeks to 2 years [1], 3 months in our case.

Differential diagnosis of MEC from other causes of tracheal obstruction should be made. Common causes of tracheal obstruction are congenital anomalies, tumors, foreign bodies and infection. Non-respiratory conditions such as gastroesophageal reflux or vascular ring (vascular anomalies forming a ring around the trachea) [35] may also cause symptoms that mimic asthma [12]. Asthma usually coexists with other diseases, so MEC should be considered in diagnosis, especially when asthma does not respond to treatment [12]. Computed tomography is the best modality to detect tracheal and bronchial lesions [8] obstructive pneumonia, lobar, segmental atelectasis, and pleural effusion [9, 36]. Nearly all MEC cases were detected by CT. Bronchial MEC is described in CT as an endobronchial "cut-off" lesion as was in our case. The tumor in our case had lobulated borders and some peripheral calcification [37]. Airways CT may at first apply using a high kVolt, magnified to be able to outline the tracheal and bronchial air column checks [9]. In our study, the tumor was clearly identified in the lobar bronchus by airway CT images. In the literature review 31/38 children had MEC located in the proximal part of the lobar and segmental bronchi [3, 11, 12, 15] and 7/38 had MEC in the trachea [1, 9, 13, 14, 16, 17]. However, chest CT can not specify the nature of the tracheal lesion. Fluorine-18-FDG PET/CT is useful in differential diagnosis reporting the biological characteristics of the tumor. Positron emission tomography without SUVmax was first reported in a 5 years old girl with low grade MEC [10]. Low grade bronchial MEC was also reported in a 37 years old female and in an another 15 years old girl

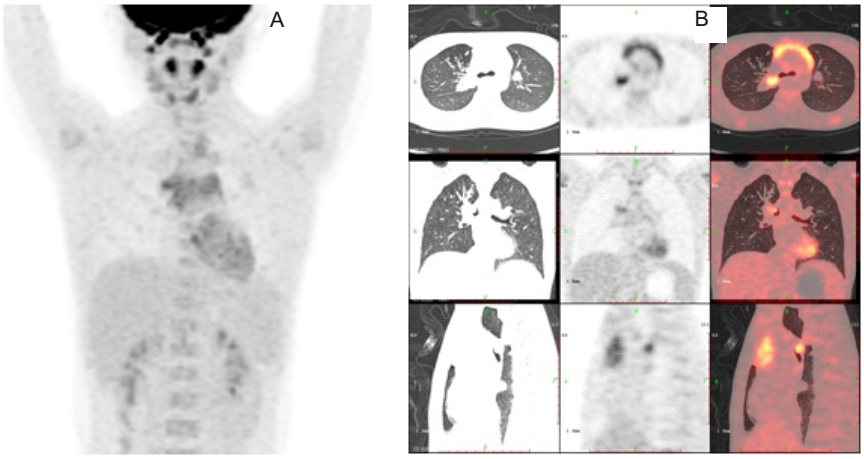

Figure 3. Maximum intensity projection (A). The transverse, coronal and sagittal ^{18}FDG PET/CT scans show increased ^{18}FDG uptake in the right upper bronchus (SUV max 3.8) (B).

with a SUVmax of 3.63 and 6.2 respectively [37]. In our case ^{18}F-FDG PET/CT showed slightly increased ^{18}F-FDG uptake (SUVmax 3.8) MEC without lymph nodes involvement in accord with the diagnosis of a low-intermediate grade of malignancy MEC. It has been reported that SUVmax in MEC can indicate the stage of malignancy and thus overall survival [38, 39]. As for radiation exposure ^{18}F-FDG PET/CT presents a particular concern for pediatric patients and is not recommended for children with low grade bronchial MEC. A chest CT scan if not an X-rays film first and then bronchoscopy with biopsy can set a diagnosis [16] and assess further the extent of the lesion [3, 9].

Differential diagnosis of MEC based on histopathology may include squamous cell carcinoma as well as adenoma of the bronchi [9]. Histological features, including nuclear pleomorphism, mitotic activity and necrosis separate low grade and high grade types of MEC. One of the cases reported in the literature with high grade MEC had peribronchial lymph node metastases but no recurrence, during a follow-up period of 11 years [18]. Other high grade MEC were reported to have poor prognosis [27]. Low grade bronchial MEC generally grow locally and are amenable to complete surgical resection with good prognosis [2, 3, 5, 6, 27]. Even if pathology reveals a low-grade MEC neoplasm, long term follow-up with CT scans, bronchoscopy and biopsies is recommended [9].

In conclusion, the authors suggest that bronchial MEC in children, although rare, should be considered if presenting with an acute unexplained onset of progressive asthma and obstructive respiratory symptoms. Our case had low grade MEC corresponding to a low SUVmax on ^{18}F-FDG PET/CT. As radiation exposure is concerned, ^{18}F-FDG PET/CT is not recommended as first diagnostic examination for pediatric patients with low grade bronchial MEC.

The authors of this study declare no conflict of interest

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Aristotle, the teacher of Alexander the Great.