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Case Report

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Carcinoid Tumour Revealed by Repeated Respiratory Infections in a Pregnant Woman, a Case Report

Djeuteu Damaris*, Zwierzijk M, Binet L and Nkouado Tchando Y

Department of Pneumology, Ambroise Pare University Hospital (HELORA), Belgium

ABSTRACT

Background: Understanding carcinoid tumours is essential, as they can often go unrecognized, leading to late diagnosis. This type of neuroendocrine tumour usually develops in the gastrointestinal tract, but can also occur in the respiratory tract. The aim of our work was firstly to review the clinical picture, the diagnostic method and the therapeutic management (while highlighting the limitations of endoscopic treatment) of a carcinoid tumour. The second aim was to raise awareness among physicians in general, and pulmonologists in particular, of the need to consider this diagnosis in the case of recurrent respiratory infection in a young patient with no exposure to tobacco and no particular medical history.

Case Report: A 32-year-old patient, Caucasian, 33 weeks pregnant, presented with recurrent respiratory infections (dry cough, wheezing, and NHYA Class II dyspnoea). Initially, she was treated with antibiotic therapy. Follow-up examinations revealed a typical carcinoid neuroendocrine tumour. In this case pregnancy was an additional factor involved in the diagnostic delay. The first-line treatment involved endoscopic resection, followed by a left S6 segmentectomy combined with a sleeve resection of the left lower lobar bronchus, performed six months later due to unfavourable developments.

Conclusion: The incidence of carcinoid tumours is increasing. Bronchial carcinoid tumours can cause recurrent infections at the same anatomical site, and can be misdiagnosed, often delaying diagnosis. Therapeutic management and prognosis depend on the histological type, which can be definitively confirmed with an operating specimen. Greater awareness among healthcare personnel of the clinical picture associated with this pathology will promote early diagnosis and treatment.

***Corresponding author**

Djeuteu Damaris, Department of Pneumology, Ambroise Pare University Hospital (HELORA), Belgium.

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Introduction

Carcinoid tumours a rare, well-differentiated growths of attenuated malignancy. They account for 1–2% of all primary bronchial tumours, with 80–90% corresponding to typical carcinoid tumours that develop from Kulchitsky cells, which are neuroendocrine cells normally present in the bronchial mucosa [1,2]. The mean age of diagnosis is 50 years with a female predominance (Ratio 2/1) [1]. Their detection may be fortuitous or secondary to a clinical picture, depending on the location of the tumour in the bronchial tree. The most common symptoms are haemoptysis, obstructive pulmonary disease, thoracic pain, dyspnoea, and carcinoid syndrome (rarely, in advanced forms) [1,3]. Carcinoid tumours are regularly observed on CT imaging and diagnosis confirmed via pathological analysis on primary biopsies collected during bronchoscopy with a very low risk of bleeding during the procedure [4]. The therapeutic management of these tumours includes surgical resection combined with lymph node dissection [5]. The 10-year survival rate is 90% for typical carcinoid tumours and 60% for atypical carcinoid tumours [6].

Observation

This work concerns Mrs. D., a 32-year-old caucasian woman, 33 weeks pregnant, with a medical history of recurrent respiratory infections for approximately four years and a long-term smoking habit. She arrived at the emergency room after undergoing an outpatient SARS-COV2 screening test—which was negative—and the symptoms a week-long dry cough associated with thoracic pain, wheezing, and NYHA Class II dyspnoea. Her vital signs, recorded in the emergency room, were normal.

A blood test revealed a significant inflammatory syndrome (C-reactive protein at 169.7 mg/dL) associated with hyperleukocytosis (18.000/mm^3). A thoracic computed tomography (CT) scan showed an impaction with partial filling in the distal portion of the left main bronchus, leading to atelectasis of the left upper lobe and an added hypo-ventilatory consolidation (Figure 1), as well as a lower left lobar infectious pneumonia (bronchiolitis.) The patient was hospitalised in the gynaecology department and treated with clavulanic amoxicillin for 7 days.

