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## Carcinoid and mucoepidermoid bronchial tumours in children

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**Abstract** The aim of the study was to determine the characteristic features and outcome of carcinoid or mucoepidermoid tumours in children. A retrospective analysis of all patients treated for a carcinoid or mucoepidermoid tumour in France between 1984 and 2001 was performed. There were 11 cases of carcinoid tumour and 6 cases of mucoepidermoid tumour. The mean age of the patients was  $10.5 \pm 3.0$  years, with a range of 5 to 15 years. Twelve and 6 patients presented with evidence of bronchial obstruction and haemoptysis, respectively. Fibre optic bronchoscopy confirmed the presence of a bronchial tumour in all cases and endobronchial biopsies were diagnostic in 11 of 12 cases. A chest CT scan revealed the presence of a hypervascular tumour in 8 of 12 patients. The distribution of the location of the tumours was equal between the right and the left lung, and, in 9 cases, the airways were totally occluded by the tumour. Complete surgical resection (lobectomy in 15 patients and pneumonectomy in 2 patients) was performed in all cases without pre-operative chemotherapy or radiotherapy. The mean

duration of follow-up was  $4.0 \pm 3.0$  years. In 2 patients, auscultation asymmetry and an episode of haemoptysis revealed the recurrence of a mucoepidermoid tumour, successfully cured by removal of the tumour and chemotherapy and radiotherapy in one child. No death was observed. **Conclusion:** Pulmonary carcinoid and mucoepidermoid tumours are rare in children. Bronchoscopic removal should not be performed. With aggressive surgical therapy, the prognosis is excellent. Fibre optic bronchoscopy confirms the presence of an endobronchial mass. A biopsy is needed for diagnosis and complete surgical removal is the treatment of choice. Long-term results are excellent but a clinical follow-up is recommended.

**Keywords** Bronchial tumour · Carcinoid tumour · Children · Mucoepidermoid carcinoma · Thoracic surgery

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### Introduction

Persistent atelectasis or recurrent pneumonia in the same location as well as persistent respiratory symptoms should raise the suspicion of obstructing lesions of the bronchus leading to the affected area. In such a situation, fibre optic bronchoscopy, looking for extraluminal or endoluminal lesions, should be performed [5]. Endobronchial tumours represent a rare cause of airway obstruction [1, 6, 14,25]. Bronchial carcinoid and mucoepidermoid tumours are considered low-grade malignant neoplasms [10,13]. These tumours are extremely rare in children and most cases have been presented as case reports in the literature, in association [1, 4, 6, 8, 14, 18,25] or not with other bronchial tumours [2, 3, 7, 9, 10, 19, 20, 21, 22, 23,28]. The present retrospective national multicentre survey was conducted to determine the characteristic clinicopathological features of bronchial carcinoid and mucoepidermoid tumours in children in France.

## Subjects and methods

A postal questionnaire was sent in 2002 to all the paediatric pulmonology, paediatric thoracic surgery, and paediatric oncology departments in France (Table 1). The physicians were asked to identify those paediatric patients (age <15 years) who had been treated for a bronchial tumour in their department since 1985. The questionnaires were distributed in May 2002 and were returned before the end of October 2002. Of the 20 departments, 15 returned a questionnaire and 8 of these 15 departments had treated patients with a bronchial tumour. The retrieved data included patients' age and sex, presenting symptoms, diagnosis delay, location and spread of tumour, methods of treatment, histological findings, and duration and outcome of follow-up. In the case of incomplete questionnaire information, a telephone contact was made to collect the missing data.

## Results

### Patients characteristics

A total of 17 patients (including 8 boys) were diagnosed as having a bronchial tumour. The mean age of the patients was  $10.5 \pm 3.0$  years, with a range of 5 to 15 years. The diagnosis delay was highly variable with a mean diagnosis delay of  $5.8 \pm 5.1$  months. The majority of patients presented with evidence of bronchial obstruction: recurrent pulmonary infections in the same location were observed in 12 patients (Table 2). This was followed by haemoptysis in 6 patients, and a variety of other symptoms, including weight loss, fatigue, fever and persistent bronchospasm, occurred in 6 patients. None of the patients was asymptomatic at presentation or had symptoms evoking a carcinoid syndrome. The clinical examination of the patients revealed no extra-respiratory abnormalities; in particular, no lymph node involvement was noticed.