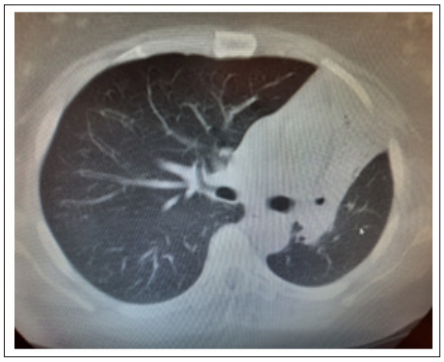

Figure 1: CT Scan Showing an Impaction with Partial Filling of the Distal Portion of the Left Main Bronchus Leading to Atelectasis of the Left Upper Lobe

Mgrs. D. attended a pulmonology consultation after a month for follow-up. Clinically, she described an overall improvement marked by the disappearance of cough and thoracic pain; however, NYHA Class II dyspnoea persisted. The control radiography (less radiation for the foetus than a CT scan) showed an absence of a pulmonary lesion (Figure 2). As a part of the additional evaluation, a pulmonary function test was performed, revealing a moderate ventilatory deficit (FEV1 at 1.86L, or 50% of the predicted value post-Broncho dilation), which was restrictive but also had an obstructive tendency and normal diffusion (Table 1). The patient was treated with a combination of a long-acting beta-2 agonist and inhaled corticosteroid.

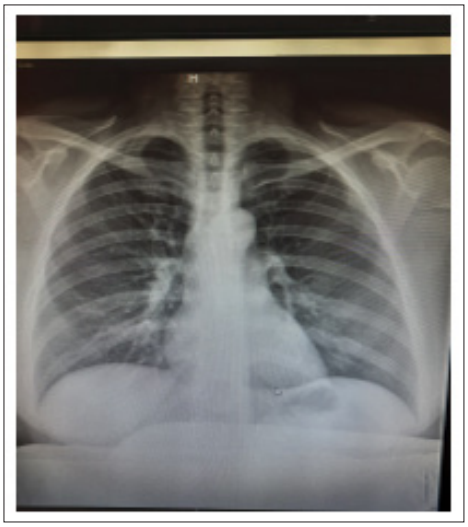

Figure 2: Thoracic Radiography with Absence of Parenchymal Lesion

Table 1: Pulmonary Function Test showing a Moderate Restrictive Ventilatory Deficit with an Obstructive Tendency and Normal Diffusion

Parameters	Pred	Actual	%Pred	Post	Post%Pre	%change
FCV (L)	4.42	2.09	47%	2.12	48%	2%
FEV1 (L)	3.68	1.75	48%	1.86	50%	6%
FEV1/FVC(%)	84	84	100%	87	104%	4%
FEF25-75% (L/sec)	3.85	1.74	45%	2.05	53%	17%
FEF 50% (L/sec)	4.62	1.80	39%	2.32	50%	29%
FEF (L/sec)	7.50	3.98	53%	3.82	51%	-4%
LUNG FONCTION						
TLC (pleth) (L)	5.69	4.39	77%			
RV (pleth) (L)	1.66	2.44	147%			
RV/TLC (pleth) (%)	30	56	186%			
DIFFUSION						
DLCO (ml/min/mm)	29.54	16.50	56%			
DLCO/VA (ml/min/mmHg/L)	5.19	6.21	120%			

FEV1 : Forced Expiratory Volume in the first second of exhalation
FCV: Forced Vital Capacity
FEF: Forced Expiratory Flow
TLC : Total Lung Capacity
RV : Residual Volume
DLCO : Diffusing capacity of the Lung for carbon monoxide
VA: Alveolar Volume

She returned for another pulmonology consultation after seven months (i.e., five months after giving birth). She was still dyspnoeic on exertion, and a respiratory function test showed a persistence of moderate ventilatory deficit (FEV1 1.88L, 53% of predicted value), without a restrictive component (Table 2). Therefore, a thoracic CT scan was performed, revealing a round opacity in the left main bronchus, with almost complete resolution of the previously described lesions (Figure 3).

Table 2: Respiratory Function Test showing a Moderate Ventilatory Deficit without Restrictive Component

Parameters	Pred	Actual	%Pred	Post	Post%Pre	%change
FCV (L)	4.29	2.16	50%	2.39	56%	11%
FEV1 (L)	3.57	1.88	53%	2.14	60%	14%
FEV1/FVC(%)	84	87	104%	89	107%	2%
FEF25-75% (L/sec)	3.75	1.98	53%	2.36	63%	20%
FEF 50% (L/sec)	4.55	2.18	48%	2.61	57%	20%
FEF (L/sec)	7.36	4.27	58%	4.91	67%	15%
LUNG FONCTION						
TLC (pleth) (L)	5.56	5.66	102%			
RV (pleth) (L)	1.64	3.14	191%			
RV/TLC (pleth) (%)	30	55	184%			
DIFFUSION						
DLCO (ml/min/mm)	28.91	20.43	71%			
DLCO/VA (ml/min/mmHg/L)	5.20	5.27	101%			

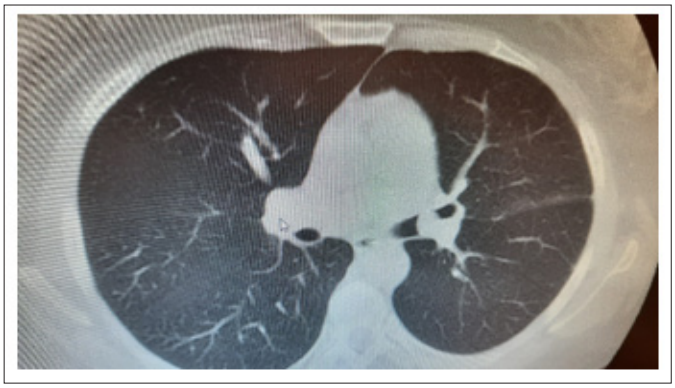

Figure 3: Thoracic CT Scan Showing a Round Opacity at the Level of the Left Main Bronchus

Subsequent bronchoscopy revealed a large, hyper-vascular budding tumour obstructing almost the entire end of the left main bronchus (Figures 4 and 5).