Two patients were regularly followed for asthma and another patient had undergone several investigations for recurrent bronchitis, without fibre optic bronchoscopy, 1 year prior to the diagnosis of his tumour. The father of patient 5 had been treated for lung cancer (histology not available) several years previously.

### Methods of diagnosis

Several chest radiographs were performed in all the patients. Atelectasis was noted in 12 patients with a small pleural effusion in 2 cases. Bronchiectasis was suspected and confirmed by chest CT scan in 2 patients.

**Table 1** Questionnaire used for the study

First name: 3 first letters and last name: 3 first letters
Date of birth
Date of diagnosis
Presenting symptoms (yes/no)
Respiratory symptoms
Cough
Dyspnoea
Haemoptysis
Chest pain
Other (specify)
Endocrinological symptoms
Cushing syndrome
Carcinoid syndrome
Acromegaly or accelerated growth
Other (specify)
General symptoms
Temperature > 38.5°C
Weight loss
Other (specify)
Duration of symptoms prior to tumour diagnosis
Duration of symptoms before histological diagnosis
Systematic chest X-ray
Chest X-ray findings (yes/no)
Atelectasis
Obstructive emphysema
Pulmonary infiltrations
Nodules
Bronchiectasis
Pleural effusion
Lymph nodes
Other (specify)
Computed tomographic scan of the lungs (specify)
Tracheobronchial endoscopy (specify)
Biology (specify)
Serum markers (values)
Alpha-fetoprotein
Carcinoembryonic antigen
$\beta$ -human chorionic gonadotropin
5-Hydroxyindoleacetic acid
Pre-operative findings (specify)
Anatomopathology of the tumour (if any)
Metastases (if any)
Chemotherapy
Radiotherapy
Pre-operative conclusions
Surgical intervention
Date
Type of procedure (specify)
Complications (specify)
Per-operative anatomopathological examination (specify)
Post-operative diagnosis
Immediate post-operative period
Duration of intensive care stay
Duration of hospital stay
Complications (specify)
Long-term follow-up
Duration of follow-up (years, months)
Number of visits
Clinical outcome (specify)
Tracheobronchial endoscopy $\pm$ biopsies (specify)
Chest X-rays (specify)
Computed tomography of the lungs (specify)
Tumour recurrence (yes/no)
If yes: pre-operative radiotherapy (yes/no)
pre-operative chemotherapy (yes/no)
Lung function tests: dates and complete results

**Table 2** Mode of presentation of the 17 patients

Presenting symptoms/signs	Number of patients ( <i>n</i> )
Recurrent pulmonary infection	12
Haemoptysis	6
Weight loss, fever and fatigue	3
Persistent bronchospasm	3
No symptoms	0

Chest CT with vascular opacification was done in 12 patients. In 8 patients, the CT scan revealed the presence of a hypervascular tumour without involvement of the ipsilateral and contralateral mediastinal lymph nodes. On the CT scan, the tumours ranged in size from 15 to 33 mm. In one patient, an involvement of the pulmonary artery was suspected but excluded by MRI. <sup>123</sup>I-metaiodobenzylguanidine imaging was performed and was normal in one patient who complained of bone pain.

Serum tumour markers (alpha-fetoprotein, carcinoembryonary antigen, beta-human chorionic gonadotropin, and 5-hydroxyindoleacetic acid) levels were within the reference range in 10 patients.

Diagnosis of the tumour was made using fibre optic bronchoscopy in all cases. Endobronchial biopsies were performed in 12 cases; however, the biopsy was not informative in one patient (patient 14). Biopsies were not performed because of spontaneous tumour bleeding in 2 patients (patients 2 and 12).

#### Tumour characteristics

Tumour location was distributed equally between the the right and the left bronchial trees (Table 3). Six tumours

arose in the right intermediate bronchus, and 2 tumours originated in the left mainstem bronchi (patients 7 and 16). None of the tumours arose in the periphery of the lungs. In 10 cases, the airways were totally occluded by the tumour.

Histopathology revealed a mucoepidermoid carcinoma in 6 patients and a carcinoid tumour in the other 11 patients. All these tumours were referred as "typical" or as "low-grade" because they were well differentiated with rare mitoses and pleomorphisms. Ipsilateral lymph node involvement was present on histological analysis in one patient (patient 7). Complete tumour and lymph nodes resection was achieved by a left pneumonectomy, and a 5-year follow-up revealed no relapse.