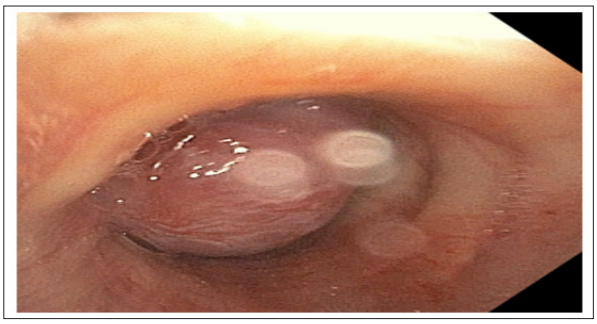

Figure 4: Large Budding Tumour Obstructing the Left Main Bronchus

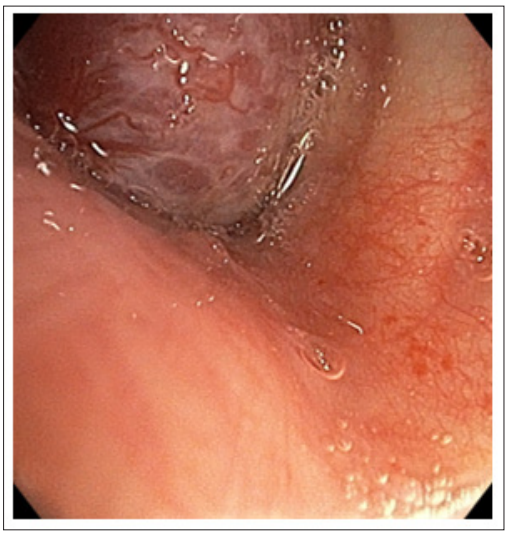

Figure 5: Hyper Vascularised Tumour Bud at the Level of the Left Main Bronchus

The biopsies collected and analysed by anatomical pathology resulted positive for NOS carcinoid tumour with criteria (small-sized cells, absence of mitosis and necrosis, Ki67 <5%, negative TTF1, and positive neuroendocrine marker), suggesting a typical carcinoid tumour. The extension assessment performed using positron emission tomography, coupled with gallium 68-marked somatostatin analogues (68Ga-DOTA-TOC PET), did not reveal any distant lesions (Figure 6). Therefore, the tumour was staged as cT1bN0M0.

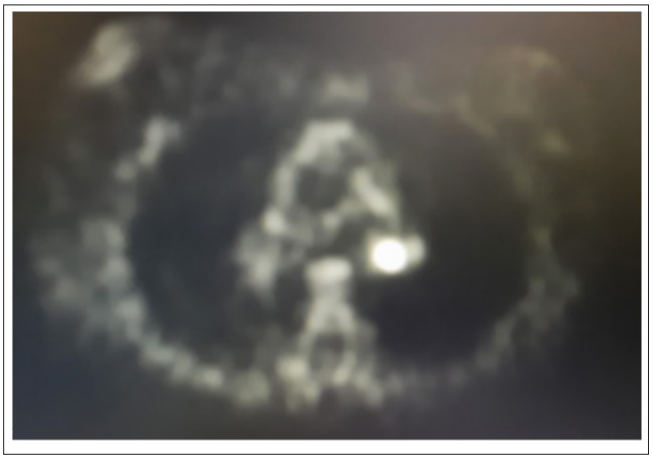

Figure 6: 68ga-Dota-Toc Pet Showing a Lesion Intensely Overexpressing Somatisation Receptors Subtype-2 in the Left Main Bronchus, Compatible with the Diagnosis of Neuroendocrine Tumour

A chromogranin test was performed, resulting normal. After multidisciplinary oncological consultations, the patient was referred to a university centre for resection of the tumour via interventional endoscopy.

Anatomopathological analysis of the surgical specimen confirmed the diagnosis of a typical carcinoid tumour.

The control bronchoscopy performed two months after the endoscopic resection of the tumour, highlighted the presence of the following two millimetric nodules: 1) at the entrance to the orifice of the left lower lobar bronchus and 2) at the level of the external surface at the entrance to the trunk of the left basal pyramid (figure 7). The patient underwent reintervention with interventional endoscopy for a flattening procedure via argonisation.

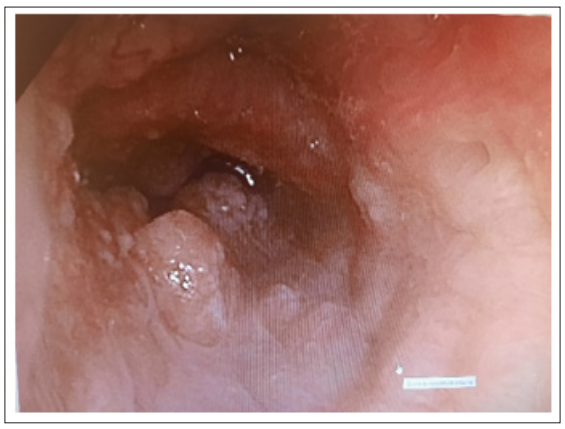

Figure 7: Millimetres-Long Nodule Entering the Orifice of the Left Lower Lobar Bronchus

A DOTA-TOC PET scan was performed one month after the second operation and demonstrated the persistence of a residual tumour (in the first hypothesis) located at the bifurcation of the left main bronchus. During the follow-up endoscopic examination, a hyper-vascularised pedunculated tumour with a diameter of 2 mm was observed at the level of the lower left lobe corresponding to segment 6 (Figures 8 and 9). Therefore, the patient was referred for surgical management.