#### Treatment

The mean delay between symptom appearance, surgical treatment and diagnosis was  $5.6 \pm 5.5$  months (Table 3). Surgical resection, with per-operative histological examination, was performed in all patients. This intra-operative histological examination showed that the bronchial resection was always performed in an area free of disease. A lobectomy, involving one (9 patients) or two lobes (5 patients), was performed in 14 patients (Table 3). A left pneumonectomy was the only therapeutic solution in the 2 patients (patients 7 and 16) who had a tumour on the left main stem bronchus. Patient 7 had an extensive tumour that had invaded the left upper and lower lobes, as well as the hilar lymph nodes. A sleeve resection was successfully performed in patient 3 who had a small tumour of the right intermediate bronchus. Successful bronchial re-implantation on the main stem bronchi was performed in patient 1 after left upper lobe resection and in patient 11 after right upper

**Table 3** Clinical presentation and outcome, tumour site, surgical treatment, tumour histology and spread of the disease. ( *LLL* left lower lobe, *LMS* left main stem bronchus, *LUL* left upper lobe,

*MEC* mucoepidermoid carcinoma, *NA* not available, *ND* not determined, *RI* right intermediate bronchus, *RLL* right lower lobe, *RML* right middle lobe, *RUL* right upper lobe)

Patient	Age (years)	Gender	Diagnosis delay (months)	Site of tumour	Surgical treatment	Tumour histology	Lymph node involvement	Recurrence	Duration of follow-up (years)
1	5	Girl	7	LUL	LUL lobectomy	MEC	No	Yes	4
2	5	Boy	1	LLL	LLL lobectomy	MEC	No	Yes	8
3	7	Boy	2	RI	Sleeve resection	MEC	ND	No	6
4	9	Boy	3	RML	RML lobectomy	Carcinoid	ND	No	8
5	9	Girl	2	Lingula	LUL lobectomy	MEC	No	No	2
6	10	Boy	6	LUL	LUL lobectomy	MEC	No	No	1
7	10	Girl	4	LMS	Left pneumonectomy	Carcinoid	Yes	No	5
8	11	Boy	7	RI	RML and RLL lobectomy	Carcinoid	No	NA	NA
9	11	Girl	7	RI	RML and RLL lobectomy	Carcinoid	No	No	3
10	11	Boy	2	RUL	RUL lobectomy	Carcinoid	No	No	1
11	12	Girl	2	RI	RML and RLL lobectomy	Carcinoid	No	No	5
12	13	Boy	7	Lingula	LUL lobectomy	Carcinoid	No	No	1
13	13	Girl	9	RI	RML and RLL lobectomy	Carcinoid	No	No	10
14	13	Girl	30	RUL	RUL lobectomy	MEC	ND	No	6
15	13	Girl	1	RI	RML and RLL lobectomy	Carcinoid	No	NA	NA
16	14	Girl	1	LMS	Left pneumonectomy	Carcinoid	ND	No	6
17	15	Boy	4	LLL	LLL lobectomy	Carcinoid	No	No	2

lobectomy. The immediate post-operative outcome was marked by a transient phrenic nerve paralysis in 2 patients. No radiotherapy or chemotherapy was administered in the immediate post-operative period.

### Follow-up

Mean duration of follow-up was  $4.0 \pm 3.0$  years. Two patients were lost to follow-up. Fibre optic bronchoscopy was performed 6 to 12 months after the surgical intervention in 8 patients because of an episode of haemoptysis in 2 patients and for systematic monitoring in the others. All the fibre optic bronchoscopies performed in the absence of clinical symptoms were normal. In one patient with haemoptysis (patient 2), however, the endoscopic examination revealed the recurrence of a mucoepidermoid carcinoid on the left main stem bronchus which was successfully removed by sleeve resection with no recurrence after 8 years. A recurrence of the tumour occurred also in patient 1 after a 3-year delay. Bronchoscopy, performed because of an asymmetry of the pulmonary auscultation, revealed an inflammatory stenosis of the remaining left lower lobe bronchus and the biopsy the recurrence of a mucoepidermoid carcinoma. Intra-operative histological analysis of the lymph nodes and the pulmonary vessels showed the presence of lymph nodes and vascular tumour extension. Chemotherapy and radiotherapy (40 Gray on the mediastinum) were administered after a left pneumonectomy. The patient is doing well and is free of disease after a follow-up of 1 year.

Finally, no death was observed, neither during the short-term evaluation nor during the follow-up.

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### Discussion

Primary pulmonary tumours are rare, especially in children, and the present national survey represents, to our knowledge, an important series of carcinoid and mucoepidermoid tumours reported in the paediatric age group. Our study has the limitations of a retrospective survey. Indeed, in the absence of prospective data, we are unable to estimate the incidence of carcinoid and mucoepidermoid tumours in children in France. Moreover, despite an extensive mailing, an underestimation of the exact number of pulmonary tumours observed during the study period is most likely. Finally, the length of the long-term follow-up was variable with 2 patients being lost to follow-up.

All our patients were symptomatic at diagnosis. This emphasises the value of fibre optic bronchoscopy which should be performed in all cases of persistent or recurrent respiratory symptoms and can confirm the presence of an endobronchial mass and allows a biopsy. Nevertheless, because of the friable nature of these tumours and their tendency to bleed [27], this pre-operative diagnosis is not always possible, as was the case in 2 of

our patients. The absence of asymptomatic patients in the present study contrasts with the experience in an adult series of pulmonary carcinoids, with 30% of the patients being asymptomatic [12]. The peripheral origin of the tumours in the adult series could explain this discrepancy. Indeed, in our patients, all tumours were located on the main or large bronchi.

Abnormalities seen on a chest X-ray film were common, as observed in 14 of the 17 patients in the present study. These abnormalities were not specific and their main value was to confirm the necessity of complementary investigations. The chest CT scan gave more interesting information. The CT scan revealed the presence of a hypervascular tumour, suspected by the occurrence of an episode of haemoptysis, in 8 of 12 patients. The accuracy of the CT scan to detect lymph node involvement has been problematic in the past. Currently, the use of high quality CT scans helps to visualise lymphadenopathies and provides anatomical localisation of both intra- and extraluminal components [17,26]. More recently, multislice-CT generated three-dimensional virtual bronchoscopy can add important information about an intraluminal tumour by showing almost identical imaging features as conventional bronchoscopy [16]. This new technique should be evaluated for patient follow-up. Calcifications, previously reported in paediatric patients with a mucoepidermoid carcinoma [28], were not observed in our patients.

Endobronchial tumours are rare in children. These tumours can be benign (such as bronchial adenomas [8], papillomas [25], leiomyomas [25], haemangiomas [25], inflammatory myofibroblastic tumours (previously called inflammatory pseudotumours or plasma cell granulomas [1,14], granular cell tumours, hamartomas [15]) or malignant, with either low-grade (such as carcinoid or mucoepidermoid tumours [1, 4, 7, 9, 14,18]), or infantile fibrosarcomas [14] or high-grade malignant tumours (such as pleuropulmonary blastomas [24], rhabdomyosarcomas [14] or lymphomas [6]). Per-endoscopic endobronchial biopsies are most often diagnostic, as in our series (11 out of 12 patients), but a definite diagnosis is provided by a complete histological analysis of the tumour. These tumours range from low-grade well-differentiated to intermediate-grade atypical and high-grade tumours. The likelihood of local recurrence is related to the histological subtype and is more common among patients with atypical subtypes [11].

Treatment consists of a careful surgical removal of the tumour, the lymph nodes and the sacrifice of as little as possible of the adjacent normal lung. When technically possible, a sleeve resection of the involved bronchus is recommended [22]; however, in most cases, the location of the lesion requires a lobectomy or a pneumonectomy for complete removal. A non-intentional bronchoscopic removal of a low-grade mucoepidermoid tumour of the intermediate bronchus has been reported in the literature [20], but this approach is not recommended because of the risk of local recurrence. Indeed, incomplete removal has been associated with the recur-

rence of these low-grade malignant tumours. In our series, 2 patients had a local recurrence of a mucoepidermoid tumour, respectively 4 and 8 years after successful removal, despite a histological examination of the airways, confirming that the resection was performed in a disease-free area. Thus, this risk of recurrence justifies a long-term clinical follow-up. Indeed, fibre optic bronchoscopy was performed because of respiratory symptoms in these two patients.

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