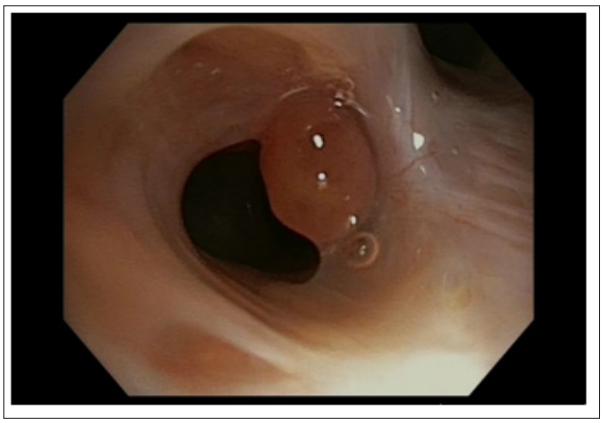

Figure 8: Hyper-Vascularised Pedunculated Tumour with a Diameter of 2 Mm at the Level of the Left Lower Lobe

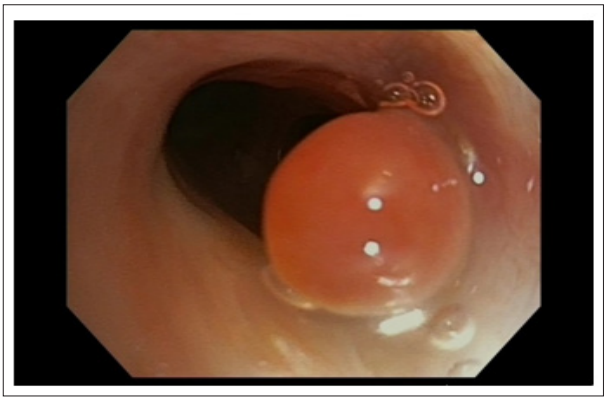

Figure 9: Pedunculated Tumour at the Level of the Left Lower Lobe

Six months after the endoscopic resection, surgery comprising a left S6 segmentectomy combined with a sleeve of the left lower lobar bronchus by VATS, converted to an anterolateral thoracotomy, was performed. Subsequently, a favourable postoperative evolution was noted.

The anatomopathological analysis facilitated performing a complete resection of the tumour at a healthy margin.

Discussion

The World Health Organization (WHO) classifies pulmonary neuroendocrine tumours into four groups based on histological type and Travis et al, as follows: typical carcinoid tumours of low-grade malignancy, intermediate-grade atypical carcinoids, and high-grade small and large cell neuroendocrine carcinomas [1,2]. The incidence of neuroendocrine tumours, including carcinoid tumours, has been increasing [7]. This may be explained by the rise in the use of thoracic scanners. The diagnostic age for carcinoid tumours varies from early childhood to the ninth decade of life (mean, 50 years) [1] . Although our patient was diagnosed at 33 years of age, her history suggests that the tumour had likely been present for at least four years. Pregnancy was an additional factor involved in the diagnostic delay. Therefore, it is important to increase awareness among clinicians regarding the clinical conditions in which a carcinoid tumour can be considered. The clinical presentation depends on the location of the tumour in the bronchial tree. Most carcinoid tumours arise in the proximal airways and the symptomatology is related to obstruction caused

by the mass, or bleeding caused by hypervascularisation [8]. The symptoms presented by our patient, such as repeated respiratory infections and dyspnoea (ventilatory disorder with obstructive tendency to EFR), were secondary to the obstruction caused by the mass at the level of the left main bronchus. Assuming that the tumour was present during previous episodes of respiratory infections, imaging would likely have shown recurrent pneumonia in the same lobe. Thus, patients presenting with recurrent respiratory symptoms despite optimal medical treatment should be examined thoroughly and subjected to thoracic CT scanning and bronchoscopy to facilitate early diagnosis and adequate management.

Bronchial carcinoid tumours can overproduce vasoactive substances such as serotonin, bradykinin, histamine, and prostaglandins. Carcinoid syndrome corresponds to the excess production of these substances in the systemic circulation. It generally occurs in cases of liver metastases or when the size of the tumour is > 5 cm and is directly connected to the systemic circulation [9]. In our case, the size of the tumour was 14mm at its largest diameter. The classic clinical picture of a carcinoid syndrome includes flushing, diarrhoea, wheezing, and carcinoid crisis [3]. None of these signs or symptoms were reported or observed during the patient's treatment.

Surgery, combined with lymph node dissection, remains the only curative treatment for bronchial carcinoid tumours [1,5]. Interventional endoscopy can precede surgery, in the event of damage to large bronchial trunks, to remove atelectasis under stenosis and specify the location of the implantation foot, thereby optimising the performance of sparing parenchymal surgery [10]. Nevertheless, endoscopic treatment is effective against localised typical carcinoid tumours [11-14]. Levent D. et al. studied 29 patients, 24 of whom had a typical carcinoid tumour and 6 had an atypical carcinoid tumour; all initially treated using endoscopic resection. This study showed complete eradication of the tumour in 21 patients (72%) after follow-up for a mean duration of 49 months (range 22–94 months) [6].

The most common complications in interventional bronchoscopy are hypoxia, haemorrhage and pneumothorax, which remain rare [12]. In our case, given the location of the tumour, absence of metastases (stage cT1bN0M0), and initial pathological study with criteria indicative of a typical carcinoid tumour, we opted for endoscopic resection as the initial treatment. It included unblocking the completely obstructed left main bronchus using argon, and then debulking the endobronchial lesion using forceps.

The lesions observed during follow-up, via bronchoscopy (resected again endoscopically) and DOTA-TOC PET scan, 2 and 3 months after the initial endoscopic resection of the tumour, were considered as residual lesions, but could also potentially correspond to a loco-regional recurrence. Notably, the absence of lymph node dissection during an endoscopic resection, as is the case in surgery, may pose a risk of recurrence. This highlights that-at least in this specific case—the initial treatment of a typical carcinoid tumour located endo-bronchially without distant metastases via endoscopic means may be insufficient.

The surgical technique used in the treatment of carcinoid tumours depends on the histological type. Conservative surgery (e.g.: segmentectomy) is recommended for typical carcinoid, whereas more extensive surgery, such as a lobectomy (high risk of recurrence), is recommended for atypical carcinoid tumours. In both cases, it should be associated with a complete mediastinum lymph node dissection [15,16]. In our case, the surgical treatment comprised a left S6 segmentectomy combined with a sleeve of the left lower lobar bronchus, due to the location of the tumour at the entrance to the G main bronchus. An extensive lymph node dissection was also performed.

Currently, there are no clear recommendations based on prospective studies regarding post-operative monitoring modalities. Nevertheless, following-up a patient for a minimum of 10 years is recommended the follow-up schedule of our patient was based (for a start) on the clinical evaluation, radiological imaging by thoracic CT scan, and bronchoscopy every quarter [1].

Conclusion

The incidence of bronchial carcinoid tumours, rare and progressive malignant growths, is increasing. Such tumours should be considered as a differential diagnosis of patients showing recurrent respiratory infections despite appropriate treatment. Indeed, bronchial carcinoid tumours can cause recurrent infections at the same anatomical site, and can be misdiagnosed, often delaying diagnosis. Therapeutic management and prognosis depend closely on the histological type, which can only be confirmed on an operating specimen. Endoscopic resection in interventional bronchoscopy, used as initial treatment in patients with typical carcinoid tumours, may prove to be insufficient. Greater awareness among healthcare personnel about the clinical characteristics associated with this pathology is required to promote early diagnosis and treatment, thereby ensuring a better prognosis for patients.

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